Specialty Drug Utilization Criteria

Contents

DISCLAIMER................................................................................................................................. 7
ACTEMRA® (TOCILIZUMAB)‡........................................................................................................... 9
ADCIＲCA® (TADALAFIL).................................................................................................................. 12
AFINITOR® (EVEROLIMUS)............................................................................................................ 14
ALCENSA® (ALECTINIB HYDROCHLORIDE)................................................................................... 16
ALKERAN® (MELPHALAN HYDROCHLORIDE)................................................................................. 17
ALUNBRIC™ (BRIGATINIB)............................................................................................................. 18
AMPYRA® (Dalfampridine)............................................................................................................. 19
ANTHIM® (OBILTOXAXIMAB)......................................................................................................... 21
ARALAST NP® (ALPHA-1 PROTEINASE INHIBITOR)...................................................................... 22
ARANESP® (DARBEPOETIN ALFA).................................................................................................. 24
AUBAGIO® (TERIFLUNOMIDE)...................................................................................................... 26
AUSTEDO® (DEUTETRABENAZINE)............................................................................................... 28
AVONEX® (INTERFERON BETA-1A)................................................................................................. 30
BARACLUDE® (ENTECAVIR)......................................................................................................... 32
BENLYSTA® (BELIMUMAB)............................................................................................................. 34
BERINERT® (HUMAN C1- ESTERASE INHIBITOR) KIT.................................................................. 36
BETASERON® (INTERFERON BETA-1 B).......................................................................................... 37
BONIVA® (IBANDRONATE SODIUM).............................................................................................. 38
BOSULIF® (BOSUTINIB MONOHYDRATE).................................................................................... 39
BOTOX® (ONABOTULINUM TOXIN A)............................................................................................ 41
CABOMETYX® (CABOZANTINIB)................................................................................................... 44
CALQUENCE® (ACALABRUTINIB).................................................................................................... 45
CAPRELSA® (VANDETANIB)......................................................................................................... 47
CAYSTON® (AZTREONAM)............................................................................................................ 48
CIMZIA® (CERTOLIZUMAB PEGOL).............................................................................................. 49
CINQAIR® (RESLIZUMAB)............................................................................................................ 52
CINRYZE® (HUMAN C1- ESTERASE INHIBITOR) ........................................................................................................54
COMETRIQ® (CABOZANTINIB) .......................................................................................................................................56
COPAXONE®, GLATOPA™ (GLATIRAMER ACETATE) ..................................................................................................58
COPIKTRA™ (DUVELISIB) † ........................................................................................................................................60
COSENTYX™ (SECUKINUMAB) ..................................................................................................................................62
COTELLIC™ (COBIMETINIB) ......................................................................................................................................64
CUVPOSAR® (GLYCOPYRROLATE) ..............................................................................................................................66
DAKLINZA™ (DACLATASVIR) .....................................................................................................................................67
DAURISMO™ (GLASDEGIB) ..........................................................................................................................................69
DUPIXENT® (DUPILUMAB) ..........................................................................................................................................71
DYSPORT® (BOTULINUM TOXIN TYPE A) ..................................................................................................................74
EMFLAZA® (DEFLAZACORT) ......................................................................................................................................76
ENBREL® (ETANERCEPT) ...............................................................................................................................................78
ENTYVIO® (VEDOLIZUMAB) .......................................................................................................................................81
EPCLUSA® (VELPATASVIR/SOFOSBUVIR) ..................................................................................................................83
ERIVEDGE® (VISMODEGIB) ......................................................................................................................................85
ERLEADA® (APALUTAMIDE) ......................................................................................................................................86
ESBRIET® (PIRfenidone) ..............................................................................................................................................87
EXJADE® (DEFERASIROX) .........................................................................................................................................89
EXTAVIA® (INTERFERON BETA-1B) ............................................................................................................................90
EYLEA® (AFLIBERCEPT) ..............................................................................................................................................92
FASENRA™ (BENRALIZUMAB) ..................................................................................................................................94
FIRAZYR® (ICATIBANT ACETATE) ............................................................................................................................96
FORTEO® (TERIPARATIDE) .........................................................................................................................................98
GILENYA® (FINGOLIMOD) .........................................................................................................................................100
GILOTIF® (AFATINIB) ...............................................................................................................................................102
GLEEVEC® (IMATINIB MESYLATE) ........................................................................................................................103
GROWTH HORMONE (SOMATROPIN) ..................................................................................................................105
HARVONI® (LEDIPASVIR/SOFOSBUVIR) ................................................................................................................108
H.P. ACTHAR GEL® (REPOSITORY CORTICOTROPIN) ..........................................................................................111
HUMIRA® (adalimumab) .............................................................................................................................................113
IBRANCE™ (PALBOCICLIB) .......................................................................................................................................118
ICLUSIG® (PONATINIB HYDROCHLORIDE) ...........................................................................................................120
IMBRUVICA® (IBRUTINIB) .........................................................................................................................................122
<table>
<thead>
<tr>
<th>Medicine Name</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>INCRELEX® (MECASERMIN)</td>
<td>124</td>
</tr>
<tr>
<td>INGREGA™ (VALBENAZINE)</td>
<td>126</td>
</tr>
<tr>
<td>INLYTA® (AXITINIB)</td>
<td>128</td>
</tr>
<tr>
<td>INTRON A® (INTERFERON ALFA-2B)</td>
<td>129</td>
</tr>
<tr>
<td>INTRAHEMATIC IRON (INFED®, DEXFERRUM®, FERRLECIT®, NULECIT®, VENOHER®, FERAHEM®, INJECTAFER®)</td>
<td>131</td>
</tr>
<tr>
<td>JAKAFI® (RUXOLITINIB)</td>
<td>134</td>
</tr>
<tr>
<td>JUXTAPID® (LOMITAPIDE)</td>
<td>135</td>
</tr>
<tr>
<td>KALBITOR® (ECALLANTIDE)</td>
<td>139</td>
</tr>
<tr>
<td>KALYDECO® (IVACAFTOR)</td>
<td>140</td>
</tr>
<tr>
<td>KEVZARA® (SARILUMAB)</td>
<td>142</td>
</tr>
<tr>
<td>KINERET® (ANAKINRA)</td>
<td>144</td>
</tr>
<tr>
<td>KISQALI® (RIBOCICLIB)</td>
<td>146</td>
</tr>
<tr>
<td>KRISTEXXXA® (PEGLOTICASE)</td>
<td>148</td>
</tr>
<tr>
<td>LEMTRADA™ (ALEMTUZUMAB)</td>
<td>150</td>
</tr>
<tr>
<td>LENVIMA® (LEVATINIB)†</td>
<td>152</td>
</tr>
<tr>
<td>LETAIRIS® (AMBRISIDENT)</td>
<td>154</td>
</tr>
<tr>
<td>LEUKINE® (SARGRAMOSTIM)</td>
<td>156</td>
</tr>
<tr>
<td>LORBRENA® (LORLATINIB)</td>
<td>157</td>
</tr>
<tr>
<td>LUCENTIS® (RANIBIZUMAB)</td>
<td>159</td>
</tr>
<tr>
<td>LUPRON DEPOT®/ELIGARD® (LEUROLIDE ACETATE)</td>
<td>161</td>
</tr>
<tr>
<td>LUXTURN® (VORETIGENE NEPARYVEC-RZYL)†</td>
<td>164</td>
</tr>
<tr>
<td>MAKENA® (HYDROXYPROGESTERONE CAPROATE)</td>
<td>166</td>
</tr>
<tr>
<td>MAVYRET® (GLECAPREVIR/PIBRENTASVIR)</td>
<td>168</td>
</tr>
<tr>
<td>MEKINIST® (TRAMETINIB)</td>
<td>170</td>
</tr>
<tr>
<td>MYOBLOC® (RIMABOTULINUMTOXINB)</td>
<td>172</td>
</tr>
<tr>
<td>NERLYNX™ (NERATINIB)</td>
<td>173</td>
</tr>
<tr>
<td>NEOLASTA® (PEGFILGRASTIM), FULPHILA™ (PEGFILGRASTIM-JMDB), UDENYCA™ (PEGFILGRASTIM-CBQV)</td>
<td>175</td>
</tr>
<tr>
<td>NEUMEGA® (OPRELVEKIN)</td>
<td>180</td>
</tr>
<tr>
<td>NEUPOGEN® (FILGRASTIM), GRANIX™ (TBO-FILGRASTIM), ZARXIO™ (FILGRASTIM-SNZ)†</td>
<td>181</td>
</tr>
<tr>
<td>NEXAVAR® (SORAFENIB)</td>
<td>187</td>
</tr>
<tr>
<td>NINLARO® (IXAZOMIB)</td>
<td>189</td>
</tr>
<tr>
<td>NORTHERA® (DROXIDOPA)</td>
<td>191</td>
</tr>
<tr>
<td>NUCALA® (MEPOLIZUMAB)</td>
<td>193</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Page</td>
</tr>
<tr>
<td>----------------------------</td>
<td>------</td>
</tr>
<tr>
<td>OCALIVA® (OBETICHOLIC ACID)</td>
<td>195</td>
</tr>
<tr>
<td>OCREVUS® (OCRELIZUMAB)</td>
<td>197</td>
</tr>
<tr>
<td>OFEV® (NINTEDANIB)</td>
<td>199</td>
</tr>
<tr>
<td>OLYSIO® (SIMEPREVIR)</td>
<td>201</td>
</tr>
<tr>
<td>ORENCIA® (ABA TACEPT)</td>
<td>203</td>
</tr>
<tr>
<td>ORKAMBI® (LUMACAFOR/IVACAFTOR)</td>
<td>205</td>
</tr>
<tr>
<td>OTEZLA® (APREMILAST)</td>
<td>207</td>
</tr>
<tr>
<td>PEGASYS® (PEGINTERFERON ALFA-2A)</td>
<td>209</td>
</tr>
<tr>
<td>PEGINTRON® (PEGINTERFERON ALFA-2B)</td>
<td>211</td>
</tr>
<tr>
<td>PLEGRIDY® (PEGINTERFERON BETA-1A)</td>
<td>212</td>
</tr>
<tr>
<td>POMALYST® (POMALIDOMIDE)</td>
<td>214</td>
</tr>
<tr>
<td>PRALUENT® (ALIROCUMAB)</td>
<td>216</td>
</tr>
<tr>
<td>EPOGEN® (EPOETIN), PROCRIT® (EPOETIN ALFA), RETACRIT (EPOETIN ALFA-EPBX)</td>
<td>219</td>
</tr>
<tr>
<td>PROLIA® (DENOSUMAB)</td>
<td>222</td>
</tr>
<tr>
<td>PROMACTA® (ELTROMBOPAG OLAMINE)</td>
<td>224</td>
</tr>
<tr>
<td>PULMOZYME® (DORNASE ALFA)</td>
<td>226</td>
</tr>
<tr>
<td>RAVICTI® (GLYCEROL PHENYL BUTYRATE)</td>
<td>227</td>
</tr>
<tr>
<td>REBIF® (INTERFERON BETA-1A)</td>
<td>228</td>
</tr>
<tr>
<td>RECLAST® (ZOLEDRONIC ACID)</td>
<td>230</td>
</tr>
<tr>
<td>REMICADE® (INFlixIMAB), INFLECTRA® (INFlixIMAB-DYYB), RENFLEXIS™ (INFlixIMAB-ABDA)</td>
<td>232</td>
</tr>
<tr>
<td>REPATHA® (EVLOU MBA)</td>
<td>236</td>
</tr>
<tr>
<td>REVATIO® (SILDENAFIL CITRATE)</td>
<td>239</td>
</tr>
<tr>
<td>REVLIMID® (LENALIDOMIDE)</td>
<td>241</td>
</tr>
<tr>
<td>RIBAVIRIN</td>
<td>243</td>
</tr>
<tr>
<td>RIDAURA® (AURANO F I N)†</td>
<td>245</td>
</tr>
<tr>
<td>RITUXAN® (RITUXIMAB)</td>
<td>247</td>
</tr>
<tr>
<td>RUBRACA™ (RUCAPARIB)</td>
<td>250</td>
</tr>
<tr>
<td>RUCONEST® (C1- ESTERASE INHIBITOR [RECOMBINANT])</td>
<td>252</td>
</tr>
<tr>
<td>RYDAPT® (MIDOSTAURIN)</td>
<td>253</td>
</tr>
<tr>
<td>SAMS CA® (TOLVAPTAN)</td>
<td>255</td>
</tr>
<tr>
<td>SANCUSO® (GRANISETRON)</td>
<td>257</td>
</tr>
<tr>
<td>SENSIPAR® (CINACALCET)</td>
<td>259</td>
</tr>
<tr>
<td>SEROSTIM® (SOMATROPIN)</td>
<td>261</td>
</tr>
<tr>
<td>SILIQ™ (BRODALUMAB)</td>
<td>263</td>
</tr>
</tbody>
</table>
SIMPONI®, SIMPONI ARIA® (GOLIMUMAB)..........................................................265
SKYRIZI™ (RISANKIZUMAB-RZAA).................................................................266
SOVALDI® (SOFOBUVIR) ..................................................................................268
SPINRAZA™ (NUSINERSEN) .............................................................................269
SPRAVATO™ (ESKETAMINE HYDROCHLORIDE SOLUTION)..........................271
SPRYCEL® (DASANTINIB) ..................................................................................273
STELARA® (USTEKINUMAB) .............................................................................275
STIVARGA® (REGORAFENIB) .........................................................................277
STRENSIQ™ (ASFOTASE ALFA) ......................................................................279
SUTENT® (SUNITINIB) ........................................................................................281
SYMDEKO™ (TEZACAFTOR/IVACAFTOR) .....................................................283
SYNAGIS® (PALIVIZUMAB) .............................................................................285
SYPRINE® (TRIENTINE) ....................................................................................287
TAFINLAR® (DABRAFENIB) ..............................................................................288
TAGRISSO™ (OSIMERTINIB) ............................................................................290
TAKHZYRO™ (LANADELUMAB-FLYO)† ..........................................................292
TALTZ™ (IXEKIZUMAB)† ..................................................................................294
TARCEVA® (ERLOTINIB HYDROCHLORIDE) ..................................................296
TARGETRETIN® (BEXAROTENE) ....................................................................298
TASIGNA® (NILOTINIB) ....................................................................................300
TECFIDERA® (DIMETHYL FUMARATE) ..........................................................302
TECHNIVIE® (PARITAPREVIR/RITONAVIR/OMBITASVIR) ...............................304
TEMODAR® (TEMOZOLOMIDE) .......................................................................306
THALOMID® (THALIDOMIDE) .........................................................................308
TIBSOVO® (IVOSONIDEB)† ...............................................................................310
TOBRAMYCIN FOR INHALATION (BETHKIS®, KITABIS PAK®, TOBI®, AND TOBI® PODHALER®) .................................................................312
TREMFYA® (GUSELKUMAB) .............................................................................314
TYKERB® (LAPATINIB) ....................................................................................316
TYMLOS® (ABALOPARATIDE) ..........................................................................318
TYSABRI® (NATALIZUMAB) ..............................................................................320
UPTRAVI® (SELEXIPAG) ..................................................................................322
VEMLIDY® (TENOFOVIR ALAFENAMIDE)† ....................................................324
VENCLEXTA™ (VENETOCLAX) .......................................................................326
VERZENIO™ (ABEMACICLID)† .........................................................................328
VIEKIRA PAK™, VIEKIRA XR™ (OMBITASVIR, PARITAPREVIR, RITONAVIR, DASABUVIR) .......................................................... 330
VIVITROL® (NALTREXONE FOR EXTENDED-RELEASE INJECTABLE SUSPENSION) .............................................................................. 332
VIZIMPRO® (DACOMITINIB) † .................................................................................................................................................. 334
VOSEVI® (SOFSBUVIR/VELPASVIR/VOXILAPREVIR) ........................................................................................................... 336
VOTRIENT® (PAZOPANIB HYDROCHLORIDE) ...................................................................................................................... 338
XALKORI® (CRIZOTINIB) ...................................................................................................................................................... 340
XELJANZ®, XELJANZ® XR (TOFACITINIB CITRATE) ........................................................................................................... 341
XELODA® (CAPECITABINE) .................................................................................................................................................. 343
XEOMIN® (INCOBOTULINUMTOXINA) ..................................................................................................................................... 345
XERMELO® (TELOTISTAT ETHYL) ........................................................................................................................................ 347
XIAFLEX™ (COLLAGENASE CLOSTRIDIUM HISTOLYTICUM) .......................................................................................... 348
XOLAIR® (OMALIZUMAB) .................................................................................................................................................. 350
XOSPATA® (GILTERITINIB) .................................................................................................................................................... 351
XTANDI® (ENZALUTAMIDE) .................................................................................................................................................. 353
XYREM® (SODIUM OXYBATE) .............................................................................................................................................. 355
ZEJULA® (NIRAPARIB) ....................................................................................................................................................... 357
ZELBORAF® (VEMURAFENIB) ............................................................................................................................................... 358
ZEPATIER™ (ELBASVIR/GRAZOPREVIR) ........................................................................................................................... 359
ZOLADEX® (GOSERELIN ACETATE) ...................................................................................................................................... 361
ZOLGENSMA (ONASEMNOGENE ABEPARVOVEC-XIOI) ........................................................................................................ 362
ZOLINZA® (VORINOSTAT) ................................................................................................................................................... 365
ZYDELIG™ (IDELALISIB) .................................................................................................................................................... 366
ZYKADIA™ (CERITINIB) .................................................................................................................................................... 368
ZYTGIA® (ABIRATERONE) ................................................................................................................................................... 369
Disclaimer

Recommended utilization criteria have been developed to assist in making coverage determinations. Recommendations are for informational purposes only and are not practice guidelines or medical advice. Treating health care professionals are solely responsible for diagnosis, treatment and medical advice. Recommendations are adopted after careful review of FDA approved labeling, published and peer-reviewed scientific literature, evidence-based guidelines from national professional organizations, and/or local standards of practice in diagnosis and treatment. Providers are advised to review this site periodically for changes.

When a treatment requires coverage review to determine appropriateness, but formal utilization recommendations have not been established by us or our delegate, decisions will be based upon FDA approved labeling, published and peer-reviewed scientific literature, and/or evidence-based guidelines.

Coverage determinations are subject to all terms and conditions of the member’s plan, including specific exclusions and limitations, and to applicable federal and state law. Eligibility and benefits are determined by the plan contract that is in effect at the time that a service is provided to the member. Members are encouraged to review the utilization criteria with their health care providers to insure mutual understanding. Utilization criteria do not constitute plan authorization, an explanation of benefits, or a guarantee of payment. Because medical technology is constantly changing, criteria are periodically reviewed and subject to change without notice. We are not responsible for the continuing viability of the website addresses listed as references. Additional criteria may be developed from time to time and some may be withdrawn from use.

Some benefit plans, such as some self-funded employer plans or governmental plans, may not use criteria for their coverage determinations. Members and their providers will need to consult the member’s benefit plan to determine if there is any exclusion or other benefit limitations applicable to the service or supply. The member’s benefit plan ultimately determines coverage.

The doctors, hospitals, and other providers which are part of the plan network are independent contractors who exercise independent judgment and over whom the health plan has no control or right of control. They are not agents or employees of the health plan.

This disclaimer applies to all present and past recommended utilization criteria.

For questions regarding these criteria, please call PA Navigator™ at 888-515-1357. For questions regarding a member’s specific benefits, please contact Member / Customer Services as identified on the member’s insurance card.

Conflict of Interest Disclosure: “In accordance with 2019 Wisconsin Act 12, the reviewers who create, update, edit and publish clinical utilization management criteria have no affiliations with or involvement in any organization or entity with financial interest (e.g., educational grants, consultant work, speakers bureau, employment, stock ownership) or non-financial interest (e.g., receipt of gifts, personal or professional relationships relationships) relative to pharmaceutical manufacturers.”
Specialty Drug Criteria and Utilization Recommendations

Updated criteria:

- Actemra
- Adcirca
- Afinitor
- Alecensa
- Alkeran
- Alunbrig
- Ampyra
- Anthem
- Aralast NP
- Aranesp
- Aubagio
- Austedo
- Avonex
- Baraclude
- Benlysta
- Berinert
- Betaseron
- Boniva
- Bosulif
- Botox
- Cabometyx
- Calquence
- Caprelsa

- Cayston
- Cimzia
- Cinqair
- Cinryze
- Cometriq
- Copaxone
- Copiktra
- Cosentyx
- Cotellic
- Cuvposa
- Kaklinza
- Daurismo
- Dysport
- Emflaza
- Enbrel
- Entyvio
- Eplueva
- Erivedge
- Humira
- Infliximab
- Orkambi
- Stelara
Actemra® (tocilizumab)‡

**FDA Approved Indication(s)**

- For the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs)
- For the treatment of giant cell arteritis (GCA) in adult patients
- For the treatment of active polyarticular juvenile idiopathic arthritis (PJIA) in patients 2 years of age and older
- For the treatment of active systemic juvenile idiopathic arthritis (SJIA) in patients 2 years of age and older
- For the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome in adults and pediatric patients 2 years of age and older

**FDA Recommended Dose**

- **Rheumatoid arthritis**
  - IV: 4 mg/kg IV every 4 weeks followed by an increase to 8 mg/kg every 4 weeks based on clinical response. Doses exceeding 800 mg per infusion are not recommended.
  - SC:
    - Less than 100 kg: 162 mg SC every other week, followed by an increase to every week based on clinical response
    - Greater than or equal to 100 kg: 162 mg SC every week
- **Giant cell arteritis**
  - 162 mg SC once every week, in combination with a tapering course of glucocorticoids
- **Polyarticular juvenile idiopathic arthritis**
  - Less than 30 kg: 10 mg/kg IV every 4 weeks or 162 mg SC every 3 weeks
  - Greater than or equal to 30 kg: 8 mg/kg IV every 4 weeks or 162 mg SC every 2 weeks
- **Systemic juvenile idiopathic arthritis**
  - Less than 30 kg: 12 mg/kg IV every 2 weeks or 162 mg SC every 2 weeks
  - Greater than or equal to 30 kg: 8 mg/kg IV every 2 weeks or 162 mg SC once every week
- **Cytokine release syndrome**
  - Less than 30 kg: 12 mg/kg IV. If no clinical improvement in the signs and symptoms of CRS occurs after the first dose, up to 3 additional doses may be administered, with an interval between consecutive doses of at least 8 hours.
  - Greater than or equal to 30 kg: 8 mg/kg IV. If no clinical improvement in the signs and symptoms of CRS occurs after the first dose, up to 3 additional doses may be administered, with an interval between consecutive doses of at least 8 hours.
  - Doses exceeding 800 mg per infusion are not recommended
  - See package insert for dose modifications with elevated liver enzymes, neutropenia, and thrombocytopenia

**How Supplied**

- 80 mg/4 mL, 200 mg/10 mL and 400 mg/20 mL single-use vials for IV administration
- 162 mg/0.9 mL single-use prefilled syringe for SC administration

**Utilization Criteria**

*For initial review:

- Member has a documented negative TB test prior to initiation of therapy, AND
- Member must use subcutaneous formulation of product, unless otherwise contraindicated or unable to self-administer, as detailed within supplied clinical documentation, AND
• Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
• RA:
  • Has tried and failed at least one non-biologic DMARD
• GCA:
  • Has tried and failed high doses of corticosteroids (i.e. prednisone 40-60 mg daily)
• PJIA:
  • Has tried and failed at least one non-biologic DMARD
• SJIA:
  • Has tried and failed at least one corticosteroid or NSAID

For continuation:
• Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
• Member has an active infection, OR
• Concurrent use with other biologic DMARD therapies
• ANC < 2000/mm³, platelet count < 100,000/mm³, ALT or AST > 1.5 times ULN

Required Medical Information
• Diagnosis
• TB test result
• Weight
• Dose
• Lipid panel, absolute neutrophil count (ANC), and platelets

Age Restrictions
• Polyanarticular Juvenile Idiopathic Arthritis or Systemic Juvenile Idiopathic Arthritis, Cytokine Release Syndrome – 2 years of age and older
• Rheumatoid Arthritis, Giant Cell Arteritis – 18 years of age and older

Prescriber Restrictions
• Must be prescribed by a rheumatologist

Coverage Duration (months)
• 12

Quantity/Partial Fill Restrictions
• None

Other Information
• Mechanism of action: Tocilizumab binds specifically to both soluble and membrane-bound IL-6 receptors (sIL-6R and mIL-6R), and has been shown to inhibit IL-6-mediated signaling through these receptors
• Black Box Warning: Risk of serious infections

References

# Adcirca® (tadalafil)

### FDA Approved Indication(s)
- To improve exercise ability in patients with pulmonary arterial hypertension (PAH) (WHO Group 1)

### FDA Recommended Dose
- 40 mg (two 20 mg tablets) taken once daily with or without food

### How Supplied
- 20 mg tablets

### Utilization Criteria

**For initial review:**
- PAH confirmed by right heart catheterization or Doppler echocardiogram in infants, AND
- Patient must have documented treatment failure of generic sildenafil

**For continuation:**
- Above criteria met, AND
- Patient must have a documented increase in 6-minute walk distance (6MWD) since therapy initiation

### Exclusion Criteria
- Patient is currently receiving nitrate therapy, OR
- Patient is currently receiving guanylate cyclase (GC) stimulators

### Required Medical Information
- Diagnosis
- Age
- Concurrent medications
- Dose
- Treatment history
- Six-minute walk distance (6MWD)

### Age Restrictions
- Age 18 years and older

### Prescriber Restrictions
- Must be prescribed by a cardiologist

### Coverage Duration (months)
- Initial: 6 months
- Continuation: 12 months

### Quantity/Partial Fill Restrictions
- None

### Other Information
- Mechanism of action: Tadalafil is an inhibitor of phosphodiesterase type 5 (PDE5), the enzyme responsible for the degradation of cyclic guanosine monophosphate (cGMP). Pulmonary arterial hypertension is associated with impaired release of nitric oxide by the vascular endothelium and consequent reduction of cGMP concentrations in the pulmonary vascular smooth muscle. PDE5 is the predominant phosphodiesterase in the pulmonary vasculature. Inhibition of PDE5 by tadalafil increases the concentrations of cGMP resulting in relaxation of pulmonary vascular smooth muscle cells and vasodilation of the pulmonary vascular bed.

### References
**Afinitor® (everolimus)**

**FDA Approved Indication(s)**

- Afinitor®:
  - For the treatment of postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer, in combination with exemestane, after failure of treatment with letrozole or anastrozole
  - For the treatment of adult patients with progressive neuroendocrine tumors of pancreatic origin (PNET) that are unresectable, locally advanced or metastatic
  - For the treatment of adult patients with progressive, well-differentiated, non-functional NET of gastrointestinal or lung origin with unresectable, locally advanced or metastatic disease
  - For the treatment of adult patients with advanced renal cell carcinoma (RCC) after treatment failure with sunitinib or sorafenib
  - For the treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery
  - For the treatment of adult and pediatric patients aged 1 year and older with tuberous sclerosis complex (TSC) for the treatment of subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected
- Afinitor® Disperz™:
  - For the treatment of pediatric and adult patients with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected
  - For the adjunctive treatment of adult and pediatric patients aged 2 years and older with TSC-associated partial-onset seizures

**FDA Recommended Dose**

- Breast Cancer: 10 mg orally once daily
- Neuroendocrine tumors of pancreatic origin: 10 mg orally once daily
- Renal cell carcinoma: 10 mg orally once daily
- TSC-Associated Renal Angiomyolipoma: 10 mg orally once daily
- TSC-Associated SEGA: 4.5 mg/m² orally once daily; adjust dose to attain trough concentrations of 5-15 ng/mL
- TSC-Associated Partial-Onset Seizures: 5 mg/m² orally once daily; adjust dose to attain trough concentrations of 5-15 ng/mL

**Utilization Criteria**

*For initial review:*
- Patient must have a diagnosis of an FDA-approved indication

*For continuation:*
- Patient must have documented response to therapy, as detailed within clinical notes

**Exclusion Criteria**

- None

**Required Medical Information**

- Diagnosis
- Age
- Dose
- Previous treatment history (if indicated for HR+, HER2-negative breast cancer)
• Concurrent medications
• SEGA with TSC: Trough level along with height and weight for BSA calculation

Age Restrictions
• None

Prescriber Restrictions
• Must be prescribed by an oncologist

Coverage Duration (months)
• 3 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions
• 14 tablets for 14 day supply for the first 6 fills

Other Information
• Mechanism of action: Everolimus binds to an intracellular protein, FKBP-12, resulting in an inhibitory complex formation with mTOR complex 1 (mTORC1) and thus inhibition of mTOR kinase activity

References
• Afinitor® [Package Insert]. East Hanover, NJ: Novartis Pharmaceuticals; April 2018.

Last Reviewed November 6, 2019
Alecensa® (alectinib hydrochloride)

FDA-Approved Indication(s)
- For the treatment of patients with anaplastic lymphoma kinase (ALK)-positive, metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test

FDA-Recommended Dose
- 600 mg orally twice daily with food until disease progression or unacceptable toxicity

How Supplied
- 150 mg hard capsules available in bottles of 240 capsules

Utilization Criteria
For initial review:
- Member must have a diagnosis of ALK-positive metastatic NSCLC

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Severe hepatic dysfunction
  - ALT or AST >3x Upper Limit of Normal (ULN), OR
  - Total bilirubin >2x ULN in absence of cholestasis or hemolysis
- Presence of Interstitial Lung Disease (ILD)/Pneumonitis
- Grade 4 renal impairment
- Pregnancy

Required Medical Information
- Diagnosis
- Dose
- Concomitant and previous therapies
- Liver function tests

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 3 months (initial), 12 months (continuation)

Other Information
- Mechanism of action: Alectinib is a tyrosine kinase inhibitor that targets ALK and RET. In nonclinical studies, alectinib inhibited ALK phosphorylation and ALK-mediated activation of the downstream signaling proteins STAT3 and AKT, and decreased tumor cell viability in multiple cell lines harboring ALK fusions, amplifications, or activating mutations. The major active metabolite of alectinib, M4, showed similar in vitro potency and activity.

References
Alkeran® (melphalan hydrochloride)

FDA Approved Indication(s)
- For the palliative treatment of multiple myeloma for whom oral therapy is not appropriate

FDA Recommended Dose
- 16 mg/m² via intravenous (IV) administration

How Supplied
- 50 mg/10 mL single-use vial

Utilization Criteria
For initial review:
- Confirmed diagnosis of multiple myeloma, AND
- Patient must be intolerant to or have failed oral chemotherapy, AND
- Patient must be currently receiving prednisone

For continuation:
- Above criteria are met, AND
- Must have a documented benefit to therapy, as assessed by oncologist or another qualified provider.

Exclusion Criteria
- None

Required Medical Information
- Diagnosis
- Age
- Dose
- Weight
- Height
- Concurrent medications

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 3 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Melphalan is an alkylating agent of the bischloroethylamine type.
- Black Box Warning: Severe bone marrow suppression with resulting infection or bleeding may occur.

References

Last Reviewed November 6, 2019
**Alunbrig™ (brigatinib)**

**FDA Approved Indication(s)**
- For the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib

**FDA Recommended Dose**
- 90 mg orally once daily for the first 7 days, then increase to 180 mg orally once daily if tolerated
- Reduce dose for symptomatic bradycardia and other adverse effects per package insert

**How Supplied**
- 30 mg, 90 mg, and 180 mg tablets

**Utilization Criteria**

*For initial review:*
- Member must have a diagnosis of metastatic NSCLC, AND
- Must have documentation of ALK-positive disease, as detected by an FDA approved test, AND
- Member must have progressed on, or had intolerance to, crizotinib

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Presence of interstitial lung disease or pneumonitis

**Required Medical Information**
- Diagnosis
- Dose
- Therapeutic history

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration (months)**
- 3 months (initial), 12 months (continuation)

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: Brigatinib is a tyrosine kinase inhibitor with in vitro activity at clinically achievable concentrations against multiple kinases including ALK, ROS1, insulin-like growth factor-1 receptor (IGF-1R), and FLT-3 as well as EGFR deletion and point mutations.

**References**

*Last Reviewed November 6, 2019*
Ampyra® (dalfampridine)

FDA Approved Indication(s)
- To improve walking (gait) in patients with multiple sclerosis (MS)

FDA Recommended Dose
- 10 mg twice daily (approximately 12 hours apart)

How Supplied
- 10 mg extended release tablets

Utilization Criteria
For initial review:
- A confirmed diagnosis of MS, AND
- Documented gait impairment secondary to MS disease progression, AND
- Creatinine clearance (CrCl) > 50mL/min, AND
- Receiving concurrent therapy with a disease modifying agent (i.e., an interferon product, glatiramer acetate, teriflunomide, fingolimod, or dimethyl fumerate) unless member has a documented intolerance to multiple disease modifying therapies, AND
- A baseline timed 25-foot walking test

For Continuation:
- At 12 weeks, member must have a documented 10% or greater improvement from baseline in a timed 25-foot walking test, AND
- At 12 months, documentation must confirm that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider, AND
- Member has remained on a disease modifying agent

Exclusion Criteria
- History of seizure disorder
- Previous treatment failure or intolerance to dalfampridine
- CrCl ≤ 50 mL/min
- Concurrent use of any product containing 4-aminopyridine (4-AP, fampridine)

Required Medical Information
- Confirmed Diagnosis of MS
- Creatinine clearance (CrCl)
- Baseline walking speed
- Concurrent medications
- History of seizure disorder
- Age
- Dose

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a neurologist

Coverage Duration
- 12 weeks initial; 12 months following documented improvement in walking speed

Quantity/Partial Fill Restrictions
• None

**Other Information**

• Black Box Warning: None

**References**

## Anthim® (obiltoxaximab)

### FDA-Approved Indication(s)
- Treatment of inhalational anthrax due to *B. anthracis* in combination with appropriate antibacterial drugs and for prophylaxis of inhalational anthrax when alternative therapies are not available or are not appropriate

### FDA-Recommended Dose
- **Adults:** 16 mg/kg
- **Pediatric patients:**
  - >40 kg: 16 mg/kg
  - 15 to 40 kg: 24 mg/kg
  - ≤15 kg: 32 mg/kg

### How Supplied
- 600 mg/6 mL (100mg/mL) solution in a single-dose vial

### Utilization Criteria

**For initial review:**
- Member must have documented inhalational anthrax due to *B. anthracis*, OR
- Documented reasoning for needed prophylaxis of inhalational anthrax

**For continuation:**
- Continued coverage will not be considered as this is a one-time dose.

### Exclusion Criteria
- None

### Required Medical Information
- Age
- Weight
- Dose

### Age Restrictions
- None

### Prescriber Restrictions
- None

### Coverage Duration (months)
- One dose

### Quantity/Partial-Fill Restrictions
- None

### Other Information
- Obiltoxaximab is a monoclonal antibody that binds the protective antigen component of *B. anthracis* toxin
- Black Box Warning: Hypersensitivity and anaphylaxis

### References

*Last Reviewed November 6, 2019*
Aralast NP® (alpha-1 proteinase inhibitor)

**FDA-Approved Indication(s)**
- For the treatment of Congenital Alpha1–Proteinase Inhibitor (α1–PI) deficiency in patients having congenital deficiency of α1–PI with clinically evident emphysema

**FDA-Recommended Dose**
- 60 mg/kg body weight, administered at a rate not exceeding 0.2 mL/kg body weight/minute, once weekly

**How Supplied**
- 500 mg and 1,000 mg sterile, non-pyrogenic, lyophilized powder in single-dose vials

**Utilization Criteria**

*For initial review:*
- Member must have documented α1–PI deficiency, as confirmed by documented sub-therapeutic levels of α1–PI, AND
- Member must have confirmed high-risk genotype of PiZZ, PiZ (null), or Pi (null/null), AND
- Member must have clinical evident emphysema, concurrently treated according to standard of care

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Member must not be a current smoker

**Required Medical Information**
- Diagnosis
- Age
- Dose

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a pulmonologist or hematologist

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: α1–PI functions in the lungs to inhibit serine proteases, which function to degrade protein components of the alveolar walls. Severe forms of the deficiency are associated with slowly progressive emphysema that often results in significantly lower life expectancy.
- Black Box Warning: None

**References**
**Aranesp® (darbepoetin alfa)**

**FDA Approved Indication(s)**
- For the treatment of anemia due to Chronic Kidney Disease (CKD)
- For the treatment of anemia due to myelosuppressive effects of chemotherapy when, upon initiation, there is a minimum of two additional months of planned chemotherapy

**FDA Recommended Dose**
- Recommended starting dose for adult CKD patients on dialysis:  
  - 0.45 mcg/kg intravenously or subcutaneously weekly as needed; OR
  - 0.75 mcg/kg intravenously or subcutaneously every 2 weeks as needed
- Recommended starting dose for adult patients with CKD not on dialysis:  
  - 0.45 mcg/kg intravenously or subcutaneously at 4-week intervals as needed
- Recommended starting dose for pediatric CKD patients on dialysis:  
  - 0.45 mcg/kg intravenously or subcutaneously weekly as needed
- Recommended starting dose for pediatric CKD patients not on dialysis:  
  - 0.45 mcg/kg intravenously or subcutaneously weekly as needed; OR
  - 0.75 mcg/kg intravenously or subcutaneously every 2 weeks as needed
- Recommended starting dose for cancer patients on chemotherapy:  
  - 2.25 mcg/kg subcutaneously weekly, OR
  - 500 mcg subcutaneously every 3 weeks

**How Supplied**
- Single-dose vials: 25, 40, 60, 100, 200, and 300 mcg/1 mL; 150 mcg/0.75 mL
- Single-dose prefilled syringes: 10 mcg/0.4 mL, 25 mcg/0.42 mL, 40 mcg/0.4 mL, 60 mcg/0.3 mL, 100 mcg/0.5 mL, 150 mcg/0.3 mL, 200 mcg/0.4 mL, 300 mcg/0.6 mL, and 500 mcg/1 mL

**Utilization Criteria**

*For initial review:*
- Anemia associated with CKD on dialysis:  
  - Hemoglobin (Hgb) level is less than 10 g/dL
- Anemia associated with CKD not on dialysis:  
  - Hgb is less than 10 g/dL, AND
  - The rate of Hgb decline indicates the likelihood of requiring a RBC transfusion, AND
  - Reducing the risk of alloimmunization and/or other RBC transfusion-related risks is a goal
- Anemia associated with concomitant myelosuppressive chemotherapy:  
  - Member has documented hemoglobin (Hgb) level equal or less than 10 g/dL, AND
  - Member is currently being treated with myelosuppressive chemotherapy, AND
  - Member has a minimum of two additional months of planned chemotherapy

*For continuation:*
- Anemia associated with CKD:  
  - Member has documented Hgb level equal to or less than 11 g/dL (on dialysis) or 10 g/dL (not on dialysis)
- Anemia associated with concomitant myelosuppressive chemotherapy:  
  - Member has documented hemoglobin (Hgb) level equal or less than 10 g/dL, AND
- Member has a minimum of two additional months of planned chemotherapy

**Exclusion Criteria**
- Members with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy
• Members with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure
• Use as a substitute for RBC transfusions in patients who require immediate correction of anemia
• Member has documented Hgb greater than or equal to 11 g/dL
• Member has completed their course of myelosuppressive chemotherapy
• Member that has uncontrolled hypertension
• Member has pure red cell aplasia (PRCA) that begins after treatment with Aranesp or other erythropoietin protein drugs

**Required Medical Information**

- Diagnosis
- Age
- Weight
- Complete blood count with differential
- Concurrent medications

**Age Restrictions**

- 1 year of age and older

**Prescriber Restrictions**

- Must be prescribed by a specialist in the disease being treated

**Coverage Duration (months)**

- CKD: 3 months
- Myelosuppressive chemotherapy: 2 months

**Quantity/Partial Fill Restrictions**

- 30-day supply, no partial fill

**Other Information**

- Mechanism of action: Darbepoetin alfa stimulates erythropoiesis by the same mechanism as endogenous erythropoietin
- Black Box Warnings
  - CKD: Patients may be placed at greater risk of death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL
  - Cancer: ESAs shortened overall survival and/or increased the risk of tumor progression or recurrence in clinical studies of patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers
  - Cancer: Prescribers and hospitals must enroll in and comply with the ESA APPRISE Oncology Program to prescribe and/or dispense darbepoetin alfa to patients with cancer
  - Cancer: Discontinue following completion of a chemotherapy course
- Darbepoetin alfa has not been shown to improve quality of life, fatigue, or patient well-being in patients with cancer.

**References**


*Last Reviewed November 6, 2019*
**Aubagio® (teriflunomide)**

**FDA Approved Indication(s)**
- For the treatment of patients with relapsing forms of multiple sclerosis

**FDA Recommended Dose**
- 7 mg or 14 mg orally once daily

**How Supplied**
- 7 mg and 14 mg tablets

**Utilization Criteria**

*For initial review:*
- Must have diagnosis of relapsing form of multiple sclerosis (RRMS, PRMS); AND
- Must have a baseline complete blood count; AND
- Must have liver enzymes (ALT, AST) and bilirubin monitored at baseline and ALT levels monitored at least monthly for the first six months; AND
- Must have tuberculin skin test or blood test for mycobacterium tuberculosis infection; AND
- Check blood pressure prior to start of treatment and periodically thereafter; AND
- Liver enzymes must be, and remain, less than two times upper limit of normal; AND
- Must have tried and failed all plan-specific step therapy requirements, as applicable

*For continuation:*
- Member must have documentation of annual assessment from a neurologist

**Exclusion Criteria**
- Currently receiving one or more alternative disease modifying therapies
- Pregnancy
- Currently receiving leflunomide

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Concomitant medications

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a neurologist

**Coverage Duration (months)**
- 6 month initial, 12 months maintenance

**Quantity/Partial Fill Restrictions**
- 30 day supply

**Other Information**
- Teriflunomide is a pyrimidine synthesis inhibitor. The exact mechanism by which teriflunomide exerts its therapeutic effect in multiple sclerosis is unknown but may involve a reduction in the number of activated lymphocytes in the CNS.
- Black Box Warning: Hepatotoxicity and Risk of Teratogenicity

**References**


Austedo® (deutetrabenazine)

FDA Approved Indication(s)

- For the treatment of chorea associated with Huntington’s disease
- For the treatment of tardive dyskinesia in adults

FDA Recommended Dose

- Dosing is individualized to the patient based on reduction of chorea or tardive dyskinesia and tolerability
- See package insert for FDA recommended dosing when switching from tetrabenazine
- Maximum dose: 48 mg/day

How Supplied

- 6 mg, 9 mg, and 12 mg tablets

Utilization Criteria

For initial review:

- Member must have a documented diagnosis of Huntington’s chorea or tardive dyskinesia

For continuation:

- Member must have documentation of treatment response, as verified per progress notes

Exclusion Criteria

- Member has a history of depression, suicide attempts, and/or suicidal ideation
- Member is using concomitantly with tetrabenazine
- Member has severe hepatic impairment
- Member is using concomitantly with a monoamine oxidase inhibitor (MAOI)
- Member is using concomitantly with reserpine
- Member is using concomitantly with tetrabenazine or valbenazine

Required Medical Information

- Diagnosis
- Current medication list
- Therapeutic history

Age Restrictions

- 18 years of age and older

Prescriber Restrictions

- Must be prescribed by a neurologist

Coverage Duration (months)

- 12 months

Quantity/Partial Fill Restrictions

- Maximum of 240 – 6mg tablets per 30-day period
- Maximum of 150 – 9 mg tablets per 30-day period
- Maximum of 120 – 12 mg tablets per 30-day period
- Any combination of available tablets that does not exceed 48 mg/day

Other Information

- Huntington’s disease (HD) is a rare and fatal genetic disorder that causes progressive neurodegeneration. Symptoms of HD include motor dysfunction, progressive psychiatric symptoms and eventually dementia. HD typically presents between the ages of 30 to 50; a key feature for diagnosis is chorea, which is characterized as involuntary, rapid movement of the face, trunk, and
limbs. HD is most common in people of European descent; the Huntington’s Disease Society of America estimates that HD affects approximately 30,000 people in the United States.

- Tardive dyskinesia causes repetitive, unintentional movements, that can be seen in the following areas: face and mouth, arms and hands, leg, and feet, and trunk. The severity of tardive dyskinesia can vary from person to person, but even mild symptoms can be bothersome.
- Mechanism: The metabolites of Austedo are inhibitors of vesicular monoamine transporter (VMAT2), a protein involved in neurotransmitter transport. By inhibiting VMAT2, deutetrabenazine reduces the number of neurotransmitters near nerve terminals.
- Deutetrabenazine is the first deuterated product approved by the FDA, and second medication approved for chorea associated with HD. Replacing certain hydrogen atoms with deuterium slows the metabolism of deutetrabenazine, allowing for decreased dosing frequency.

**References**

- Austedo™ deutetrabenazine [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; July 2019.
- Huntington’s Disease Society of America. What is Huntington’s Disease? Available from: http://hdsa.org/what-is-hd/

_Last Reviewed November 6, 2019_
**Avonex® (interferon beta-1a)**

**FDA Approved Indication(s)**
- For the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults

**FDA Recommended Dose**
- 30 mcg injected intramuscularly once weekly; may be started at a dose of 7.5 mcg and increased by 7.5 mcg each week until the recommended dose of 30 mcg is achieved to reduce incidence and severity of flu-like symptoms that may occur

**How Supplied**
- 30 mcg lyophilized powder single-use vial
- 30 mcg/0.5 mL single-use prefilled syringe
- 30 mcg/0.5 mL single-use prefilled autoinjector

**Utilization Criteria**

*For initial review:*
- Diagnosis of a relapsing form multiple sclerosis; AND
- Must have an MRI scan that demonstrated features consistent with a diagnosis of MS

*For continuation:*
- Review of therapy by a neurologist confirms that there is a continued beneficial response to therapy

**Exclusion Criteria**
- Concurrent use of alternative disease-modifying therapy, such as interferon beta-1b, interferon beta-1a, glatiramer acetate, dimethyl fumarate, fingolimod, or teriflunomide

**Required Medical Information**
- Diagnosis
- Concurrent medications
- Age
- Dose
- Complete baseline blood count with differential
- Liver function tests (ALT, AST)

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a neurologist

**Coverage Duration (months)**
- 12 months

**Quantity/Partial Fill Restrictions**
- 4 injections per 28 day supply

**Other Information**
- The mechanism of action through which interferon beta-1a exerts its effects on multiple sclerosis is unknown.

**References**
## Baraclude® (entecavir)

### FDA-Approved Indication(s)
- Chronic hepatitis B virus infection with evidence of active viral replication and either persistently elevated serum aminotransferases (ALT or AST) or histologically active disease.

### FDA-Recommended Dose
- Nucleoside-inhibitor-treatment-naïve with compensated liver disease in those ≥ 16 years of age: 0.5 mg orally once daily on an empty stomach
- Nucleoside-inhibitor naïve and lamivudine-experienced pediatric patients (≥ 2 years of age) and weighing at least 10 kg: dosing based on weight (see package insert)
- Lamivudine-refractory or known lamivudine or telbivudine resistance substitutions in those ≥ 16 years of age with compensated liver disease: 1 mg orally once daily on an empty stomach
- Adults with decompensated liver disease: 1 mg orally once daily on an empty stomach
- Dose adjust for renal impairment (CrCl < 50 mL/min)

### How Supplied
- 0.5 mg and 1 mg film-coated tablet
- 0.05 mg/mL oral solution

### Utilization Criteria

#### For initial review:
- Member must have a diagnosis of chronic hepatitis B (CHB) virus infection, AND
- Evidence of immune-active CHB, defined as:
  - Serial elevation of ALT >2 ULN (>60 U/L in males, >38 U/L in females) OR evidence of significant histological disease; AND
  - HBV DNA >2,000 IU/mL (HBeAg negative) or >20,000 IU/mL (HBeAg positive); OR
  - Compensated cirrhosis and low levels of viremia (<2,000 IU/mL)
- Documentation of HIV status
- For patients who are coinfected, treatment of HBV needs to be coordinated with HIV therapy

#### For continuation:
- Persistent low-level viremia (<2,000 IU/mL) on entecavir therapy
- HBeAg-negative immune active CHB
- HBeAg-positive with cirrhosis who seroconvert

### Exclusion Criteria
- Immune-tolerant CHB, defined as ALT <30 U/L for men and <19 U/L for women, within the previous six months
- Previous history of lamivudine resistance
- For continuation, in patients with HBeAg-positive adults without cirrhosis who seroconvert to anti-HBe, entecavir should be discontinued after 12 months of persistently normal ALT levels and undetectable HBV DNA levels

### Required Medical Information
- Diagnosis
- Age
- Weight (if <16 years of age)
- Dose
- Renal Function
- LFTs
- HBV status
<table>
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<th><strong>Age Restrictions</strong></th>
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<td>• 2 years of age</td>
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<th><strong>Prescriber Restrictions</strong></th>
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<tr>
<td>• Must be prescribed by a gastroenterologist, hepatologist, or infectious disease specialist</td>
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<th><strong>Coverage Duration (months)</strong></th>
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<td>• 12 months</td>
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<th><strong>Quantity/Partial-Fill Restrictions</strong></th>
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<td>• None</td>
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<th><strong>Other Information</strong></th>
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<tr>
<td>• Entecavir has anti-HIV activity and treatment of HBV needs to be coordinated with HIV therapy in patients who are co-infected</td>
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<tr>
<td>• Black Box Warnings</td>
</tr>
<tr>
<td>• Severe acute exacerbations of hepatitis B have been documented after treatment discontinuation. Liver function should be monitored for several months after discontinuation.</td>
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<tr>
<td>• Patients co-infected with HIV should be receiving HAART in addition to entecavir.</td>
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<tr>
<td>• Lactic acidosis and hepatomegaly with steatosis (including fatal cases) have been reported in patients receiving nucleoside analogs.</td>
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<th><strong>References</strong></th>
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_Last Reviewed November 18, 2019_
Benlysta® (belimumab)

FDA Approved Indication(s)
- For the treatment of patients aged 5 years and older with active, autoantibody-positive, systemic lupus erythematosus who are receiving standard therapy

FDA Recommended Dose
- IV: 10 mg/kg, infused over one hour, at two-week intervals for the first three doses and at four-week intervals thereafter
- SC: (adults only) 200 mg subcutaneously once weekly

How Supplied
- 120 mg/5 mL and 400 mg/20 mL lyophilized powder single-use vials
- 200 mg/mL prefilled autoinjector
- 200 mg/mL prefilled syringe

Utilization Criteria
For initial review:
- Must have a diagnosis of systemic lupus erythematosus (SLE); AND
- Must have a positive antinuclear antibody (ANA) test result of ≥ 1:80 or anti-dsDNA result of ≥ 30 IU/mL; AND
- Must be receiving standard of care SLE medications

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Diagnosis of severe active lupus nephritis or severe active central nervous system lupus
- Use in combination with other biologics or intravenous cyclophosphamide

Required Medical Information
- Diagnosis
- Concurrent Medications
- Weight
- Age
- Dose

Age Restrictions
- 5 years and older

Prescriber Restrictions
- Must be prescribed by a rheumatologist or dermatologist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Belimumab is a BLYS-specific inhibitor that blocks the binding of soluble BLYS, a B-cell survival factor, to its receptors on B cells.

References

Last Reviewed November 18, 2019
**Berinert® (human c1- esterase inhibitor) kit**

**FDA Approved Indication(s)**
- For the treatment of acute abdominal, facial, or laryngeal attacks of hereditary angioedema (HAE) in adult and adolescent patients

**FDA Recommended Dose**
- 20 IU/kg

**How Supplied**
- 500 IU single use vial for reconstitution

**Utilization Criteria**

*For initial review:*
- Member must have a diagnosis of classic HAE, where diagnosis is based on evidence of a normal C1 level and a low C4 level (C4 less than 14 mg/dL; normal range 14 to 40 mg/dL, or C4 below the lower limit of normal as defined by the laboratory performing the test)

*For continuation:*
- Documentation of ongoing HAE attacks and response to medication

**Exclusion Criteria**
- Not to be used for prophylactic therapy
- Patient is receiving one or more biologic therapy to treat acute HAE attacks (e.g., Firazyr or Ruconest)

**Required Medical Information**
- Diagnosis
- Dose
- Weight

**Age Restrictions**
- 12 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an allergist, immunologist, or hematologist

**Coverage Duration (months)**
- 1 month

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: C1 esterase inhibitor has an important inhibiting potential on several of the major cascade systems of the human body, including the complement system, the intrinsic coagulation (contact) system, the fibrinolytic system, and the coagulation cascade. Regulation of these systems is performed through the formation of complexes between the proteinase and the inhibitor, resulting in inactivation of both and consumption of the C1 esterase inhibitor.
- Black Box Warning: none

**References**
# Betaseron® (interferon beta-1b)

## FDA Approved Indication(s)
- For the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults

## FDA Recommended Dose
- The recommended starting dose is 0.0625 mg (0.25 mL) subcutaneously every other day, with dose increases over a six-week period to the recommended dose of 0.25 mg (1 mL) every other day

## How Supplied
- 0.3 mg lyophilized powder in a single-use vial with a pre-filled single-use syringe containing 1.2 mL sodium chloride (0.54%)

## Utilization Criteria

**For initial review:**
- Diagnosis of a relapsing form of multiple sclerosis

**For continuation:**
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

## Exclusion Criteria
- Concurrent use of alternative disease-modifying therapy, such as interferon beta-1a, glatiramer acetate, dimethyl fumarate, fingolimod, or teriflunomide
- History of hypersensitivity to natural or recombinant interferon beta, albumin or mannitol

## Required Medical Information
- Diagnosis
- Concurrent medications
- Age
- Dose
- Complete baseline blood count with differential
- Liver function tests (ALT, AST)

## Age Restrictions
- 18 years of age and older

## Prescriber Restrictions
- Must be prescribed by a neurologist

## Coverage Duration (months)
- 12 months

## Quantity/Partial Fill Restrictions
- None

## Other Information
- Mechanism of action: The mechanism of action of interferon beta-1b in patients with multiple sclerosis is unknown.

## References

*Last Reviewed November 18, 2019*
Boniva® (ibandronate sodium)

FDA Approved Indication(s)
- For the treatment of osteoporosis in postmenopausal women

FDA Recommended Dose
- 3 mg every 3 months, administered over a period of 15 to 30 seconds intravenously

How Supplied
- 3 mg/3 mL single-use, clear glass, 5 mL prefilled syringe

Utilization Criteria
For initial review:
- Member must be postmenopausal as confirmed by a physician, AND
- Member is concurrently receiving supplemental calcium and vitamin D unless contraindicated, AND
- Member must have a documented bone mineral density (BMD) T-score of ≤ -2.5, AND
- Member is intolerant or has a contraindication to at least one oral bisphosphonate as documented in provider notes

For continuation:
- Benefit of therapy evidenced by increased BMD, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s provider

Exclusion Criteria
- Hypocalcemia
- Hypersensitivity to ibandronate injection

Required Medical Information
- Diagnosis
- Age
- Dose
- Therapeutic history

Age Restrictions
- 18 years of and older

Prescriber Restrictions
- None

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Ibandronate is a bisphosphonate that inhibits osteoclast activity and reduces bone resorption and turnover
- Limitations of Use: Optimal duration of use has not been determined. For patients at low-risk for fracture, consider drug discontinuation after 3 to 5 years of use

References
Bosulif® (bosutinib monohydrate)

FDA Approved Indication(s)
- For the treatment of chronic, accelerated or blast phase Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) with resistance or intolerance to prior therapy
- For the treatment of newly-diagnosed chronic phase Ph+ CML

FDA Recommended Dose
- Chronic, accelerated or blast phase Ph+ CML with resistance or intolerance to prior therapy:
  - 500 mg orally once daily with food
- Newly diagnosed chronic phase Ph+ CML:
  - 400 mg orally once daily with food

How Supplied
- 100 mg, 400 mg, and 500 mg tablets

Utilization Criteria
For initial review:
- Member must have a diagnosis of chronic, accelerated, or blast phase Philadelphia chromosome-positive chronic myelogenous leukemia, OR
- Member must have a diagnosis of newly diagnosed chronic phase Ph+ CML

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Pregnancy

Required Medical Information
- Diagnosis
- Age
- Dose
- Treatment history

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist or hematologist

Coverage Duration
- 3 months (initial)
- 12 months (continuation)

Quantity/Partial Fill Restrictions
- 15 tablets for a 15-day supply for the first three months

Other Information
- Mechanism of action: Bosutinib is a tyrosine kinase inhibitor, targeting the Bcr-Abl kinase that promotes CML, as well as the Src-family kinases.

References
# Botox® (onabotulinum toxin a) ‡

## FDA Approved Indication(s)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication</td>
<td></td>
</tr>
<tr>
<td>Treatment of urinary incontinence due to detrusor overactivity associated with a neurological condition (e.g., spinal cord injury, multiple sclerosis) in adults with inadequate response to or are intolerant of an anticholinergic medication</td>
<td></td>
</tr>
<tr>
<td>Prophylaxis of headaches in adult patients with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer)</td>
<td></td>
</tr>
<tr>
<td>Treatment of upper or lower limb spasticity in adult patients</td>
<td></td>
</tr>
<tr>
<td>Treatment of upper or lower limb spasticity in pediatric patients 2 to 17 years of age</td>
<td></td>
</tr>
<tr>
<td>Treatment of cervical dystonia in adult patients</td>
<td></td>
</tr>
<tr>
<td>Treatment of severe axillary hyperhidrosis that is inadequately managed by topical agents</td>
<td></td>
</tr>
<tr>
<td>Treatment of blepharospasm and strabismus associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and older</td>
<td></td>
</tr>
</tbody>
</table>

## FDA Recommended Dose

- The appropriate dose for botulinum toxin for an FDA-approved indication varies by disease state and patient response; however, the maximum cumulative dose should generally not exceed 400 Units in adults and the lesser of 8 units/kg or 300 Units in pediatrics in a 3-month interval. Exceptions are listed below.
  - OAB – the maximum dose is 100 units per treatment no sooner than every 12 weeks
  - Detrusor overactivity associated with a neurological condition – the maximum dose is 200 units per treatment no sooner than every 12 weeks
  - Blepharospasm – the cumulative dose in a 30-day period should not exceed 200 units
  - Pediatric upper or lower Limb Spasticity - Recommended total dose 3 Units/kg to 6 Units/kg (maximum 340 Units when treating upper and lower limbs) divided among affected muscles

## How Supplied

- 100 Unit and 200 Unit single-use vials

## Utilization Criteria

**For initial review:**
- The indicated diagnosis (including any applicable test results) and medication usage must comply with FDA-approved indications and be supported by documentation from the patient’s medical records
- For Migraine Prophylaxis:
  - Member must have tried and failed at least three oral preventative medications across two or more unique therapeutic classes (i.e., beta-blockers, antidepressants, and anticonvulsants), unless otherwise contraindicated
  - Member must have 15 or more days with migraines per month, as supported by clinical records
- For Urinary Incontinence:
  - Member must have tried and failed at least two anticholinergic medications, unless otherwise contraindicated
- For Hyperhidrosis:
  - Member must have failed topical therapy
  - Coverage of hyperhidrosis may be excluded per plan-specific policies
For upper or lower limb spasticity in pediatric patients 2 to 17 years of age:

- Member must have failed at least two spasticity treatments across two or more unique therapeutic classes (i.e. muscle relaxants, benzodiazepines)
- Consider coverage when upper or lower limb spasticity is:
  - Impeding gross or fine motor function
  - Comprimising care and hygiene
  - Causing pain
  - Disturbing sleep
  - Impeding tolerance of other treatments, such as orthoses

For continuation:
- The indicated diagnosis and medication usage must continue to comply with FDA-approved indications
- The member must have documented improvement in symptoms, as supported by the member’s medical records

Exclusion Criteria
- Medication is being used in combination with a calcitonin gene-related peptide (CGRP) inhibitor
- Medication is to be used for cosmetic purposes
- Infection at the proposed injection site
- Intradermator Injections: Urinary tract infection or urinary retention
- Pregnancy

Required Medical Information
- Diagnosis
- Age
- Dose

Age Restrictions
- 2 years of age or older for treatment of upper or lower limb spasticity in pediatric patients; 12 years of age and older for the treatment of blepharospasm and strabismus; 16 years of age and older for cervical dystonia; 18 years and older for all other indications

Prescriber Restrictions
- Must be prescribed by a provider skilled in the treatment of neurologic conditions, such as neurologist, otolaryngologist, ophthalmologist, physical therapist, or physiatrist

Coverage Duration (months)
- Initial coverage may be limited to 6 months to establish efficacy
- 12 months (continuation)

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Botulinum toxin blocks neuromuscular transmission by binding to acceptor sites on motor or sympathetic nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine.
- Black Box Warning: Distant spread of toxin effect

References
- Bajwa, Z. Preventive treatment of migraine in adults. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. 2018.
Cabometyx® (cabozantinib)

FDA Approved Indication(s)
- For the treatment of patients with advanced renal cell carcinoma (RCC)
- For the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib

FDA Recommended Dose
- 60 mg once daily
- If used with a strong inhibitor or inducer of CYP3A4, the daily dose should be reduced or increased by 20 mg, respectively

How Supplied
- 20, 40, and 60 mg tablets

Utilization Criteria
For initial review:
- Member must have documentation of a diagnosis consistent with an FDA-approved indication

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Members that have or are at risk for severe hemorrhage

Required Medical Information
- Diagnosis with treatment plan

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 3 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions
- 15 tablets for a 15-day supply for the first six (6) fills

Other Information
- Cabozantinib inhibits the tyrosine kinase activity of RET, MET, VEGFR-1, 2, and 3, KIT, TRKB, FLT-3, AXL, and TIE-2

References
Calquence® (acalabrutinib)

FDA Approved Indication(s)
- For the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy

FDA Recommended Dose
- 100 mg orally every 12 hours
- See prescribing information for dose modifications

How Supplied
- 100 mg capsules in a 60-count bottle

Utilization Criteria
For initial review:
- Member must have a diagnosis of MCL, AND
- Member must have received at least one prior therapy for the treatment of MCL

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Member received prior treatment with Bruton’s tyrosine kinase (BTK) or BCL-2 inhibitor
- Member is concurrently receiving warfarin or equivalent vitamin K antagonist
- Pregnancy

Required Medical Information
- Diagnosis
- Age
- Dose
- Concurrent medications
- Treatment history

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a hematologist or oncologist

Coverage Duration (months)
- 3 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Small molecule inhibitor of BTK, a signaling molecule of the B-cell antigen receptor and cytokine receptor signaling pathways.
- Warnings and precautions: Serious hemorrhagic events, including fatal events, have occurred in patients with hematologic malignancies treated with acalabrutinib monotherapy. Acalabrutinib may further increase risk of hemorrhage in patients receiving anti-platelet or anticoagulant therapies, and patients should be monitored for signs of bleeding. Monitor for signs of infection, monitor complete blood counts monthly during treatment, advise patients to use sun protection as second
primary malignancies including non-skin carcinomas have occurred in 11% of patients studied, and
monitor for atrial fibrillation and atrial flutter as appropriate.

- Black Box warning: None

References

- National Comprehensive Cancer Network (NCCN), Clinical Practice Guidelines in Oncology. B-cell
  cell.pdf

Last Reviewed November 18, 2019
### Caprelsa® (vandetanib)

**FDA Approved Indication(s)**
- Symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease

**FDA Recommended Dose**
- 300 mg taken orally once daily

**How Supplied**
- 100 mg and 300 mg tablets

**Utilization Criteria**
- Member has diagnosis of unresectable locally advanced or metastatic medullary thyroid cancer

**Exclusion Criteria**
- **For initial review:**
  - Member has congenital long QT syndrome
  - Member is receiving medication that may prolong the QT interval
- **For continuation:**
  - Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Required Medical Information**
- Diagnosis
- Dose
- Treatment history and concurrent medications
- Documented assessment of QT-prolongation risk (chart note or EKG)

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist and certified with the Caprelsa® REMS program

**Coverage Duration (months)**
- 6

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: In vitro studies have shown that vandetanib inhibits the tyrosine kinase activity of the EGFR and VEGFR families, RET, BRK, TIE2, and members of the EPH receptor and Src kinase families. These receptor tyrosine kinases are involved in both normal cellular function and pathologic processes such as oncogenesis, metastasis, tumor angiogenesis, and maintenance of the tumor microenvironment. In addition, the N-desmethyl metabolite of the drug, representing 7 to 17.1% of vandetanib exposure, has similar inhibitory activity to the parent compound for VEGF receptors (KDR and Flt-1) and EGFR.
- Black Box Warning: QT prolongation, torsades de pointes, and sudden death

**References**

*Last Reviewed September 3, 2019*
Cayston® (aztreonam)

**FDA Approved Indication(s)**
- To improve respiratory symptoms in cystic fibrosis (CF) patients with *Pseudomonas aeruginosa* infection

**FDA Recommended Dose**
- One single-use vial (75 mg of aztreonam) reconstituted with 1 mL of sterile diluent, administered 3 times a day via Altera® Nebulizer System for a 28-day course followed by 28 days off

**How Supplied**
- 28-day kit of 84 sterile vials and 88 ampules of sterile diluent

**Utilization Criteria**
- Member must have a diagnosis of CF with *Pseudomonas aeruginosa*
- Susceptibility results indicating that the *Pseudomonas aeruginosa* is sensitive to aztreonam
- Member must have documentation of FEV1 between 25% and 75% of predicted volume

**Exclusion Criteria**
- Patient is currently receiving tobramycin

**Required Medical Information**
- Diagnosis
- Documentation of positive *Pseudomonas aeruginosa* culture and sensitivity
- Dose
- Current medications

**Age Restrictions**
- 7 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a pulmonary specialist

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: Aztreonam is a monobactam antibacterial drug that binds to penicillin binding proteins within cell walls of susceptible bacteria, resulting in cell death.

**References**

Last Reviewed November 18, 2019
# Cimzia® (certolizumab pegol)

## FDA Approved Indication(s)
- Reducing signs and symptoms of Crohn's disease (CD) and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy
- Treatment of adults with moderately to severely active rheumatoid arthritis (RA)
- Treatment of adult patients with active psoriatic arthritis (PsA)
- Treatment of adult patients with active ankylosing spondylitis (AS)
- Treatment of adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation
- Treatment of adults with moderate-to-severe plaque psoriasis (PsO) who are candidates for systemic therapy or phototherapy

## FDA Recommended Dose

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD</td>
<td>400 mg subcutaneously at weeks 0, 2 and 4. If response is documented, continue therapy at 400 mg every four weeks</td>
</tr>
<tr>
<td>RA, PsA, AS</td>
<td>400 mg subcutaneously at weeks 0, 2 and 4, followed by 200 mg every other week or 400 mg every four weeks. Non-radiographic Axial Spondyloarthritis 400 mg initially and at weeks 2 and 4, followed by 200 mg every other week or 400 mg every 4 weeks.</td>
</tr>
<tr>
<td>PsO</td>
<td>400 mg subcutaneously every other week. For some patients (with body weight ≤ 90 kg) a dose of 400 mg subcutaneously at weeks 0, 2 and 4, followed by 200 mg every other week may be considered</td>
</tr>
</tbody>
</table>

## How Supplied
- Prefilled syringe starter kit
- Six single-use prefilled syringes containing 200 mg/1 mL of active product
- Prefilled syringe
- Two single-use prefilled syringes containing 200 mg/1 mL of active product
- Powder for reconstitution
- Two type-1 glass vials containing 200 mg of lyophilized powder for reconstitution

## Utilization Criteria

For initial review:
- For all conditions: Member has a negative TB test prior to initiating therapy, AND
- As applicable, member has tried and failed two or more of the plan’s preferred biologic therapies, AND
- Crohn’s Disease
  - Prescriber is a gastroenterologist, AND
  - Member must have documented failure, intolerance, or contraindication to ≥ 2 conventional therapies (e.g., corticosteroids, 5-ASA agents, immunosuppressants, immunomodulators)
- Rheumatoid arthritis
  - Prescriber is a rheumatologist, AND
• Member must have documented failure, intolerance, or contraindication to methotrexate or at least one other disease modifying anti-rheumatic therapy (DMARD)
  • Psoriatic arthritis
    • Prescriber is a dermatologist, AND
    • Member has tried and failed treatment with methotrexate
  • Ankylosing spondylitis
    • Prescriber is a rheumatologist, AND
    • Member has tried and failed ≥ 2 NSAIDs, steroid products, or methotrexate
  • Non-radiographic axial spondyloarthritis
    • Prescriber is a rheumatologist, AND
    • Patient has objective signs of inflammation, AND
    • Member has tried and failed ≥ 2 NSAIDs, steroid products, or methotrexate
  • Plaque psoriasis
    • Prescriber is a dermatologist, AND
    • Patient has ≥ 10% BSA involvement or affected area includes palms, soles, head, neck, or genitalia, AND
    • Member has documented failure, intolerance, or contraindication to topical agents, topical immunomodulators, systemic therapy (i.e., methotrexate, cyclosporine, or acitretin), or phototherapy

For continuation:
• Crohn’s Disease
  • Member has demonstrated clinical response after induction therapy
• All other indications:
  • Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
• Member is receiving additional biologic DMARD therapy, OR
• Member has active infection, OR
• Member will be receiving a live vaccination

Required Medical Information
• Diagnosis
• Concurrent medications
• Therapeutic history
• Age
• Dose
• TB Test

Age Restrictions
• 18 years of age and older

Prescriber Restrictions
• Must be prescribed by a gastroenterologist, rheumatologist, or dermatologist

Coverage Duration (months)
• CD: Four weeks (initial), 12 months (continuation)
• RA, PsA, AS, PsO, SpA: 12 months

Quantity/Partial Fill Restrictions
• None
Other Information

- Mechanism of action: Certolizumab pegol binds to human TNFα
- Warnings and Precautions: Patients treated with certolizumab are at an increased risk for developing serious infections involving various organ systems and sites that may lead to hospitalizations or death. In the controlled portions of clinical studies of some TNF blockers, more cases of malignancies have been observed among patients receiving TNF blockers compared to control patients.

References


Last Reviewed November 18, 2019
Cinqair® (reslizumab)

FDA Approved Indication(s)
- Add-on maintenance treatment of patients with severe asthma with an eosinophilic phenotype

FDA Recommended Dose
- 3 mg/kg administered via IV infusion once every 4 weeks

How Supplied
- 100 mg/10 mL single-use vial

Utilization Criteria

For initial review:
- Patient must have a diagnosis of severe, sub-optimally controlled asthma (i.e., asthma symptoms two days per week or more, or exacerbations requiring systemic corticosteroids more than two times per year), AND
- Patient must have an inadequate response to a three-month course of inhaled corticosteroids and a long-acting beta2-agonist, AND
- Have a blood eosinophil count of ≥ 400 cells/µL, AND
- Patient is currently receiving long-acting beta2-agonist, inhaled corticosteroid therapy, montelukast, and short-acting beta2-agonist as rescue therapy, unless otherwise contraindicated

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider. Such assessment must include an objective measurement of response, such as a quantitative decrease in asthma symptoms, exacerbation rate, or improvement in FEV1.

Exclusion Criteria
- Treatment of other eosinophilic conditions
- Relief of acute bronchospasm or status asthmaticus
- Current smoker

Required Medical Information
- Diagnosis
- Age
- Dose
- Concurrent medications
- Treatment history
- Baseline eosinophil count

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a pulmonologist, allergist, or immunologist

Coverage Duration (months)
- 6 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Reslizumab is an interleukin-5 (IL-5) antagonist. IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils.
Reslizumab binds to IL-5 and reduces the production and survival of eosinophils; however, the mechanism of reslizumab action in asthma has not been definitively established.

- Anaphylaxis has been observed in a small (0.3%) number of patients. Administration should initially be performed in a healthcare setting by a healthcare professional prepared to manage anaphylaxis.

References

# Cinryze® (human c1- esterase inhibitor)

## FDA Approved Indication(s)
- Cinryze® is a C1 esterase inhibitor indicated for routine prophylaxis against angioedema attacks in adults, adolescents and pediatric patients (6 years of age and older) with Hereditary Angioedema (HAE)

## FDA Recommended Dose
- **Adults and adolescents (12 years old and above):** 1,000 Units Cinryze® can be administered every 3 or 4 days for routine prophylaxis against angioedema attacks in HAE patients
- **Children (6 to 11 years old):** 500 Units Cinryze® can be administered every 3 or 4 days for routine prophylaxis against angioedema attacks in HAE patients; doses up to 1,000 units every 3 to 4 days may be considered

## How Supplied
- 500 unit/8 mL vial

## Utilization Criteria
### For initial review:
- Patient must have a diagnosis of Hereditary Angioedema (HAE)
- Patient must have epinephrine available for acute hypersensitivity reactions

### For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

## Exclusion Criteria
- Used in combination with another biologic prophylaxis medication to treat HAE

## Required Medical Information
- Diagnosis
- Age
- Dose

## Age Restrictions
- 6 years of age or older

## Prescriber Restrictions
- None

## Coverage Duration (months)
- 12

## Quantity/Partial Fill Restrictions
- None

## Other Information
- Mechanism of action: C1 inhibitor is a normal constituent of human blood and is one of the serine proteinase inhibitors (serpins). The primary function of C1 inhibitor is to regulate the activation of the complement and intrinsic coagulation (contact system) pathway. C1 inhibitor also regulates the fibrinolytic system.

## References

*Last Reviewed November 18, 2019*
## Cometriq® (cabozantinib)

### FDA Approved Indication(s)
- Progressive, metastatic medullary thyroid cancer

### FDA Recommended Dose
- 140 mg (one 80-mg and three 20-mg capsules) daily
- If used with a strong inhibitor or inducer of CYP3A4, the daily dose should be reduced or increased by 40 mg, respectively

### How Supplied
- 20 mg, 80 mg capsules

### Utilization Criteria

**For initial review:**
- Must have a diagnosis of progressive, metastatic medullary thyroid cancer

**For continuation:**
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

### Exclusion Criteria
- None

### Required Medical Information
- Diagnosis
- Age
- Gender
- Dose

### Age Restrictions
- 18 years of age and older

### Prescriber Restrictions
- Must be prescribed by an oncologist

### Coverage Duration (months)
- 3 months (initial), 12 months (continuation)

### Quantity/Partial Fill Restrictions
- 14 capsules (80 mg) or 42 capsules (20 mg) for 14 days supply for the first 6 fills

### Other Information
- Cabozantinib inhibits the tyrosine kinase activity of RET, MET, VEGFR-1, 2, and 3, KIT, TRKB, FLT-3, AXL, and TIE-2
- Black Box Warning: Perforations and fistulas were reported in a small (3% and 1%, respectively) population of patients. Severe hemorrhage occurred in 3% of patients in clinical trials. Do not administer product to patients with either perforations and fistulas or hemorrhage.

### References
- Patricia Keegan; Center for Drug Evaluation and Research. Division director summary review: NDA 203756-cabozantinib.
**Copaxone®, Glatopa™ (glatiramer acetate)**

**FDA Approved Indication(s)**
- For the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults

**FDA Recommended Dose**
- **Copaxone®, Glatopa™, glatiramer acetate**: 20 mg subcutaneously once daily
- **Copaxone®, Glatopa™, glatiramer acetate**: 40 mg subcutaneously three times per week, at least 48 hours apart

**How Supplied**
- **Copaxone®, Glatopa™, glatiramer acetate**: Single-use 20 mg/mL prefilled syringe
- **Copaxone®, Glatopa™, glatiramer acetate**: Single-use 40 mg/mL prefilled syringe

**Utilization Criteria**

*For initial review:*
- Must have diagnosis of relapsing-form of MS, AND
- Must have an MRI scan that demonstrated features consistent with a diagnosis of MS

*For continuation:*
- Confirmation by neurologist that the patient has had a beneficial response to therapy

**Exclusion Criteria**
- Member is receiving other disease-modifying therapy (i.e., interferons, natalizumab, fingolimod, teriflunomide, or dimethyl fumarate)
- Member is requesting branded formulation of product

**Required Medical Information**
- Diagnosis
- Documentation of MRI
- Concurrent medications
- Dose

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a neurologist

**Coverage Duration**
- 12 months

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: glatiramer acetate is thought to act by modifying immune processes that are believed to be responsible for the pathogenesis of MS.

**References**

• Olek M. Treatment of relapsing-remitting multiple sclerosis in adults. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. 2019.
**Copiktra™ (duvelisib) †**

**FDA Approved Indication(s)**
- For the treatment of adults with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies
- For the treatment of adults with relapsed or refractory follicular lymphoma (FL) after at least two prior systemic therapies

**FDA Recommended Dose**
- 25 mg orally twice daily
- Prophylaxis for pneumocystis jirovecii (PJP) infection is recommended during treatment with duvelisib
- Consider prophylaxis to prevent cytomegalovirus (CMV) infection including CMV reactivation
- See prescribing information for dose modification

**How Supplied**
- 25 mg capsules: cartons containing 2 x 28-count blister packs, and 56-count bottles
- 15 mg capsules: cartons containing 2 x 28-count blister packs, and 56-count bottles

**Utilization Criteria**
*For initial review:*
- Member must have a documented diagnosis of chronic lymphocytic leukemia, small lymphocytic lymphoma, or follicular lymphoma, AND
- CLL/SLL: Member must have failed, or did not tolerate, at least two prior therapies
- FL: Member must have failed, or did not tolerate at least two prior systemic therapies
*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Pregnancy
- AST/ALT > 20 x ULN
- Confirmed PJP infection
- Concurrent use of strong CYP3A inducers

**Required Medical Information**
- Diagnosis
- Concurrent medications
- Age
- Dose
- Treatment history
- Labs: hepatic function, complete blood count

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration (months)**
- 3 months (initial), 12 months (continuation)

**Quantity/Partial Fill Restrictions**
- Split fill for the first 3 months of therapy
Other Information

- Mechanism of action: Inhibits phosphoinositide 3-kinase (primarily PI3K-δ and PI3K-γ) in normal and malignant B-cells; inhibits B-cell receptor signaling, CXCR12-mediated chemotaxis of malignant B cells, CXCL12-induced T cell migration, and M-CSF and IL-4 driven M2 polarization of macrophages
- Black Box Warning: Fatal and/or serious infections (31%), diarrhea or colitis (18%), cutaneous reactions (5%), and pneumonitis (5%) occurred in patients during clinical trials
- When co-administered with strong CYP3A4 inhibitors, reduce dose to 15 mg twice daily

References

- Copiktra (duvelisib) [prescribing information]. Needham, MA: Verastem, Inc; September 2018.
Cosentyx™ (secukinumab)

FDA Approved Indication(s)

- For the treatment of moderate to severe plaque psoriasis (PsO) in adults who are candidates for systemic therapy or phototherapy
- For the treatment of adults with active psoriatic arthritis (PsA)
- For the treatment of adults with active ankylosing spondylitis (AS)

FDA Recommended Dose

For PsO:
- 300 mg by subcutaneous injection at Weeks 0, 1, 2, 3 and 4, followed by 300 mg every 4 weeks
- A dose of 150 mg may be acceptable for some patients

For PsA:
- 150 mg by subcutaneous injection every 4 weeks; a loading dose is not required
  - A dose increase to 300 mg every 4 weeks may be required in patients who continue to have active PsA

For AS:
- 150 mg by subcutaneous injection every 4 weeks; a loading dose is not required

How Supplied

- 150 mg/mL solution in a single-use prefilled syringe Sensoready® pen
- 150 mg/mL solution in a single-use Sensoready® (i.e., auto-injector) device
- 150 mg lyophilized powder in a single-use vial for reconstitution (healthcare provider use only)

Utilization Criteria

For initial review:
- Member must have a diagnosis of moderate to severe PsO, PsA, or AS, AND
- Member must have documentation of a negative TB test, AND
- Member must have tried and failed, or did not tolerate, a 3-month course of at least 1 conventional or non-biologic disease modifying therapy, such as methotrexate, cyclosporine, PUVA or UVB, AND
- Member must have experienced a failure with, or intolerance to, at least 1 anti-Tumor Necrosis Factor (TNF) agent, such as infliximab, etanercept, or adalimumab

Based upon member’s benefit structure, additional step therapy may be required

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria

- None

Required Medical Information

- Diagnosis, with documentation of disease severity and BSA coverage
- Age
- Dose
- Treatment history

Age Restrictions

- 18 years of age and older

Prescriber Restrictions

- Must be prescribed by a dermatologist or rheumatologist

Coverage Duration (months)

- 12 months
Quantity/Partial Fill Restrictions

- None

Other Information

- Mechanism of action: secukinumab is a human IgG1 monoclonal antibody that selectively binds to the interleukin-17A (IL-17A) cytokine, inhibiting its interaction with the IL-17 receptor

References


Last Reviewed November 18, 2019
## Cotelllíc™ (cobimetinib)

### FDA-Approved Indication(s)
- For the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib

### FDA-Recommended Dose
- 60 mg (three 20 mg tablets) orally taken once daily for the first 21 days of each 28-day cycle until disease progression or unacceptable toxicity

### How Supplied
- 20 mg film-coated tablet available in bottles of 63 tablets

### Utilization Criteria

#### For initial review:
- Member must have a diagnosis of unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, AND
- Must be taken in combination with vemurafenib

#### For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

### Exclusion Criteria
- Presence of wild-type BRAF melanoma
- Left ventricular ejection fraction (LVEF) below 50%
- Existing serous retinopathy or retinal vein occlusion
- Pregnancy

### Required Medical Information
- Diagnosis
- Confirmation of BRAF V600E or V600K mutation
- Dose
- Concurrent therapies

### Age Restrictions
- 18 years and older

### Prescriber Restrictions
- Must be prescribed by an oncologist

### Coverage Duration (months)
- 12 months

### Quantity/Partial Fill Restrictions
- None

### Other Information
- Mechanism of action: Cobimetinib is a reversible inhibitor of mitogen-activated protein kinase (MAPK)/extracellular signal regulated kinase 1 (MEK1) and MEK2. MEK proteins are upstream regulators of the extracellular signal-related kinase (ERK) pathway, which promotes cellular proliferation. BRAF V600E and K mutations result in constitutive activation of the BRAF pathway which includes MEK1 and MEK2. In mice implanted with tumor cell lines expressing BRAF V600E, cobimetinib inhibited tumor cell growth.

### References
- [Cotellic™ [package insert]. San Francisco, CA: Genentech, Inc; January 2018.](#)
Cuvposa® (glycopyrrolate)

**FDA Approved Indication(s)**
- For the treatment of chronic, severe drooling in patients 3-16 years with neurologic conditions associated with problem drooling (e.g., cerebral palsy)

**FDA Recommended Dose**
- 0.02 mg/kg orally three times daily; titrate in increments of 0.02 mg/kg every 5-7 days based on therapeutic response and adverse reactions

**How Supplied**
- 1 mg/5 mL clear, cherry-flavored solution in a 16 oz bottle

**Utilization Criteria**
- **For initial review:**
  - The indicated diagnosis (including any applicable labs and/or tests) and medication usage must be supported by documentation from the patient’s medical records
  - Clinically diagnosed with a neurologic condition associated with chronic severe drooling (sialorrhea)
  - Failed or intolerant to glycopyrrolate generic tablets, or inability to safely consume tablet

- **For continuation:**
  - Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Medical conditions that preclude anticholinergic therapy
- Concomitant use of solid oral dosage forms of potassium chloride

**Required Medical Information**
- Diagnosis
- Age
- Weight
- Dose

**Age Restrictions**
- Within 3-16 years of age

**Prescriber Restrictions**
- None

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: Glycopyrrolate is a competitive inhibitor of acetylcholine receptors that are located on certain peripheral tissues, including salivary glands. Glycopyrrolate indirectly reduces the rate of salivation by preventing the stimulation of these receptors.

**References**
## Daklinza™ (daclatasvir)

### FDA-Approved Indication(s):
- For use with sofosbuvir, with or without ribavirin, for the treatment of chronic HCV genotype 1 or 3 infection
- Limitation of use: Sustained virologic response (SVR) rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving daclatasvir in combination with sofosbuvir for 12 weeks

### FDA-Recommended Dose
- 60 mg taken orally once daily with or without food in combination with sofosbuvir with or without ribavirin for 12 weeks
- See package insert for dosage modifications when co-administered with strong or moderate inhibitors of CYP3A enzymes

### How Supplied
- 30 mg, 60 mg, 90 mg tablets

### Utilization Criteria

**For initial review:**
- Member must have a diagnosis of chronic HCV genotype 1 (GT1) or genotype 3 (GT3), with a documented viral load collected within the previous three months, AND
- Member must have documentation of current fibrosis staging, as determined via a Metavir, transient elastography/Fibroscan, FibroTest, or equivalent test, AND
- Physician must attest to the patient’s ability and dedication to remain adherent to the entire course of therapy, AND
- Physician must confirm that alcohol and illicit substance abuse is absent for the previous six months, or patient is currently seeing an addiction specialist, AND
- Member must receive concurrent sofosbuvir therapy

### Exclusion Criteria
- Concurrent use with simeprevir or ledipasvir/sofosbuvir, OR
- Concurrent use with strong CYP3A inducers, OR
- Decompensated cirrhosis, OR
- Coverage may be revoked if patient is non-adherent through the first two months of therapy, as evidenced by claim records or verbal confirmation of poor adherence

### Required Medical Information
- Age
- Diagnosis, including genotype
- Viral load
- Dose and duration of therapy
- Concurrent medications
- Treatment history
- Fibrosis stage

### Age Restrictions
- Must be 18 years of age or older

### Prescriber Restrictions
- Must be prescribed by a gastroenterologist, hepatologist, or infectious disease specialist

### Coverage Duration (months)
- 3 months

### Quantity/Partial Fill Restrictions
Other Information

- Mechanism of action: Daclatasvir is a nonstructural protein 5A (NS5A) inhibitor that interferes with hepatitis C virus RNA replication and virion assembly.
- There is a risk of symptomatic bradycardia when daclatasvir is used in combination with sofosbuvir and amiodarone. The co-administration of daclatasvir, sofosbuvir, and amiodarone is not recommended.
- Black Box Warning: Risk of hepatitis B virus reactivation in patients coinfected with HCV and HBV.

References

Daurismo™ (glasdegib)

FDA Approved Indication(s)
- Used in combination with low-dose cytarabine for the treatment of patients 75 years of age or older with newly diagnosed acute myeloid leukemia (AML) or for patients who may not tolerate intensive induction chemotherapy due to comorbidities

FDA Recommended Dose
- 100 mg orally once daily on days 1 through 28 in combination with cytarabine 20 mg subcutaneously twice daily on days 1 through 10 of each 28-day cycle; treat in the absence of unacceptable toxicity or loss of disease control. For patients without unacceptable toxicity, treat for a minimum of 6 cycles to allow time for clinical response.

How Supplied
- 100 mg tablet in 30-count bottle
- 25 mg tablet in 60-count bottle

Utilization Criteria
For initial review:
- Documented new diagnosis of acute myeloid leukemia (AML), AND
- Member must be 75 years of age or older, OR
- Member has comorbidities that prevent the use of intensive induction chemotherapy
- Prescribed in combination with cytarabine

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- None

Required Medical Information
- Diagnosis
- Age
- Concurrent medication
- Treatment history
- Pregnancy testing for females of reproductive potential
- Baseline ECG, creatinine kinase, CBC, electrolytes, renal and hepatic function

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist or hematologist

Coverage Duration (months)
- Initial: 3
- Maintenance: 12

Quantity/Partial Fill Restrictions
- Initial: 6 fills for quantity 14

Other Information
- Mechanism of action: glasdegib inhibits the Hedgehog pathway via binding and inhibiting the transmembrane protein, Smoothened, which is involved in hedgehog signal transduction
- Black Box Warning: Embroyo-fetal toxicity
References


Last Viewed June 27, 2019
**Dupixent® (dupilumab)**

**FDA Approved Indication(s)**
- For treatment of patients 12 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable
- As add-on maintenance therapy for patients 12 years and older with moderate-to-severe asthma and an eosinophilic phenotype or corticosteroid (oral) dependent asthma

**FDA Recommended Dose**
- Administered subcutaneously
  - Atopic Dermatitis
    - Adults: 600 mg (two 300 mg injections) once, followed by 300 mg every other week
    - Adolescents:
      - Less than 60 kg: 400 mg (two 200 mg injections), once, followed by 200 mg every other week
      - 60 kg or more: 600 mg (two 300 mg injections), once, followed by 300 mg every other week
  - Asthma
    - 400 mg (two 200 mg injections), once, followed by 200 mg given every other week, OR
    - 600 mg (two 300 mg injections), once, followed by 300 mg given every other week
    - Patients requiring concomitant oral corticosteroids or with co-morbid moderate-to-severe atopic dermatitis for which Dupixent® is indicated, start with an initial dose of 600 mg followed by 300 mg every other week
  - Chronic Rhinosinusitis with Nasal Polyposis
    - 300 mg every other week

**How Supplied**
- Available only in cartons containing 2 syringes
- 200 mg/1.14 mL Pre-filled Syringe with needle shield
- 300 mg/2 mL Pre-filled Syringe with needle shield

**Utilization Criteria**

*For initial review:*
- Atopic Dermatitis
  - Member must have a documented diagnosis of moderate to severe atopic dermatitis; AND
  - Member must have clinical documentation of functional impairment due to atopic dermatitis, which may include (but is not limited to) documentation of limitation of activities of daily living (ADLs), such as skin infections or sleep disturbances; AND
  - Member must have documentation of an inadequate response, intolerance or contraindication to the following topical therapies:
    - A moderate to very high-potency topical corticosteroid, AND
    - A topical calcineurin inhibitor
- Asthma
  - Member must have a diagnosis of severe, sub-optimally controlled asthma resulting in at least one exacerbation within the previous year that required treatment with systemic corticosteroids, an emergency department visit, hospitalization or requires daily corticosteroids, OR
Must have an absolute eosinophil count of: greater than or equal to 300 cells/microL within the past 12 months, AND

Must have documentation of inadequate response to a three-month course of inhaled corticosteroids, montelukast, and a long-acting beta2-agonist, AND

Member must be concurrently receiving a long-acting beta2-agonist, inhaled corticosteroid therapy, montelukast, and short-acting beta2-agonist as rescue therapy, unless otherwise contraindicated, AND

Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable

Chronic Rhinosinusitis with Nasal Polyposis

Must have documentation of inadequate response to a three-month course of intranasal corticosteroids, AND

Previous sino-nasal surgery or recent (within previous two years) treatment with systemic corticosteroids, AND

Documented history of recurrent rhinosinusitis infection

For continuation:

Member must have documentation of treatment response, as verified per progress notes

Exclusion Criteria

Patient is currently utilizing one or more biologic therapies

Required Medical Information

Diagnosis
Current medication list
Therapeutic history

Age Restrictions

18 years of age and older

Prescriber Restrictions

Must be prescribed by a dermatologist, pulmonologist, allergist, immunologist or rheumatologist

Coverage Duration (months)

Atopic dermatitis and asthma: 14-day initial dose/6 months maintenance
Chronic rhinosinusitis with nasal polyposis: 6 months initial
12 months thereafter

Quantity/Partial Fill Restrictions

Maximum of 2 syringes (4 mL) per 14 days (initial), 2 syringes (4 mL) per 28 days maintenance

Other Information

Dupilumab is an interleukin-4 receptor antagonist used in the treatment of moderate to severe atopic dermatitis when conventional therapy is not effective.

Treatment guidelines for Atopic Dermatitis recommend the use of topical corticosteroids in patients who have failed to respond to good skin care and regular use of emollients alone. Topical calcineurin inhibitors are recommended as second-line agents.

References

• Dupixent® (dupilumab) [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; March 2019.

Last Reviewed August 6, 2019
# Dysport® (botulinum toxin type a)

## FDA Approved Indication(s)
- Treatment of cervical dystonia in adult patients
- Temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and corrugator muscle activity in adult patients less than 65 years of age
- Treatment of upper limb spasticity in adult patients
- Treatment of lower limb spasticity in pediatric patients two years of age and older

## FDA Recommended Dose
- **Cervical dystonia**
  - 500 Units given intramuscularly as a divided dose among affected muscles
  - Dose adjustments can be made in 250 Unit steps according to the individual patient’s response, with re-treatment every 12 weeks or longer, as necessary
  - Doses above 1000 Units have not been systematically evaluated
- **Glabellar lines**
  - 50 Units given intramuscularly no more frequently than every three months
- **Upper and lower limb spasticity**
  - Dosing should be tailored to the individual
  - In pivotal clinical trials, doses of 500 Units and 1000 Units were divided among selected muscles no more frequently than every 12 weeks

## How Supplied
- 300 Unit and 500 Unit single-use vials

## Utilization Criteria

### For initial review:
- The indicated diagnosis (including any applicable test results) and medication usage must comply with FDA-approved indications and be supported by documentation from the patient’s medical records

### For continuation:
- The indicated diagnosis and medication usage must continue to comply with FDA-approved indications
- The member must have documented improvement in symptoms, as supported by the member’s medical records

## Exclusion Criteria
- To be used for cosmetic purposes
- Pregnancy

## Required Medical Information
- Diagnosis
- Age
- Dose

## Age Restrictions
- 18 years of age and older

## Prescriber Restrictions
- Must be prescribed by a provider skilled in the treatment of neurologic conditions, such as neurologist, otolaryngologist, ophthalmologist, physical therapist, or physiatrist

## Coverage Duration (months)
• Initial coverage may be limited to 6 months to establish efficacy
• 12 months (continuation)

Quantity/Partial Fill Restrictions

• None

Other Information

• Mechanism of action: Botulinum toxin blocks neuromuscular transmission by binding to acceptor sites on motor or sympathetic nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine.
• Black Box Warning: Distant spread of toxin effect

References

Emflaza® (deflazacort)

**FDA Approved Indication(s)**
- For the treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older

**FDA Recommended Dose**
- 0.9 mg/kg/day once daily

**How Supplied**
- 6 mg, 18 mg, 30 mg, and 36 mg tablets
- 22.75 mg/ml suspension

**Utilization Criteria**

*For initial review:*
- Member must have a documented diagnosis of Duchenne muscular dystrophy (DMD); AND
- Member must have documented mutation of the dystrophin gene; AND
- Member must have documented onset of weakness before 5 years of age; AND
- Member must have documented serum creatinine kinase activity at least 10 times the upper limit of normal (ULN) at some stage in their illness; AND
- Member must have documented inadequate treatment response, intolerance, or contraindication to prednisone

*For continuation:*
- Member must have documentation of treatment response, as verified per progress notes

**Exclusion Criteria**
- Active infection (e.g. tuberculosis, or hepatitis B virus)

**Required Medical Information**
- Diagnosis
- Weight
- Current medication list
- Therapeutic history

**Age Restrictions**
- 2 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a provider who specializes in the treatment of Duchenne Muscular Dystrophy (DMD) and/or neurologist

**Coverage Duration (months)**
- 6 months

**Quantity/Partial Fill Restrictions**
- Maximum of quantity sufficient for 30 days at a dose of 0.9 mg/kg/day once daily

**Other Information**
- DMD is an inherited disorder that results in a deficiency of dystrophin, which occurs primarily in boys, and is rapidly progressive, resulting in loss of muscle function and weakness. There is no cure.
- Deflazacort (Emflaza) is a corticosteroid prodrug, which converts to active corticosteroid in the body. Corticosteroids decrease inflammation and suppress the immune system. It is unknown exactly how deflazacort (Emflaza) works for patients with DMD.

**References**
- Emflaza® (deflazacort) [prescribing information]. Northbrook, IL: Marathon Pharmaceuticals, LLC; June 2019.
Enbrel® (etanercept)

FDA Approved Indication(s)

- For the treatment of moderately to severely active rheumatoid arthritis (RA), alone or in combination with methotrexate
- For the treatment of moderately to severely active polyarticular juvenile idiopathic arthritis (JIA) in patients aged 2 years or older
- For the treatment of psoriatic arthritis (PsA), alone or in combination with methotrexate
- For the treatment of active ankylosing spondylitis (AS)
- For the treatment of chronic moderate to severe plaque psoriasis (PsO) in patients 4 years or older, who are candidates for systemic therapy or phototherapy

FDA Recommended Dose

- Adult RA, AS, PsA
  - 50 mg per week
- Adult PSO
  - 50 mg twice weekly for 3 months, then 50 mg once weekly
- Pediatric JIA or PsO
  - 63 kg or more – 50 mg weekly
  - 63 kg or less – 0.8 mg/kg weekly

How Supplied

- 50 mg/1 mL prefilled syringe, carton of 4
- 50 mg/1 mL single-use prefilled SureClick autoinjector
- 50 mg/mL solution in Enbrel Mini® single-dose prefilled cartridge for use with the AutoTouch® reusable autoinjector only
- 25 mg/0.5 mL single-use prefilled syringe, carton of 4
- 25 mg multiple-use vial, carton of 4

Utilization Criteria

For initial review:

- All disease states: Member must have a negative TB test, documented within the previous 12 months
- Rheumatoid Arthritis
  - Prescriber is a rheumatologist, AND
  - Dose is ≤ 50 mg weekly, AND
  - Currently receiving methotrexate, OR
  - Member has tried and failed ≥ 1 non-biologic DMARD therapy for at least 60 days of use
- Juvenile Idiopathic Arthritis
  - Member is ≥ 2 years of age, AND
  - Prescriber is a rheumatologist, AND
  - Member has tried and failed ≥ 1 non-biologic DMARD for at least 60 days of use, AND
  - Dose is ≤ 50 mg weekly
- Psoriatic Arthritis/Ankylosing Spondylitis
  - Prescriber is a rheumatologist, AND
  - Patient is intolerant to sulfasalazine, COX-2, NSAIDs, or corticosteroids, AND
  - Dose is ≤ 50 mg weekly
- Plaque Psoriasis
  - Prescriber is a dermatologist, AND
• Intolerant to monotherapy with topical agents, topical immunomodulators, systemic therapy, or phototherapy
  • ≥ 10% BSA involvement, OR
  • Affected area includes palms, soles, head, neck, or genitalia, AND
  • Dose is ≤ 100mg weekly (adult) or dose is ≤ 50 mg weekly (pediatric)
  • Coverage of doses exceeding FDA-approved limits requires documentation of progression of disease after an adequate trial (typically three months), of FDA-approved dosing

For continuation:
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
• Patient is receiving additional biologic DMARD therapy, OR
• Patient is allergic to latex, OR
• Patient is receiving cyclophosphamide

Required Medical Information
• Diagnosis
• Concurrent medications
• Baseline LFT, CBC, and hepatitis profile
• Age
• Dose
• Weight (Pediatric patients only)

Age Restrictions
• Member must be 2 years of age and older

Prescriber Restrictions
• Must be prescribed by a rheumatologist or dermatologist

Coverage Duration (months)
• 12

Quantity/Partial Fill Restrictions
• For Adult Plaque Psoriasis: Eight 50 mg injections per month for 3 months; followed by four 50 mg injections per month.

Other Information
• Mechanism of action: Etanercept inhibits binding of TNF-α and TNF-β (lymphotoxin alpha [LT-α]) to cell surface TNFRs, rendering TNF biologically inactive
• Black Box Warning: Increased risk of serious infections leading to hospitalization or death and increased risk of malignancies

References
Entyvio® (vedolizumab)

**FDA Approved Indication(s)**

- For the treatment of adult patients with moderately to severely active Crohn’s disease who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids:
  - **Crohn’s Disease**
    - inducing and maintaining clinical response and clinical remission
    - achieving corticosteroid-free remission
  - **Ulcerative Colitis**
    - inducing and maintaining clinical response and remission
    - improving endoscopic appearance of the mucosa
    - achieving corticosteroid-free remission

**FDA Recommended Dose**

- Crohn’s disease and Ulcerative Colitis
- 300 mg administered by intravenous infusion over 30 minutes at zero (0), two (2) and six(6) weeks and then every eight (8) weeks thereafter
- Discontinue therapy if no evidence of therapeutic benefit by Week 14

**How Supplied**

- 300 mg/20 mL vial for intravenous infusion

**Utilization Criteria**

*For initial review:*

- Member must have a diagnosis consistent with an FDA-approved indication
- Member must be up to date with immunizations, according to current immunization guidelines
- Member must have a negative TB test
- Member must have had inadequate response to a three-month trial or is intolerant to:
  - Conventional therapy such as azathioprine, 6-mercaptopurine, methotrexate, or aminosalicylate; AND
  - Two or more self-administered anti-TNF agents
- Disease is steroid-dependent

*For continuation:*

- Member must have a response to therapy at week 14

**Exclusion Criteria**

- Member is concomitantly receiving biologic DMARD therapy
- Member has an active or chronic infection

**Required Medical Information**

- Diagnosis
- Age
- Dose
- Treatment history
- TB test with date
- Immunization record

**Age Restrictions**

- 18 years of age and older

**Prescriber Restrictions**
• Must be prescribed by a gastroenterologist

**Coverage Duration (months)**

• 4 months initially; 12 months for continuation

**Quantity/Partial Fill Restrictions**

• None

**Other Information**

• Mechanism of action: Vedolizumab is a humanized monoclonal antibody that specifically binds to the α4β7 integrin and blocks the interaction of α4β7 integrin with mucosal addressin cell adhesion molecule-1 (MAdCAM-1) and inhibits the migration of memory T-lymphocytes across the endothelium into inflamed gastrointestinal parenchymal tissue. The interaction of the α4β7 integrin with MAdCAM-1 has been implicated as an important contributor to the chronic inflammation that is a hallmark of ulcerative colitis and Crohn’s disease.

**References**


_Last Reviewed November 18, 2019_
**Epclusa® (velpatasvir/sofosbuvir)**

**FDA-Approved Indication(s)**
- For the treatment of adult patients with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis, or with decompensated cirrhosis in combination with ribavirin

**FDA-Recommended Dose**
- One tablet by mouth once daily, with or without ribavirin (see indications below)

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Treatment Regimen and Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients without cirrhosis and patients with compensated cirrhosis (Child-Pugh A)</td>
<td>Epclusa® for 12 weeks</td>
</tr>
<tr>
<td>Patients with decompensated cirrhosis (Child-Pugh B or C)</td>
<td>Epclusa® plus ribavirin for 12 weeks</td>
</tr>
</tbody>
</table>

**How Supplied**
- 100 mg velpatasvir/400 mg sofosbuvir tablet supplied in a 28-count bottle

**Utilization Criteria**

For initial review:
- Member must have a diagnosis of chronic HCV with documented genotype and viral load collected within the previous three months, AND
- Member must documentation of current fibrosis staging, as determined via a Metavir, transient elastography/Fibroscan, FibroTest, or equivalent test, AND
- Must be given with ribavirin if member has documented decompensated cirrhosis, AND
- Physician must attest to the member’s ability and dedication to remain adherent to the entire course of therapy, AND
- Physician must confirm that alcohol and illicit substance abuse is absent for the previous six months, or Member is currently seeing an addiction specialist

**Exclusion Criteria**
- Acute HCV infection that is known to have occurred within the previous six months, OR
- Coverage may be revoked if member is non-adherent through the first two months of therapy, as evidenced by claim records or verbal confirmation of poor adherence

**Required Medical Information**
- Dose and duration of therapy
- HCV genotype and subtype
- HCV treatment history
- Baseline ALT
- Liver status

**Age Restrictions**
- 18 years of age or older

**Prescriber Restrictions**
- Must be prescribed by a gastroenterologist or infectious disease specialist

**Coverage Duration (months)**
- 3 months

**Quantity/Partial-Fill Restrictions**
- Split fill – 14 days supply

**Other Information**
• Mechanism of action: Sofosbuvir is a nucleotide analog NS5B polymerase inhibitor. Velpatasvir is an inhibitor of the HCV NS5A protein.
• Black Box Warning: Risk of Hepatitis B virus reactivation in patients coinfected with HCV and HBV

References

Last Reviewed November 18, 2019
**Erivedge® (vismodegib)**

**FDA Approved Indication(s)**
- For the treatment of adults with metastatic basal cell carcinoma, or with locally advanced basal cell carcinoma that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation.

**FDA Recommended Dose**
- 150 mg taken orally once daily

**How Supplied**
- 150 mg capsule

**Utilization Criteria**

*For initial review:*
- Diagnosis of metastatic basal cell carcinoma
- Diagnosis of locally advanced basal cell carcinoma that has recurred after surgery
- Diagnosis of locally advanced basal cell carcinoma and patient is not a candidate for radiation or surgery

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- None

**Required Medical Information**
- Diagnosis
- Age
- Dose

**Age Restrictions**
- 18 and over

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration (months)**
- 3 months (initial), 12 months (continuation)

**Quantity/Partial Fill Restrictions**
- 14 capsules for a 14 days supply for the first 6 fills

**Other Information**
- Mechanism of action: Vismodegib is an inhibitor of the Hedgehog pathway. Vismodegib binds to and inhibits Smoothened, a transmembrane protein involved in Hedgehog signal transduction.
- Black Box Warning: Embryo-fetal death and Severe birth defects

**References**
Erleada™ (apalutamide)

FDA Approved Indication(s)
- For the treatment of patients with non-metastatic castration-resistant prostate cancer

FDA Recommended Dose
- Four 60 mg tablets (240 mg total) administered orally once daily with or without food

How Supplied
- 60 mg tablets; supplied in 120 count bottles

Utilization Criteria
For initial review:
- Member must have a diagnosis of non-metastatic castration-resistant prostate cancer, AND
- Member must be receiving a gonadotropin-releasing hormone (GnRH) analog concurrently, OR
- Member must have documentation of a bilateral orchiectomy

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Concurrent treatment with abiraterone or enzalutamide
- History of seizure

Required Medical Information
- Diagnosis
- Dose
- Baseline CBC, CMP, lipid panel, glucose
- Concurrent medications
- Treatment history

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 3 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Apalutamide is an androgen receptor inhibitor that binds directly to the ligand-binding domain of the androgen receptor. Apalutamide inhibits androgen receptor nuclear translocation, inhibits DNA binding, and impedes AR-mediated transcription.
- Warnings and precautions: Based on animal studies, Apalutamide can cause fetal harm and potential loss of pregnancy. Effective contraception during treatment and for 3 months after last dose is required. Monitor for fall risk which may result in fractures. Patients should be advised of the potential for seizures.

References
**Esbriet® (pirfenidone)**

**FDA Approved Indication(s)**
- For the treatment of idiopathic pulmonary fibrosis (IPF)

**FDA Recommended Dose**
- Initial titration recommended as follows:
  - Days one through seven: One capsule three times a day with meals (801 mg)
  - Days eight through 14: Two capsules three times a day with meals (1602 mg)
  - Days 15, onward: Three capsules three times a day with meals (2403 mg)
- Dose reductions may be required for elevated LFTs, concomitant use of CYP1A2 inhibitors, current smokers, and photosensitivity or gastrointestinal reactions

**How Supplied**
- Each capsule contains 267 mg of pirfenidone, supplied via the following:
  - 14-day titration blister pack (63 capsules)
  - 28-day blister pack (252 capsules)
  - 30-day bottle (270 capsules)

**Utilization Criteria**

For initial review:
- Patient must have diagnosis of idiopathic pulmonary fibrosis (IPF) determined per the following diagnostic features
  - No identifiable causes of Interstitial Lung Diseases, AND
  - Pattern of usual interstitial pneumonia (UIP) per criteria in IPF guidelines determined on the high-resolution computed tomography (HRCT) as
    - Definite UIP, or
    - Possible UIP with a surgical lung biopsy pattern of definite or probable UIP
- Must complete the 14 days initial titration (re-initiate if ≥ 14 days of therapy missed or stopped)

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- AST/ALT >3x ULN with symptoms or >5x ULN with/without symptoms of hyperbilirubinemia

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Treatment history
- Concomitant medications
- HRCT pattern (and lung biopsy pattern, if applicable)
- Baseline liver function tests (AST, ALT, bilirubin)
- Baseline pulmonary function tests (FVC)

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an pulmonologist
**Coverage Duration (months)**
- 12 months

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Limited Distribution Drug
- The mechanism of action is currently unknown

**References**

*Last Reviewed November 9, 2015*
Exjade® (deferasirox)

FDA Approved Indication(s)
- Chronic Iron overload due to chronic blood transfusions in patients 2 years of age and older
- Chronic iron overload due to non-transfusion dependent thalassemia (NTDT) syndromes and with a liver iron concentration (LIC) of at least 5 mg/g of dry weight and a serum ferritin level greater than 300 mcg/L in patients 10 years of age and older

FDA Recommended Dose
- 20 mg per kg body weight orally, once daily.

How Supplied
- 125 mg, 250 mg and 500 mg tablets for oral suspension

Utilization Criteria
For initial review:
- Chronic iron overload due to blood transfusions
  - Serum ferritin level ≥ 1000mcg/L within last 60 days
  - Member will have serum ferritin, serum creatinine, creatinine clearance, serum transaminases, and bilirubin monitored monthly
- Chronic iron overload due to non-transfusion dependent thalassemia (NTDT) syndromes
  - Liver iron concentration (LIC) of at least 5 mg/g of dry weight and a serum ferritin level greater than 300 mcg/L
  - Member will have serum ferritin, serum creatinine, creatinine clearance, serum transaminases, and bilirubin monitored monthly

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- None

Required Medical Information
- Diagnosis
- Weight
- Baseline serum ferritin, creatinine, transaminases, and bilirubin

Age Restrictions
- 2 years of age and older

Prescriber Restrictions
- Must be prescribed by a hematologist

Coverage Duration (months)
- 3

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Deferasirox is an iron chelator
- Black Box Warning: Deferasirox may cause renal failure, hepatic failure, and gastrointestinal hemorrhage and requires close clinically monitoring of renal and hepatic function

References
Extavia® (interferon beta-1b)

FDA Approved Indication(s)
- For the treatment of relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations

FDA Recommended Dose
- 0.25 mg injected subcutaneously every other day

How Supplied
- 0.3 mg lyophilized powder in a 3 mL single-use vial

Utilization Criteria

For initial review:
- Member has a diagnosis of relapsing multiple sclerosis, AND
- Diagnosis has been confirmed by MRI, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Concurrent use of alternative disease-modifying therapy, such as interferon beta-1a, glatiramer acetate, dimethyl fumerate, fingolimod, or teriflunomide

Required Medical Information
- Diagnosis
- Concurrent medications
- Age
- Dose
- Complete baseline blood count with differential
- Liver function tests (ALT, AST)

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a neurologist

Coverage Duration (months)
- 12 months

Quantity/Partial Fill Restrictions
- None

Other Information

References

Last Reviewed November 10, 2015
# Eylea® (aflibercept)

## FDA Approved Indication(s)
- Neurovascular age-related macular degeneration (AMD)
- Macular edema following ocular vein occlusion (RVO)
- Diabetic macular edema (DME)
- Diabetic retinopathy (DR) in patients with DME

## FDA Recommended Dose
- AMD: 2 mg administered by intravitreal injection every 4 weeks for the first 12 weeks (3 months), followed by 2 mg once every 8 weeks
- RVO: 2 mg administered once every 4 weeks
- DME/DR: 2 mg administered every 4 weeks for the first 5 injections, followed by 2 mg administered once every 8 weeks

## How Supplied
- Single-use 3 ml vial that provides 0.05 mL (2 mg) of solution for intravitreal injection

## Utilization Criteria

### For initial review:
- Member must have diagnosis of an FDA-approved indication, AND
- For AMD, DME, and DR:
  - Member must have tried and failed, or is intolerant to, treatment with intravitreal bevacizumab, OR
  - Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

### For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

## Exclusion Criteria
- Member has concurrent ocular or periocular infections, or intraocular inflammation
- Hypersensitivity to aflibercept

## Required Medical Information
- Diagnosis
- Age
- Dose
- Treatment history

## Age Restrictions
- 18 years of age and older

## Prescriber Restrictions
- Must be prescribed by an ophthalmologist or optometrist

## Coverage Duration (months)
- 12 months

## Quantity/Partial Fill Restrictions
- Coverage of doses exceeding FDA-approved limits requires documentation of progression of disease after an adequate trial (typically three months), of FDA-approved dosing
Other Information

- Mechanism of action: Aflibercept acts as a soluble decoy receptor that binds VEGF-A and PIGF, and thereby can inhibit the binding and activation of VEGF receptors
- Black box warning: none

References

- Arroyo JG. Age-related macular degeneration: Treatment and prevention. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA.
**Fasenra™ (benralizumab)**

**FDA Approved Indication(s)**
- Add-on maintenance treatment of patients with severe asthma aged 12 years and older and with an eosinophilic phenotype.

**FDA Recommended Dose**
- 30 mg subcutaneous injection every 4 weeks for the first 3 doses, followed by once every 8 weeks thereafter.

**How Supplied**
- 30 mg/mL single-dose prefilled syringe

**Utilization Criteria**
For initial review:
- Member must have a diagnosis of severe, sub-optimally controlled asthma (i.e., asthma symptoms two days per week or more, or exacerbations requiring systemic corticosteroids more than two times per year), AND
- Must have an inadequate response to a three-month course of inhaled corticosteroids and a long-acting beta2-agonist, AND
- Must have an absolute eosinophil count of:
  - ≥ 150 cells/microL within the past 6 weeks, OR
  - ≥ 300 cells/microL within the past 12 months, AND
- Member is currently receiving long-acting beta2-agonist, inhaled corticosteroid therapy, montelukast, and short-acting beta2-agonist as rescue therapy, unless otherwise contraindicated, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable

For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider. Such assessment must include an objective measurement of response, such as a quantitative decrease in asthma symptoms, exacerbation rate, or improvement in FEV1.

**Exclusion Criteria**
- Treatment of other eosinophilic conditions
- Relief of acute bronchospasm or status asthmaticus
- Current smoker
- Pre-existing parasitic (helminth) infections

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Concurrent medications
- Treatment history
- Baseline eosinophil count

**Age Restrictions**
- 12 years of age and older
### Prescriber Restrictions
- Must be prescribed by an allergist, immunologist, or pulmonologist

### Coverage Duration (months)
- 3 months (initial), 12 months (continuation)

### Quantity/Partial Fill Restrictions
- None

### Other Information
- **Mechanism of action**: Benralizumab is an interleukin-5 (IL-5) antagonist. IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils. Benralizumab binds to IL-5 and reduces the production and survival of eosinophils; however, the mechanism of benralizumab action in asthma has not been definitively established.
- **Warnings and precautions**: Benralizumab should be administered by a healthcare professional. In line with clinical practice, monitoring of patients after administration of biologic agents is recommended. Hypersensitivity reactions (e.g., anaphylaxis, angioedema, urticaria, rash) have occurred following administration. These reactions generally occur within hours of administration, but in some instances have a delayed onset (i.e., days). In the event of a hypersensitivity reaction, benralizumab should be discontinued.

### References

_Last Reviewed April 3, 2018_
Firazyrr® (icatibant acetate)

FDA Approved Indication(s)

- For the treatment of acute attacks of hereditary angioedema (HAE) in adults 18 years of age and older

FDA Recommended Dose

- 30 mg administered by subcutaneous (SC) injection in the abdominal area; additional doses (up to 3) may be administered at intervals of at least 6 hours in a 24 hour period if response is inadequate or if symptoms recur

How Supplied

- 30 mg/3 mL prefilled syringe

Utilization Criteria

For initial review:

- Member must have a diagnosis of HAE, where diagnosis is based on evidence of a normal C1 level and a low C4 level (C4 less than 14 mg/dL; normal range 14 to 40 mg/dL, or C4 below the lower limit of normal as defined by the laboratory performing the test), AND
- Member must be having an attack associated with HAE (e.g., airway swelling, severe abdominal pain, facial swelling, painful facial distortion), AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

For continuation:

- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria

- None

Required Medical Information

- Diagnosis
- Age
- Dose

Age Restrictions

- 18 years of age and older

Prescriber Restrictions

- Must be prescribed by an immunologist or hematologist

Coverage Duration (months)

- 12

Quantity/Partial Fill Restrictions

- 3 syringes for 30 days

Other Information

- Mechanism of action: Icatibant is a competitive antagonist selective for the bradykinin B2 receptor, with an affinity similar to bradykinin. Icatibant inhibits bradykinin from binding the B2 receptor and thereby treats the clinical symptoms of an acute, episodic attack of HAE.
References

**Forteo® (teriparatide)**

**FDA Approved Indication(s)**
- For the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy
- To increase bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy
- For the treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy (daily dosage equivalent to 5 mg or greater of prednisone) at high risk for fracture, defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy

**FDA Recommended Dose**
- 20 mcg subcutaneously once daily

**How Supplied**
- 2.4 mL prefilled delivery device

**Utilization Criteria**
- **For initial review:**
  - Member is at high risk for fracture, AND
  - Member is concurrently receiving supplemental calcium and vitamin D unless contraindicated, AND
  - Bone mineral density (BMD) T-score ≤ -2.5, AND
  - Member has tried at least one oral bisphosphonate for at least 3 – 6 months and failed, OR
  - Member is intolerant or has a contraindication to at least one oral bisphosphonate as evidenced by documentation in provider notes, AND
  - Member meets one of the following:
    - Female with postmenopausal osteoporosis
    - Male with primary or hypogonadal osteoporosis
    - Male or female with osteoporosis associated with sustained glucocorticoid therapy
      - Has received a mean daily dose of 5 mg or more of prednisone or its equivalent for 3 or more consecutive months
  - Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable
- **For continuation:**
  - Benefit of therapy evidenced by increased BMD, AND
  - Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s prescriber, AND
  - Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

**Exclusion Criteria**
- Member has Paget’s disease, OR
- Member has received teriparatide or abaloparatide for more than 24 months

**Required Medical Information**
- Diagnosis
- Age
- Dose
• Concurrent medications
• Treatment history

Age Restrictions
• 18 and older

Prescriber Restrictions
• None

Coverage Duration (months)
• 12
• 24-month total max

Quantity/Partial Fill Restrictions
• None

Other Information
• Mechanism of action: Endogenous 84-amino acid parathyroid hormone (PTH) is the primary regulator of calcium and phosphate metabolism in bone and kidney
• Black Box Warning: Potential risk of osteosarcoma

References
• Forteo® [package insert]. Indianapolis, IN; Lilly USA, LLC; March 2017.

Last Reviewed August 11, 2017
Gilenya® (fingolimod)

FDA Approved Indication(s)

- For the treatment of relapsing forms of multiple sclerosis (MS) in patients 10 years of age and older

FDA Recommended Dose

- Adults and pediatric patients 10 years of age and older weighing > 40 kg:
  - 0.5 mg orally once daily
- Pediatric patients 10 years of age and older weighing ≤ 40 kg:
  - 0.25 mg orally once daily

How Supplied

- 0.25 mg and 0.5 mg capsules, supplied in 30-count bottles and blister cards of 7 capsules

Utilization Criteria

For initial review:

- Must have diagnosis of relapsing form of multiple sclerosis (RRMS, SPMS, PRMS), AND
- Must have a baseline complete blood count, AND
- Must have liver enzymes (ALT, AST) monitored at baseline and within normal limits, AND
- Must have baseline eye exam, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

For continuation:

- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria

- Member is currently receiving one or more alternative disease modifying therapies, OR
- Member has a history (within last 6 months) of myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization or Class II/IV heart failure, OR
- Member has a history of Mobitz Type II 2nd degree or 3rd degree AV block or sick sinus syndrome, unless patient has a pacemaker, OR
- Member’s baseline QTc interval ≥ 500 msec, OR
- Member is concurrently receiving Class Ia or Class III anti-arrhythmic drugs

Required Medical Information

- Diagnosis
- Treatment history
- Age
- Dose
- Concurrent medications
- Comorbid conditions

Age Restrictions

- 10 years of age and older

Prescriber Restrictions

- Must be prescribed by a neurologist

Coverage Duration (months)
• 12 months

**Quantity/Partial Fill Restrictions**

- 30-day supply

**Other Information**

- Mechanism of action: fingolimod is a sphingosine 1-phosphate receptor modulator
- Warnings and precautions: The first dose should be administered in the presence of a health care professional due to risk of bradyarrhythmia and atrioventricular blocks

**References**


*Last Reviewed February 4, 2019*
**Gilotrif® (afatinib)**

**FDA Approved Indication(s)**
- For the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test

**FDA Recommended Dose**
- 40 mg orally, once daily

**How Supplied**
- 20 mg, 30 mg, and 40 mg film-coated, round, biconvex, bevel-edged tablets

**Utilization Criteria**

*For initial review:*
- EGFR exon 19 deletions OR exon 21 (L858R) substitution mutations, as detected by an FDA-approved test

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Patient has not undergone genetic testing for required mutations

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Genetic test results

**Age Restrictions**
- None

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- 30 day supply (no partial fill)

**Other Information**
- Gilotrif® must be administered on an empty stomach, 1 hour before or 2 hours after a meal

**References**

*Last Reviewed November 10, 2015*
**Gleevec® (imatinib mesylate)**

**FDA Approved Indication(s)**

- Newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (CML) in chronic phase
- Patients with Philadelphia chromosome positive chronic myeloid leukemia in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy
- Adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (ALL)
- Pediatric patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) in combination with chemotherapy
- Adult patients with myelodysplastic/myeloproliferative diseases associated with PDGFR (platelet-derived growth factor receptor) gene re-arrangements
- Adult patients with aggressive systemic mastocytosis without the D816V c-Kit mutation or with c-Kit mutational status unknown
- Adult patients with hypereosinophilic syndrome and/or chronic eosinophilic leukemia who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFRα fusion kinase negative or unknown
- Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans
- Patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors
- Adjuvant treatment of adult patients following complete gross resection of Kit (CD117) positive GIST

**FDA Recommended Dose**

- Adult Patients with Ph+ CML CP: 400 mg/ day
- Adult Patients with Ph+ CML AP or BC: 600 mg/day
- Pediatric Patients with Ph+ CML CP: 340 mg/m²/day; Not to exceed 600 mg
- Adults Patients with Ph+ ALL: 600 mg/day in patients with relapsed/refractory Ph+ ALL
- Pediatric Patients with Ph+ ALL: 340mg/m²/day; Not to exceed 600mg
  - MDS/MPD: 400 mg/day
- ASM:
  - Without D816V c-Kit mutation: 400 mg/day
  - ASM associated with eosinophilia: 100 mg/day
- HES/CEL
  - 400 mg/day
  - FIP1L1-PDGFRα fusion kinase: 100 mg/day
- DFSP: 800 mg/day
- Metastatic or Unresectable GIST: 400 mg/day
  - A dose increase up to 800 mg daily (given as 400 mg twice daily) may be considered
- Adjuvant GIST: 400 mg/day

**How Supplied**

- 100 mg, tablets
- 400 mg tablets

**Utilization Criteria**

For initial review:

- Patient has a diagnosis aligned with an FDA-approved indication, AND
- For increased doses from FDA-recommended starting doses:
• Member has a diagnosis of CML in any phase, or ASM, or HES/CEL, or metastatic or unresectable GIST; AND
• Member shows no evidence of adverse drug reactions, AND
• Member demonstrates insufficient response to FDA-recommended dose

For continuation:
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
• Medication is being used for the treatment of idiopathic pulmonary fibrosis (IPF)
• Member is requesting branded formulation of product

Required Medical Information
• Diagnosis, including phase or mutation status
• Height and weight (Pediatric members only)

Age Restrictions
• 1 year of age and older

Prescriber Restrictions
• Must be prescribed by an oncologist or hematologist

Coverage Duration (months)
• 12

Quantity/Partial Fill Restrictions
• None

Other Information
• Mechanism of action: Imatinib inhibits proliferation and induces apoptosis in bcr-abl positive cell lines as well as fresh leukemic cells from Philadelphia chromosome positive chronic myeloid leukemia.

References

Last Reviewed February 1, 2017
# Growth Hormone (Somatropin)

## FDA Approved Products and Indications

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Pediatric GH Deficiency</th>
<th>Adult GH Deficiency</th>
<th>Idiopathic Short Stature</th>
<th>Small for Gestational Age</th>
<th>Turner Syndrome</th>
<th>Noonan Syndrome</th>
<th>Chronic Renal Insufficiency</th>
<th>Prader-Willi Syndrome</th>
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## FDA Recommended Dose

- Specific to product, refer to package insert per authorization

## How Supplied

- Specific to product, refer to package insert per authorization

## Utilization Criteria

### For initial review:

- Pediatric patients:
  - Diagnosis of chronic renal failure and growth retardation; OR
  - Diagnosis of hypothalamic-pituitary lesions or panhypopituitarism; OR
  - Diagnosis of growth hormone (GH) deficiency;
    - Patient must meet all of the following criteria for documentation of growth failure:
      - Height is >2 standard deviations below the mean for age and sex (less than 3rd percentile for age)
      - Growth velocity is subnormal (age specific growth rate at less than the 25th percentile, or less than 4 cm per year)
      - Bone age is delayed
      - Documented failure of at least one GH stimulation tests (defined as a peak growth hormone level of less than 10mcg/L after GH stimulation by insulin, arginine, clonidine, glucagon, or levodopa). GH stimulation tests not required with diagnosis of Turner Syndrome, Noonan Syndrome, or Prader-Willi Syndrome

- Adult patients
  - Diagnosis of HIV and an unintentional weight loss of 10% over 12 months, 7.5% over 6 months or a BMI <20mg/kg; OR
  - Diagnosis of hypothalamic-pituitary lesions or panhypopituitarism; OR
  - Documented GH deficiency; OR
  - Diagnosis of Short Bowel Syndrome;
• Patient is currently receiving specialized nutrition support directed by a healthcare professional (Total Parenteral Nutrition (TPN), Peripheral Parenteral Nutrition (PPN), or high-complex carbohydrate, low-fat diet) and maintaining appropriate daily caloric intake requirements

• Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

*For continuation:*

• Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND

• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider, AND

• For pediatric growth hormone deficiency, documentation must confirm epiphyses have not closed

### Exclusion Criteria

• 65 years of age and older

### Required Medical Information

• Diagnosis
• Age
• Dose
• Weight
• Treatment history
• Growth chart with velocity

### Age Restrictions

• None

### Prescriber Restrictions

• Must be prescribed by an endocrinologist or pediatric endocrinologist

### Coverage Duration (months)

• 12

### Quantity/Partial Fill Restrictions

• None

### Other Information

• Mechanism of action: GH binds to dimeric GH receptors located within the cell membranes of target tissue cells. This interaction results in intracellular signal transduction and subsequent induction of transcription and translation of GH-dependent proteins including IGF-I, IGF BP-3 and acid-labile subunit. GH has direct tissue and metabolic effects, including stimulation of chondrocyte differentiation, stimulation of lipolysis and stimulation of hepatic glucose output. In addition, some effects of somatropin are mediated indirectly by IGF-I, including stimulation of protein synthesis and chondrocyte proliferation.

### References

• Snyder, PJ. Growth hormone deficiency in adults. In: UpToDate, Basow, DS (Ed), UpToDate. Waltham, MA, 2013.

• Rogol, AD. Treatment of growth hormone deficiency in children. In: UpToDate, Basow, DS (Ed), UpToDate. Waltham, MA, 2013.

• Rogol, AD. Growth hormone treatment for children born small for gestational age. In: UpToDate, Basow, DS (Ed), UpToDate. Waltham, MA, 2013.

Last Reviewed November 9, 2015
Harvoni® (ledipasvir/sofosbuvir)

**FDA Approved Indication(s)**
- For the treatment of adult patients with chronic hepatitis C (HCV):
  - Genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis
  - Genotype 1 infection with decompensated cirrhosis, for use in combination with ribavirin
  - Genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, for use in combination with ribavirin
- For the treatment of pediatric patients 12 years of age and older or weighing at least 35 kg with HCV genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis

**FDA Recommended Dose**
- For adults and pediatric patients 12 years of age and older or weighing at least 35 kg:
  - One tablet orally once daily, with or without food

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patient Population</th>
<th>Treatment Regimen and Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1</td>
<td>Treatment-naive without cirrhosis or with compensated cirrhosis (Child-Pugh A) (Adult and pediatric)</td>
<td>Harvoni® x 12 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment-experienced without cirrhosis (Adult and pediatric)</td>
<td>Harvoni® x 12 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment-experienced with compensated cirrhosis (Child-Pugh A) (Adult and pediatric)</td>
<td>Harvoni® x 24 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment-naive or treatment-experienced with decompensated cirrhosis (Child-Pugh B or C) (Adult)</td>
<td>Harvoni® + ribavirin x 12 weeks</td>
</tr>
<tr>
<td>Genotype 1 or 4</td>
<td>Treatment-naive and treatment-experienced liver transplant recipients without cirrhosis, or with compensated cirrhosis (Child-Pugh A) (Adult)</td>
<td>Harvoni® + ribavirin x 12 weeks</td>
</tr>
<tr>
<td>Genotype 4, 5, or 6</td>
<td>Treatment-naive and treatment-experienced, without cirrhosis or with compensated cirrhosis (Child-Pugh A) (Adult and pediatric)</td>
<td>Harvoni® x 12 weeks</td>
</tr>
</tbody>
</table>

- 8 weeks of treatment can be considered in treatment-naive genotype 1 adult patients without cirrhosis who have pretreatment HCV RNA levels less than 6 million IU/mL
- Treatment-experienced adult patients have failed a peginterferon alfa + ribavirin based regimen with or without an HCV protease inhibitor
- Treatment-experienced pediatric patients have failed an interferon based regimen with or without ribavirin
- Harvoni + ribavirin for 12 weeks can be considered in treatment-experienced genotype 1 patients with cirrhosis who are eligible for ribavirin
- For further information on ribavirin dosing and dosage modifications, refer to prescribing information

**How Supplied**
- 90mg (ledipasvir)/400 mg (sofosbuvir) tablets supplied in a 28 count bottle

**Utilization Criteria**
For Initial Review:
- Member must have a diagnosis of chronic HCV with documented genotype and viral load collected within the previous three months, AND
- Physician must attest to the member’s ability and dedication to remain adherent to the entire course of therapy, AND
- Physician must confirm that alcohol and illicit substance abuse is absent for the previous six months, or member is currently seeing an addiction specialist, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

Exclusion Criteria
- Concurrent use with sofosbuvir, simeprevir or other HCV protease inhibitors, or peginterferon, OR
- Concurrent use of P-glycoprotein inhibitors (i.e., St. John’s Wort, rifampin, select anti-convulsants), OR
- Severe renal impairment (CrCl < 30 ml/min, or End Stage Renal Disease), OR
- Acute HCV infection that is known to have occurred within the previous six months, OR
- Concurrent use of amiodarone
- Coverage may be revoked if Member is non-adherent through the first two months of therapy, as evidenced by claim records or verbal confirmation of poor adherence

Required Medical Information
- Diagnosis, including genotype
- Viral load
- Age
- Dose and duration of therapy
- Concurrent medications
- Treatment history

Age Restrictions
- Must be 12 years of age or older

Prescriber Restrictions
- Must be prescribed by a gastroenterologist or infectious disease specialist

Coverage Duration (months)
- Coverage duration will depend on required duration of therapy

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Sofosbuvir is a nucleotide analog NS5B polymerase inhibitor. Ledipasvir is an inhibitor of the HCV NS5A protein.
- Ledipasvir was fully active against the sofosbuvir resistance-associated substitution S282T in NS5B, while all ledipasvir resistance-associated substitutions in NS5A were fully susceptible to sofosbuvir. Both sofosbuvir and ledipasvir were fully active against substitutions associated with resistance to other classes of direct-acting antivirals with different mechanisms of actions, such as NS5B non-nucleoside inhibitors and NS3 protease inhibitors.

References


# H.P. Acthar Gel® (repository corticotropin)

## FDA Approved Indication(s)
- For the treatment of infantile spasms in children under 2 years of age
- For the treatment of exacerbations of multiple sclerosis (MS) in adults
- For the short-term treatment of rheumatic, collagen, dermatologic, allergic, ophthalmic, respiratory, and edematous disorders and disease states

## FDA Recommended Dose

- **Infantile spasms**
  - 150 U/m² (divided into twice daily intramuscular injections of 75 U/m²) administered over a 2-week period. Dosing should then be gradually tapered over a 2-week period to avoid adrenal insufficiency.
- **MS exacerbations**
  - 80-120 units intramuscularly or subcutaneously once daily for 2-3 weeks for acute exacerbations
- **Treatment of other disorders and diseases**
  - Dosing will need to be individualized depending on disease and medical condition of the patient. The usual dose is 40-80 units intramuscularly or subcutaneously every 24-72 hours.

## How Supplied
- 5 mL multi dose vial (80 U/mL)

## Utilization Criteria

### For initial review:
- **Infantile Spasm (West Syndrome)**
  - Patient is less than 2 years of age; AND
  - The medication is being prescribed by a pediatric neurologist and/or neurologist
- **Multiple sclerosis (MS) with acute exacerbation**
  - Patient is currently being treated with an immunomodulatory therapy; AND
  - The patient has limited/unsatisfactory response (i.e. no difference in symptoms) to corticosteroids (i.e. IV methylprednisolone, IV dexamethasone, or high dose oral steroids); OR
  - The patient has documented intolerance (i.e., severe anaphylaxis) or treatment limitations (i.e., poor venous access) to corticosteroids, determined by poor tolerance to intravenous (IV methylprednisolone, IV dexamethasone) or oral (high dose oral steroids) treatment trials; AND
  - Treatment is limited to 3 weeks
- **Other diagnoses**
  - The patient has limited/unsatisfactory response (i.e. no difference in symptoms) to corticosteroids (i.e. IV methylprednisolone, IV dexamethasone, or high dose oral steroids); OR
  - The patient has documented intolerance (i.e. severe anaphylaxis) or treatment limitations (i.e., poor venous access) to corticosteroids determined by poor tolerance to intravenous (IV methylprednisolone, IV dexamethasone) or oral (high dose oral steroids) treatment trials; OR

### Coverage of other diagnoses may be excluded per plan-specific policies

### For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

## Exclusion Criteria
• Planned use as MS pulse therapy
• When congenital infections are suspected in infants
• Patient has other contraindication to corticotropin, such as scleroderma, osteoporosis, systemic fungal infections, ocular herpes simplex, recent surgery, history of or the presence of a peptic ulcer, congestive heart failure, uncontrolled hypertension, primary adrenocortical insufficiency, adrenocortical hyperfunction or sensitivity to proteins or porcine origin

Required Medical Information

• Diagnosis
• Age
• Dose
• Weight
• Height

Age Restrictions

• Infantile spasms: Less than 2 years of age
• MS with acute exacerbation: 18 years of age and older

Prescriber Restrictions

• Must be prescribed by a neurologist or pediatric neurologist

Coverage Duration (weeks)

• 3

Quantity/Partial Fill Restrictions

• None

Other Information

• Mechanism of action: Corticotropin and endogenous ACTH stimulate the adrenal cortex to secrete cortisol, corticosterone, aldosterone, and a number of weakly androgenic substances. Prolonged administration of large doses of corticotropin induces hyperplasia and hypertrophy of the adrenal cortex and continuous high output of cortisol, corticosterone and weak androgens. The release of endogenous ACTH is under the influence of the nervous system via the regulatory hormone released from the hypothalamus and by a negative corticosteroid feedback mechanism. Elevated plasma cortisol suppresses ACTH release. Corticotropin is also reported to bind to melanocortin receptors.

References

Humira® (adalimumab)

FDA Approved Indication(s)

- Rheumatoid Arthritis (RA): For reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active Rheumatoid Arthritis (RA)
- Juvenile Idiopathic Arthritis (JIA): For reducing signs and symptoms of moderately to severely active polyarticular Juvenile Idiopathic Arthritis (JIA) in pediatric patients 4 years of age and older
- Psoriatic Arthritis (PsA): For reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active Psoriatic Arthritis (PsA)
- Ankylosing Spondylitis (AS): For reducing signs and symptoms in adult patients with active Ankylosing Spondylitis (AS)
- Adult Crohn's Disease (CD): For reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy. Reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab
- Pediatric Crohn's Disease: For reducing signs and symptoms and inducing and maintaining clinical remission in patients 6 years of age and older with moderately to severely active Crohn's disease who have had an inadequate response to corticosteroids or immunomodulators such as azathioprine, 6-mercaptopurine, or methotrexate
- Ulcerative Colitis (UC): For inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP)
- Plaque Psoriasis (PsO): For the treatment of adult patients with moderate to severe chronic plaque psoriasis (PsO) who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate
- Hidradenitis Suppurativa (HS): For the treatment of moderate to severe hidradenitis suppurativa
- Uveitis (UV): For the treatment of non-infectious intermediate, posterior and panuveitis in adult patients

FDA Recommended Dose

- RA, PsA, and AS
  - 40 mg subcutaneously every other week
  - For RA, dose may be increased to 40 mg every week
- JIA
  - 22 – 33 lbs: 10 mg every other week
  - 33-66 lbs: 20 mg every other week
  - Greater than 66 lbs: 40 mg every other week
- Adult CD and UC
  - Day 1: 160 mg day one or 80 mg per day for two consecutive days
  - Day 15: 80 mg
  - Day 29/Maintenance: 40 mg every other week
- Pediatric CD
  - 37 – 88 lbs
    - Day 1: 80 mg
    - Day 15: 40 mg
    - Day 29/Maintenance: 20 mg every other week
  - ≥88 lbs
• Day 1: 160 mg or 80 mg per day for two consecutive days
  • Day 15: 80 mg
  • Day 29/Maintenance: 40 mg every other week

• PsO, UV
  • 80 mg day one, then 40 mg every other week

• HS
  • Day 1: 160 mg or 80 mg per day for two consecutive days
  • Day 15: 80 mg
  • Day 29/Maintenance: 40 mg every week

How Supplied

• 40mg/1 mL Single-Use Pen
• 40 mg/1 mL Pre-Filled Syringe
• 20 mg/0.5 mL Pre-Filled Syringe

Utilization Criteria

For initial review:

• For all conditions: Patient has a negative TB test prior to initiating therapy, AND
• Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
• Moderate to Severe Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, and Psoriatic Arthritis
  • Prescriber is a rheumatologist, AND
  • Patient is at least 4 years of age, AND
  • Patient has tried and failed, or is intolerant to, methotrexate monotherapy, OR
  • Patient has tried and failed at least one non-biologic DMARD for at least 6-12 weeks
• Ankylosing spondylitis
  • Prescriber is a rheumatologist, AND
  • Patient has tried and failed ≥ 2 NSAIDs, steroid products, or methotrexate
• Plaque psoriasis
  • Prescriber is a dermatologist, AND
  • Patient has ≥ 10% BSA involvement or affected area includes palms, soles, head, neck, or genitalia, AND
  • Intolerant to topical agents, topical immunomodulators, systemic therapy (i.e., methotrexate, cyclosporine, or acitretin), or phototherapy
• Adult Crohn’s Disease, Ulcerative Colitis
  • Prescriber is gastroenterologist, AND
  • Member has tried and failed 2 or more of the following for at least 60 days:
    • Azathioprine
    • Balsalazine disodium
    • Budesonide
    • Cyclosporine
    • Mercaptopurine
    • Mesalamine
    • Methotrexate
    • Osalazine sodium
    • Prednisone
    • Sulfasalazine
• Pediatric Crohn’s Disease
• Prescriber is a gastroenterologist, AND
• Patient is at least 6 years of age, AND
• Patient has had an inadequate response to ≥ 1 of the following:
  • Corticosteroids
  • Azathioprine
  • 6-Mercaptopurine
  • Methotrexate
• Hidradenitis Suppurativa
  • Prescriber is a dermatologist, AND
  • Patient has had an inadequate response to ≥ 1 of the following:
    • Topical clindamycin
    • Tetracycline, doxycycline, minocycline, dapsone, or a combination of clindamycin and rifampin
• Uveitis
  • Prescriber is an ophthalmologist, AND
  • Patient has had an inadequate response to the following:
    • One or more intraocular glucocorticoid injections, AND
    • One or more of the following systemic immunosuppressive agents:
      • Azathioprine
      • Mycophenolate mofetil
      • Methotrexate
      • Cyclosporine
      • Tacrolimus
      • Cyclophosphamide

For continuation:
• Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
• Review of therapy by the respective specialist confirms that the patient continues to have a beneficial response to therapy, AND
• For Ulcerative Colitis:
  • Member must have evidence of clinical remission by week 8 of adalimumab therapy
Special considerations:
• Request for shortened interval following initial treatment
  o Requires the following:
    ▪ Crohn’s Disease, Ulcerative Colitis
      • Serum drug trough concentration and antibody levels, AND
      • Documentation member experienced secondary loss of response via:
        o Colonoscopy, computed tomography enterography, magnetic resonance enterography results (preferred), OR
        o Fecal calprotectin and significantly increased disease symptoms (e.g., # stools per day)
    ▪ Plaque Psoriasis
      • Will consider reauthorization for induction dose if:
        o Member experienced lapse in therapy or adherence issues that are now resolved
    ▪ Any indication
      • Will consider 1 extra fill for missed dose(s)
Coverage duration

- Crohn’s Disease, Ulcerative Colitis
  - Initial: determined by earliest clinical trial data collection points
  - Maintenance:
    - Avoid continuing therapy with shortened interval unless medically necessary
    - Documented clinical rationale by provider stating shortened interval medically necessary (e.g., following shortened interval dosing – positive antibody levels, serum drug trough concentration within normal limits and symptoms resolved) – 6 months

- Plaque Psoriasis
  - 1 month

Exclusion Criteria

- Receiving additional biologic DMARD therapy

Required Medical Information

- Diagnosis
- Treatment history
- Age
- Dose
- Weight (Pediatric patients only)
- TB Test

Age Restrictions

- 4 years of age and older

Prescriber Restrictions

- Must be prescribed by a gastroenterologist, dermatologist, ophthalmologist, or rheumatologist, per diagnosis

Coverage Duration (months)

- For Ulcerative Colitis, the initial coverage will be for 2 months, followed by 12 months continuation
- For all other conditions, 12 months

Quantity/Partial Fill Restrictions

- Rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, and uveitis
  - 40 mg every 2 weeks
  - For RA, 40 mg every week may be considered on a case-by-case basis
- Adult Crohn’s disease
  - Ten 40 mg syringes in the initial 3 month period (induction), then 40 mg every 2 weeks thereafter
- Ulcerative Colitis
  - Eight 40 mg syringes in the initial 2 months; followed by two 40 mg syringes per month if continuation is authorized.
- Pediatric CD
  - < 40 kg: Three 40 mg syringes for first month; followed by two 20 mg syringes per month
  - ≥ 40 kg: Six 40 mg syringes for first month; followed by two 40 mg syringes per month
- Chronic plaque psoriasis
  - Four 40 mg syringes (160 mg) in the first month; followed by two 40 mg syringes per month
- Hidradenitis Suppurativa
- Six 40 mg syringes in the first month (induction); followed by four 40 mg syringes per month

**Other Information**

- Mechanism of action: Adalimumab binds specifically to TNF-alpha and blocks its interaction with the p55 and p75 cell surface TNF receptors.
- Black Box Warning: Increased risk of serious infections and malignancy

**References**

- Margesson L. Treatment of hidradenitis suppurativa (acne inversa). In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed December 15, 2015.)
- Rosenbaum J. Uveitis: treatment. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed July 25, 2016.)

*Last Reviewed June 19, 2017*
Ibrance™ (palbociclib)

FDA Approved Indication(s)

- For the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:
  - An aromatase inhibitor as initial endocrine based therapy in postmenopausal women, or
  - Fulvestrant in women with disease progression following endocrine therapy

FDA Recommended Dose

- One 125 mg capsule taken daily for the first 21 days of each 28 day cycle

How Supplied

- 125 mg, 100 mg, and 75 mg capsules

Utilization Criteria

For initial review:

- Member has a confirmed diagnosis of (ER)-positive, (HER-2)-negative advanced or metastatic breast cancer, AND
  - Medication is prescribed as initial endocrine-based therapy, AND
  - Medication is being used in combination with an aromatase inhibitor, OR
- Member has a confirmed diagnosis of (HR)-positive, (HER-2)-negative advanced or metastatic breast cancer, AND
  - Member has documentation of disease progression following endocrine therapy, AND
  - Medication is being used in combination with fulvestrant

For continuation:

- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria

- None

Required Medical Information

- Diagnosis
- Age
- Dose
- Treatment history
- Concurrent medications

Age Restrictions

- 18 years of age and older

Prescriber Restrictions

- Must be prescribed by an oncologist

Coverage Duration (months)

- 12 months

Quantity/Partial Fill Restrictions

- None

Other Information

- Mechanism of action: Palbociclib is an inhibitor of cyclin-dependent kinase (CDK) 4 and 6, which are downstream of signaling pathways which lead to cellular proliferation. Palbociclib has been shown to reduce cellular proliferation of estrogen receptor (ER)-positive breast cancer cell lines.
- Approval was granted via accelerated approval, and confirmatory clinical trials are on-going.
References

**Iclusig® (ponatinib hydrochloride)**

**FDA Approved Indication(s)**
- For the treatment of adult patients with chronic, accelerated phase, or blast phase chronic myeloid leukemia (CML) or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) for whom no other tyrosine kinase inhibitor (TKI) therapy is indicated.
- For the treatment of adult patients with T315I-positive CML (chronic phase, accelerated phase, or blast phase) or T315I-positive Ph+ ALL.

**FDA Recommended Dose**
- Recommended starting dose: 45 mg orally once daily

**How Supplied**
- 15 mg, 30 mg and 45 mg tablets

**Utilization Criteria**

*For initial review:*
- Member must have documentation of a diagnosis consistent with an FDA-approved indication, AND
- Must have documentation of T315I-positivity, if applicable

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- None

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Treatment history
- Baseline liver function status (AST, ALT, bilirubin)

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration**
- 3 months

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: Ponatinib is a multi-kinase inhibitor.
- Black Box Warning: Increased risk for arterial occlusion, venous thromboembolism, heart failure, and hepatotoxicity

**References**
Imbruvica® (ibrutinib)

FDA Approved Indication(s)
• For the treatment of adult patients with:
  • Mantle cell lymphoma (MCL) who have received at least one prior therapy
  • Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), with or without 17p deletion
  • Waldenström’s macroglobulinemia (WM)
  • Marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy
  • Chronic graft-versus-host disease (cGVHD) after failure of one or more lines of systemic therapy

FDA Recommended Dose
• MCL and MZL: 560 mg orally once daily
• CLL/SLL, WM, and cGVHD: 420 mg orally once daily

How Supplied
• 70 mg and 140 mg capsules
• 140 mg, 280 mg, 420 mg and 560 mg tablets

Utilization Criteria
For initial review:
• Member must have a diagnosis of MCL and have received at least one prior chemotherapy regimen, OR
• Member must have a diagnosis of CLL or WM, OR
• Member must have a diagnosis MZL and have received at least one prior rituximab-containing chemotherapy regimen, OR
• Member must have a diagnosis of cGVHD with failure of one or more lines of systemic therapy

For continuation:
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
• Pregnancy
• Severe hepatic impairment (Child-Pugh class C)

Required Medical Information
• Diagnosis
• Age
• Dose
• Concurrent medications
• Treatment history

Age Restrictions
• Must be 18 years of age or older

Prescriber Restrictions
• Must be prescribed by an oncologist or hematologist

Coverage Duration (months)
• 3 months

Quantity/Partial Fill Restrictions
• 15 days supply for the first six fills

**Other Information**

• Mechanism of action: Ibrutinib is an inhibitor of Bruton’s tyrosine kinase (BTK). Ibrutinib forms a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK enzymatic activity. BTK is a signaling molecule of the B-cell antigen receptor (BCR) and cytokine receptor pathways. BTK's role in signaling through the B-cell surface receptors results in activation of pathways necessary for B-cell trafficking, chemotaxis, and adhesion.

**References**


*Last Reviewed June 12, 2019*
Increlex® (mecasermin)

FDA Approved Indication(s)
- Severe primary IGF-1 deficiency

FDA Recommended Dose
- Starting dose: 0.04 to 0.08 mg/kg SubQ twice daily
- Maximum dose: 0.12 mg/kg SubQ twice daily

How Supplied
- 10 mg/mL in multi-dose vials (40 mg/vial)

Utilization Criteria
For initial review:
- Presence of:
  - Growth failure due to severe IGF-1 deficiency defined by:
    - Height standard deviation score <= -3.0
    - Basal IGF-1 standard deviation score <= -3.0
    - Normal or elevated growth hormone level
    - OR
  - Growth hormone gene deletion and has developed neutralizing antibodies to GH
  - Documentation of open epiphyses for patients who are Tanner stage III or greater
For continuation:
- Epiphyses must not be closed
- Growth rate velocity is >= 2.5 cm/year

Exclusion Criteria
- Active or suspected neoplasia
- Closed epiphyses

Required Medical Information
- Diagnosis
- Standard deviation score for height and basal IGF-1
- Documentation of open epiphyses
- Age
- Dose

Age Restrictions
- 2 years to 18 years

Prescriber Restrictions
- Must be prescribed by a pediatric endocrinologist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
• Mechanism of action: Insulin-like growth factor-1 (IGF-1) is a key hormonal mediator on statural growth. Under normal circumstances, growth hormone (GH) binds to its receptor in the liver, and other tissues, and stimulates the synthesis/secretion of IGF-1. In target tissues, the Type 1 IGF-1 receptor, which is homologous to the insulin receptor, is activated by IGF-1, leading to intracellular signaling which stimulates multiple processes resulting in statural growth. The metabolic actions of IGF-1 are in part directed at stimulating the uptake of glucose, fatty acids, and amino acids so that metabolism supports growing tissues.

• Black Box Warning: None

Reference

Ingrezza™ (valbenazine)

FDA Approved Indication(s)
- For the treatment of adults with tardive dyskinesia

FDA Recommended Dose
- 40 mg orally once daily for one week, followed by 80 mg once daily
- Continuation of 40 mg once daily may be considered for some patients

How Supplied
- 40 mg capsules

Utilization Criteria
For initial review:
- Member must have a diagnosis of moderate to severe tardive dyskinesia, AND
- Member must have documented inadequate treatment response, intolerance, or contraindication to at least two of the following:
  - A benzodiazepine
  - A second generation antipsychotic
  - Tetrabenazine

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Member has documented congenital long QT syndrome or with arrhythmias associated with a prolonged QT interval, OR
- Member is concomitantly on a monoamine oxidase inhibitor (MAOI)

Required Medical Information
- Diagnosis
- Dose
- Therapeutic history

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- None

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: The mechanism of action of valbenazine in the treatment of tardive dyskinesia is unknown, but is thought to be mediated through the reversible inhibition of vesicular monoamine transporter 2 (VMAT2), a transporter that regulates monoamine uptake from the cytoplasm to the synaptic vesicle for storage and release.
- Valbenazine may prolong the QT interval, although the degree of QT prolongation is not clinically significant at concentrations expected with recommended dosing. For patients who are CYP2D6 poor metabolizers or are taking a strong CYP2D6 inhibitor, dose reduction may be necessary. For patients taking a strong CYP3A4 inhibitor, reduce the dose of valbenazine to 40 mg once daily.
Valbenazine should be avoided in patients with congenital long QT syndrome or with arrhythmias associated with a prolonged QT interval.

References

- Tarsy D. Tardive Dyskinesia: Prevention and Treatment. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. 2017.
Inlyta® (axitinib)

FDA Approved Indication(s)
- Advanced renal cell carcinoma after failure of one prior systemic therapy

FDA Recommended Dose
- 5 mg orally twice daily

How Supplied
- 1 mg and 5 mg tablets

Utilization Criteria

For initial review:
- Patient has a diagnosis of advanced renal cell carcinoma
- Patient has documented failure of ≥ one prior systemic therapy

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- None

Required Medical Information
- Diagnosis
- Age
- Dose
- Concurrent medications
- Treatment history

Age Restrictions
- 18 and over

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Axitinib has been shown to inhibit receptor tyrosine kinases including vascular endothelial growth factor receptors (VEGFR)-1, VEGFR-2, and VEGFR-3 at therapeutic plasma concentrations. These receptors are implicated in pathologic angiogenesis, tumor growth, and cancer progression. VEGF-mediated endothelial cell proliferation and survival were inhibited by axitinib in vitro and in mouse models. Axitinib was shown to inhibit tumor growth and phosphorylation of VEGFR-2 in tumor xenograft mouse models.

References
Intron A® (interferon alfa-2b)

FDA Approved Indication(s)
- For the treatment of hairy cell leukemia
- For the treatment of malignant melanoma in adult patients who are free of disease but are at high risk for systemic recurrence, within 56 days of surgery
- For the initial treatment of clinically aggressive Follicular Non-Hodgkin’s Lymphoma, in conjunction with anthracycline-containing combination chemotherapy in patients 18 years of age or older
- For the treatment of AIDS related Kaposi’s Sarcoma
- For intralesional treatment of selected patients 18 years of age or older with condylomata acuminata involving external surfaces of the genital and perianal areas
- For the treatment of chronic hepatitis C in patients 18 years of age or older with compensated liver disease who have a history of blood or blood-product exposure and/or are HCV antibody positive
- For the treatment of chronic hepatitis B in patients 1 year of age or older with compensated liver disease

FDA Recommended Dose
- **Hairy Cell Leukemia:** 2 million IU/m2 administered intramuscularly or subcutaneously 3 times a week for up to 6 months
  - Patients with platelet counts of less than 50,000/mm3 should not be administered Intron A® intramuscularly, but instead by subcutaneous administration
- **Malignant Melanoma:** 20 million IU/m2 as an intravenous infusion, over 20 minutes, 5 consecutive days per week, for 4 weeks; then 10 million IU/m2 as a subcutaneous injection three times per week for 48 weeks
- **Follicular Lymphoma:** 5 million IU subcutaneously three times per week for up to 18 months in conjunction with anthracycline-containing chemotherapy regimen and following completion of the chemotherapy regimen
- **AIDS related Kaposi’s Sarcoma:** 30 million IU/m2/dose administered subcutaneously or intramuscularly three times a week until disease progression or maximal response has been achieved after 16 weeks of treatment
- **Condylomata Acuminata:** 1.0 million IU per lesion in a maximum of 5 lesions in a single course. The lesions should be injected three times weekly on alternate days for 3 weeks. An additional course may be administered at 12 to 16 weeks
- **Chronic HCV:** 3 million IU three times a week administered subcutaneously or intramuscularly
- **Chronic HBV:** is 30 to 35 million IU per week, administered subcutaneously or intramuscularly, either as 5 million IU daily or as 10 million IU three times a week for 16 weeks
  - **Pediatric HBV:** 3 million IU/m2 three times a week for the first week of therapy followed by dose escalation to 6 million IU/m2 three times a week (maximum of 10 million IU three times weekly) administered subcutaneously for a total duration of 16 to 24 weeks

How Supplied
- 10 million IU, 18 million IU, and 50 million IU vials

Utilization Criteria

**For initial review:**
- Patient must have documentation of diagnosis of an FDA-approved indication, excluding hepatitis C
- For the diagnosis of condylomata acuminata, documented failure of, or intolerance to, traditional treatment modalities (e.g., podofilox, imiquimod, acid-therapy, or surgical options)
- For the diagnosis of chronic HBV, patients must have documented liver disease and hepatitis B viral replication
For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Patient has decompensated liver disease

Required Medical Information
- Diagnosis
- Age
- Dose
- Complete blood count with differential

Age Restrictions
- For diagnosis of hairy cell leukemia, malignant melanoma, follicular lymphoma, AIDS related Kaposi’s Sarcoma, and CML, patients must be >18 years of age
- For diagnosis of HBV, patient must be >1 year of age

Prescriber Restrictions
- Must be prescribed by an oncologist or infectious disease specialist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Interferons exert their cellular activities by binding to specific membrane receptors on the cell surface. Once bound to the cell membrane, interferons initiate a complex sequence of intracellular events.
- Black Box Warning: Alpha interferons may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders.

References

Last Reviewed January 28, 2019
Intravenous Iron (INFeD®, Dexferrum®, Ferrlecit®, Nulecit®, Venofer®, Feraheme®, Injectafer®)

FDA-Approved Products and Indications

- For the treatment of iron deficiency:

<table>
<thead>
<tr>
<th>Agent</th>
<th>Oral therapy is unsatisfactory or impossible</th>
<th>Anemia associated with CKD</th>
<th>Age restriction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron dexran (INFeD®, Dexferrum®)</td>
<td>x</td>
<td></td>
<td>≥ 4 months</td>
</tr>
<tr>
<td>Sodium ferric gluconate (Ferrlecit®, Nulecit®)</td>
<td></td>
<td>x (supplemental to ESA)</td>
<td>≥ 6 years</td>
</tr>
<tr>
<td>Iron sucrose (Venofer®)</td>
<td>x</td>
<td></td>
<td>≥ 2 years</td>
</tr>
<tr>
<td>Ferumoxytol (Feraheme®)</td>
<td>x</td>
<td></td>
<td>≥ 18 years</td>
</tr>
<tr>
<td>Ferric carboxymaltose (Injectafer®)</td>
<td>x</td>
<td></td>
<td>≥ 18 years</td>
</tr>
</tbody>
</table>

CKD = chronic kidney disease, ND = non-dialysis, HD = hemodialysis, PD = peritoneal dialysis, ESA = erythropoiesis-stimulating agent

FDA Recommended Dose and How Supplied

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose (iron replacement)</th>
<th>How Supplied (single-use vials)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron dexran (INFeD®, Dexferrum®)</td>
<td>Refer to package insert for equation</td>
<td>100 mg/2 mL, 50 mg/1 mL</td>
</tr>
<tr>
<td>Sodium ferric gluconate (Ferrlecit®, Nulecit®)</td>
<td>Adults: 125 mg/treatment x 8 sessions</td>
<td>62.5 mg/5 mL</td>
</tr>
<tr>
<td>Iron sucrose (Venofer®)</td>
<td>Adult ND: 200 mg/treatment on 5 different occasions over 14 d</td>
<td>200 mg/10 mL, 100 mg/5 mL, 50 mg/2.5 mL</td>
</tr>
<tr>
<td></td>
<td>HD: 100 mg/treatment x 8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PD: 3 doses – 300 mg day 1, 300 mg day 14, 400 mg day 28</td>
<td></td>
</tr>
<tr>
<td>Ferumoxytol (Feraheme®)</td>
<td>Two 510 mg doses: the first on day 1, the second 3-8 days later</td>
<td>510 mg/17 mL</td>
</tr>
<tr>
<td>Ferric carboxymaltose (Injectafer®)</td>
<td>≥50 kg: 750 mg separated by ≥7 d for total 1500 mg per course</td>
<td>750 mg/15 mL</td>
</tr>
<tr>
<td></td>
<td>&lt;50 kg: two 15 mg/kg doses separated by ≥7 d</td>
<td></td>
</tr>
</tbody>
</table>

- Iron replacement generally consists of administration of 1000 mg elemental iron over 2 to 3 weeks
- Iron maintenance dosing is generally 25 to 100 mg elemental iron every 1 to 2 weeks

Utilization Criteria

For initial review:

- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Anemia associated with CKD
  - The member must have anemia, defined by Hb < 13 g/dL in males and < 12 g/dL in females, AND
  - The member must have TSAT ≤ 30% and ferritin ≤ 500 ng/mL, AND
  - If ND patient, the member must have insufficient response to oral iron therapy
• Iron deficiency in whom oral therapy is unsatisfactory or impossible
  • The member must have iron deficiency confirmed by serum ferritin < 100 ng/mL or TSAT < 20%, AND
  • The member must have documentation of why oral therapy is unsatisfactory or impossible

For continuation:
• Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
• Product hypersensitivity

Required Medical Information
• Diagnosis
• Age
• Dose
• Iron indices (Hb, MCV, TSAT, ferritin)

Age Restrictions
• See “FDA-Approved Products and Indications”

Prescriber Restrictions
• Must be prescribed by a provider specialized in the disease being treated

Coverage Duration (months)
• 3

Quantity/Partial Fill Restrictions
• None

Other Information
• Anemia evaluation:
  • Evaluate whether or not a person is anemic by assessing Hb. Anemia indicated by Hb < 13 g/dL in males and < 12 g/dL in females.
  • Assess potential cause of anemia by evaluating mean corpuscular volume (MCV). If MCV low (< 80 fl), iron deficiency is a likely cause. If MCV is within normal range (80-100 fl), anemia could be due to a variety of causes such as an acute bleed, CKD, or malignancy. If MCV is elevated (> 100 fl), the cause is likely folate or B12 deficiency.
  • Assess whether a person may have multiple anemias by evaluating red blood cell distribution width (RDW). If the RDW is elevated (> 15%), it is likely more than one type of anemia present.

• Mechanism of action: Intravenous iron products are colloids that are taken up by macrophages in the reticuloendothelial system where their carbohydrate shell is metabolized, releasing iron. Iron, complexed with transferrin, is transported to erythroid precursor cells to be incorporated into hemoglobin as the cells mature into red blood cells.
• Black box warning for iron dextran and ferumoxytol (verbiage varies with each product):
  • Anaphylactic-type reactions, including fatalities, have followed the parenteral administration of iron dextran injection and ferumoxytol products. Initial symptoms may include hypotension, syncope, unresponsiveness, and cardiac/cardiorespiratory arrest.

References
Jakafi® (ruxolitinib)

FDA Approved Indication(s)

- For the treatment of patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis
- For treatment of patients with polycythemia vera who have had an inadequate response to or are intolerant to hydroxyurea
- For the treatment of patients with steroid-refractory acute graft-versus-host disease in patients 12 years and older

FDA Recommended Dose

- Myelofibrosis: starting dose based on platelet count

<table>
<thead>
<tr>
<th>Platelet Count</th>
<th>Starting Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 200 x 10⁹/L</td>
<td>20 mg orally twice daily</td>
</tr>
<tr>
<td>100 x 10⁹/L to 200 x 10⁹/L</td>
<td>15 mg orally twice daily</td>
</tr>
<tr>
<td>50 x 10⁹/L to &lt; 100 x 10⁹/L</td>
<td>5 mg orally twice daily</td>
</tr>
</tbody>
</table>

- Polycythemia vera: 10 mg twice daily
- Acute Graft Versus Host Disease: starting dose is 5 mg twice daily; may increase to 10 mg twice daily 3 days after initiating starting dose if ANC and platelet counts are not decreased by 50% more more from baseline
- Refer to prescribing information for dose modifications

How Supplied

- 5, 10, 15, 20, 25 mg tablets

Utilization Criteria

For initial review:

- Member must have a diagnosis of an FDA-approved indication, AND
- Member is not receiving concurrent tyrosine kinase inhibitor or immunomodulatory agents, AND
- For the treatment of polycythemia vera, member must have documentation of inadequate response or intolerance to hydroxyurea, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

For continuation:

- All
  - Symptom improvement
  - Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND

- Myelofibrosis
  - By week 24, member must have:
    - Documented reduction in spleen volume as measured by CT or MRI (or palpable spleen length), AND
    - Decrease in symptoms from baseline

- Acute Graft Versus Host Disease
  - By week 28, decrease in symptoms from baseline

- Annually: documentation must confirm that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider
Exclusion Criteria

- None

Required Medical Information

- Diagnosis
- Age
- Dose
- Complete blood count (CBC) and platelet count
- Acute Graft Versus Host Disease: ANC, total bilirubin

Age Restrictions

- 18 years of age and older

Prescriber Restrictions

- Must be prescribed by an oncologist or hematologist

Coverage Duration (months)

- 6 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions

- None

Other Information

- Mechanism of action: Ruxolitinib, a kinase inhibitor, inhibits Janus Associated Kinases (JAKs) JAK1 and JAK2 which mediate the signaling a number of cytokines and growth factors that are important for hematopoiesis and immune function.
- Black Box Warning: None

References


Juxtapid® (lomitapide)

FDA Approved Indication(s)

- For the treatment of homozygous familial hypercholesterolemia (HoFH) as an adjunct to a low-fat diet and other lipid-lowering treatments to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B and non-high-density lipoprotein cholesterol (non-HDL-C)

FDA Recommended Dose

- Initially, 5 mg one time daily with 2 weeks in between 1st dose and increase to 10 mg, followed by at least 4 weeks in between remaining increases, to 20 mg, 40 mg and finally, up to 60 mg daily
- In conjunction with daily supplements of vitamin E 400 international units along with at least 200 mg linoleic acid, 210 mg alpha-linolenic acid, 110 mg eicosapentaenoic acid and 80 mg docosahexaenoic acid

How Supplied
• 5 mg, 10 mg, 20 mg, 30 mg, 40 mg, 60 mg capsules in bottles of 28 count

**Utilization Criteria**

**For initial review:**

- Coverage may be granted for members who meet ALL criteria listed below:
  - Documented diagnosis of HoFH determined by:
    - Functional mutations in both LDL receptor alleles or alleles known to affect LDL receptor functionality, OR
    - Skin fibroblast LDL receptor activity less than 20% normal, OR
    - Untreated total cholesterol (TC) greater than 500 mg/dL and triglycerides (TG) less than 300 mg/dL or treated TC greater than 300 mg/dL, AND one of the following:
      - Tendon or cutaneous xanthomas at age 10 or younger
      - Both parents with diagnosis of definite FH by genetic analysis, Simon-Broom Diagnostic criteria, or Dutch Lipid Clinic Network criteria, OR
      - Both parents with documented untreated TC greater than 250 mg/dL, OR
      - Both parents with documented atherosclerotic cardiovascular disease (ASCVD)
  - Prior to initiation of treatment with Juxtapid, member is/was receiving at least one of the following treatment options listed below:
    - Liver transplant; OR
    - LDL apheresis; OR
    - Combination lipid-lowering regimen including the following for at least 3 months with an inadequate response†:
      - Maximally tolerated or maximum FDA-approved doses of high-intensity statin therapy (e.g., atorvastatin or rosuvastatin); AND
      - Non-Statin therapy (e.g., ezetimibe, fibrates, bile acid sequestrants, niacin, etc.); AND
      - Proprotein convertase subtilisin kexin 9 (PCSK9) inhibitor therapy (e.g., alirocumab or evolocumab)
    - Therapy is in conjunction with a low-fat diet (less than 20% of energy from fat)

† Inadequate response may be demonstrated by one of the following:

- Treated LDL greater than or equal to 100 mg/dL
- Treated LDL greater than or equal to 70 mg/dL with a history of one of the following:
  - Myocardial infarction (MI)
  - Coronary artery bypass graft (CABG) surgery
  - Significant coronary artery disease (CAD) or percutaneous transluminal coronary angioplasty (PTCA) with/without atherectomy or coronary stent placement
  - Significant angina pectoris with positive thallium or other heart scanning stress test
  - Predicted 10-year ASCVD risk greater than or equal to 7.5%
  - Peripheral artery disease defined as claudication with ankle-brachial index less than 0.85 or previous revascularization or amputation
  - Ischemic stroke or transient ischemic attack
  - Diabetes

For continuation:
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider
  • Minimum 40% reduction in LDL-C from baseline

Exclusions
  • Patient’s with hypercholesterolemia who do not have HoFH
  • Not used in combination with a PCSK9 inhibitor
  • Not used in combination with Kynamro® ( mipomersen)

Required Medical Information
  • Confirmed diagnosis
  • Therapeutic history
  • Fasting lipid panel
  • Liver function tests
  • Alkaline phosphatase
  • Total bilirubin
  • Serum creatinine
  • Negative pregnancy test for females of reproductive potential

Age Restrictions
  • 18 years of age and older

Prescriber Restrictions
  • Must be prescribed by a cardiologist, endocrinologist or lipid specialist authorized to participate in the Juxtapid Risk Evaluation and Mitigation Strategy (REMS) Program

Coverage Duration (months)
  • 12

Quantity/Partial Fill Restrictions
  • Initial: 6 months
  • Continuation: 12 months

Other Information
  • Mechanism of action: Juxtapid binds to and inhibits the microsomal triglyceride transfer protein (MTP), preventing the assembly of apo B-containing lipoproteins in enterocytes and hepatocytes. This prevents the synthesis of chylomicrons and VLDL. Preventing the synthesis of VLDL reduces levels of plasma LDL-C.
  • Black Box Warning: Risk of Hepatotoxicity
  • Simon-Broom Diagnostic Criteria – definite FH:
    • Total cholesterol levels > 290 mg/dL (7.5 mmol/L) or LDL-C > 190 mg/dL (4.9 mmol/L)
    • Tendon xanthomas, or tendon xanthomas in first or second degree relative
  • Dutch Lipid Clinic Network
    • Total score > 8

References
  • Juxtapid® [product insert]. Cambridge, MA. Aegerion Pharmaceuticals, Inc. December 2018

Last Reviewed June 12, 2019
# Kalbitor® (ecallantide)

## FDA Approved Indication(s)
- For the treatment of acute attacks of hereditary angioedema (HAE) in patients 16 years of age and older

## FDA Recommended Dose
- 30 mg (3 mL) administered subcutaneously in three 10 mg (1 mL) injections
- An additional 30 mg may be administered following 24 hours of initial dose and insufficient clinical improvement

## How Supplied
- Each carton contains three single-use 10 mg/1 mL vials

## Utilization Criteria

### For initial review:
- Patient must have documented diagnosis of HAE, as confirmed by serum complement factor testing or family history of HAE, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

## Exclusion Criteria
- Patient has a history of anaphylactic response to ecallantide administration

## Required Medical Information
- Diagnosis
- Concurrent medications
- Treatment history

## Age Restrictions
- Must be 16 years of age and older

## Prescriber Restrictions
- Must be prescribed by an allergist or hematologist

## Coverage Duration (months)
- 1 month

## Quantity/Partial Fill Restrictions
- Patient will be able to fill for 60 mg (6 mL) per authorization

## Other Information
- Black Box Warning: Anaphylaxis has been reported after administration of Kalbitor®. Because of the risk of anaphylaxis, Kalbitor® should only be administered by a healthcare professional with appropriate medical support to manage anaphylaxis and hereditary angioedema.

## References

*Last Reviewed November 10, 2015*
Kalydeco® (ivacaftor)

FDA Approved Indication(s)
- For the treatment of cystic fibrosis (CF) in patients age 2 years and older who have one mutation in the CFTR gene that is responsive to ivacaftor potentiation based on clinical and/or in vitro assay data
- If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

FDA Recommended Dose
- Adults and children ages 6 years and older:
  - One 150 mg tablet taken orally every 12 hours (300 mg total daily dose) with fat-containing food
- Pediatric patients ages 2 to less than 6 years:
  - Less than 14 kg: one 50 mg packet every 12 hours (100 mg/day)
  - 14 kg or greater: one 75 mg packet every 12 hours (150 mg/day)
- See package insert for dose modification recommendations

How Supplied
- 150 mg tablets
- 50 mg and 75 mg unit-dose packets of oral granules

Utilization Criteria
For initial review:
- Member must have a diagnosis of cystic fibrosis, AND
- Must have presence of a mutation in the CFTR gene that is responsive to ivacaftor, as detected by an FDA-cleared CF mutation test, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Documentation of homozygous F508del mutations in the CFTR gene

Required Medical Information
- Diagnosis
- Copy of mutational test results
- Age
- Weight
- Dose

Age Restrictions
- 2 years of age and older

Prescriber Restrictions
- Must be prescribed by a pulmonary specialist

Coverage Duration (months)
Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Ivacaftor is a potentiator of the CFTR protein. The CFTR protein is a chloride channel present at the surface of epithelial cells in multiple organs. Ivacaftor facilitates increased chloride transport by potentiating the channel-open probability (or gating) of the G551D-CFTR protein.
- Black Box Warning: None

References
Kevzara® (sarilumab)

FDA Approved Indication(s)
- For the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs).

FDA Recommended Dose
- 200 mg injected subcutaneously once every two weeks
- Dose reduction to 150 mg injected subcutaneously once every two weeks possible if patient experiences neutropenia, thrombocytopenia and elevated liver enzymes

How Supplied
- 150 mg/1.14 mL, and 200 mg/1.14 mL pre-filled syringes (available as packs of two syringes)

Utilization Criteria
For initial review:
- Member must have a documented diagnosis of moderately to severely active RA; AND
- Member must have tried and failed therapy with at least one non-biologic DMARD including methotrexate (e.g. sulfasalazine, leflunomide, hydroxychloroquine); AND
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable

For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Member must have documentation of treatment response, as verified per progress notes

Exclusion Criteria
- Member is on concomitant therapy with another biologic medication
- Member is on long term concomitant therapy with corticosteroids
- Member has an active infection

Required Medical Information
- Diagnosis
- Current medication list
- Therapeutic history

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a rheumatologist

Coverage Duration (months)
- 12 months

Quantity/Partial Fill Restrictions
- Maximum of two pre-filled syringes per 28 days

Other Information
- Sarilumab may be used as monotherapy or in combination with a conventional DMARD such as methotrexate.
• Sarilumab is a human recombinant monoclonal antibody of the IgG1 subclass that binds to the IL-6 receptor.

References

Kineret® (anakinra)

FDA Approved Indication(s)
- Active rheumatoid arthritis (RA)
- Cryopyrin-Associated Periodic Syndromes (CAPS)

FDA Recommended Dose
- Rheumatoid Arthritis
  - 100 mg subcutaneously per day
- Cryopyrin-Associated Periodic Syndromes
  - 1-2 mg/kg subcutaneously per day

How Supplied
- 100 mg/0.67 mL pre-filled glass syringes

Utilization Criteria
For initial review:
- Patient has a negative TB test, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- RA
  - A treatment course of methotrexate was ineffective after at least a 6-12 week treatment course unless contraindicated or not tolerated
- Cryopyrin-Associated Periodic Syndromes
  - Treatment with at least one oral systemic agent (i.e., methotrexate, glucocorticoids) was ineffective or not tolerated

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Patient is receiving concurrent biologic DMARD therapy

Required Medical Information
- Diagnosis
- Age
- Dose
- Weight (if for Cryopyrin-Associated Periodic Syndromes)
- Renal function (CrCl)

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a rheumatologist or autoimmune specialist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
Mechanism of action: Anakinra blocks the biologic activity of IL-1 alpha and beta by competitively inhibiting IL-1 binding to the interleukin-1 type I receptor (IL-1RI), which is expressed in a wide variety of tissues and organs.

References

# Kisqali® (ribociclib)

## FDA Approved Indication(s)
- For the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer, in combination with an aromatase inhibitor

## FDA Recommended Dose
- 600 mg (three 200 mg tablets) by mouth, once daily for 21 consecutive days followed by 7 days off treatment; resulting in a complete cycle of 28 days
- Letrozole 2.5 mg should be taken once daily throughout the 28-day cycle

## How Supplied
- 200 mg film-coated tablets
  - Blister pack (21 tablets) – each blister pack contains 21 tablets (3 blister packs/ container)
  - Blister pack (14 tablets) – each blister pack contains 14 tablets (3 blister packs/ container)
  - Blister pack (21 tablets) – each blister pack contains 21 tablets (1 blister pack/ container)

## Utilization Criteria
**For initial review:**
- Member must have a documented diagnosis of HR-positive, HER2-negative advanced or metastatic breast cancer; AND
- Member must be postmenopausal; AND
- Must be used in combination with an aromatase inhibitor; AND
- Review of an ECG must be documented in the member’s submitted chart note

**For continuation:**
- Member must have documentation of treatment response, as verified per progress notes

## Exclusion Criteria
- N/A

## Required Medical Information
- Diagnosis
- Current medication list
- Therapeutic history

## Age Restrictions
- 18 years of age and older

## Prescriber Restrictions
- Must be prescribed by an oncologist

## Coverage Duration (months)
- 3 months initially; 6 months for continuation

## Quantity/Partial Fill Restrictions
- Maximum of 63 tablets per 28 day period

## Other Information
- **MOA:** Ribociclib is an inhibitor of cyclin-dependent kinase (CDK) 4 and 6. These kinases are activated upon binding to D-cyclins and play a crucial role in signaling pathways which lead to cell cycle progression and cellular proliferation. The cyclin D-CDK4/6 complex regulates cell cycle progression through phosphorylation of the retinoblastoma protein (pRb).
• NCCN currently has Kisqali + letrozole as a category 1 option in patients who are postmenopausal, and who have no prior endocrine therapy within the past year.

References

• Kisqali® (ribociclib) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2017.
## Krystexxa® (pegloticase)

### FDA Approved Indication(s)
- Treatment of chronic gout in adult patients refractory to conventional therapy

### FDA Recommended Dose
- 8 mg (uricase protein) given as an intravenous infusion every two weeks.

### How Supplied
- Single-use vial with 8 mg of uricase protein in 1 mL

### Utilization Criteria

**For initial review:**
- Presence of symptomatic gout with one or more of the following:
  - Three gouty flares in previous 18 months
  - Presence of 1 or more tophi
  - Chronic gouty arthritis
  - Baseline serum uric acid level ≥ 8 mg/dL
- Member has tried and failed or is intolerant to allopurinol and febuxostat, OR
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

**For continuation:**
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

### Exclusion Criteria
- Asymptomatic hyperuricemia
- G6PD deficiency

### Required Medical Information
- Diagnosis
- Age
- Dose

### Age Restrictions
- 18 and over

### Prescriber Restrictions
- N/A

### Coverage Duration (months)
- 12

### Quantity/Partial Fill Restrictions
- None

### Other Information
- Mechanism of action: Pegloticase is a uric acid specific enzyme which is a recombinant uricase and achieves its therapeutic effect by catalyzing the oxidation of uric acid to allantoin, thereby lowering serum uric acid. Allantoin is an inert and water soluble purine metabolite. It is readily eliminated, primarily by renal excretion.
- Black Box Warning: Anaphylaxis and infusion reactions

### References
# Lemtrada™ (alemtuzumab)

## FDA Approved Indication(s)
- For the treatment of patients with relapsing forms of multiple sclerosis (MS) who have had an inadequate response to two or more drugs indicated for the treatment of MS

## FDA Recommended Dose
- First Treatment Course: 12 mg/day on 5 consecutive days (60 mg total dose)
- Second Treatment Course: 12 mg/day on 3 consecutive days (36 mg total dose) administered 12 months after the first treatment course

## How Supplied
- Single-use vial that delivers 12 mg/1.2 mL (10 mg/mL)

## Utilization Criteria

**For initial review:**
- Member has a diagnosis of relapsing multiple sclerosis, AND
- Member must have documented failure of, or intolerance to, 2 or more of their plan’s preferred product(s), as applicable, AND
- CBC with differential, serum creatinine, urinalysis with urine cell count, and test of thyroid function (TSH) collected prior to treatment, AND
- Baseline skin exam for melanoma prior to treatment, AND
- Requirements of REMS program are met

**For continuation:**
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

## Exclusion Criteria
- HIV infection
- Diagnosis of chronic-progressive MS

## Required Medical Information
- Diagnosis
- Age
- Dose
- Treatment history
- Pertinent labs

## Age Restrictions
- 18 years of age and older

## Prescriber Restrictions
- Must be prescribed by a neurologist

## Coverage Duration (months)
- 12 months

## Quantity/Partial Fill Restrictions
- None

## Other Information
- Mechanism of action: The precise mechanism by which alemtuzumab exerts its effects in MS is unknown but is presumed to involve binding to CD52, a cell surface antigen present on T and B
lymphocytes, natural killer cells, monocytes, and macrophages. Following cell surface binding to T and B lymphocytes, alemtuzumab results in antibody-dependent cellular cytolysis and complement-mediated lysis

- Black box warning:
  - Autoimmunity: causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease.
  - Infusion reactions: must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions
  - Malignancies: increased risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders

References


Last Reviewed October 19, 2018
**Lenvima® (lenvatinib)†**

### FDA Approved Indication(s)
- For the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC)
- For the treatment of patients with advanced renal cell carcinoma (RCC), in combination with everolimus, following one prior anti-angiogenic therapy
- For the first-line treatment of patients with unresectable hepatocellular carcinoma (HCC).

### FDA Recommended Dose
- **DTC**: 24mg orally once daily
- **RCC**: 18mg orally once daily, in combination with everolimus 5mg orally once daily
- **HCC**: 12mg orally once daily for patients ≥ 60kg, 8mg orally once daily for patients < 60kg
- See package insert for dose modifications due to adverse reactions or renal/hepatic impairment

### How Supplied
- Capsules: 4mg and 10mg
- All capsules are supplied in cartons of 6 cards. Each card is a 5-day supply blister pack.

<table>
<thead>
<tr>
<th>Total Dose</th>
<th>Combination of Capsule Strengths</th>
</tr>
</thead>
<tbody>
<tr>
<td>24mg</td>
<td>Ten 10mg capsules and five 4mg capsules in each card</td>
</tr>
<tr>
<td>20mg</td>
<td>Ten 10mg capsules in each card</td>
</tr>
<tr>
<td>18mg</td>
<td>Five 10mg capsules and ten 4mg capsules in each card</td>
</tr>
<tr>
<td>14mg</td>
<td>Five 10mg capsules and five 4mg capsules in each card</td>
</tr>
<tr>
<td>12mg</td>
<td>Fifteen 4mg capsules in each card</td>
</tr>
<tr>
<td>10mg</td>
<td>Five 10mg capsules in each card</td>
</tr>
<tr>
<td>8mg</td>
<td>Ten 4mg capsules in each card</td>
</tr>
<tr>
<td>4mg</td>
<td>Five 4mg capsules in each card</td>
</tr>
</tbody>
</table>

### Utilization Criteria

**For initial review:**
- Member must documentation of a diagnosis consistent with an FDA-approved indication, AND
- **DTC**: Member must have documentation of iodine-refractory disease
- **RCC**: Member must have documentation of prior anti-angiogenic therapy, AND
  - Treatment plan must include everolimus

**For continuation:**
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

### Exclusion Criteria
- Uncontrolled hypertension
- Pregnancy

### Required Medical Information
Diagnosis
• Age
• Treatment history
• Dose
• Baseline lab work, including CBC, CMP, liver function tests, and TSH as appropriate

Age Restrictions
• 18 years of age and older

Prescriber Restrictions
• Must be prescribed by an oncologist

Coverage Duration (months)
• 3 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions
• None

Other Information
• Mechanism of action: Lenvatinib is a kinase inhibitor that inhibits the kinase activities of vascular endothelial growth factor (VEGF) receptors VEGFR1 (FLT1), VEGFR2 (KDR), and VEGFR3 (FLT4). Lenvatinib inhibits other kinases that have been implicated in pathogenic angiogenesis, tumor growth, and cancer progression in addition to their normal cellular functions, including fibroblast growth factor (FGF) receptors FGFR1, 2, 3, and 4; platelet derived growth factor receptor alpha (PDGFRα), KIT, and RET. Lenvatinib also exhibits antiproliferative activity in hepatocellular carcinoma cell lines dependent on activated FGFR signaling with a concurrent inhibition of FGF-receptor substrate 2α (FRS2α) phosphorylation.
• Warnings and Precautions: Serious complications of poorly controlled hypertension have been reported. Control blood pressure prior to initiating therapy. Monitor blood pressure after 1 week, then every 2 weeks for the first 2 months, and then at least monthly thereafter during treatment. Monitor patients for clinical symptoms or signs of cardiac dysfunction. Monitor and correct electrolyte abnormalities at baseline and periodically during treatment. Monitor liver function prior to initiating lenvatinib, then every 2 weeks for the first 2 months, and at least monthly thereafter during treatment. Monitor for proteinuria prior to initiating therapy and periodically during treatment, and initiate prompt management of diarrhea or dehydration/hypovolemia.

References
• Lenvima® [package insert]. Woodcliff Lake, NJ; Eisai Inc.; August 2018.
Letairis® (ambrisentan)

FDA Approved Indication(s)
- For the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability and delay clinical worsening

FDA Recommended Dose
- 5 mg orally, once daily; may increase to 10 mg orally once daily as tolerated

How Supplied
- 5 mg and 10 mg tablets

Utilization Criteria
For initial review:
- Patient must have a confirmed diagnosis of pulmonary arterial hypertension (WHO Group 1) with WHO class II or III symptoms (i.e., comfortable at rest but symptomatic with routine, or less than ordinary, physical activity)
- Patient must have tried and failed a calcium channel blocker therapy
- Patient must have tried and failed, or have a contraindication to, a short acting vasodilator (i.e., sildenafil), OR
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Pregnancy

Required Medical Information
- Diagnosis
- Age
- Dose
- Sex
- Baseline liver function tests (ALT, AST, bilirubin)

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a pulmonologist or cardiologist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Letairis® is an endothelin receptor antagonist. In patients with PAH, serum endothelin concentrations are increased and correlate with increased mean right atrial pressure and disease severity.
- Black Box Warning: Pregnancy Category X; embryo-fetal toxicity
References

- Hopkins W, Rubin L. “Treatment of Pulmonary Hypertension in Adults.” In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2013.
### Leukine® (sargramostim)

#### FDA Approved Indication(s)
- For use following induction chemotherapy in older adult patients with acute myelogenous leukemia (AML) to shorten time to neutrophil recovery and to reduce the incidence of severe and life-threatening infections and infections resulting in death
- For the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis
- For acceleration of myeloid recovery in patients with non-Hodgkin’s lymphoma (NHL), acute lymphoblastic leukemia (ALL) and Hodgkin’s disease undergoing autologous bone marrow transplantation (BMT)
- For acceleration of myeloid recovery in patients undergoing allogeneic BMT from HLA-matched related donors
- Indicated in patients who have undergone allogeneic or autologous bone marrow transplantation (BMT) in whom engraftment is delayed or has failed

#### FDA Recommended Dose
- 250 mcg/m²/day administered IV or SC depending on use; duration also depends on use; see package insert

#### How Supplied
- 250 mcg lyophilized vial
- 500 mcg/mL multi-use vial

#### Utilization Criteria

**For initial review:**
- Member must have one of the listed FDA approved indications, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

**For continuation:**
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

#### Exclusion Criteria
- Excessive leukemic myeloid blasts in bone marrow or peripheral blood (>= 10%)
- Concomitant use with chemotherapy or radiotherapy

#### Required Medical Information
- Diagnosis
- WBC with differential
- ANC
- Age
- Dose

#### Age Restrictions
- None

#### Prescriber Restrictions
- Must be prescribed by an oncologist or hematologist

#### Coverage Duration (months)
Lorbrena® (lorlatinib)

FDA Approved Indication(s)
- Treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) whose disease progressed while treated with:
  - Crizotinib and at least one other ALK inhibitor for metastatic disease, OR
  - Alectinib as first ALK inhibitor therapy for metastatic disease, OR
  - Ceritinib as first ALK inhibitor therapy for metastatic disease

FDA Recommended Dose
- 100 mg one time daily until disease progression or unacceptable toxicity

How Supplied
- 25 mg tablet as 30-count bottle
- 100 mg tablet as 30-count bottle

Utilization Criteria
For initial review:
- Member has confirmed diagnosis of ALK-positive metastatic NSCLC, AND
  - Previous treatment with crizotinib and one other ALK inhibitor for metastatic disease, OR
  - Previous treatment with alectinib, OR
  - Previous treatment with ceritinib

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- None

Required Medical Information
- Diagnosis
- Age
- Dose
- Concurrent medication
- Treatment history
- Serum cholesterol and triglycerides, ECG

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a hematologist or oncologist
## Coverage Duration (months)
- Initial: 3 months
- Maintenance: 12 months

## Quantity/Partial Fill Restrictions
- 15-day supply first six fills

## Other Information
- Mechanism of action: lorlatinib is a kinase inhibitor with in vitro activity against ALK and ROS1, along with TYK1, FER, FPS, TRKA, TRKB, TRKC, FAK, FAK2 and ACK. Mice implanted with tumors containing EML4 fusions with ALK variant 1 or ALK mutations that included G1202R and I1171T mutations, lorlatinib demonstrated anti-tumor activity.
- Black Box Warning: None

## References
**Lucentis® (ranibizumab)**

**FDA Approved Indication(s)**
- Neurovascular age-related macular degeneration (AMD)
- Macular edema following ocular vein occlusion (RVO)
- Diabetic Macular Edema (DME)
- Diabetic Retinopathy (DR)
- Myopic Choroidal Neovascularization (mCNV)

**FDA Recommended Dose**
- AMD: 0.5 mg (0.05 mL of 10 mg/ml solution) is recommended to be administered by intravitreal injection once a month
- RVO: 0.5 mg (0.05 mL of 10 mg/ml solution) is recommended to be administered by intravitreal injection once a month
- DME and DR: 0.3 mg (0.05 mL of 6 mg/mL solution) is recommended to be administered by intravitreal injection once a month
- mCNV: 0.5 mg (0.05 mL of 10 mg/mL solution) is recommended to initially be administered by intravitreal injection once a month for up to 3 months

**How Supplied**
- 0.5 mg carton contains a single-use, 2-cc vial designed to deliver 0.05 mL of 10 mg/mL ranibizumab
- 0.3 mg carton contains a single-use, 2-cc vial designed to deliver 0.05 mL of 6 mg/mL ranibizumab

**Utilization Criteria**
*For initial review:*
- Patient is diagnosed with an FDA approved indication
- For AMD, RVODME, DR and mCNV: Must be intolerant to or failed treatment with bevacizumab, OR
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

*For continuation:*
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Patients with ocular or periocular infections
- Hypersensitivity to ranibizumab

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Past treatment history

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an ophthalmologist or optometrist

**Coverage Duration (months)**
- 12 months

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: binds to the receptor binding site of active forms of VEGF-A, including the biologically active, cleaved form of this molecule, VEGF110. VEGF-A has been shown to cause neovascularization and leakage in models of ocular angiogenesis and vascular occlusion and is thought to contribute to pathophysiology of neovascular AMD, macular edema following RVO, and DME
- Black box warning: none

**References**
Lupron Depot®/Eligard® (leuprolide acetate)

FDA Approved Indication(s)
- Palliative treatment of advanced prostate cancer
- Endometriosis (Lupron Depot® only)
- Uterine Leiomyoma (fibroids) (Lupron Depot® only)
- Central Precocious Puberty (CPP) (Lupron Depot-Ped® only)

FDA Recommended Dose
- Prostate cancer
  - 7.5 mg every 4 weeks, OR
  - 22.5 mg every 12 weeks, OR
  - 30 mg every 16 weeks, OR
  - 45 mg every 24 weeks
- Endometriosis
  - 3.75 mg (1 month)
  - 11.25 mg (3 month)
- Fibroids
  - 3.75 mg (1 month)
  - 11.25 mg (3 month)
- CPP (Lupron Depot-Ped®)
  - 1 month kit (7.5, 11.25, 15 mg)
  - 3 month kit (11.25, 30 mg)

How Supplied
- 3.75, 7.5, 15, 22.5, 30 and 45mg injectable suspension
- 1 mg/0.2 mL 2.8 mL multi-dose vial (solution)

Utilization Criteria

For initial review:
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Lupron Depot® and Eligard®
  - Advanced Prostate Carcinoma
    - Being used for the palliative treatment of advanced prostate cancer
- Lupron Depot®
  - Endometriosis
    - Diagnosis of endometriosis, AND
    - Documented treatment failure of three to six month course of analgesics and oral contraceptives, AND
    - ≥ 18 years of age
- Uterine Leiomyoma (fibroids)
  - Being used to treat anemia caused by uterine leiomyoma, AND
  - Patient has not responded to iron therapy, AND
  - Being used prior to surgery, OR
  - Being used prior to surgery to reduce the size of fibroids to facilitate the surgical procedure
- Central Precocious Puberty (Lupron Depot-Ped®)
- Clinical diagnosis of CPP with onset of secondary sexual characteristics earlier than 8 years in females and 9 years in males, AND
- Diagnosis confirmed by pubertal response to GnRH stimulation test or bone age advanced one year beyond chronological age
- Ovarian suppression in premenopausal women diagnosed with breast cancer
  - Diagnosis of breast cancer, AND
  - Being used for ovarian suppression in women who are premenopausal at diagnosis, AND
  - Dosing is once monthly
- Gender Dysphoria in Adolescents
  - The member meets DSM-V or ICD-10 criteria for the diagnosis of gender identity disorder, AND
  - The adolescent has experienced puberty to at least Tanner stage 2, AND
  - Documentation that the adolescent has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed), AND
  - Any co-existing psychological, medical, or social problems that could interfere with treatment have been addressed and member has adequate psychological and social support for treatment, AND
  - Member has given informed consent to begin treatment
  - If the adolescent has not reached the age of medical consent, the parent(s)/legal guardian(s) have consented to the treatment, AND
  - Prescriber is an endocrinologist

For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Pregnancy, OR
- Breast feeding, OR
- Undiagnosed abnormal vaginal bleeding

Required Medical Information
- Diagnosis
- Age
- Dose
- Treatment history

Age Restrictions
- 2-12 for central precocious puberty18 and over for other diagnoses

Prescriber Restrictions
- Must be prescribed by an oncologist, endocrinologist, gynecologist, or pediatric specialist

Coverage Duration (months)
- 3 for uterine leiomyomata
- 6 for endometriosis
- 12 for prostate cancer, CPP, breast cancer, and gender dysphoria
Quantity/Partial Fill Restrictions

- None

Other Information

- Mechanism of action: Leuprolide acetate, a gonadotropin releasing hormone (GnRH) agonist, acts as a potent inhibitor of gonadotropin secretion when given continuously in therapeutic doses.
- The use of leuprolide for ovarian suppression is recognized in the NCCN treatment guidelines for breast cancer in women who are premenopausal at diagnosis. Leuprolide should be given as monthly injections as the 3-month depots do not reliably suppress estrogen levels in all patients.

References

- World Professional Association for Transgender Health. Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People. V7. Available at www.wpath.org

Last Reviewed August 14, 2017
**Luxturna® (voretigene neparvovec-rzyl)†**

### FDA Approved Indication(s)
- For the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy. Patients must have viable retinal cells as determined by the treating physician(s).

### FDA Recommended Dose
- The recommended dose for each eye is $1.5 \times 10^{11}$ vector genomes (vg), administered by subretinal injection in a total volume of 0.3 mL.
- Perform subretinal administration to each eye on separate days within a close interval, but no fewer than 6 days apart. See prescribing information for complete details on administration.
- Systemic oral corticosteroids equivalent to prednisone at 1 mg/kg/day (maximum of 40 mg/day) for a total of 7 days (starting 3 days before administration of voretigene neparvovec-rzyl to the first eye), followed by tapering the dose during the following 10 days. The same corticosteroid dosing regimen applies for the administration to the second eye. If the corticosteroid taper following administration to the first eye is not complete three days prior to the planned administration to the second eye, then the corticosteroid regimen for the second eye replaces the taper for the first eye.

### How Supplied
- 0.5 mL extractable volume in a 2 mL single dose vial at a concentration of $5 \times 10^{12}$ vg/mL
- Diluent supplied in two single-use 2 mL vials

### Utilization Criteria
**For initial review:**
- Member must have documentation of an FDA-approved indication, AND
- Genetic testing documenting biallelic mutations of the RPE65 gene, as determined by an FDA-approved test, AND
- Sufficient viable retinal cells as determined by optical coherence tomography (OCT) and/or ophthalmoscopy:
  - An area of retina within the posterior pole of $>100 \mu$m thickness shown on OCT, OR
  - $\geq 3$ disc areas of retina without atrophy or pigmentary degeneration within the posterior pole, OR
  - Remaining visual field within 30 degrees of fixation as measured by a III4e isopter or equivalent, AND
- Member has not previously received RPE65 gene therapy in eye(s) to be treated

### Exclusion Criteria
- Pregnancy
- Intraocular surgery within the past 6 months

### Required Medical Information
- Diagnosis
- Age
- Therapeutic history
- Treatment and monitoring plan

### Age Restrictions
- 12 months of age and older

### Prescriber Restrictions
- Must be prescribed by an ophthalmologist or retinologist

### Coverage Duration (months)
- 1
Quantity/Partial Fill Restrictions

- Limit 1 injection per eye per lifetime

Other Information

- Mechanism of action: Voretigene neparvovec-rzyl is a suspension of an adeno-associated virus vector-based gene therapy designed to deliver a normal copy of the gene encoding the human retinal pigment epithelial 65 kDa protein (RPE65) to cells of the retina in persons with reduced or absent levels of biologically active RPE65.

- Warnings and Precautions: Endophthalmitis may occur following any intraocular surgical procedure or injection. Permanent decline in visual acuity, retinal abnormalities, and increased intraocular pressure may occur after subretinal injection of voretigene neparvovec-rzyl. Following the injection, monitor patients to permit early detection and treatment.

- Instruct patients to avoid air travel, travel to high elevations or scuba diving until the air bubble formed following administration has completely dissipated from the eye. A change in altitude while the air bubble is still present can result in irreversible vision loss. Verify the dissipation of the air bubble through ophthalmic examination.

References


Last Reviewed October 24, 2018
# Makena® (hydroxyprogesterone caproate)

## FDA-Approved Indication(s)
- To reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth

## FDA-Recommended Dose
- **Autoinjector:** 275 mg subcutaneously once weekly
- **Single- and multi-dose vials:** 250 mg intramuscularly once weekly
- To be administered by a healthcare provider
- Begin treatment between 16 weeks, 0 days and 20 weeks, 6 days of gestation
- Continue administration once weekly through 36 weeks, 6 days of gestation or delivery

## How Supplied
- **Subcutaneous injection:**
  - 275 mg/1.1 mL single-use auto-injector
- **Intramuscular injection:**
  - 250 mg/mL single-dose vials
  - 1250 mg/5 mL (250 mg/mL) multiple-dose vials

## Utilization Criteria
### For initial review:
- Member must have a history of singleton spontaneous preterm birth (before 37 weeks gestation), AND
- There is a confirmed singleton pregnancy with gestational age between 16 weeks 0 days and 20 weeks 6 days

## Exclusion Criteria
- Current or history of thrombosis or thromboembolic disorders
- Known or suspected breast cancer, other hormone-sensitive cancer, or history of these conditions
- Undiagnosed abnormal vaginal bleeding unrelated to pregnancy
- Cholestatic jaundice of pregnancy
- Liver tumors, benign or malignant, or active liver disease
- Uncontrolled hypertension
- Multiple gestations

## Required Medical Information
- Diagnosis
- Age
- Dose

## Age Restrictions
- Must be 16 years of age or older

## Prescriber Restrictions
- Must be prescribed by an OB/GYN

## Coverage Duration (months)
- 5

## Quantity/ Partial Fill Restrictions
- None

## Other Information
Mechanism of action: Hydroxyprogesterone caproate is a synthetic progestin. The mechanism by which hydroxyprogesterone caproate reduces the risk of recurrent preterm birth is not known.

Black Box Warning: None

References

- Robinson J. Risk factors for preterm labor and delivery. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. 2018.
Mavyret® (glecaprevir/pibrentasvir)

FDA-Approved Indication(s)

- For the treatment of:
  - Adult patients with chronic hepatitis C (HCV) genotypes 1–6 without cirrhosis or with compensated cirrhosis (Child-Pugh A)
  - Adult patients with HCV genotype 1 who have previously been treated with a regimen containing an HCV NS5A or an NS3/4A inhibitor, but not both

FDA-Recommended Dose

- Three tablets by mouth once daily

<table>
<thead>
<tr>
<th>HCV Genotype</th>
<th>Treatment History</th>
<th>Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No Cirrhosis</td>
</tr>
<tr>
<td>1,2,3,4,5, or 6</td>
<td>Naïve</td>
<td>8 weeks</td>
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<tr>
<td>1</td>
<td>NS5A inhibitor without prior treatment with an NS3/4A protease inhibitor</td>
<td>16 weeks</td>
</tr>
<tr>
<td></td>
<td>NS3/4A protease inhibitor without prior treatment with an NS5A inhibitor</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1,2,4,5 or 6</td>
<td>Interferon, ribavirin, and/or sofosbuvir</td>
<td>8 weeks</td>
</tr>
<tr>
<td>3</td>
<td>Interferon, ribavirin, and/or sofosbuvir</td>
<td>16 weeks</td>
</tr>
</tbody>
</table>

Compensated Cirrhosis (Child-Pugh A)

- 16 weeks

How Supplied

- Supplied as a 4-week or 8-week carton containing weekly cartons of seven daily-dose wallets

Utilization Criteria

For initial review:

- Member must have a diagnosis of chronic HCV with documented genotype and viral load collected within the previous three months, AND
- Physician must attest to the member’s ability and dedication to remain adherent to the entire course of therapy, AND
- Physician must confirm that alcohol and illicit substance abuse is absent for the previous six months, or member is currently seeing an addiction specialist, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

Exclusion Criteria

- Acute HCV infection that is known to have occurred within the previous six months, OR
- Coverage may be revoked if member is non-adherent through the first two months of therapy, as evidenced by claim records or verbal confirmation of poor adherence

Required Medical Information

- Dose and duration of therapy
- HCV genotype and subtype
- HCV treatment history
- Baseline ALT

**Age Restrictions**
- 18 years of age or older

**Prescriber Restrictions**
- Must be prescribed by a gastroenterologist, hepatologist, or infectious disease specialist

**Coverage Duration (months)**
- 8 weeks to 16 weeks

**Quantity/Partial-Fill Restrictions**
- 28 days supply

**Other Information**
- Mechanism of action: Glecaprevir inhibits NS3/4A, pibrentasvir inhibits NS5A
- It is generally well tolerated but attention is required to avoid drug interactions.

**References**
Mekinist® (trametinib)

FDA Approved Indication(s)

- Indicated as a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test
- Indicated in combination with dabrafenib for:
  - The treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test
  - The adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection
  - The treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test
  - The treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options

FDA Recommended Dose

- 2 mg orally once daily, taken at least 1 hour before or 2 hours after a meal

How Supplied

- 0.5 mg and 2 mg tablets

Utilization Criteria

For initial review:

Unresectable or Metastatic Melanoma:
- Member must have documentation of BRAF V600E mutation, as detected by an FDA-approved test, AND
  - Medication is being used as a single agent, OR
- Member has documentation of BRAF V600E or V600K mutation, as detected by an FDA-approved test, AND
  - Medication is being used in combination with dabrafenib

Resectable Melanoma:
- Member must have documentation of BRAF V600E or V600K mutation, as detected by an FDA-approved test, AND
- Documentation of lymph node involvement, AND
- Medication is being used as adjuvant treatment after complete resection in combination with dabrafenib

NSCLC:
- Member must have documentation of BRAF V600E mutation, as detected by an FDA-approved test, AND
- Medication is being used in combination with dabrafenib

Locally Advanced or Metastatic ATC:
- Member has documentation of BRAF V600E mutation, as detected by an FDA-approved test, AND
- Medication is being used in combination with dabrafenib, AND
- Prescriber confirms no satisfactory locoregional treatment options are available

For continuation:
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria

• Previous treatment with vemurafenib or dabrafenib

Required Medical Information

• Diagnosis
  • Age
  • Dose
  • Concurrent medications
  • BRAF V600E or V600K mutation status

Age Restrictions

• 18 years of age and older

Prescriber Restrictions

• Must be prescribed by an oncologist

Coverage Duration (months)

• 3 months (initial), 12 months continuation

Quantity/Partial Fill Restrictions

• 30 day supply – no split fill
• Must not remove from original packaging

Other Information

• Mechanism of action: reversible inhibition of mitogen-activated extracellular signal regulated kinase 1 (MEK1) and MEK2 activation and of MEK1 and MEK2 kinase activity
• Warnings and precautions: New primary cutaneous and non-cutaneous malignancies, hemorrhage, colitis and gastrointestinal perforation, venous thromboembolism, cardiomyopathy, ocular toxicities, interstitial lung disease, serious febrile reactions, and serious skin toxicity can occur when dabrafenib is administered as a single agent or when used with dabrafenib.

References


Last Reviewed June 18, 2018
Myobloc® (rimabotulinumtoxinb)

FDA Approved Indication(s)
- For the treatment of adults with cervical dystonia to reduce the severity of abnormal head position and neck pain associated with cervical dystonia

FDA Recommended Dose
- 2,500 to 5,000 Units divided among affected muscles
- Dose should be tailored to an individual’s response

How Supplied
- 2,500 Units/0.5 mL, 5,000 Units/1 mL, and 10,000 Units/2 mL glass vials
- 5,000 Units/3.5 mL single-use glass vial

Utilization Criteria
For initial review:
- Patient has a confirmed diagnosis of cervical dystonia, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Off-label use

Required Medical Information
- Diagnosis
- Age
- Dose

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a neurologist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: RimabotulinumtoxinB is a neurotoxin that acts at the neuromuscular junction to produce flaccid paralysis
- Black Box Warning: All botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects

References

Last Reviewed November 9, 2015
<table>
<thead>
<tr>
<th><strong>Nerlynx™ (neratinib)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDA Approved Indication</strong></td>
</tr>
<tr>
<td>• For the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer with node positive disease, following adjuvant trastuzumab-based therapy</td>
</tr>
<tr>
<td><strong>FDA Recommended Dose</strong></td>
</tr>
<tr>
<td>• 240 mg orally (6 tablets) once daily with food.</td>
</tr>
<tr>
<td>• Hepatic impairment: recommended starting dose of 80 mg in patients with severe hepatic impairment (Child Pugh C)</td>
</tr>
<tr>
<td><strong>How Supplied</strong></td>
</tr>
<tr>
<td>• 40 mg tablets</td>
</tr>
<tr>
<td><strong>Utilization Criteria</strong></td>
</tr>
<tr>
<td><em>For initial review:</em></td>
</tr>
<tr>
<td>• Member must have documentation of HER2 overexpression, as detected by an FDA-approved test, AND</td>
</tr>
<tr>
<td>• Member must have been treated for early breast cancer with standard of care duration of trastuzumab within previous 2 years, AND</td>
</tr>
<tr>
<td>• Member must have appropriate antidiarrheal prophylaxis and monitoring in place, as indicated in treatment plan</td>
</tr>
<tr>
<td><em>For continuation:</em></td>
</tr>
<tr>
<td>• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider</td>
</tr>
<tr>
<td><strong>Exclusion Criteria</strong></td>
</tr>
<tr>
<td>• N/A</td>
</tr>
<tr>
<td><strong>Required Medical Information</strong></td>
</tr>
<tr>
<td>• Diagnosis, with documentation of HER2 overexpression</td>
</tr>
<tr>
<td>• Baseline AST, ALT, alkaline phosphatase, and bilirubin levels</td>
</tr>
<tr>
<td>• Age</td>
</tr>
<tr>
<td>• Dose</td>
</tr>
<tr>
<td>• Concurrent medications</td>
</tr>
<tr>
<td>• Treatment history</td>
</tr>
<tr>
<td><strong>Age Restrictions</strong></td>
</tr>
<tr>
<td>• 18 years of age and older</td>
</tr>
<tr>
<td><strong>Prescriber Restrictions</strong></td>
</tr>
<tr>
<td>• Must be prescribed by an oncologist</td>
</tr>
<tr>
<td><strong>Coverage Duration (months)</strong></td>
</tr>
<tr>
<td>• 3 months (initial), 12 months (continuation)</td>
</tr>
<tr>
<td><strong>Quantity/Partial Fill Restrictions</strong></td>
</tr>
<tr>
<td>• None</td>
</tr>
<tr>
<td><strong>Other Information</strong></td>
</tr>
<tr>
<td>• Mechanism of action: Neratinib is a kinase inhibitor that irreversibly binds to intracellular EGFR, HER2, and HER4, leading to a reduction in autophosphorylation of EGFR and HER2, downstream MAPK and AKT signaling pathways, and antitumor activity in EGFR and/or HER2 expressing carcinoma cell lines.</td>
</tr>
</tbody>
</table>
• Warnings and precautions: In the clinical trial that brought the drug to market (ExteNET), diarrhea was reported in 95% of patients therefore loperamide should be initiated for antidiarrheal prophylaxis. Dose adjustments may be necessary depending on the severity of diarrhea and liver abnormalities experienced per package insert.

References

• RED BOOK Online®. Truven Health Analytics LLC Micromedex® Solutions; July 2017.ncc

Last Reviewed July 26, 2017
Neulasta® (pegfilgrastim), Fulphila™ (pegfilgrastim-jmdb), Udenyca™ (pegfilgrastim-cbqv)

FDA Approved Indication(s)
- To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia
- To increase survival in patients acutely exposed to myelosuppressive doses of radiation (Neulasta® only)

FDA Recommended Dose
- Patients with cancer receiving myelosuppressive therapy
  - Subcutaneous injection of 6 mg administered once per chemotherapy cycle in adults. Do not administer pegfilgrastim between 14 days before and 24 hours after administration of cytotoxic chemotherapy.
- Patients with hematopoietic subsyndrome of acute radiation syndrome
  - Two doses, 6 mg each, administered subcutaneously one week apart in adults. Administer the first dose as soon as possible after suspected or confirmed exposure to radiation levels greater than 2 gray. Administer the second dose one week after the first dose.

How Supplied
- Neulasta®:
  - 6 mg/0.6 mL prefilled syringe
  - 6 mg/0.6 mL prefilled syringe plus On-Body Injector for Neulasta® (Onpro® kit)
- Fulphila™:
  - 6 mg/0.6 mL prefilled syringe

Utilization Criteria
For initial review:
- All uses: Prescriber must be an oncologist or hematologist, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Primary prophylaxis
  - Patient must be receiving a myelosuppressive chemotherapy regimen associated with a ≥20% risk of febrile neutropenia (See below for list of recognized regimens), OR
  - Patient may have ≥ 10% risk if any of the following are present:
    - Older patient, notably patients 65 years of age and older
    - Previous chemotherapy or radiation therapy
    - Preexisting neutropenia or bone marrow involvement with tumor
    - Preexisting neutropenia, infection/open wounds, and/or recent surgery
    - Poor performance status or poor nutritional status
    - Poor renal function (creatinine clearance < 50)
    - Liver dysfunction, most notably elevated bilirubin > 2.0
    - Multiple comorbid conditions
    - Cardiovascular disease
    - HIV infection
    - Advanced cancer
- Secondary prophylaxis
- Patient must have had a neutropenic complication during a previous cycle of chemotherapy for which primary prophylaxis was not received and a dose reduction will compromise disease-free survival, overall survival, or treatment outcome.

- Treatment of chronic neutropenia
  - Patient is chronically receiving pegfilgrastim to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia, AND
  - ANC ≤ 1 x 10^9/L
  - Patient is receiving pegfilgrastim for a reduction in the duration of neutropenia and neutropenia-related infectious complications and is undergoing myeloablative chemotherapy followed by autologous or allogeneic bone marrow transplantation (BMT)
  - Therapeutic use in high-risk, febrile, neutropenic patients (Patient risk factors for poor clinical outcomes resulting from febrile neutropenia or infection)
    - Must have one of the following:
      - Age greater than 65 years
      - Hospitalization at the time of the development of fever
      - Sepsis syndrome
      - Hypotension
      - Invasive fungal infection
      - Multi-organ dysfunction (sepsis syndrome)
      - Pneumonia
      - Prolonged (greater than 10 days) and profound (absolute neutrophil count less than 1 x 10^9/L) neutropenia
      - Prior episode of febrile neutropenia
      - Uncontrolled primary disease
  - Patients with any of the following characteristics:
    - Receiving induction or consolidation chemotherapy for AML, OR
    - Patients with ALL after completion of the first few days of chemotherapy of the initial induction or first post-remission course, OR
    - Patients with advanced HIV infection and neutropenia (absolute neutrophil count less than 1 x 10^9/L) to allow scheduled dosing of myelosuppressive anti-retroviral medication (e.g., zidovudine and ganciclovir).
    - Planned exposure to potentially lethal doses of total-body radiotherapy
  - Acute Radiation Syndrome
    - Patient has confirmed diagnosis of acute radiation syndrome

For continuation:
- Above criteria is met, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

Exclusion Criteria
- None

Required Medical Information
- Diagnosis
- Laboratory parameters
- Age
- Dose
- Concurrent medications

### Age Restrictions
- None

### Prescriber Restrictions
- Must be prescribed by a hematologist or oncologist

### Coverage Duration (months)
- 3 months

### Quantity/Partial Fill Restrictions
- 2 injections per 28 days

### Common Chemotherapy Regimens with ≥20% Risk of Febrile Neutropenia

- **Acute Lymphoblastic Leukemia (ALL)**
  - Select ALL regimens as directed by treatment protocol
- **Bladder Cancer**
  - Dose-dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
- **Breast Cancer**
  - Dose-dense AC followed by T (doxorubicin, cyclophosphamide, paclitaxel)
  - TAC (docetaxel, doxorubicin, cyclophosphamide)
  - TC (docetaxel, cyclophosphamide)
  - TCH (docetaxel, carboplatin, trastuzumab)
- **Head and Neck Cancer**
  - TPF (docetaxel, cisplatin, 5-fluorouracil)
  - Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
  - Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
- **Hodgkin Lymphoma**
  - Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
- **Kidney Cancer**
  - Doxorubicin/gemcitabine
- **Non-Hodgkin’s Lymphomas**
  - Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
  - ICE (ifosfamide, carboplatin, etoposide)
  - Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone)
  - MINE (mesna, ifosfamide, mitoxantrone, etoposide)
  - DHAP (dexamethasone, cisplatin, cytarabine)
  - ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine)
  - HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone)
- **Melanoma**
  - Dacarbazine-based combo with IL-2, interferon alfa (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)
- **Multiple Myeloma**
• DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide) +/- bortezomib (VTD-PACE)

• Ovarian Cancer
  • Topotecan
  • Docetaxel

• Soft Tissue Sarcoma
  • MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
  • Doxorubicin
  • Ifosfamide/doxorubicin

• Small Cell Lung Cancer
  • Topotecan

• Testicular Cancer
  • VeIP (vinblastine, ifosfamide, cisplatin)
  • VIP (etoposide, ifosfamide, cisplatin)
  • BEP (bleomycin, etoposide, cisplatin)
  • TIP (paclitaxel, ifosfamide, cisplatin)

Common Chemotherapy Regimens with 10-20% Risk of Febrile Neutropenia

• Occult Primary – Adenocarcinoma
  • Gemcitabine/docetaxel

• Breast Cancer
  • Docetaxel
  • AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
  • FEC (fluorouracil, epirubicin, cyclophosphamide) + sequential docetaxel
  • Paclitaxel every 21 days

• Cervical Cancer
  • Cisplatin/topotecan
  • Paclitaxel/cisplatin
  • Topotecan
  • Irinotecan

• Colorectal Cancer
  • FOLFOX (fluorouracil, leucovorin, oxaliplatin)

• Esophageal and Gastric Cancers
  • Irinotecan/cisplatin
  • Epirubicin/cisplatin/5-fluorouracil
  • Epirubicin/cisplatin/capecitabine

• Non-Hodgkin’s Lymphomas
  • GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
  • CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone), including regimens with pegylated liposomal doxorubicin

• Non-Small Cell Lung Cancer
  • Cisplatin/paclitaxel
  • Cisplatin/vinorelbine
  • Cisplatin/docetaxel
  • Cisplatin/etoposide
  • Carboplatin/paclitaxel
  • Docetaxel
- Ovarian Cancer
  - Carboplatin/docetaxel
- Pancreatic Cancer
  - FOLFIRINOX
- Prostate Cancer
  - Cabazitaxel
- Small Cell Lung Cancer
  - Etoposide/carboplatin
- Testicular Cancer
  - Etoposide/cisplatin
- Uterine Sarcoma
  - Docetaxel

Other Information

- Mechanism of action: Pegfilgrastim is a colony-stimulating factor that acts on hematopoietic cells by binding to specific cell surface receptors, thereby stimulating proliferation, differentiation, commitment, and end cell functional activation.
- Black Box Warning: None

References

# Neumega® (oprelvekin)

## FDA Approved Indication(s)
- For the prevention of severe thrombocytopenia and the reduction of the need for platelet transfusions following myelosuppressive chemotherapy in adult patients with nonmyeloid malignancies who are at high risk of severe thrombocytopenia

## FDA Recommended Dose
- 50 mcg/kg given once daily as a single subcutaneous injection

## How Supplied
- 5 mg vial of lyophilized powder for reconstitution

## Utilization Criteria

### For initial review:
- Patient must be at high risk of severe thrombocytopenia (i.e., patient experienced severe thrombocytopenia and/or required platelet transfusion(s) following previous chemotherapy cycle)
- Patient must be receiving myelosuppressive chemotherapy

### For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

## Exclusion Criteria
- Creatinine clearance (CrCl) < 30 mL/min
- Patient has received myeloablative chemotherapy

## Required Medical Information
- Diagnosis
- Age
- Dose
- CrCl
- Treatment history
- Chemotherapy schedule

## Age Restrictions
- 18 years of age and older

## Prescriber Restrictions
- Must be prescribed by an oncologist/hematologist

## Coverage Duration (months)
- 1

## Quantity/Partial Fill Restrictions
- None

## Other Information
- Mechanism of action: The primary hematopoietic activity of Neumega® is stimulation of megakaryocytopoiesis and thrombopoiesis.
- Black Box Warning: Neumega® has led to severe allergic reactions including anaphylaxis

## References

*Last Reviewed November 9, 2015*
Neupogen® (filgrastim), Granix™ (tbo-filgrastim), Zarxio™ (filgrastim-sndz)

FDA Approved Indication(s)

- To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever (All products)
- For reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with AML (Neupogen® and Zarxio™ only)
- To reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation (Neupogen® and Zarxio™ only)
- For the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis (Neupogen® and Zarxio™ only)
- For chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia (Neupogen® and Zarxio™ only)
- To increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome) (Neupogen® only)

FDA Recommended Dose

- Bone marrow transplant
  - The recommended dose of filgrastim following BMT is 10 mcg/kg/day given as an IV infusion no longer than 24 hours. For patients receiving BMT, the first dose of filgrastim should be administered at least 24 hours after cytotoxic chemotherapy and at least 24 hours after bone marrow infusion. See package insert for dose titration recommendations.
- Peripheral blood progenitor cell collection
  - The recommended dose of filgrastim for the mobilization of PBPC is 10 mcg/kg/day given by subcutaneous injection. It is recommended that filgrastim be given for at least 4 days before the first leukapheresis procedure and continued until the last leukapheresis.
- Chronic neutropenia
  - Congenital neutropenia: Starting dose 6 mg/kg SC twice daily, followed by maintenance dose 6 mcg/kg SC one time daily
  - Idiopathic neutropenia: 5 mcg/kg SC injection one time daily
  - Chronic daily administration is required to maintain clinical benefit. Absolute neutrophil count should not be used as the sole indication of efficacy. The dose should be individually adjusted based on the patient's clinical course as well as ANC.
- Myelosuppressive Chemotherapy or AML Induction/Consolidation
  - 5 mcg/kg/day, administered as single daily SC injection, by short IV infusion (15 to 30 min), or by continuous IV infusion. Doses may be increased in increments of 5 mcg/kg for each chemotherapy cycle, according to the duration and severity of the ANC nadir. Filgrastim should be administered no earlier than 24 hours after the administration of cytotoxic chemotherapy. Filgrastim should not be administered in the period 24 hours before the administration of chemotherapy. Filgrastim therapy should be discontinued if the ANC surpasses 10,000/mm³ after the expected chemotherapy-induced neutrophil nadir.
- Hematopoietic Syndrome of Acute Radiation Syndrome
  - 10 mcg/kg daily as single SC injection. Filgrastim administration should continue until the ANC remains greater than 1,000/mm³ for 3 consecutive CBCs or exceeds 10,000/mm³
How Supplied

- Neupogen®
  - Vial
    - 300 mcg/mL, 1 mL vial
    - 300 mcg/mL, 1.6 mL vial (480 mcg/1.6 mL)
  - Prefilled syringe
    - 600 mcg/mL (300 mcg/0.5 mL)
    - 600 mcg/mL (480 mcg/0.8 mL)

- Zarxio™
  - Prefilled syringe
    - 600 mcg/mL (300 mcg/0.5 mL)
    - 600 mcg/mL (480 mcg/0.8 mL)

- Granix™
  - Prefilled syringe
    - 600 mcg/mL (300 mcg/0.5 mL)
    - 600 mcg/mL (480 mcg/0.8 mL)

Utilization Criteria

For initial review:

- All uses: Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Primary prophylaxis
  - Patient must be receiving a myelosuppressive chemotherapy regimen associated with a ≥20% risk of febrile neutropenia (See below for list of recognized regimens)
  - Patient may have ≥ 10% risk if any of the following are present:
    - Older patient, notably patients age 65 and over
    - Previous chemotherapy or radiation therapy
    - Preexisting neutropenia or bone marrow involvement with tumor
    - Preexisting neutropenia, infection/open wounds, and/or recent surgery
    - Poor performance status or poor nutritional status
    - Poor renal function (creatinine clearance < 50)
    - Liver dysfunction, most notably elevated bilirubin > 2.0
    - Multiple comorbid conditions
    - Cardiovascular disease
    - HIV infected patient
    - Advanced cancer
- Secondary prophylaxis
  - Patient must have had a neutropenic complication during a previous cycle of chemotherapy for which primary prophylaxis was not received and a dose reduction will compromise disease-free survival, overall survival, or treatment outcome.
- Treatment of Chronic Neutropenia
  - Patient is chronically receiving filgrastim to reduce the incidence and duration of sequelae of neutropenia (eg, fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia, AND
  - ANC ≤ 1 x 10⁹/L
• Patient is receiving filgrastim for a reduction in the duration of neutropenia and neutropenia-related infectious complications and is undergoing myeloablative chemotherapy followed by autologous or allogeneic bone marrow transplantation (BMT)
• Patient is receiving filgrastim as an adjunct to progenitor cell-transplantation to mobilize peripheral-blood progenitor-cells (PBPC) often in conjunction with chemotherapy and their administration after autologous, but not allogeneic transplant.
• Therapeutic use in high-risk, febrile, neutropenic patients (Patient risk factors for poor clinical outcomes resulting from febrile neutropenia or infection)
  • Must have one of the following:
    • Age greater than 65 years
    • Hospitalization at the time of the development of fever
    • Sepsis syndrome
    • Hypotension
    • Invasive fungal infection
    • Multi-organ dysfunction
    • Pneumonia
    • Prolonged (greater than 10 days) and profound (absolute neutrophil count less than 1 x 10^9/L) neutropenia
    • Prior episode of febrile neutropenia
    • Uncontrolled primary disease
• Patients with any of the following characteristics:
  • Receiving induction or consolidation chemotherapy for AML, OR
  • Patients with ALL after completion of the first few days of chemotherapy of the initial induction or first post-remission course, OR
  • Patients with advanced HIV infection and neutropenia (absolute neutrophil count less than 1 x 10^9/L) to allow scheduled dosing of myelosuppressive anti-retroviral medication (e.g., zidovudine and ganciclovir).
• Acute Radiation Syndrome
  • Patient has confirmed diagnosis of acute radiation syndrome

*For continuation:*
• Above criteria is met, AND
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider, AND
• Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

**Exclusion Criteria**

• Member has myeloid malignancy

**Required Medical Information**

• Diagnosis
• Laboratory parameters
• Age
• Dose
• Concurrent medications

**Age Restrictions**

• None

**Prescriber Restrictions**
• Must be prescribed by an oncologist or hematologist

**Coverage Duration (months)**
- 6 months for chronic neutropenia indications
- 3 months for all other indications

**Quantity/Partial Fill Restrictions**
- None

**Common Chemotherapy Regimens with ≥20% Risk of Febrile Neutropenia**
- Acute Lymphoblastic Leukemia (ALL)
  - Select ALL regimens as directed by treatment protocol
- Bladder Cancer
  - Dose-dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
- Breast Cancer
  - Dose-dense AC followed by T (doxorubicin, cyclophosphamide, paclitaxel)
  - TAC (docetaxel, doxorubicin, cyclophosphamide)
  - TC (docetaxel, cyclophosphamide)
  - TCH (docetaxel, carboplatin, trastuzumab)
- Hodgkin Lymphoma
  - Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
- Kidney Cancer
  - Doxorubicin/gemcitabine
- Non-Hodgkin’s Lymphomas
  - Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
  - ICE (ifosfamide, carboplatin, etoposide)
  - Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone)
  - MINE (mesna, ifosfamide, mitoxantrone, etoposide)
  - DHAP (dexamethasone, cisplatin, cytarabine)
  - ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine)
  - HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone)
- Melanoma
  - Dacarbazine-based combo with IL-2, interferon alfa (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)
- Multiple Myeloma
  - DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)
  - +/- bortezomib (VTD-PACE)
- Ovarian Cancer
  - Topotecan
  - Docetaxel
- Soft Tissue Sarcoma
  - MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
  - Doxorubicin
  - Ifosfamide/doxorubicin
- Small Cell Lung Cancer
  - Topotecan
- Testicular Cancer
  - VeIP (vinblastine, ifosfamide, cisplatin)
• VIP (etoposide, ifosfamide, cisplatin)
• BEP (bleomycin, etoposide, cisplatin)
• TIP (paclitaxel, ifosfamide, cisplatin)

**Common Chemotherapy Regimens with 10-20% Risk of Febrile Neutropenia**

- **Occult Primary – Adenocarcinoma**
  - Gemcitabine/docetaxel
- **Breast Cancer**
  - Docetaxel
  - AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
  - FEC (fluorouracil, epirubicin, cyclophosphamide) + sequential docetaxel
  - Paclitaxel every 21 days
- **Cervical Cancer**
  - Cisplatin/topotecan
  - Paclitaxel/cisplatin
  - Topotecan
  - Irinotecan
- **Colorectal Cancer**
  - FOLFOX (fluorouracil, leucovorin, oxaliplatin)
- **Esophageal and Gastric Cancers**
  - Irinotecan/cisplatin
  - Epirubicin/cisplatin/5-fluorouracil
  - Epirubicin/cisplatin/capecitabine
- **Non-Hodgkin’s Lymphomas**
  - GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
  - CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone), including regimens with pegylated liposomal doxorubicin
- **Non-Small Cell Lung Cancer**
  - Cisplatin/paclitaxel
  - Cisplatin/vinorelbine
  - Cisplatin/docetaxel
  - Cisplatin/etoposide
  - Carboplatin/paclitaxel
  - Docetaxel
- **Ovarian Cancer**
  - Carboplatin/docetaxel
- **Pancreatic Cancer**
  - FOLFIRINOX
- **Prostate Cancer**
  - Cabazitaxel
- **Small Cell Lung Cancer**
  - Etoposide/carboplatin
- **Testicular Cancer**
  - Etoposide/cisplatin
- **Uterine Sarcoma**
  - Docetaxel

**Other Information**
Mechanism of action: Colony-stimulating factors are glycoproteins which act on hematopoietic cells by binding to specific cell surface receptors and stimulating proliferation, differentiation commitment, and some end-cell functional activation.

References

- Granix™ [package insert], North Wales, PA; Teva Pharmaceuticals. August 2018.
Nexavar® (sorafenib)

FDA Approved Indication(s)
- For the treatment of patients with:
  - Unresectable hepatocellular carcinoma (HCC)
  - Advanced renal cell carcinoma (RCC)
  - Locally recurrent or metastatic, progressive, differentiated thyroid carcinoma (DTC) that is refractory to radioactive iodine treatment

FDA Recommended Dose
- 400 mg (2 x 200 mg tablets) twice daily without food (at least 1 hour before or 2 hours after a meal)
- See package insert for dose modification recommendations

How Supplied
- 200 mg tablets

Utilization Criteria
For initial review:
- Documented diagnosis of an FDA-approved indication
For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Severe hypersensitivity to sorafenib
- Member is prescribed sorafenib in combination with carboplatin and paclitaxel in squamous cell lung cancer
- Congenital long QT syndrome
- Pregnancy

Required Medical Information
- Diagnosis
- Age
- Dose

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 3 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Sorafenib was shown to inhibit multiple intracellular (CRAF, BRAF and mutant BRAF) and cell surface kinases (KIT, FLT-3, RET, VEGFR-1, VEGFR-2, VEGFR-3, and PDGFR-ß). Several of these kinases are thought to be involved in tumor cell signaling, angiogenesis, and apoptosis. Sorafenib inhibited tumor growth and angiogenesis of human hepatocellular carcinoma and renal cell carcinoma, and several other human tumor xenografts in immunocompromised mice.
- Black Box Warning: None

References
Ninlaro® (ixazomib)

FDA-Approved Indication(s)
- For the treatment of multiple myeloma, in combination with lenalidomide and dexamethasone, in patients who have received at least one prior therapy

FDA-Recommended Dose
- 4 mg taken orally on Days 1, 8, and 15 of a 28-day cycle in combination with lenalidomide and dexamethasone

How Supplied
- 2.3 mg, 3 mg, and 4 mg gelatin capsules available as single and triple capsule blister packs

Utilization Criteria

For initial review:
- Member must have a documented diagnosis of multiple myeloma, AND
- Member must have a documented trial of at least one prior multiple myeloma regimen, AND
- Must be treated with lenalidomide and dexamethasone as part of the 28-day cycle regimen, AND
- Must be used as maintenance therapy following response to either stem cell transplant or primary induction therapy

For continuation:
- Member must meet the above listed requirements, AND
- Member must have a documented benefit to therapy, as assessed by their oncologist

Exclusion Criteria
- Member has shown to be resistant to lenalidomide therapy
- Member has shown to be resistant to Proteasome Inhibitor based therapy
- Member has a platelet count less than 30,000/mm3
- Member has an absolute neutrophil count (ANC) less than 500/mm3
- Member is pregnant

Required Medical Information
- Diagnosis
- Dose
- Treatment history
- Concurrent medications
- CBC w/ Differential
- Pregnancy Determination

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- Three months (initial), 12 months (maintenance)

Quantity/Partial-Fill Restrictions
- None

Other Information
- Mechanism of Action: Ixazomib is a reversible proteasome inhibitor. Ixazomib preferentially binds and inhibits the chymotrypsin-like activity of the beta 5 subunit of the 20S proteasome. In doing this it promotes the apoptosis, or destruction, of the myeloma cells.
• Requires co-administration with lenalidomide (Revlimid®) and dexamethasone
• The recommended starting dose of lenalidomide is 25 mg administered daily on Days 1 through 21 of a 28-day treatment cycle.
• The recommended starting dose of dexamethasone is 40 mg administered on Days 1, 8, 15, and 22 of a 28-day treatment cycle.

References

Last Reviewed February 01, 2017
**Northera® (droxidopa)**

**FDA Approved Indication(s)**
- For the treatment of orthostatic dizziness, lightheadedness, or the “feeling that you are about to black out” in adult patients with symptomatic neurogenic orthostatic hypotension (nOH) caused by primary autonomic failure (Parkinson’s disease [PD], multiple system atrophy, and pure autonomic failure), dopamine beta-hydroxylase deficiency, and non-diabetic autonomic neuropathy

**FDA Recommended Dose**
- The recommended starting dose is 100 mg by mouth three times during the day. Last dose to be administered at least 3 hours prior to bedtime.
- Must be administered consistently with or without food.
- Titrate to symptomatic response, in increments of 100 mg three times daily every 24 to 48 hours up to a maximum dose of 600 mg three times daily (maximum total daily dose of 1,800 mg).

**How Supplied**
- 100 mg, 200 mg, and 300 mg capsules

**Utilization Criteria**

*For initial review:*
- Member must have documentation of a clinical diagnosis of symptomatic neurogenic orthostatic hypotension caused by one of the following:
  - Primary autonomic failure (Parkinson’s disease, multiple system atrophy, or pure autonomic failure)
  - Dopamine beta-hydroxylase deficiency
  - Non-diabetic autonomic neuropathy, AND
- Member must have tried and failed or is intolerant to a sympathomimetic agent (eg. Midodrine), AND
- Member must have a decrease of at least 20 mmHg in systolic blood pressure or 10 mmHg in diastolic blood pressure within three minutes after standing from a sitting position

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider, AND
- Documented decrease in symptoms of nOH

**Exclusion Criteria**
- None

**Required Medical Information**
- Diagnosis
- Dose
- Concomitant and previous therapies
- Blood pressure readings (standing and sitting)

**Age Restrictions**
- 18 years of age or older

**Prescriber Restrictions**
- Must be prescribed by a specialist in the area of practice related to the patient’s diagnosis, such as a cardiologist or neurologist

**Coverage Duration (months)**
- 2 weeks
Quantity/Partial Fill Restrictions

- None

Other Information

- Mechanism of Action: unknown but thought to exert its effects through norepinephrine which increases BP by inducing peripheral arterial and venous vasoconstriction.
- Supine BP should be measured prior to initiating droxidopa and after dose increases.
- Warnings and precautions: Hyperpyrexia and confusion have occurred with use of droxidopa. Patients with existing cardiac issues (e.g. ischemic heart disease, arrhythmias, and congestive heart failure) may have exacerbation of cardiac symptoms.

References


Last Reviewed April 3, 2018
Nucala® (mepolizumab)

FDA Approved Indication(s)
- Add-on maintenance treatment of patients aged 12 years and older with severe asthma with an eosinophilic phenotype
- Treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA)

FDA Recommended Dose
- Severe Asthma:
  - 100 mg injected subcutaneously once every 4 weeks
- Eosinophilic Granulomatosis with Polyangiitis:
  - 300 mg injected subcutaneously once every 4 weeks as 3 separate 100 mg injections into the upper arm, thigh, or abdomen

How Supplied
- 100 mg single-dose vial

Utilization Criteria

For initial review:
- Severe Asthma:
  - Member must have a diagnosis of severe, sub-optimally controlled asthma (i.e., asthma symptoms two days per week or more, or exacerbations requiring systemic corticosteroids more than two times per year), AND
  - Must have documentation of inadequate response to a three-month course of inhaled corticosteroids, montelukast, and a long-acting beta\textsubscript{2}-agonist, AND
  - Must have an absolute eosinophil count of:
    - ≥ 150 cells/microL within the past 6 weeks, OR
    - ≥ 300 cells/microL within the past 12 months, AND
  - Member must be concurrently receiving a long-acting beta\textsubscript{2}-agonist, inhaled corticosteroid therapy, montelukast, and short-acting beta\textsubscript{2}-agonist as rescue therapy, unless otherwise contraindicated, AND
  - Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable
- EGPA:
  - Member must have a documentation of relapsing/refractory EGPA, AND
  - Must have documented treatment failure or contraindication to cyclophosphamide, methotrexate, and azathioprine, AND
  - Must have a blood eosinophil level >10% or absolute eosinophil count > 1000 cells/mm\textsuperscript{3}
  - Must be concurrently receiving glucocorticoids, AND
  - Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable

For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Treatment of other eosinophilic conditions
- Relief of acute bronchospasm or status asthmaticus
### Required Medical Information
- Diagnosis
- Age
- Dose
- Concurrent medications
- Treatment history
- Baseline CBC

### Age Restrictions
- Severe asthma: 12 years of age and older
- EGPA: 18 years of age and older

### Prescriber Restrictions
- Must be prescribed by a pulmonologist, allergist, or immunologist

### Coverage Duration (months)
- 6 months (initial), 12 months (continuation)

### Quantity/Partial Fill Restrictions
- None

### Other Information
- **Mechanism of Action:** Mepolizumab is an interleukin-5 antagonist (IgG1 kappa). IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils. Mepolizumab binds to IL-5 and reduces the production and survival of eosinophils; however, the mechanism of mepolizumab action in asthma has not been definitively established.
- Use may result in an opportunistic infection of herpes zoster; consider herpes zoster vaccination prior to initiation of therapy with mepolizumab.

### References
- Wenzel S. Treatment of severe asthma in adolescents and adults. In: UpToDate, Post TW (Ed), Waltham, MA. 2018.
Ocaliva® (obeticholic acid)

FDA Approved Indication(s)
- For the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA

FDA Recommended Dose
- Starting dose: 5 mg orally once daily in adults who have not achieved an adequate response to an appropriate dosage of UDCA for at least 1 year or are intolerant to UDCA
- Dose titration: If adequate reduction in ALP and/or total bilirubin has not been achieved after 3 months of Ocaliva® 5 mg once daily and the patient is tolerating Ocaliva®, increase dosage to 10 mg once daily.
- Maximum dose is 10 mg once daily

How Supplied
- 5 mg and 10 mg tablets, administered orally

Utilization Criteria
For initial review:
- Must be used for an FDA-approved indication, AND
- Alkaline phosphatase, serum transaminases and total bilirubin levels collected prior to treatment, AND
- Member must have documented inadequate response to UDCA, OR
  - Member must have clinical documentation that patient is unable to tolerate UDCA

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed by a decrease in serum ALP by the member’s specialist provider

Exclusion Criteria
- Members who have complete biliary obstruction, or who have developed complete biliary obstruction while taking Ocaliva®

Required Medical Information
- Diagnosis
- Age
- Dose
- Pertinent labs

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a gastroenterologist or hepatologist

Coverage Duration (months)
- 3 months initially, followed by 12 months thereafter

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Ocaliva® is an agonist for FXR, a nuclear receptor expressed in the liver and intestine. FXR is a key regulator of bile acid, inflammatory, fibrotic, and metabolic pathways. FXR
activation decreases the intracellular hepatocyte concentrations of bile acids by suppressing de novo synthesis from cholesterol as well as by increased transport of bile acids out of the hepatocytes. These mechanisms limit the overall size of the circulating bile acid pool while promoting choleresis, thus reducing hepatic exposure to bile acids.

- Ocaliva® for PBC is approved under accelerated approval based on a reduction in alkaline phosphatase (ALP). An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
- In a landmark study published by Hirschfield et al., Ocaliva® was randomized to three different doses (10, 25, or 50 mg once daily), which all had significant reductions of serum ALP, GGTP, AST, and bilirubin levels compared to patients in the placebo arm.

References

Ocrevus™ (ocrelizumab)

FDA Approved Indication(s)
- For the treatment of adult patients with relapsing or primary progressive forms of multiple sclerosis (MS).

FDA Recommended Dose
- Initial dose: 300 mg administered by intravenous infusion, followed two weeks later by a second 300 mg intravenous infusion
- Maintenance dose: 600 mg administered by intravenous infusion once every six months

How Supplied
- 300 mg/10 mL (30 mg/mL) single dose vial

Utilization Criteria

For initial review:
- Relapsing forms of MS:
  - Member must have a documented diagnosis of a relapsing form of MS; AND
  - Member must have tried and failed two or more preferred agents for the treatment of MS, as evidenced by continued clinical relapse or worsening of the disease. Clinical relapse is defined as one of the following while at steady state on therapy:
    - Member experiences at least one relapse within the past 12 months
    - Member continues to have CNS lesion progression as measured by MRI
  - Member must not be using in combination with another MS disease modifying agent
- Primary Progressive Multiple Sclerosis (PPMS):
  - Member must have a documented diagnosis of PPMS; AND
  - Member must not be using in combination with another MS disease modifying agent

For continuation:
- Member must have documentation of treatment response, as verified per progress notes

Exclusion Criteria
- Member is at risk for hepatitis B virus (HBV) infection and HBV infection has not been ruled out; OR
- Member has HBV and treatment has not been initiated; OR
- Member has experienced a life-threatening infusion reaction to ocrelizumab in the past

Required Medical Information
- Diagnosis
- Current medication list
- Therapeutic history

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a neurologist, or an MS specialist provider

Coverage Duration (months)
- 6 months initially, 12 months thereafter

Quantity/Partial Fill Restrictions
- Maximum of three infusions in a six month period

Other Information
Multiple sclerosis (MS) is a chronic, progressive, autoimmune disease of the central nervous system (CNS), including the brain, spinal cord and optic nerve. It affects approximately 400,000 Americans and 2.5 million people worldwide.

Relapsing remitting multiple sclerosis is the most common form of MS and has many available treatments, whereas few medications have demonstrated efficacy in treating primary progressive multiple sclerosis (PPMS). PPMS is less common, and comprises approximately 10% of the total MS cases in the United States.

Mechanism of action: ocrelizumab is a recombinant humanized monoclonal antibody that targets CD-20 expressing B-cells. These immune cells are thought to play a role in the pathogenesis of several forms of MS. Through the binding of the CD-20 cell surface antigen, ocrelizumab stimulates an antibody-dependent cellular cytolysis and complement-mediated lysis of the B-cell.

References


Last Reviewed May 24, 2017
Ofev® (nintedanib)

FDA Approved Indication(s)

- Treatment of idiopathic pulmonary fibrosis

FDA Recommended Dose

- 150 mg twice daily taken approximately 12 hours apart with food

How Supplied

- 100 mg and 150 mg capsules; 60 capsules per bottle

Utilization Criteria

For initial review:

- Patient must have diagnosis of idiopathic pulmonary fibrosis (IPF) determined per the following diagnostic features
  - No identifiable causes of Interstitial Lung Diseases, AND
  - Pattern of usual interstitial pneumonia (UIP) per criteria in IPF guidelines determined on the high-resolution computed tomography (HRCT) as
    - Definite UIP, or
    - Possible UIP with a surgical lung biopsy pattern of definite or probable UIP

For continuation:

- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria

- AST/ALT >5x ULN, or > 3x ULN with signs and symptoms of severe liver damage
- Airway obstruction or requiring lung transplant
- Recent history of acute myocardial ischemia
- High risk of bleeding, or concurrent anticoagulation treatment
- Pregnancy (Category D)

Required Medical Information

- Diagnosis
- Age
- Dose
- Concomitant medications
- HRCT pattern (and lung biopsy pattern, if applicable)
- Forced Vital Capacity (FVC)
- Liver function tests (AST, ALT, bilirubin)

Age Restrictions

- 18 years of age and older

Prescriber Restrictions

- Must be prescribed by a pulmonologist

Coverage Duration (months)

- 3 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions

- None

Other Information

- Limited Distribution
- Mechanism of action:
• Inhibits multiple receptor tyrosine kinases (RTKs) and non-receptor tyrosine kinases (nRTKs), few of which have been implicated in IPF pathogenesis
• Binds competitively to the adenosine triphosphate (ATP) binding pocket of these receptors and blocks the intracellular signaling which is crucial for the proliferation, migration, and transformation of fibroblasts

References


Last Reviewed November 9, 2015
Olysio® (simeprevir)

FDA Approved Indication(s)
- For the treatment of chronic hepatitis C (HCV) genotype 1 infection as a component of a combination antiviral treatment regimen
- Limitations of use:
  - Simeprevir efficacy is substantially reduced in patients infected with HCV genotype 1a with an NS3 Q80K polymorphism
  - Simeprevir is not recommended in patients with moderate or severe hepatic impairment
  - Simeprevir is not recommended in patients who have previously failed therapy with a treatment regimen that included simeprevir or other HCV protease inhibitors

FDA Recommended Dose
- 150 mg orally daily, with food
- Duration of therapy:
  - Simeprevir/peginterferon alfa/ribavirin combination therapy
    - 12 weeks for treatment naïve or experienced patients
  - Simeprevir/sofosbuvir combination therapy
    - Treatment naïve or experienced without cirrhosis – 12 weeks
    - Treatment naïve or experienced with cirrhosis – 24 weeks

How Supplied
- 150 mg capsules in 28-count and 7-count (emergency supply) bottles

Utilization Criteria
For initial review:
- Member must have a diagnosis of HCV genotype 1, with documented viral load collected within the previous three months, AND
- Physician must attest to the patient’s ability and dedication to remain adherent to the entire course of therapy, AND
- Physician must confirm that alcohol and illicit substance abuse is absent for the previous six months, or patient is currently seeing an addiction specialist, AND
- Patient must be concurrently receiving peginterferon alfa and ribavirin OR sofosbuvir
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable

For continuation:
- Members receiving simeprevir/peginterferon alfa/ribavirin therapy:
  - HCV RNA must be obtained at week 0, 4, 12, and 24 of therapy
  - If HCV RNA < 25 IU/mL at week 4, approve simeprevir for an additional 7 weeks

Exclusion Criteria
- Member has a diagnosis of HCV with NS3 Q80K polymorphism, OR
- Member has previously received simeprevir, boceprevir or telaprevir therapy, OR
- Medication is prescribed as monotherapy

Required Medical Information
- Diagnosis, including genotype
- NS3 Q80K polymorphism status
- Viral loads
- Age
- Dose and duration
• Concurrent medications
• Treatment history

**Age Restrictions**
• Must be 18 years of age or older

**Prescriber Restrictions**
• Must be prescribed by a gastroenterologist or infectious disease specialist

**Coverage Duration (months)**
• Initial coverage: 5 weeks
• Continued coverage: up to 19 weeks (total duration – 6 months)

**Quantity/Partial Fill Restrictions**
• None

**Other Information**
• Mechanism of action: Simeprevir is a direct-acting antiviral (DAA) and inhibits the HCV NS3/4A protease.

**References**
• Olysio® [Package Insert]. Titusville, NJ: Janssen Therapeutics; May 2018.

Orencia® (abatacept)

**FDA Approved Indication(s)**
- For the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA), as monotherapy or concomitantly with disease-modifying antirheumatic drugs (DMARDs) other than tumor necrosis factor (TNF) antagonists
- For the treatment of patients 2 years of age and older with moderately to severely active polyarticular juvenile idiopathic arthritis (JIA), as monotherapy or concomitantly with methotrexate
- For the treatment of adult patients with active psoriatic arthritis (PsA)

**FDA Recommended Dose**
- **Adult RA:**
  - Subcutaneous injection: 125 mg once weekly without loading intravenous infusion
  - Intravenous infusion: Initial infusion on day one based on weight, followed by IV infusion at 2 and 4 weeks after the first infusion and every 4 weeks thereafter
    - Less than 60 kg: 500 mg (2 vials)
    - 60 to 100 kg: 750 mg (3 vials)
    - 100+ kg: 1000 mg (4 vials)
- **Juvenile Idiopathic Arthritis:**
  - Subcutaneous injection (2 years of age and older):
    - 10 kg to <25 kg: 50 mg once weekly
    - 25 kg to <50 kg: 87.5 mg once weekly
    - 50 kg or more: 125 mg once weekly
  - Intravenous infusion (6 years of age and older):
    - If less than 75 kg, administer 10 mg/kg
    - Patients weighing greater than 75 kg should be dosed based on adult recommendations
- **Adult Psoriatic Arthritis:**
  - Subcutaneous injection: 125 mg once weekly without loading intravenous infusion
  - Intravenous infusion: Initial infusion on day one based on weight, followed by IV infusion at 2 and 4 weeks after the first infusion and every 4 weeks thereafter
    - Less than 60 kg: 500 mg (2 vials)
    - 60 to 100 kg: 750 mg (3 vials)
    - 100+ kg: 1000 mg (4 vials)

**How Supplied**
- 250 mg/15 mL vial for intravenous infusion
- 50 mg/0.4 mL, 87.5 mg/0.7 mL, and 125 mg/1 mL prefilled glass syringes
- 125 mg/1 mL single-dose disposable prefilled autoinjector

**Utilization Criteria**
*For initial review:*
- Member must have a negative TB test before initiating therapy, AND
- Documented failure of, intolerance or contraindication to, two other disease modifying antirheumatic drugs (DMARDs) (e.g., methotrexate, sulfasalazine, azathioprine, or hydroxychloroquine), AND
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
• Coverage of infused formulation requires documented intolerance to, or inability to safely administer, self-injectable product

For continuation:
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
• Member is concurrently receiving TNF antagonists or other biologic DMARD therapy

Required Medical Information
• Diagnosis
• Weight
• Concurrent medications
• Age
• Dose
• Treatment history

Age Restrictions
• 2 years of age or older

Prescriber Restrictions
• Must be prescribed by a rheumatologist

Coverage Duration (months)
• 12

Quantity/Partial Fill Restrictions
• None

Other Information
• Mechanism of action: Abatacept, a selective costimulation modulator, inhibits T cell (T lymphocyte) activation by binding to CD80 and CD86, thereby blocking interaction with CD28.
• For IV administration, administer over 30 minutes. Reconstituted product must be administered using a filter.

References

Last Reviewed February 7, 2018
Orkambi™ (lumacaftor/ivacaftor)

**FDA Approved Indication(s)**

- For the treatment of cystic fibrosis (CF) in patients age 6 years and older who are homozygous for the F508del mutation in the CFTR gene
  - If the patient’s genotype is unknown, and FDA-cleared CF mutation test should be used to detect the presence of the F508del mutation on both alleles of the CFTR gene
  - Limitations of Use: Efficacy and safety of lumacaftor/ivacaftor has not been established in patients with CF other than those homozygous for the F508del mutation

**FDA Recommended Dose**

<table>
<thead>
<tr>
<th>Age</th>
<th>Orkambi Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 through 5 years weighing less than 14 kg</td>
<td>lumacaftor 100 mg/ivacaftor 125 mg packet every 12 hours with fat-containing food</td>
</tr>
<tr>
<td>2 through 5 years weighing 14 kg or greater</td>
<td>lumacaftor 150 mg/ivacaftor 188 mg packet every 12 hours with fat-containing food</td>
</tr>
<tr>
<td>6 through 11 years</td>
<td>lumacaftor 100 mg/ivacaftor 125 mg – 2 tablets every 12 hours with fat-containing food</td>
</tr>
<tr>
<td>12 years and older</td>
<td>lumacaftor 200 mg/ivacaftor 125 mg – 2 tablets every 12 hours with fat-containing food</td>
</tr>
</tbody>
</table>

**How Supplied**

- Lumacaftor 100 mg/ivacaftor 125 mg tablets; supplied in a 112–count tablet box containing a 4-week supply (4 weekly cartons of 7 daily blister strips with 4 tablets per strip)
- Lumacaftor 100 mg/ivacaftor 125 mg granules; supplied in 56-unit-dose packets
- Lumicaftor 150 mg/ivacaftor 188 mg granules; supplied in 56-unit-dose packets
- Lumacaftor 200 mg/ivacaftor 125 mg tablets; supplied in a 112–count tablet box containing a 4-week supply (4 weekly cartons of 7 daily blister strips with 4 tablets per strip)

**Utilization Criteria**

*For initial review:*

- Diagnosis of cystic fibrosis, AND
- Documentation of two copies of the F508del mutation, AND
- Member is 6 years of age or older, AND
- Documentation of significant impairment of forced expiratory volume (FEV1), or presence of symptoms secondary to the decline in FEV1

*For continuation:*

- Documented clinical benefit, as evidenced by an improvement in FEV1

**Exclusion Criteria**

- Member has diagnosis of CF without the homozygous F508del mutation

**Required Medical Information**

- Age
- Weight
• Dose
• Documentation of mutation test results
• Forced expiratory volume (FEV1)

**Age Restrictions**
• 6 years of age and older

**Prescriber Restrictions**
• Must be prescribed by a pulmonary specialist

**Coverage Duration (months)**
• 12

**Quantity/Partial Fill Restrictions**
• None

**Other Information**
• Mechanism of action: Lumacaftor improves the conformation stability of F508del-CFTR, resulting in increased processing and trafficking of mature protein to the cell surface. Ivacaftor is a CFTR potentiator that facilitates increased chloride transport by potentiating the channel-open probability (or gating) of the CFTR protein at the cell surface.
• Black Box Warning: None

**References**

*Last Reviewed November 26, 2019*
**Otezla® (apremilast)**

**FDA Approved Indication(s)**
- For the treatment of active psoriatic arthritis
- For the treatment of moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy

**FDA Recommended Dose**
- For psoriatic arthritis or plaque psoriasis:
  - Requires a five-day initial dose titration as follows to avoid the associated GI symptoms:
    | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 |
    |-------|-------|-------|-------|-------|
    | AM 10mg | AM 10mg | PM 10mg | AM 10mg | PM 20mg |
    | AM 20mg | PM 20mg | AM 20mg | PM 30mg |
  - Maintenance dose begins day six onward with 30 mg twice daily

**How Supplied**
- Two-Week Starter Pack containing 10 mg, 20 mg, and 30 mg tablets
- 28-Day Starter Pack or Carton containing 10 mg, 20 mg and 30 mg tablets
- 30 mg tablets, bottle of 60

**Utilization Criteria**

*For initial review:*
- Member must have a diagnosis of active psoriatic arthritis or moderate to severe plaque psoriasis, **AND**
- Plaque psoriasis:
  - Member must have documented failure, intolerance, or contraindication to methotrexate and at least one other traditional therapy (e.g. PUVA, UVB, acitretin, or cyclosporine), **AND**
  - Has tried and failed all preferred biologic products, as applicable
- Psoriatic arthritis:
  - Peripheral disease
    - Member must have documented failure, intolerance or contraindication to methotrexate
  - Has tried and failed all preferred biologic products, as applicable
  - **•**
  - Axial disease
    - Member must have documented failure, intolerance or contraindication to non-steroidal anti-inflammatory drugs (NSAIDs)
  - Has tried and failed all preferred biologic products, as applicable
- Behcet’s syndrome
  - Member must have documented failure, intolerance, or contraindication to colchicine and at least one other traditional therapy (e.g., azathioprine) plus an oral corticosteroid (e.g., prednisone), **AND**
  - For all indications, member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable

*For continuation:*
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, **AND**
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member's specialist provider

Exclusion Criteria

• Patient is currently receiving one or more biologic DMARD therapies, OR
• Patient has history of depression and/or suicidal ideation

Required Medical Information

• Diagnosis
• Age
• Dose
• Treatment history
• Concomitant medications

Age Restrictions

• 18 years and older

Prescriber Restrictions

• Must be prescribed by a dermatologist or rheumatologist

Coverage Duration (months)

• 12 months

Quantity/Partial Fill Restrictions

• 14 day induction, 28/30-day maintenance (depends on package type)

Other Information

• Apremilast is an oral small-molecule inhibitor of phosphodiesterase 4 (PDE4) specific for cyclic adenosine monophosphate (cAMP). PDE4 inhibition results in increased intracellular cAMP levels. The specific mechanism(s) by which apremilast exerts its therapeutic action in psoriatic arthritis patients and psoriasis patients is not well defined.

References

Pegasys® (peginterferon alfa-2a)

FDA Approved Indication(s)

- For the treatment of chronic hepatitis C virus (HCV) in:
  - Patients ≥ 5 years of age with compensated liver disease not previously treatment with interferon alfa
  - Patients with histological evidence of cirrhosis and compensated liver disease
  - Adults with chronic HCV/HIV co-infection and CD4 count > 100 cells/mm³
- For the treatment of adult patients with chronic hepatitis B (HBV) infection who have compensated liver disease and evidence of viral replication and liver inflammation
- For the treatment of patients 3 years of age and older who are HBeAg-positive CHB and non-cirrhotic with evidence of viral replication and elevations in serum alanine aminotransferase (ALT)

FDA Recommended Dose

- Adult patients:
  - HCV/HBV (as monotherapy): 180 mcg once weekly for 48 weeks
  - HCV (in combination with ribavirin): 180 mcg once weekly for 48 weeks (Genotypes 1, 4, or co-infection with HIV) or 24 weeks (Genotypes 2, 3)
- Pediatric patients:
  - HCV (in combination with ribavirin): 180 mcg/1.73m² BSA once weekly, to a maximum of 180 mcg, for 48 weeks (Genotypes 1, 4) or 24 weeks (Genotypes 2, 3)

How Supplied

- 180 mcg/mL Vial for single use
- 180 mcg/0.5 mL Prefilled Syringe for single use
- 180 mcg/0.5 mL Autoinjector for single use
- 135 mcg/0.5 mL Autoinjector for single use

Utilization Criteria

- Patient has diagnosis of HBV or HCV with detectable viral load
- Patient is naive to interferon-based therapy
- If for HCV,
  - Member must have tried and failed at least one interferon-free HCV regimen
  - Approval is for 48 weeks (Genotypes 1, 4, or co-infected with HIV) or 24 weeks (Genotypes 2, 3), provided that HCV-RNA levels are not indicative of treatment futility
  - Prior authorization will be rescinded if patient has not achieved a 2 log₁₀ reduction from baseline in HCV RNA titer by 12 weeks of therapy or has detectable HCV RNA after 24 weeks of therapy
- If for HBV,
  - Patient must have evidence of viral replication and compensated liver disease

Exclusion Criteria

- Patient has hepatic decompensation (Child-Pugh score ≥ 6) with cirrhosis before treatment

Required Medical Information

- Diagnosis
- Age
- Dose
- Weight (if under 18 years of age)
- Complete blood count with differential

Age Restrictions
- 3 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a gastroenterologist, hepatologist, infectious disease specialist

**Coverage Duration (months)**
- Patient specific based on therapy outcomes

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: Pegylated recombinant human interferon alfa-2a is an inducer of the innate antiviral immune response
- Black Box Warning: May cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Monitor closely and withdraw therapy with persistently severe or worsening signs or symptoms of the above disorders.

**References**

*Last Reviewed January 28, 2019*
# Pegintron® (peginterferon alfa-2b)

<table>
<thead>
<tr>
<th>FDA Approved Indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• For the treatment of chronic hepatitis C (CHC/HCV) for patients with HCV genotype 1 infection and compensated liver disease, in combination with ribavirin and an approved HCV NS3/4A protease inhibitor</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FDA Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Adult patients: 1.5 mcg/kg/week</td>
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<tr>
<td>• Pediatric patients: 60 mcg/m²/week</td>
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<table>
<thead>
<tr>
<th>How Supplied</th>
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<tbody>
<tr>
<td>• 50 mcg per 0.5 mL, 80 mcg per 0.5 mL, 120 mcg per 0.5 mL, 150 mcg per 0.5 mL Pegintron® Redipen® and single-use vials</td>
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<tr>
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<td><strong>For initial review:</strong></td>
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<td>• Patient is naïve to interferon-based therapy</td>
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<tr>
<td>• Patient must have tried and failed an interferon-free HCV regimen</td>
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<td>• Approval is for 48 weeks (Genotypes 1) or 24 weeks (Genotypes 2,3), provided that HCV-RNA levels are not indicative of treatment futility</td>
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<td>• Prior authorization will be rescinded if patient has not achieved a $2 \log_{10}$ reduction from baseline in HCV RNA titer by 12 weeks of therapy or has detectable HCV RNA after 24 weeks of therapy</td>
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<tr>
<td>• Dose</td>
</tr>
<tr>
<td>• Weight</td>
</tr>
<tr>
<td>• Complete blood count with differential</td>
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<td>• 3 years of age and older</td>
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<table>
<thead>
<tr>
<th>Coverage Duration (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 12, pending patient-specific factors as noted above</td>
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<table>
<thead>
<tr>
<th>Quantity/Partial Fill Restrictions</th>
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<tbody>
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<td>• None</td>
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<thead>
<tr>
<th>Other Information</th>
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<tbody>
<tr>
<td>• Mechanism of action: Pegylated recombinant human interferon alfa-2b is an inducer of the innate antiviral immune response</td>
</tr>
<tr>
<td>• Black Box Warning: May cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Monitor closely and withdraw therapy with persistently severe or worsening signs or symptoms of the above disorders.</td>
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<table>
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<th>References</th>
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</table>
# Plegridy® (peginterferon beta-1a)

## FDA Approved Indication(s)
- For the treatment of patients with relapsing forms of multiple sclerosis

## FDA Recommended Dose
- Titration required per table below, followed by maintenance dose of 125 mcg injected subcutaneously every 14 days
  - Day 1: 63 mcg
  - Day 15: 94 mcg
  - Day 29: 125 mcg

## How Supplied
- Starter packs:
  - One 63 mcg and one 94 mcg prefilled syringe
  - One 63 mcg and one 94 mcg pen
- Maintenance packs:
  - Two 125 mcg prefilled syringes
  - Two 125 mcg pens

## Utilization Criteria
### For initial review:
- Patient has a diagnosis of a relapsing form of multiple sclerosis, AND
- Diagnosis has been confirmed by MRI, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

### For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

## Exclusion Criteria
- Concurrent use of alternative disease-modifying therapy, such as interferon beta-1b, glatiramer acetate, dimethyl fumarate, fingolimod, or teriflunomide

## Required Medical Information
- Diagnosis
- Age
- Dose
- Concomitant medications
- Complete baseline blood count with differential
- Liver function tests (ALT, AST)

## Age Restrictions
- 18 years of age and older

## Prescriber Restrictions
- Must be prescribed by a neurologist

## Coverage Duration (months)
### Quantity/Partial Fill Restrictions
- None

### Other Information
- The mechanism of action of interferon therapy in the treatment of MS is currently unknown

### References

*Last Reviewed February 4, 2019*
Pomalyst® (pomalidomide)

**FDA Approved Indication(s)**
- Multiple Myeloma in patients that have received at least two prior therapies including lenalidomide and bortezomib and have demonstrated disease progression on or within 60 days of completion of the last therapy

**FDA Recommended Dose**
- Recommended starting dose:
  - 4 mg orally daily on days 1-21 of repeated 28-day cycles
  - See package insert for recommended dose adjustments

**How Supplied**
- 1 mg, 2 mg, 3 mg, and 4 mg capsules

**Utilization Criteria**

*For initial review:*
- Patient must have a diagnosis of relapsed and refractory multiple myeloma
- Patient must have tried and failed bortezomib and lenalidomide
- Disease progression must be present and indicative of refractory disease

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Pregnancy
- AST/ALT > 3 times the upper limit of normal
- Serum bilirubin >2 mg/dL
- Serum creatinine >3 mg/dL

**Required Medical Information**
- Diagnosis
- Therapy history and timeframe of disease progression post-previous therapy
- Age
- Gender
- Pregnancy status
- Liver function tests (AST, ALT, serum bilirubin)
- Serum creatinine
- Dose

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist or hematologist

**Coverage Duration (months)**
- 6

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Black Box Warnings: Pregnancy category X (embryo-fetal toxicity) and increased risk of deep venous thrombosis (DVT) and pulmonary embolism (PE)

References

- Pomalyst® [Package Insert]. Summit, NJ: Celgene Corporation; May 2014.
Praluent® (alirocumab)

FDA Approved Indication(s)
- For the additional lowering of low density lipoprotein cholesterol (LDL-C) in adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), in combination with diet and maximally tolerated statin therapy

FDA Recommended Dose
- Recommended starting dose is 75 mg injected subcutaneously every two weeks
  - If response to 75 mg every two weeks is inadequate after 4-8 weeks, dosage may be increased to a maximum dosage of 150 mg every two weeks
- Alternative starting dose is 300 mg injected subcutaneously every 4 weeks (monthly)
  - If response to 300 mg every 4 weeks is inadequate after 4-8 weeks, dosage may be adjusted to 150 mg every two weeks

How Supplied
- 75 mg/mL single-dose pre-filled pen or syringe
- 150 mg/mL single-dose pre-filled pen or syringe

Utilization Criteria

For initial review:
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

Heterozygous familial hypercholesterolemia (HeFH)
- Member must have diagnosis confirmed through genetic testing of LDL receptor mutation(s), OR
- Member must have documentation of ‘definite FH’ as defined by the Simon Broome Familial Hypercholesterolemia Register or Dutch Lipid Clinic Network diagnostic criteria; AND
- Member must have documented trial and failure of, or intolerance\(^1\) to, three-month therapies of both high-intensity atorvastatin (40-80 mg) and rosuvastatin (20-40 mg) therapies, unless otherwise contraindicated\(^2\), AND
- Member must have tried and failed at least one non-statin therapy\(^3\) after failure of high-intensity statin therapy, AND
- Member must have documentation of baseline fasting LDL-C levels of greater than 100 mg/dL if currently on high-intensity statin therapy plus non-statin therapy\(^3\), OR greater than 190 mg/dL if intolerant\(^2\) to high-intensity statin therapy plus non-statin therapy.

Clinical ASCVD
- Member must have documentation of acute coronary syndrome, a history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization procedure, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin, OR
  - Member must be at high risk for ASCVD with an estimated 10-year ASCVD risk of ≥ 7.5% based on ACC/AHA pooled cohort risk calculator, AND
- Member must have documented trial and failure of, or intolerance\(^1\) to, three-month therapies of both high-intensity atorvastatin (40-80 mg) and rosuvastatin (20-40 mg) therapies, unless otherwise contraindicated\(^2\), AND
- Member must have tried and failed at least one non-statin therapy\(^3\) after failure of high-intensity statin therapy, AND
- Member must have documentation of baseline fasting LDL-C level of ≥ 70 mg/dL

\(^1\) Statin intolerance is defined as:
- Skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]), AND
- The skeletal-related muscle symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin at the maximally tolerated dose, AND
- The skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy with return of symptoms when reinstated on alternative statin, OR
- Statin-induced hepatitis (with all other causes of hepatitis ruled out), documented liver function tests greater than five times the ULN over 30 days despite dose reduction, AND return of hepatitis when reinstated on alternative statin

2 Accepted contradictions to both atorvastatin and rosuvastatin:
- Unexplained ALT of three times the upper limit of normal (ULN)
- Pregnancy
- Nursing Mothers
- Documentation of rhabdomyolysis, confirmed by medical records and the documentation of CPK levels 10 times the upper limit of normal

3 Accepted Non-Statin Therapies:
- Cholestyramine
- Colestipol
- Colesevelam
- Fenofibrate
- Niacin
- Ezetimibe
- Lomitapide
- Mipomersen

For continuation:
- Documentation must confirm that member is continuing to receive maximally tolerated statin therapy plus non-statin therapy (unless member has documentation of statin intolerance), AND
- At week eight: Member must have documentation of reduction in fasting LDL-C levels by week eight of therapy
- At month twelve: Member must have documentation of continuously suppressed fasting LDL-C levels
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

Exclusion Criteria
- Patients with HIV, HCV, or other inflammatory states that may impact hepatocytes to synthesize PCSK9

Required Medical Information
- Diagnosis
- Age
- Dose
- Fasting lipid panel, baseline and history prior to initiating statin therapy
- Therapeutic history
- Baseline CPK and liver function test (LFT) panel

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a cardiologist or lipid specialist
**Coverage Duration (months)**
- 2 months (initial), 12 months (continuation)

**Quantity/Partial Fill Restrictions**
- Initial coverage will be limited to 75 mg every 14 days; requests for doses greater than 75 mg every 14 days may be considered on a case by case basis.

**Other Information**
- Mechanism of action: Alirocumab is a fully human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9). PCSK9 targets LDL receptors for degradation reducing the liver's ability to remove LDL-C from the blood. Alirocumab attaches to PCSK9 to inhibit the binding to LDL receptors on the liver surface. With reduced PCSK9 activity, more LDL receptors become available to remove LDL-C from the blood.

**References**
- 2016 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk. Journal of the American College of Cardiology Jul 2016, 68 (1) 92-125; DOI: 10.1016/j.jacc.2016.03.519

_Last Reviewed February 26, 2018_
Epogen® (epoetin), Procrit® (epoetin alfa), Retacrit (epoetin alfa-epbx)‡

FDA Approved Indication(s)
- For the treatment of anemia due to:
  - Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis
  - Zidovudine administration in patients with HIV-infection
  - Effects of concomitant myelosuppressive chemotherapy, in patients with non-myeloid malignancies
- For reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery

FDA Recommended Dose
- CKD Patients:
  - Initial dose: 50 to 100 Units/kg intravenously or subcutaneously 3 times weekly (adults) and 50 Units/kg intravenously or subcutaneously 3 times weekly (pediatric patients)
  - Individualize maintenance dose
  - Intravenous route recommended for patients on hemodialysis
- Zidovudine-treated HIV-infected Patients: 100 Units/kg intravenously or subcutaneously 3 times weekly
- Cancer Patients on Chemotherapy: 40,000 Units subcutaneously weekly or 150 Units/kg subcutaneously 3 times weekly (adults); 600 Units/kg intravenously weekly (children ≥ 5 years)
- Surgery Patients: 300 Units/kg per day subcutaneously for 15 days total, or 600 Units/kg subcutaneously once weekly for four doses

How Supplied
- Procrit®
  - Single-dose vial: 2000, 3000, 4000, 10,000, and 40,000 Units/1 mL
  - Multi-dose vial: 20,000 Units/2 mL and 20,000 Units/1 mL
- Retacrit®
  - Single-dose vial: 2000, 3000, 4000, 10,000, and 40,000 Units/1 mL

Utilization Criteria
For initial review:
- For all indications: Member has documentation of an FDA-approved indication, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Anemia associated with CKD on dialysis:
  - Hemoglobin (Hgb) level is less than 10 g/dL
- Anemia associated CKD not on dialysis:
  - Hgb is less than 10 g/dL, AND
  - The rate of Hgb decline indicates the likelihood of requiring a RBC transfusion, AND
  - Reducing the risk of alloimmunization and/or other RBC transfusion-related risks is a goal
- Anemia associated with concomitant myelosuppressive chemotherapy:
  - Member has documented hemoglobin (Hgb) level equal or less than 10 g/dL, AND
  - Member is currently being treated with myelosuppressive chemotherapy, AND
  - Member has a minimum of two additional months of planned chemotherapy

For Continuation of Coverage:
• Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
• Anemia associated with CKD:
  • Member has documented Hgb level equal to or less than 11 g/dL (on dialysis) or 10 g/dL (not on dialysis)
• Anemia due to chemotherapy:
  • Member has documented hemoglobin (Hgb) level equal or less than 10 g/dL, AND
  • Member has a minimum of two additional months of planned chemotherapy

Exclusion Criteria
• Members with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy
• Members with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure
• Members with cancer receiving myelosuppressive chemotherapy in whom the anemia can be managed by transfusion
• Members scheduled for surgery who are willing to donate autologous blood
• Use as a substitute for RBC transfusions in patients who require immediate correction of anemia
• Member has documented Hgb greater than or equal to 11 g/dL
• Member has completed their course of myelosuppressive chemotherapy

Required Medical Information
• Diagnosis
• Age
• Weight
• Dose
• Concurrent therapies
• Complete blood count with differential

Age Restrictions
• None

Prescriber Restrictions
• Must be prescribed by a specialist in the disease being treated

Coverage Duration (months)
Initial Coverage:
• CKD: 3 months
• HIV treatment with zidovudine: 2 months
• Myelosuppressive chemotherapy: 2 months
• Perisurgery: 1 month

Continuation of Coverage:
• Duration of continued coverage will depend on indication and response to therapy

Quantity/Partial Fill Restrictions
• 30 day supply, no partial fill

Other Information
• Mechanism of action: Epoetin alfa stimulates erythropoiesis by the same mechanism as endogenous erythropoietin.
• Black Box Warnings
• CKD: In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL.

• Cancer: ESAs shortened overall survival and/or increased the risk of tumor progression or recurrence in clinical studies of patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers; ESAs are not indicated for patients receiving myelosuppressive chemotherapy when the anticipated outcome is cure; Discontinue following the completion of a chemotherapy course.

• Perisurgery: Due to increased risk of Deep Venous Thrombosis (DVT), DVT prophylaxis is recommended.

References


Last Reviewed October 25, 2018
Prolia® (denosumab)

FDA Approved Indication(s)

- For the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or members who have failed or are intolerant to other available osteoporosis therapy
- For treatment to increase bone mass in men with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or members who have failed or are intolerant to other available osteoporosis therapy
- For the treatment of glucocorticoid-induced osteoporosis in men and women at high risk of fracture who are either initiating or continuing systemic glucocorticoids in a daily dosage equivalent to 7.5 mg or greater of prednisone and expected to remain on glucocorticoids for at least 6 months
- To increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer
- To increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

FDA Recommended Dose

- 60 mg administered as a single subcutaneous injection once every 6 months in the upper arm, the upper thigh, or the abdomen
- All patients should receive calcium 1000 mg daily and at least 400 IU vitamin D daily

How Supplied

- 60 mg/1 mL single use vial
- 60 mg/1 mL prefilled syringe

Utilization Criteria

For Initial Review:

- Member must be receiving concurrent calcium (1000 mg daily) and vitamin D (400 IU daily) supplementation, AND
- Postmenopausal women and men with osteoporosis
  - Must be at high risk for fracture with a history of osteoporotic fracture or multiple risk factors for fracture, AND
  - Bone mineral density (BMD) T-score ≤ -2.5, AND
  - Member must have tried and failed, or is intolerant to, at least one oral bisphosphonate
- Glucocorticoid-induced osteoporosis:
  - Must be at high risk for fracture with a history of osteoporotic fracture or multiple risk factors for fracture, AND
  - Bone mineral density (BMD) T-score ≤ -2.5, AND
  - Member must have tried and failed, or is intolerant to, at least one oral bisphosphonate, AND
  - Member must be receiving systemic glucocorticoids at a daily dosage equivalent to 7.5 mg or greater of prednisone, AND
  - Expected duration of treatment must be ≥ 6 months
- Men receiving androgen deprivation therapy
  - Must have a diagnosis of nonmetastatic prostate cancer, AND
  - Must be currently receiving androgen deprivation therapy (LHRH agonists, flutamide, nilutamide, or bicalutamide)
- Women receiving aromatase inhibitor therapy
  - Must have a diagnosis of breast cancer, AND
Must be currently receiving an aromatase inhibitor (anastrozole, exemestane, or letrozole)

For Continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s prescriber

Exclusion Criteria
- Pre-existing hypocalcemia, OR
- Pregnancy, OR
- Member is receiving other denosumab therapy (Xgeva®)

Required Medical Information
- Diagnosis
- Age
- Dose
- Fracture history and risk factors
- Concurrent medications
- Comorbid conditions
- BMD T-score

Age Restrictions
- 18 and older

Prescriber Restrictions
- None

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Denosumab binds to RANKL, a transmembrane or soluble protein essential for the formation, function, and survival of osteoclasts, the cells responsible for bone resorption. Denosumab prevents RANKL from activating its receptor, RANK, on the surface of osteoclasts and their precursors. Prevention of the RANKL/RANK interaction inhibits osteoclast formation, function, and survival, thereby decreasing bone resorption and increasing bone mass and strength in both cortical and trabecular bone.

References
Promacta® (eltrombopag olamine)

FDA Approved Indication(s)
- For the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.
- For the treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy.
- For the treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy.

FDA Recommended Dose
- Chronic ITP: 50 mg once daily. Dose should not exceed 75 mg per day.
- Chronic hepatitis C-associated thrombocytopenia: Initiate at 25 mg once daily. Dose should not exceed 100 mg per day.
- Severe aplastic anemia: Initiate at 50 mg once daily. Dose should not exceed 150 mg per day.

How Supplied
- 12.5 mg, 25 mg, 50 mg, 75 mg, and 100 mg oral tablets
- 25 mg unit-dose powder packets for oral suspension

Utilization Criteria
For initial review:
- Chronic ITP:
  - Initial platelet count must be < 30,000/microL, AND
  - One or more of the following apply:
    - Insufficient response to corticosteroids
    - Insufficient response to immunoglobulins
    - Splenectomy
- Hepatitis C-associated thrombocytopenia:
  - Planning to initiate and maintain interferon-based treatment or currently receiving interferon-based treatment not in combination with direct antivirals (boceprevir, telaprevir), AND
  - Initial platelet count must be < 75,000/microL
- Severe aplastic anemia:
  - Initial platelet count must be < 30,000/microL, AND
  - Insufficient response to immunosuppressive therapy

For continuation:
- Alanine aminotransferase (ALT) levels < 3 times upper limit of normal (ULN) or < 3 times baseline in patients with pretreatment elevations in transaminases, AND
- Chronic ITP:
  - Increase in platelet count to ≥ 50,000/microL, OR
  - Increase in platelet level that is sufficient to avoid clinically important bleeding after at least 4 weeks of max eltrombopag dose, AND
  - Dose is ≤ 75 mg per day
- Hepatitis C-associated thrombocytopenia:
  - Platelet count must be 30,000-150,000, AND
  - Dose is ≤ 100 mg per day
- Severe aplastic anemia:
Platelet count must increase to 20,000/microL above baseline, OR
Platelet count must be stable with transfusion independence for a minimum of 8 weeks, AND
Dose is ≤ 150 mg per day

Exclusion Criteria
- Receiving direct-acting antiviral therapy (i.e., boceprevir or telaprevir). Use in combination with these agents has not been studied.

Required Medical Information
- Diagnosis
- Age
- Dose
- Concurrent therapies
- Complete blood count with differential
- Baseline serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin

Age Restrictions
- 6 years of age and older (ITP)
- 18 years of age and older (other indications)

Prescriber Restrictions
- Must be prescribed by a hematologist, hepatologist, or infectious disease specialist

Coverage Duration (months)
- Initial approval for three months
- Continuation approval for 12 months

Quantity/Partial Fill Restrictions
- 30 day supply

Other Information
- Mechanism of action: Eltrombopag is an orally bioavailable, small-molecule thrombopoietin (TPO) receptor agonist that interacts with the transmembrane domain of the human TPO-receptor and initiates signaling cascades that induce proliferation and differentiation of megakaryocytes from bone marrow progenitor cells.
- Black Box Warning: Risk for hepatotoxicity, especially when combined with interferon and ribavirin in patients with chronic hepatitis C. Discontinue eltrombopag if liver enzymes surpass three times ULN.

References
- Promacta® [Package Insert]. Research Triangle Park, NC: GlaxoSmithKline; August 2015.
- Schrier, SL. Treatment of aplastic anemia in adults. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed March 4, 2016.)

Last Reviewed March 4, 2016
## Pulmozyme® (dornase alfa)

### FDA Approved Indication(s)
- To improve pulmonary function in the management of patients with cystic fibrosis (CF)

### FDA Recommended Dose
- 2.5 mg inhaled once daily

### How Supplied
- 2.5 mg/2.5 mL single-use ampules

### Utilization Criteria

**For initial review:**
- Patient must have a confirmed diagnosis of cystic fibrosis,

**For continuation:**
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

### Exclusion Criteria
- None

### Required Medical Information
- Diagnosis
- Age
- Dose
- Previous and concurrent therapies

### Age Restrictions
- None

### Prescriber Restrictions
- Must be prescribed by a pulmonologist

### Coverage Duration (months)
- 12

### Quantity/Partial Fill Restrictions
- None

### Other Information
- Mechanism of action: Dornase alfa is a highly purified solution of recombinant human deoxyribonuclease I (rhDNase), an enzyme which selectively cleaves DNA

### References

*Last Reviewed June 12, 2019*
**Ravicti® (glycerol phenylbutyrate)**

**FDA Approved Indication(s)**
- Ravicti® is indicated for use as a nitrogen-binding agent for chronic management of adult and pediatric patients ≥2 years of age with urea cycle disorders (UCDs) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone.

**FDA Recommended Dose**
- Administer in 3 equally divided dosages, each rounded up to the nearest 0.5 mL
  - The maximum total daily dosage is 17.5 mL (19 g)

**How Supplied**
- 1.1 g/mL, 25 mL glass vials

**Utilization Criteria**

*For initial review:*
- Must be used in line with the FDA approved indication

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Use for the treatment of acute hyperammonemia in patients with UCDs

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Previous Therapies

**Age Restrictions**
- 2 years of age and older

**Prescriber Restrictions**
- None

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: UCDs are inherited deficiencies of enzymes or transporters necessary for the synthesis of urea from ammonia (NH3, NH4+). Absence of these enzymes or transporters results in the accumulation of toxic levels of ammonia in the blood and brain of affected patients. Ravicti is a triglyceride containing 3 molecules of phenylbutyrate (PBA). PAA, the major metabolite of PBA, conjugates with glutamine (which contains 2 molecules of nitrogen) via acetylation in the liver and kidneys to form PAGN, which is excreted by the kidneys.
- Black Box Warning: None

**References**
- Ravicti® [package insert]. Lyme Laboratories; Brockton, MA; February 2013.

*Last Reviewed November 9, 2015*
Rebif® (interferon beta-1a)

FDA Approved Indication(s)

- For the treatment of patients with relapsing forms of multiple sclerosis to decrease the frequency of clinical exacerbations and delay the accumulation of physical disability

FDA Recommended Dose

- 22 mcg or 44 mcg injected subcutaneously three times per week
- See package insert for dose titration schedules

How Supplied

- 8.8 mcg, 22 mcg, and 44 mcg prefilled syringes
- 8.8 mcg, 22 mcg, and 44 mcg Rebidose™ autoinjector

Utilization Criteria

For initial review:
- Patient has a diagnosis of relapsing multiple sclerosis, AND
- Diagnosis has been confirmed by MRI, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria

- Chronic progressive multiple sclerosis, OR
- Concurrent use of alternative disease-modifying therapy, such as interferon beta-1b, glatiramer acetate, dimethyl fumarate, fingolimod, or teriflunomide

Required Medical Information

- Diagnosis
- Concurrent medications
- Age
- Dose
- Complete baseline blood count with differential
- Liver function tests (ALT, AST)

Age Restrictions

- 18 years of age and older

Prescriber Restrictions

- Must be prescribed by a neurologist

Coverage Duration (months)

- 12 months

Quantity/Partial Fill Restrictions

- None

Other Information

- Mechanism of action: The specific interferon-induced proteins and mechanisms by which interferon beta-1a exerts its effects in multiple sclerosis have not been fully defined.

References

Last Reviewed February 4, 2019
Reclast® (zoledronic acid)

**FDA Approved Indication(s)**
- For the treatment and prevention of postmenopausal osteoporosis
- For the treatment to increase bone mass in men with osteoporosis
- For the treatment and prevention of glucocorticoid-induced osteoporosis
- For the treatment of Paget’s disease of bone in men and women

**FDA Recommended Dose**
- Treatment of osteoporosis in men and postmenopausal women, and treatment and prevention of glucocorticoid-induced osteoporosis
  - 5 mg infusion once a year given intravenously over no less than 15 minutes.
- Prevention of Osteoporosis in Postmenopausal Women
  - 5 mg infusion given once every 2 years intravenously over no less than 15 minutes.
- Treatment of Paget’s Disease of Bone
  - One 5 mg infusion given over no less than 15 minutes

**How Supplied**
- 5 mg/100 mL ready-to-infuse vial

**Utilization Criteria**

*For initial review:*
- Member has a diagnosis consistent with FDA-approved indications for use, AND
- Member has tried and failed one or more oral bisphosphonate therapies, AND
- For glucocorticoid-induced osteoporosis:
  - Member must be receiving systemic glucocorticoids at a daily dosage equivalent to ≥ 7.5 mg prednisone, AND
  - Expected duration of glucocorticoid therapy must be ≥ 12 months
- Criteria specific to Paget’s disease:
  - Serum Alk Phos levels ≥ 2 x ULN for age-specific reference range, AND
  - Symptomatic disease (bone pain, hearing loss, bone deformities, fractures, arthritis), AND
  - At risk of complications from Paget’s disease (ex. osteoarthritis, heart failure, kidney stones, broken bones), AND
  - Member also receiving calcium (1500 mg daily) and vitamin D (800 IU daily)

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s prescriber
- For Paget’s disease:
  - Retreatment can be considered in members who have relapsed, based on increases in serum alkaline phosphatase, or in those who failed to achieve normalization of their serum alkaline phosphatase, or in those members with symptoms
- For osteoporosis
  - Demonstrated increase in BMD

**Exclusion Criteria**
- CrCl < 35 mL/min
- Pre-existing hypocalcemia or other disturbances of mineral metabolism, OR
- Member is receiving other zoledronic acid therapy (Zometa®)

**Required Medical Information**
- Diagnosis
• Age
• Dose
• Treatment history
• Concurrent medications

### Age Restrictions
- 18 years of age or older

### Prescriber Restrictions
- None

### Coverage Duration (months)
- 12

### Quantity/Partial Fill Restrictions
- 1 infusion per year

### Other Information
- Mechanism of action: Zoledronic acid is a bisphosphonate and acts primarily on bone. It is an inhibitor of osteoclast-mediated bone resorption.

### References
- Reclast® [package insert]. Novartis Pharmaceuticals Corporation; East Hanover, NJ. April 2016.
Remicade® (infliximab), Inflectra® (infliximab-dyyb), Renflexis™ (infliximab-abda)

FDA Approved Indication(s)

• Crohn’s Disease:
  • For reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
  • For reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing disease.

• Pediatric Crohn’s Disease:
  • For reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy.

• Ulcerative Colitis:
  • For reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.

• Pediatric Ulcerative Colitis:
  • Remicade® only: For reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy.

• Rheumatoid Arthritis:
  • For reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active disease, in combination with methotrexate.

• Ankylosing Spondylitis:
  • For reducing signs and symptoms in patients with active disease.

• Psoriatic Arthritis:
  • For reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function.

• Plaque Psoriasis:
  • For the treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.

FDA Recommended Dose

• Crohn’s Disease, Pediatric Crohn’s Disease, Ulcerative Colitis
  • 5 mg/kg given as an intravenous induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks thereafter

• Pediatric Ulcerative Colitis (Remicade® only)
  • 5 mg/kg given as an intravenous induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks thereafter

• Rheumatoid Arthritis
  • 3 mg/kg given as an intravenous induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 3 mg/kg every 8 weeks thereafter, in combination with methotrexate
• Ankylosing Spondylitis
  • 5 mg/kg given as an IV induction regimen at 0, 2, and 6 weeks, followed by a maintenance regimen of 5 mg/kg every 6 weeks thereafter

• Psoriatic Arthritis and Plaque Psoriasis
  • 5 mg/kg given as an IV induction regimen at weeks 0, 2, and 6, followed by a maintenance regimen of 5 mg/kg every 8 weeks thereafter

How Supplied
• 100 mg/20 mL vial for intravenous infusion

Utilization Criteria
For initial review:
• For all disease states:
  • Member must have a diagnosis consistent with an FDA-approved indication, AND
  • Member must have a negative TB test, AND
  • Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable

• Rheumatoid Arthritis
  • Prescriber is a rheumatologist, AND
  • Member is concurrently receiving methotrexate, AND
  • Member must have documented failure, intolerance, or contraindication to methotrexate and at least one other disease modifying anti-rheumatic therapy (DMARD)

• Ankylosing Spondylitis
  • Prescriber is a rheumatologist, AND
  • Member must have documented failure, intolerance, or contraindication to at least 1 month of treatment with sulfasalazine, COX-2 inhibitors, NSAIDs, or corticosteroids, AND

• Plaque Psoriasis
  • Prescriber is a dermatologist, AND
  • Member has greater than 10% BSA involvement, or affected area includes palms, soles, head, neck, or genitalia, AND
  • Member must have documented failure, intolerance, or contraindication to methotrexate, AND
  • Member must have documented failure, intolerance, or contraindication to topical agents, topical immunomodulators, systemic therapy, or phototherapy in previous 6 months

• Psoriatic Arthritis
  • Prescriber is a rheumatologist, AND
  • Member must have documented failure, intolerance, or contraindication to methotrexate and at least one other disease modifying anti-rheumatic therapy (DMARD), AND

• Crohn’s Disease and Ulcerative Colitis
  • Prescriber is a gastroenterologist, AND
  • Member must have documented failure, intolerance, or contraindication to at least two conventional therapies (e.g., corticosteroids, 5-ASA agents, immunosuppressants, immunomodulators)

• Pediatric Crohn’s Disease, Fistulizing Crohn’s Disease, and Pediatric Ulcerative Colitis
  • Prescriber is a gastroenterologist, AND
  • Member must have documented failure, intolerance, or contraindication to at least one immunosuppressants or immunomodulators (e.g., 6-mercaptopurine, azathioprine, methotrexate)

For continuation:
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider, AND
• Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable

Exclusion Criteria
• Patient is receiving additional biological agents for the treatment of his or her disease, OR
• Patient has active or chronic infection, OR
• Patient has moderate to severe heart failure (NYHA Functional Class III/IV), if doses > 5 mg/kg

Required Medical Information
• Diagnosis
• Age
• Weight
• Dose
• Treatment history
• TB test with date
• Concurrent medications
• % Body Surface Area (for plaque psoriasis)

Age Restrictions
• 6 years of age and older

Prescriber Restrictions
• Must be prescribed by a gastroenterologist, rheumatologist or dermatologist

Coverage Duration (months)
• 12

Quantity/Partial Fill Restrictions
• Initial coverage is limited to FDA-recommended dosing; increased dosing may be considered on a case-by-case basis.

Other Information
• Mechanism of action: Infliximab neutralizes the biological activity of TNFα by binding with high affinity to the soluble and transmembrane forms of TNFα and inhibits binding of TNFα with its receptors
• Black Box Warning: Increased risk of serious infection and malignancy

References
Repatha® (evolomubab)

FDA Approved Indication(s)
- To reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease
- As an adjunct to diet, alone or in combination with other lipid-lowering therapies, for treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia (HeFH)) to reduce low-density lipoprotein cholesterol (LDL-C)
- As an adjunct to diet and other LDL-lowering therapies in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C

FDA Recommended Dose
- HeFH, CVD: 140 mg subcutaneous injection every two weeks, or 420 mg subcutaneous injection once monthly
- HoFH: 420 mg subcutaneous injection once monthly

How Supplied
- 140 mg/mL single-use prefilled syringe
- 140 mg/mL single-use prefilled SureClick® autoinjector
- 420 mg/3.5 mL single-use Pushtronex® system (on-body infuser with prefilled cartridge)

Utilization Criteria

For initial review:
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

Homozygous familial hypercholesterolemia (HoFH)
- Member must have diagnosis of HoFH confirmed through genetic testing of LDL receptor mutation(s), OR
- Member must have clinical diagnosis of HoFH with:
  - History of untreated LDL-C concentration greater than 500 mg/dL, OR
  - Treated LDL-C concentration greater than 300 mg/dL, together with either xanthoma before 10 years of age or evidence of HoFH in both parents, AND
- Member must have documented trial and failure of, or intolerance¹ to, three-month therapies of both high-intensity atorvastatin (40-80 mg) and rosuvastatin (20-40 mg) therapies, unless otherwise contraindicated², AND
- Member must have tried and failed at least one non-statin therapy³ after failure of high-intensity statin therapy, AND
- Member must have documentation of baseline fasting LDL-C levels of greater than 100 mg/dL if currently on high-intensity statin therapy plus non-statin therapy³, OR greater than 190 mg/dL if intolerant¹ to high-intensity statin therapy plus non-statin therapy.

Heterozygous familial hypercholesterolemia (HeFH)
- Member must have diagnosis confirmed through genetic testing of LDL receptor mutation(s), OR
- Member must have documentation of ‘definite FH’ as defined by the Simon Broome Familial Hypercholesterolemia Register or Dutch Lipid Clinic Network diagnostic criteria; AND
- Member must have documented trial and failure of, or intolerance¹ to, three-month therapies of both high-intensity atorvastatin (40-80 mg) and rosuvastatin (20-40 mg) therapies, unless otherwise contraindicated², AND
- Member must have tried and failed at least one non-statin therapy³ after failure of high-intensity statin therapy, AND
• Member must have documentation of baseline fasting LDL-C levels of greater than 100 mg/dL if currently on high-intensity statin therapy plus non-statin therapy\(^3\), OR greater than 190 mg/dL if intolerant\(^2\) to high-intensity statin therapy plus non-statin therapy.

**Clinical ASCVD**

- Member must have documentation of acute coronary syndrome, a history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization procedure, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin, OR
  - Member must be at high risk for ASCVD with an estimated 10-year ASCVD risk of ≥ 7.5% based on ACC/AHA pooled cohort risk calculator, AND
- Member must have documented trial and failure of, or intolerance\(^3\) to, three-month therapies of both high-intensity atorvastatin (40-80 mg) and rosuvastatin (20-40 mg) therapies, unless otherwise contraindicated\(^2\), AND
- Member must have tried and failed at least one non-statin therapy\(^3\) after failure of high-intensity statin therapy, AND
- Member must have documentation of baseline fasting LDL-C level of ≥70 mg/dL

\(^1\)Statin intolerance is defined as:
  - Skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]), AND
  - The skeletal-related muscle symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin at the maximally tolerated dose, AND
  - The skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy with return of symptoms when reinstated on alternative statin, OR
  - Statin-induced hepatitis (with all other causes of hepatitis ruled out), documented liver function tests greater than five times the ULN over 30 days despite dose reduction, AND return of hepatitis when reinstated on alternative statin

\(^2\)Accepted contradictions to both atorvastatin and rosuvastatin:
  - Unexplained ALT of three times the upper limit of normal (ULN)
  - Pregnancy
  - Nursing Mothers
  - Documentation of rhabdomyolysis, confirmed by medical records and the documentation of CPK levels 10 times the upper limit of normal

\(^3\)Accepted Non-Statin Therapies:
- Cholestyramine
- Colestipol
- Colesevelam
- Fenofibrate
- Niacin
- Ezetimibe
- Lomitapide
- Mipomersen

*For continuation:*
- Documentation must confirm that member is continuing to receive maximally tolerated statin therapy plus non-statin therapy (unless member has documentation of statin intolerance)\(^1\), AND
- At week eight: Member must have documentation of reduction in fasting LDL-C levels by week eight of therapy
• At month twelve: Member must have documentation of continuously suppressed fasting LDL-C levels

Exclusion Criteria
• Patients with HIV, HCV, or other inflammatory states that may impact hepatocytes to synthesize PCSK9

Required Medical Information
• Diagnosis
• Age
• Dose
• Fasting lipid panel, baseline and history prior to initiating statin therapy
• Therapeutic history
• Baseline CPK and liver function test (LFT) panel

Age Restrictions
• HoFH: 13 years of age and older
• HeFH or ASCVD: 18 years of age and older

Prescriber Restrictions
• Must be prescribed by a cardiologist or lipid specialist

Coverage Duration (months)
• 2 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions
• None

Other Information
• Mechanism of action: Evolocumab is a human monoclonal antibody that inhibits human proprotein convertase subtilisin kexin type 9 (PCSK9). PCSK9 targets LDL receptors for degradation, reducing the liver's ability to remove LDL-C from the blood. With reduced PCSK9 activity, more LDL receptors within the liver become available to remove LDL-C from the blood, thus lowering concentration of serum LDL-C.

References
• Scott R. Evolocumab, Endocrinologic and Metabolic Drugs Advisory Committee. FDA. 2015.
• 2016 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk. Journal of the American College of Cardiology Jul 2016, 68 (1) 92-125; DOI: 10.1016/j.jacc.2016.03.519

Last Reviewed February 26, 2018
**Revatio® (sildenafil citrate)**

**FDA Approved Indication(s)**
- For the treatment of pulmonary arterial hypertension (WHO Group I) in adults to improve exercise ability and delay clinical worsening

**FDA Recommended Dose**
- Tablets and oral suspension
  - 20 mg three times daily
  - 10 mg IV bolus three times daily

**How Supplied**
- 20 mg tablets
- 10 mg/12.5 mL single use vial
- 10 mg/mL oral suspension

**Utilization Criteria**

*For initial review:*
- Clinical diagnosis of WHO Group I pulmonary arterial hypertension, AND
- Patient has New York Heart Association Functional Class II-IV symptoms

*For continuation:*
- Member has had clinical benefit as evidenced by increased six minute walk distance

**Exclusion Criteria**
- Concomitant use of organic nitrates in any form, either regularly or intermittently, because of the greater risk of hypotension, OR
- Concomitant use of riociguat, a guanylate cyclase stimulator, OR
- Medication is being used for the treatment of idiopathic pulmonary fibrosis (IPF)

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Six minute walk distance
- Concurrent medications

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a cardiologist or a PAH specialist

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- Only generic sildenafil tablets will be covered

**Other Information**
- Mechanism of action: Sildenafil is an inhibitor of cGMP specific phosphodiesterase type-5 (PDE-5) in the smooth muscle of the pulmonary vasculature, where PDE-5 is responsible for degradation of cGMP. Sildenafil, therefore, increases cGMP within pulmonary vascular smooth muscle cells resulting in relaxation. In patients with PAH, this can lead to vasodilation of the pulmonary vascular bed and, to a lesser degree, vasodilatation in the systemic circulation.
In the clinical trial no greater efficacy was achieved with the use of higher doses. Treatment with doses higher than 20 mg TID is not recommended.

References

# Revlimid® (lenalidomide)

## FDA Approved Indication(s)

- For the treatment of patients with:
  - Multiple myeloma (MM), in combination with dexamethasone
  - Multiple myeloma (MM), as maintenance following autologous hematopoietic stem cell transplantation (auto-HSCT)
  - Transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes (MDS) associated with a deletion 5q abnormality with or without additional cytogenetic abnormalities
  - Mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib

## FDA Recommended Dose

- **MM**
  - Combination therapy: 25 mg orally once daily on days 1-21 of repeated 28-day cycles. Refer to prescribing information for dexamethasone dosing
  - Maintenance therapy following auto-HSCT: 10 mg orally once daily continuously on days 1-28 of repeated 28-day cycles
- **MDS**
  - 10 mg orally once daily
- **MCL**
  - 25 mg orally once daily on days 1-21 of repeated 28 day cycles

## How Supplied

- 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg capsules

## Utilization Criteria

### For initial review:

- **MM**
  - Member is using in combination with dexamethasone or melphalan and prednisone, OR
  - Member is using as maintenance therapy following autologous hematopoietic stem cell transplantation
- **MDS**
  - Member has transfusion dependent anemia or symptomatic anemia with clinically significant cytopenias, AND
  - Member’s diagnosis is associated with a deletion 5q cytogenic abnormality, AND
  - Member has tried or is intolerant to erythropoiesis-stimulating agents (ESAs) such as erythropoietin or darbepoetin
- **MCL**
  - Member has diagnosis of MCL and has relapsed or progressed after two prior therapies, one of which included bortezomib

### For continuation:

- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

## Exclusion Criteria

- Pregnancy

## Required Medical Information

- Diagnosis
• Age
• Dose
• Treatment history
• Concurrent medications

Age Restrictions
• 18 years of age and older

Prescriber Restrictions
• Must be prescribed by an oncologist certified through the REVLIMID REMS™ program

Coverage Duration (months)
• Three months initial, 12 months maintenance

Quantity/Partial Fill Restrictions
• None

Other Information
• Lenalidomide is not indicated and not recommended for the treatment of patients with chronic lymphocytic leukemia (CLL) outside of controlled clinical trials
• Mechanism of action: Lenalidomide inhibits proliferation and induces apoptosis of certain hematopoietic tumor cells including multiple myeloma, mantle cell lymphoma, and del (5q) myelodysplastic syndromes in vitro.
• Black Box Warning: Potential for human birth defects, hematologic toxicity including neutropenia and thrombocytopenia, and increased risk of deep vein thrombosis and pulmonary embolisms

References

Last Reviewed February 5, 2018
# Ribavirin

## FDA Approved Indication(s)
- Ribavirin is a nucleoside analogue indicated for the treatment of chronic hepatitis C virus (HCV) infection

## FDA Recommended Dose
- Dose is dependent on treatment regimen and product

## How Supplied
- Various; most commonly available as 200 mg tablets or capsules

## Utilization Criteria

### For initial review:
- Clinically diagnosed hepatitis C with detectable HCV RNA levels
- Must be used in combination with an FDA-approved HCV antiviral regimen
- Liver biopsy, unless contraindicated, shows fibrosis and inflammatory necrosis
- Must have documentation of intolerance of, or inability to use, generic product

## Exclusion Criteria
- Previously treated with interferon alpha
- History of significant or unstable cardiac disease
- Pregnancy

## Required Medical Information
- Diagnosis with genotype
- Treatment history
- Weight
- Renal function (CrCl)

## Age Restrictions
- 5 years of age and older

## Prescriber Restrictions
- Must be prescribed by a gastroenterologist, hepatologist, internal medicine or infectious disease

## Coverage Duration (months)
- 12

## Quantity/Partial Fill Restrictions
- None

## Other Information
- Mechanism of action: Ribavirin is an antiviral drug
- Black Box Warnings
  - Ribavirin monotherapy is not effective for the treatment of chronic hepatitis C virus infection
  - The hemolytic anemia associated with ribavirin therapy may result in worsening of cardiac disease and lead to fatal and nonfatal myocardial infarctions
  - Significant teratogenic and embryocidal effects have been demonstrated in all animal species exposed to ribavirin. Therefore, COPEGUS is contraindicated in women who are pregnant and in the male partners of women who are pregnant. Extreme care must be taken to avoid pregnancy during therapy and for 6 months after completion of
treatment in both female patients and in female partners of male patients who are taking COPEGUS therapy

References

- Ribavirin CapsulesPackage Insert]. Aurobindo Pharma USA, Inc.: East Windsor, NJ; October 2018.
Ridaura® (auranofin)†

FDA Approved Indication(s)

- For the management of adults with active classical or definite rheumatoid arthritis who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of full doses of one or more nonsteroidal anti-inflammatory drugs.

FDA Recommended Dose

- 6 mg orally daily (given as 3 mg twice daily or 6 mg once daily)
  - If response is inadequate after six months, an increase to 9 mg (3 mg three times daily) may be tolerated
  - If response remains inadequate after a three-month trial of 9 mg daily, therapy should be discontinued
- See prescribing information for dosing recommendations when transferring from injectable gold

How Supplied

- 3 mg capsules

Utilization Criteria

For initial review:

- Member must have a diagnosis of active classical or definite rheumatoid arthritis, AND
- Must have had an insufficient therapeutic response, intolerance or contraindication to, one or more nonsteroidal anti-inflammatory drugs, AND
- Must have had an insufficient therapeutic response, intolerance or contraindication to one or more conventional disease-modifying antirheumatic drugs (DMARDs), such as methotrexate, hydroxychloroquine, leflunomide, or sulfasalazine, AND
- Documentation of baseline CBC with differential, platelet count, urinalysis, renal and liver function tests, AND
- Treatment plan includes monitoring of CBC with differential, platelet count and urinalysis at least monthly

For continuation:

- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria

- Member has a history of any of the following gold-induced disorders: anaphylactic reactions, necrotizing enterocolitis, pulmonary fibrosis, exfoliative dermatitis, bone marrow aplasia or other severe hematologic disorders, OR
- Pregnancy

Required Medical Information

- Age
- Diagnosis
- Therapeutic history
- Baseline complete blood count (CBC) with differential
- Baseline platelet count
- Baseline urinalysis
- Baseline renal and liver function tests

Age Restrictions

- 18 years of age and older

Prescriber Restrictions
• Must be prescribed by a rheumatologist

**Coverage Duration (months)**

- 6 months (initial), 12 months (continuation)
- If increasing to 9 mg daily, initial approval will be limited to 3 months to determine efficacy

**Quantity/Partial Fill Restrictions**

- None

**Other Information**

- Mechanism of action: In patients with adult rheumatoid arthritis, auranofin may modify disease activity as manifested by synovitis and associated symptoms and reflected by laboratory parameters such as ESR.
- Black Box Warning: Auranofin contains gold and, like other gold-containing drugs, can cause gold toxicity, signs of which include: fall in hemoglobin, leukopenia below 4,000 WBC/cu mm, granulocytes below 1,500/cu mm, decrease in platelets below 150,000/cu mm, proteinuria, hematuria, pruritus, rash, stomatitis or persistent diarrhea. Therefore, the results of recommended laboratory work should be reviewed before prescribing auranofin.
- Unlike anti-inflammatory drugs, auranofin does not produce an immediate response. Therapeutic effects may be seen after three to four months of treatment, although improvement has not been seen in some patients before six months.
- Warnings and Precautions: Gastrointestinal reactions reported with gold therapy include diarrhea/loose stools (reported in approximately 50% of patients), nausea, vomiting, anorexia and abdominal cramps. GI reactions are generally manageable by reducing the dosage. Ulcerative enterocolitis is a rare serious gold reaction. Therefore, patients with gastrointestinal symptoms should be monitored for the appearance of gastrointestinal bleeding. Gold can produce a nephrotic syndrome or glomerulitis with proteinuria and hematuria. Blood dyscrasias including leukopenia, granulocytopenia, thrombocytopenia and aplastic anemia have all been reported as reactions to injectable gold and auranofin.

**References**

Rituxan® (rituximab)

FDA Approved Indication(s)

- For the treatment of:
  - Non-Hodgkin's Lymphoma (NHL)
  - Chronic Lymphocytic Leukemia (CLL)
  - Rheumatoid Arthritis (RA) in combination with methotrexate in adult patients with moderately-to-severely-active RA who have inadequate response to one or more TNF antagonist therapies
  - Granulomatosis with Polyangiitis (GPA)(Wegener’s Granulomatosis) and Microscopic Polyangiitis (MPA)

FDA Recommended Dose

- NHL:
  - Relapsed or Refractory, Low-Grade or Follicular, CD20-Positive, B-Cell NHL
    - 375 mg/m²: administer once weekly for 4 or 8 doses
  - Retreatment for Relapsed or Refractory, Low-Grade or Follicular, CD20-Positive, B-Cell NHL
    - 375 mg/m²: administer once weekly for 4 doses
  - Previously Untreated, Follicular, CD20-Positive, B-Cell NHL
    - 375 mg/m²: administer on Day 1 of each cycle of chemotherapy, for up to 8 doses
    - In patients with complete or partial response, initiate rituximab maintenance eight weeks following completion of rituximab in combination with chemotherapy. Administer rituximab as a single-agent every 8 weeks for 12 doses
  - Non-progressing, Low-Grade, CD20-Positive, B-cell NHL, after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy
    - 375 mg/m²: following completion of 6–8 cycles of CVP chemotherapy, administer once weekly for 4 doses at 6-month intervals to a maximum of 16 doses
  - Previously Untreated Diffuse Large B-Cell, CD20-Positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens
    - 375 mg/m²: administer on Day 1 of each cycle of chemotherapy for up to 8 infusions
    - In combination with Zevalin® (ibritumomab tiuxetan)
      - 250 mg/m²: administer as intravenous infusion on day 1, 7, 8, and 9 of therapy
- CLL:
  - 375 mg/m² the day prior to the initiation of fludarabine and cyclophosphamide (FC) chemotherapy (cycle 1); then 500 mg/m² on Day 1 of cycles 2 – 6 (every 28 days)
- RA:
  - Two-1000 mg intravenous infusions spaced two weeks apart, in combination with methotrexate
  - Maintenance infusions may be administered every 24 weeks or based on clinical evaluation, but no sooner than 16 weeks from previous infusion
- GPA, MPA:
  - 375 mg/m² intravenous infusion once weekly for 4 weeks

How Supplied

- 100 mg/10 mL and 500 mg/50 mL single-use vials

Utilization Criteria

For initial review:
Member must have a documented diagnosis consistent with an FDA-approved indication, AND
Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable
For RA:
- Prescriber must be a rheumatologist, AND
- Member aged 18 years or older and has moderate to severely active disease, AND
- Member must be receiving concurrent methotrexate therapy, unless otherwise contraindicated or not tolerated, AND
- Member must have documented treatment failure with, or contraindication to, at least one non-biologic DMARD
For CLL:
- Prescriber must be an oncologist or hematologist
For GPA, MPA:
- Prescriber must be a rheumatologist or nephrologist, AND
- Member must have documented treatment failure or contraindication to both methotrexate and azathioprine, OR
- Member must have documented concerns about fertility, high risk of malignancy, relapsing disease or cyclophosphamide resistance, AND
- Member must be concurrently receiving glucocorticoids
NHL
- Prescriber must be an oncologist or hematologist

For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider
For RA:
- Member must not have received a rituximab infusion in the previous 16 weeks

Exclusion Criteria
- Member has an active infection
- Therapy to be used in combination with other DMARD therapy

Required Medical Information
- Diagnosis
- Age
- Dose
- Height and Weight
- Therapeutic history
- Concurrent medications

Age Restrictions
- For RA, GPA, and MPA
  - Member must be 18 years of age and older
- For all other indications, there is no age restriction

Prescriber Restrictions
- Must be prescribed by an oncologist/hematologist, rheumatologist, or nephrologist.

Coverage Duration (months)
- For NHL, CLL: Treatment coverage will be tailored by diagnosis and patient-specific care plan
For RA: 6 months (two infusions)
For GPA, MPA: 12 months

Quantity/Partial Fill Restrictions
- N/A

Other Information
- Mechanism of action: Rituximab is a CD20-directed cytotoxic antibody
- Black Box Warning: Members must be monitored for fatal infusion reactions and mucocutaneous reactions within 24 hours of infusion, hepatitis B virus (HBV) reactivation, and progressive multifocal leukoencephalopathy (PML)

References
Rubraca™ (rucaparib)

**FDA-Approved Indication(s):**
- For the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy
- For the treatment of adult patients with deleterious BRCA mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies

**FDA-Recommended Dose**
- 600 mg (two 300 mg tablets) orally twice daily with or without food

**How Supplied**
- 200 mg, 250 mg and 300 mg tablets

**Utilization Criteria**
- **For initial review:**
  - Member must have a diagnosis of an FDA-approved indication
- **For continuation:**
  - Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Pregnancy

**Required Medical Information**
- Diagnosis
- Concurrent medications
- Treatment history

**Age Restrictions**
- Must be 18 years of age or older

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration (months)**
- 3 Months

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- **Mechanism of Action:** Rucaparib is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP-1, PARP-2, and PARP-3, which play a role in DNA repair
- **Warnings and Precautions:** Myelodysplastic Syndrome (MDS)/Acute Myeloid Leukemia (AML) occur uncommonly in patients treated with rucaparib, and are potentially fatal adverse reactions. In approximately 1100 treated patients, MDS/AML occurred in 12 patients (1.1%), including those in long term follow-up. Rucaparib can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings from animal studies. Advise females of reproductive potential to use effective contraception during treatment and for 6 months following the last dose of rucaparib.

**References**

Last Reviewed April 13, 2018
## Ruconest® (c1- esterase inhibitor [recombinant])

### FDA Approved Indication(s)
- Ruconest® is a C1 esterase inhibitor indicated for the acute treatment of angioedema attacks in adolescent and adult patients with Hereditary Angioedema (HAE)

### FDA Recommended Dose
- 50 IU/kg to a maximum 4200 IU dose
- No more than two doses should be administered within a 24 hour period

### How Supplied
- Single-use 2100 IU/25 mL glass vial

### Utilization Criteria

**For initial review:**
- Member must have a diagnosis of classic HAE, where diagnosis is based on evidence of a normal C1 level and a low C4 level (C4 less than 14 mg/dL; normal range 14 to 40 mg/dL, or C4 below the lower limit of normal as defined by the laboratory performing the test), AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

### Exclusion Criteria
- Must not be receiving other c1-esterase inhibitor products for prophylaxis

### Required Medical Information
- Diagnosis with previous treatment history and number of HAE attacks occurred within the past year
- Current weight

### Age Restrictions
- 13 years of age or older

### Prescriber Restrictions
- Must be an allergist or other disease-specific specialist

### Coverage Duration (months)
- 12

### Quantity/Partial Fill Restrictions
- None

### Other Information
- Mechanism of action: C1 inhibitor is a normal constituent of human blood and is one of the serine proteinase inhibitors (serpins). The primary function of C1 inhibitor is to regulate the activation of the complement and intrinsic coagulation (contact system) pathway.

### References

*Last Reviewed November 10, 2015*
Rydapt® (midostaurin)

FDA Approved Indication(s)
- For the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) who are FLT3 mutation-positive, as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation chemotherapy.
- For the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL).

FDA Recommended Dose
- AML: 50 mg orally twice daily, on days 8 through 21 of each cycle of induction with cytarabine and daunorubicin and on days 8 through 21 of each cycle of consolidation with high-dose cytarabine
- ASM, SM-AHN, MCL: 100 mg orally twice daily

How Supplied
- 25 mg capsules, in cartons of 56 or 112 capsules

Utilization Criteria
For initial review:
AML:
- Member must documentation of FLT3 mutation-positive acute myeloid leukemia, as detected by an FDA-approved test, AND
- Must be used in combination with cytarabine and daunorubicin and high-dose cytarabine consolidation chemotherapy
ASM, SM-AHN, MCL:
- Member must have a diagnosis of aggressive systemic mastocytosis, systemic mastocytosis with associated hematological neoplasm, or mast cell leukemia

For continuation:
- Member must have documentation of treatment response, as verified per progress notes

Exclusion Criteria
- Pregnancy
- Diagnosis of interstitial lung disease (ILD) or pneumonitis

Required Medical Information
- Diagnosis
- Therapeutic history
- Baseline CBC
- FLT3 mutation testing, if diagnosed with AML

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
Mechanism of action: Midostaurin is a tyrosine kinase inhibitor which inhibits multiple receptors, such as wild type FLT3, FLT3 mutant kinases ITD and TKD, KIT (wild type and D816V mutant), PDGFRα/β, VEGFR2, and members of the serine/threonine protein kinase C (PKC) family. Midostaurin inhibits FLT3 receptor signaling and cell proliferation, and induces apoptosis in ITD- and TKD- mutant expressing leukemic cells, as well as in cells overexpressing wild type FLT3 and PDGFR. It also may inhibit KIT signaling, cell proliferation, and histamine release (and induces apoptosis) in mast cells.

References

Samsca® (tolvaptan)

FDA Approved Indication(s)
- For the treatment of clinically significant hypervolemic and euvolemic hyponatremia (serum sodium <125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction), including patients with heart failure and Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

FDA Recommended Dose
- The usual starting dose for tolvaptan is 15 mg administered once daily without regard to meals. Increase the dose to 30 mg once daily, after at least 24 hours, to a maximum of 60 mg once daily, as needed to achieve the desired level of serum sodium.
- Do not administer tolvaptan for more than 30 days to minimize the risk of liver injury.

How Supplied
- 15 mg and 30 mg tablets

Utilization Criteria
For initial review:
- Patient has tried and failed other therapies (e.g. fluid restriction, loop diuretics, demeclocycline, salt tablets, hypertonic saline), AND
- Drug-induced hyponatremia (or SIADH) has been ruled out, AND
- Tolvaptan is initiated or re-initiated in the inpatient setting, AND
- Patient has a diagnosis of clinically significant hypervolemic or euvolemic hyponatremia (serum sodium < 125 mEq/L), OR
- Patient has serum sodium < 130 mEq/L with symptoms (e.g. nausea, vomiting, headache, lethargy, confusion) that have not responded to fluid restriction and have had a treatment failure, allergy, or intolerance to a trial of demeclocycline (not required if the patient is allergic to tetracyclines)

Exclusion Criteria
- Inability of the patient to sense or appropriately respond to thirst
- Hypovolemic hyponatremia
- Concomitant use of strong CYP3A inhibitors
- Anuric patients

Required Medical Information
- Diagnosis
- Age
- Dose
- Serum Sodium
- Concurrent Medications
- Treatment and monitoring plan

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an endocrinologist or nephrologist

Coverage Duration (months)
- 0.5

Quantity/Partial Fill Restrictions
- Maximum allowable dose is capped at 60 mg per day

Other Information
Mechanism of action: Tolvaptan is a selective vasopressin V2-receptor antagonist with an affinity for the V2-receptor that is 1.8 times that of native arginine vasopressin (AVP). Tolvaptan affinity for the V2-receptor is 29 times greater than for the V1a-receptor. When taken orally, 15 to 60 mg doses of tolvaptan antagonize the effect of vasopressin and cause an increase in urine water excretion that results in an increase in free water clearance (aquaresis), a decrease in urine osmolality, and a resulting increase in serum sodium concentrations. Urinary excretion of sodium and potassium and plasma potassium concentrations are not significantly changed. Tolvaptan metabolites have no or weak antagonist activity for human V2-receptors compared with tolvaptan.

Black Box Warning: Initiate and re-initiate in a hospital and monitor serum sodium.

References

Sancuso® (granisetron)

FDA Approved Indication(s)
- For the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy for up to 5 consecutive days

FDA Recommended Dose
- One patch (34.3 mg) applied 24-48 hours before chemotherapy

How Supplied
- 52 cm² patch containing 34.3 mg of granisetron

Utilization Criteria
For initial review:
- Patient must be undergoing emetogenic chemotherapy (see below), AND
- Patient is intolerant to two or more anti-emetic therapies, one of which includes ondansetron, as documented in chart notes

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Moderate to Severe emetogenic therapies include:

| Aldesleukin | Clofarabine |
| Amifostine (> 300 mg/m²) | Cyclophosphamide |
| Arsenic trioxide | Cytarabine (> 200 mg/m²) |
| Azacitidine | Dacarbazine |
| Bendamustine | Daclomycin |
| Busulfan | Daunorubicin |
| Carmustin | Doxorubicin |
| Carboplatin | Epirubicin |
| Cisplatin | Idarubicin |
| Ifosamide | Interferon alfa (≥ 10 million IU/m²) |
| Irinotecan | Mechloretamine |
| Melphalan | Methotrexate (≥ 250 mg/m²) |
| Oxaliplatin | Streptozocin |
| Temozolomide |

Exclusion Criteria
- Extended wear of the patch exceeding 5 days

Required Medical Information
- Diagnosis
- Age
- Dose
- Concurrent medications

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- Quantity will be based on the individual’s chemotherapy protocol

Other Information
- Mechanism of action: Granisetron is a selective 5-hydroxytryptamine3 (5-HT3) receptor antagonist
### References

Sensipar® (cinacalcet)

FDA Approved Indication(s)

- Secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on dialysis
- Hypercalcemia in adult patients with parathyroid carcinoma (PC)
- Hypercalcemia in adult patients with primary HPT for whom parathyroidectomy would be indicated on the basis of serum calcium levels, but who are unable to undergo parathyroidectomy

FDA Recommended Dose

- Secondary HPT in patients with CKD on dialysis
  - Starting dose is 30 mg once daily
  - Titrate dose no more frequently than every 2 to 4 weeks through sequential doses of 30, 60, 90, 120, and 180 mg once daily as necessary to achieve goal intact parathyroid hormone levels (iPTH)
- Hypercalcemia in patients with PC or hypercalcemia in patients with primary HPT
  - Starting dose is 30 mg twice daily
  - Titrate dose every 2 to 4 weeks through sequential doses of 30 mg twice daily, 60 mg twice daily, 90 mg twice daily, and 90 mg three or four times daily as necessary to normalize serum calcium levels

How Supplied

- 30, 60, and 90 mg tablets

Utilization Criteria

**For initial review:**
- Member must have a diagnosis matching an FDA-approved indication
- Therapy must be initiated at the recommended FDA-approved starting dose

**For continuation:**
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s prescriber

Exclusion Criteria

- Patient has documented serum calcium less than the lower limit of the normal range
- Prescriber initiates doses higher than the starting dose recommended by the FDA if the patient has never been on Sensipar®

Required Medical Information

- Diagnosis
- Age
- Dose
- Concurrent medications
- Treatment history
- Baseline iPTH levels
- Baseline calcium levels

Age Restrictions

- 18 years of age and older, Sensipar® is not indicated for use in pediatric patients.

Prescriber Restrictions

- None

Coverage Duration (months)

- 12
Quantity/Partial Fill Restrictions

- None

Other Information

- Mechanism of action: Cinacalcet, the active ingredient in Sensipar®, directly lowers PTH levels by increasing the sensitivity of the calcium-sensing receptor to extracellular calcium. The calcium-sensing receptor on the parathyroid gland is the principal regulator of PTH synthesis and secretion. The reduction in PTH is associated with concomitant decrease in serum calcium levels.

- In three randomized studies of patients with CKD on dialysis, the median cinacalcet dose reached was 90 mg per day and 40% of patients reached goal iPTH levels less than 250 picograms/mL compared to those receiving placebo.

- There is no all-cause or cardiovascular mortality benefit for cinacalcet plus standard therapy compared with placebo, but cinacalcet reduces the need for parathyroidectomy in patients with CKD stage 5D.

References

Serostim® (somatropin)

FDA Approved Indication(s)

- For the treatment of HIV associated wasting or cachexia

FDA Recommended Dose

- 0.1 mg/kg (up to 6 mg) subcutaneously, once daily

How Supplied

- 4 mg multiple-use vial
- 5 mg and 6 mg single-use vial

Utilization Criteria

For initial review:

- Patient is receiving concurrent antiviral therapy, AND
- Patient has involuntary weight loss greater than 10% of baseline body weight or significant weight loss (BMI < 20kg/m^2) and ≥ 1 of the following:
  - Chronic diarrhea (at least 2 loose stools per day for 30 days)
  - Chronic weakness and documented fever (for 30 days or more, intermittent or constant) in the absence of concurrent illness or any condition other than HIV infection that could explain the findings (cancer, tuberculosis, cryptosporidiosis, or other specific enteritis), AND
- The following have been verified:
  - Other potential causes of weight loss have been ruled out
  - Adequate dietary intake (receiving at least 100% of estimated caloric requirement on current nutritional regimen)
  - Written evaluation by a registered dietician that documents adequate nutrition
  - A documented baseline body weight and BMI

For continuation:

- Evidence of beneficial response to somatropin during the initial 12 weeks of therapy (2% or greater increase in body weight or BMI; AND
- Still exhibits evidence of wasting (BMI < 20 kg/m^2); OR
- BCM (body cell mass) not yet normalized (< 40% in non-obese men or < 28% in non-obese women)
- As long as patient continues to gain weight or BCM, Serostim may be extended every 28 days with prior authorization, until BCM and/or weight are normalized

Exclusion Criteria

- None

Required Medical Information

- Diagnosis
- Age
- Dose
- Weight
- Concurrent therapies

Age Restrictions

- 18 years of age and older

Prescriber Restrictions

- Must be prescribed by an HIV specialist

Coverage Duration (months)

- 12 weeks initial therapy, 28 days per authorization after
Quantity/Partial Fill Restrictions

- None

Other Information

- Mechanism of action: Serostim® is an anabolic and anticatabolic agent which exerts its influence by interacting with specific receptors on a variety of cell types including myocytes, hepatocytes, adipocytes, lymphocytes, and hematopoietic cells. Some, but not all of its effects, are mediated by insulin-like growth factor-1 (IGF-1).

References

# Siliq™ (brodalumab)

## FDA Approved Indication(s)
- For the treatment of moderate to severe plaque psoriasis (PsO) in adults who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies

## FDA Recommended Dose
- 210 mg at weeks 0, 1, and 2 followed by 210 mg every 2 weeks

## How Supplied
- 210 mg/1.5 mL single-dose prefilled syringe

## Utilization Criteria

### For initial review:
- Member must have a diagnosis of moderate-to-severe plaque psoriasis, AND
- Documented negative tuberculosis (TB) test at baseline, AND
- Member must have failed, or did not tolerate, a 3-month trial of at least one conventional or non-biologic disease modifying therapy, such as methotrexate, cyclosporine, PUVA or UVB, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable

### For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider
- Member must have evidence of clinical response by week 16 of brodalumab

## Exclusion Criteria
- Member has Crohn’s disease

## Required Medical Information
- Diagnosis, including documentation of disease severity and body surface area (BSA) coverage
- Age
- Dose
- Treatment history

## Age Restrictions
- 18 years of age and older

## Prescriber Restrictions
- Must be prescribed by a dermatologist certified through the SILIQ REMS program™

## Coverage Duration (months)
- 4 month initial approval to determine response
- 12 months continuation

## Quantity/Partial Fill Restrictions
- None

## Other Information
- Mechanism of action: Brodalumab is a human IgG2 monoclonal antibody that selectively binds to the interleukin-17A (IL-17A) cytokine, inhibiting its interaction with the IL-17 receptor.
- Black Box Warning: Suicidal ideation and behavior, including completed suicides, has been observed in clinical trials.
In the three placebo-controlled trials, the percent of subjects who achieved a Psoriasis Area and Severity Index (PASI)-75 score ranged from 83-86% by week 12 of therapy. Two of the clinical trials also compared brodalumab to ustekinumab and subjects in the brodalumab group achieved a higher PASI-75 score by week 12 of therapy that ranged from 85-86% compared to 69-70% in the ustekinumab group.

References

- Redbook Online®. Truven Health Analytics LLC Micromedex Solutions; July 2017.
Simponi®, Simponi ARIA® (golimumab)

FDA Approved Indication(s)

- For the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate (Simponi® and Simponi ARIA®)
- For the treatment of adult patients with active psoriatic arthritis (PsA) (Simponi®)
- For the treatment of adult patients with active ankylosing spondylitis (AS) (Simponi®)
- For the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response to or failed to tolerate prior treatment, or who require continuous steroid therapy (Simponi®)

FDA Recommended Dose

- Rheumatoid Arthritis, Psoriatic Arthritis and Ankylosing Spondylitis:
  - 50 mg once monthly
- Ulcerative colitis:
  - 200 mg at week 0, 100 mg at week 2, followed by 100 mg every 4 weeks
- Rheumatoid Arthritis (Simponi ARIA®):
  - 2 mg/kg IV infusion over 30 minutes at weeks 0 and 4, then every 8 weeks thereafter

How Supplied

- Simponi®:
  - 50 mg/0.5 mL in a single dose prefilled SmartJect® autoinjector
  - 50 mg/0.5 mL in a single dose prefilled syringe
  - 100 mg/1 mL in a single dose prefilled SmartJect® autoinjector
  - 100 mg/1 mL in a single dose prefilled syringe
- Simponi ARIA®:
  - 50 mg/4mL single-use vial for infusion

Utilization Criteria

For initial review:

- Member must have a negative TB baseline test, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable
- Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis:
  - Member is receiving methotrexate concomitantly, OR
  - Member has documented failure of, or intolerance to methotrexate or >1 non-biologic DMARD therapy, AND
  - Coverage of infused formulation requires documented intolerance to, or inability to safely administer, self-injectable product
- Moderate to severe Ulcerative colitis:
  - Member has documented failure of >1 conventional therapy (i.e. aminosalicylates, corticosteroids, azathioprine, or 6-mercaptopurine)

For continuation:

- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria

- Patient is receiving alternative biologic DMARD therapy
Defined Term:

**Skyrizi™ (risankizumab-rzaa)**

**FDA Approved Indication(s)**

- Treatment of moderate-to-severe plaque psoriasis (PsO) in adults who are candidates for systemic or phototherapy

**FDA Recommended Dose**

- Initial: 150 mg (two 75 mg injections) subcutaneously at Week 0 and Week 4, followed by:
  - Maintenance: 150 mg (two 75 mg injections subcutaneously every 12 weeks

**How Supplied**

- Each carton: 2 x 75 mg/0.83 mL solution as a single-dose prefilled syringe

**Utilization Criteria**

*For initial review:*

- Member must have a documented diagnosis of moderate to severe plaque psoriasis, AND
  - Documentation of a negative TB test AND
  - Documentation of psoriasis involving at least 10% body surface area (BSA), OR

**References**

- Documentation of psoriatic lesions affecting the hands, feet, or genital area leading to disability or impact on quality of life, AND
- Member must have had a previous trial of at least one or more forms of preferred conventional or non-biologic therapies, such as PUVA (Phototherapy Ultraviolet Light A), UVB (Ultraviolet Light B), acitretin, methotrexate, or cyclosporine, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable

**For continuation:**
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Member must have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Member currently receiving one or more biologic DMARD therapies

**Required Medical Information**
- Age
- Diagnosis
- Treatment history
- Concurrent medications

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a dermatologist

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: Risankizumab-rzaa is a human IgG1 monoclonal antibody that binds with high affinity and specificity to the p19 subunit of IL-23 cytokines and inhibits its interaction with the IL-23 receptor.

**References**
- Skyrizi™ [product insert]. North Chicago, IL. AbbVie Inc. April 2019

**Last Reviewed [Date]**
### Sovaldi® (sofosbuvir)

**FDA Approved Indication(s)**
- For the treatment of Chronic Hepatitis C (CHC, HCV) infection (Genotypes 1-4) as a component of a combination antiviral treatment regimen

**FDA Recommended Dose**
- One 400 mg tablet taken once daily, in combination with ribavirin and/or pegylated interferon
  - Genotypes 1,4: Sofosbuvir + Peginterferon alfa + Ribavirin for 12 weeks
  - Genotype 2: Sofosbuvir + Ribavirin for 12 weeks
  - Genotype 3: Sofosbuvir + Ribavirin for 24 weeks
- For patients with genotype 1 who are have a true contraindication with peginterferon alpha, such as a known hypersensitivity to peginterferon alpha-2a/b, autoimmune hepatitis, or hepatic decompensation with cirrhosis, 24 weeks of sofosbuvir and ribavirin may be considered (see utilization criteria below)
- For patients with hepatocellular carcinoma, treatment may continue for 48 weeks, or until liver transplantation

**How Supplied**
- 400 mg tablets dispensed in a 28-count bottle

**Utilization Criteria**

*For initial review:*
- Member must have a diagnosis of HCV genotype 1-6 with documented viral load collected within the previous three months, AND
- Physician must attest to the patient’s ability and dedication to remain adherent to the entire course of therapy, AND
- Physician must confirm that alcohol and illicit substance abuse is absent for the previous six months, or patient is currently seeing an addiction specialist, AND
- Member is concurrently receiving weight-based ribavirin, AND
- Utilization with simeprevir for patients with genotype 1 will be allowed only under the condition that the patient meets all utilization criteria for simeprevir and has a true contraindication to peginterferon alpha; such contradictions include:
  - known hypersensitivity to peginterferon alpha-2a/b
  - autoimmune hepatitis
  - hepatic decompensation with cirrhosis
  - major, uncontrolled depressive disorder
  - neutrophil count < 1,500/µL
  - platelet count < 90,000/µL
  - hemoglobin < 10 g/dL
  - preexisting cardiac disease
- Coverage of 24 weeks of sofosbuvir and ribavirin will be considered if the patient is both interferon intolerant and does not meet the criteria for simeprevir coverage
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

*For Extended Therapy:*
- Member has had a documented response to therapy based upon viral load, AND
- Member has remained adherent throughout therapy

**Exclusion Criteria**
• Prescribed for use as monotherapy, OR
• Concurrent use of P-gp inhibitors (i.e., St. John’s Wort, rifampin, select anti-convulsants), OR
• Pregnancy, OR
• Concurrent use of amiodarone and another direct acting anti-viral, OR
• Severe renal impairment (CrCl < 30 ml/min, or End Stage Renal Disease), OR
• Coverage may be revoked if patient is non-adherent through the first two months of therapy, as evidenced by claim records or verbal confirmation of poor adherence

Required Medical Information

• Diagnosis including genotype
• Viral load
• Treatment history
• Age
• Dose and duration of therapy
• Pregnancy Status
• Concurrent medications

Age Restrictions

• Must be 18 years of age or older

Prescriber Restrictions

• Must be prescribed by a gastroenterologist or infectious disease specialist

Coverage Duration (months)

• 3 months (12 weeks) if HCV Genotype 1, 2, 4, 5 or 6
• 6 months (24 weeks) if HCV genotype 3, or genotype 1 and patient is ineligible for interferon and simeprevir therapies
• Extended therapy up to 48 weeks may be considered for patients with hepatocellular carcinoma and documented response to therapy

Quantity/Partial Fill Restrictions

• None

Other Information

• Mechanism of action: Sofosbuvir is a nucleotide analog NS5B polymerase inhibitor.
• Place in therapy: Sofosbuvir may be used first line in patients who were both previously treated and who are naïve to therapy. No cross-resistance was shown in non-clinical studies with HCV replicons expressing NS3/4A, NS5B, or NS5A resistant mutations.

References


Spinraza™ (nusinersen)

FDA-Approved Indication(s):  
• For the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients

FDA-Recommended Dose
• Loading dose: 12 mg once every 14 days for 3 doses; then 12 mg once 30 days after the third dose
• Maintenance: 12 mg once every 4 months

How Supplied
• 12 mg/5 mL (2.4 mg/mL) solution in a single-dose glass vial

Utilization Criteria
For initial review:
• Documentation of confirmatory Type 1 SMA diagnosis:
  • Genetic documentation of 5q SMA homozygous gene deletion, homozygous mutation, or compound heterozygote, AND
  • Documentation of SMA-associated symptoms, such as proximal predominant weakness, reduced or absent reflexes, tongue fasciculations, and limb tremor, with onset before 6 months of age, AND
  • Baseline assessment of motor function with the Hammersmith Infant Neurologic Exam (HINE) or the Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND)

For continuation:
• Member must have objective documentation of treatment response as verified by a significant improvement in spinal muscular atrophy-associated symptoms per a standardized motor function test:
  • HINE: Improvement from baseline in more categories of motor milestones than worsening, with at least a 2-point increase in ability to kick, or at least a 1-point increase in head control, rolling, sitting, crawling, standing or walking
  • CHOP INTEND: 4-point improvement or greater from baseline

Exclusion Criteria
• Diagnosis of a non-5q-spinal muscular atrophy disorders

Required Medical Information
• Diagnosis
• Treatment history
• Baseline assessment of motor function per a standardized test, such as the HINE or CHOP INTEND

Age Restrictions
• Must be 6 months of age or older, limited to Type 1 SMA

Prescriber Restrictions
• Must be prescribed by a specialist in SMA disorders

Coverage Duration (months)
• 3 Months

Quantity/Partial Fill Restrictions
• None

Other Information
• Mechanism of Action: Nusinersen is an antisense oligonucleotide (ASO) designed to treat SMA caused by mutations in chromosome 5q that lead to SMN protein deficiency. Nusinersen binds to a specific sequence in the intron downstream of exon 7 of the SMN2 transcript.

References
• Spinraza™ (nusinersen) [prescribing information]. Cambridge, MA: Biogen; December 2016.
Spravato™ (esketamine hydrochloride solution)

**FDA Approved Indication(s)**
- Treatment-resistant depression (TRD) in adults, in conjunction with an oral antidepressant

**FDA Recommended Dose**
- Weeks 1 to 4: 56 mg day 1 then 56 mg or 84 mg twice weekly
- Weeks 5 to 8: 56 mg or 84 mg once weekly
- Maintenance: 56 mg or 84 mg every 2 weeks OR once weekly

**How Supplied**
- 56 mg Kit: two 28 mg nasal spray devices (each device delivers two sprays of 28 mg esketamine)
- 84 mg Kit: three 28 mg nasal spray devices (each device delivers two sprays of 28 mg esketamine)

**Utilization Criteria**

*For initial review:*
- Member must have a diagnosis of major depressive disorder, AND
- Member must have tried and failed at least two different antidepressants, at standard dosing or higher, for a minimum trial period of six weeks, AND
- Documentation Spravato™ is used in combination with an oral antidepressant, taken for at least two weeks before starting Spravato™ therapy

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial and peripheral arterial vessels) or arteriovenous malformation
- History of intracerebral hemorrhage

**Required Medical Information**
- Diagnosis
- Baseline blood pressure (BP)
- Therapeutic history
- Current treatments

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a psychiatrist

**Coverage Duration (months)**
- Initial: 1 month
- Induction: 3 months
- Maintenance: 8 months initial followed by 12 months

**Quantity/Partial Fill Restrictions**
- None
Other Information

- Mechanism of action: Esketamine is a non-competitive antagonist of N-methyl-D-aspartate (NMDA) receptor. Antidepressant effect of esketamine is unknown. Esketamine’s major metabolite, noresketamine, is active at the same receptor with less affinity.
- Black Box Warning: Sedation, Dissociation, Abuse and Misuse and Suicidal thoughts and behaviors

References


Last Reviewed August 5, 2019
Sprycel® (dasatinib)

FDA Approved Indication(s)
- For the treatment of adult patients with:
  - Newly diagnosed Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase
  - Chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib
  - Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy
- For the treatment of pediatric patients with:
  - Ph+ CML in chronic phase
  - Ph+ ALL, newly diagnosed, in combination with chemotherapy

FDA Recommended Dose
- Chronic phase CML in adults: 100 mg once daily
- Accelerated phase CML, myeloid or lymphoid blast phase CML, Ph+ ALL in adults: 140 mg once daily
- Pediatric dosing (1 year of age and older):

<table>
<thead>
<tr>
<th>Body Weight (kg)</th>
<th>Daily Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 kg to less than 20 kg</td>
<td>40 mg</td>
</tr>
<tr>
<td>20 kg to less than 30 kg</td>
<td>60 mg</td>
</tr>
<tr>
<td>30 kg to less than 45 kg</td>
<td>70 mg</td>
</tr>
<tr>
<td>at least 45 kg</td>
<td>100 mg</td>
</tr>
</tbody>
</table>

- See prescribing information for dose modification and dose escalation

How Supplied
- 20 mg, 50 mg, 70 mg, 80 mg, 100 mg and 140 mg tablets

Utilization Criteria

For initial review:
- Patient has documentation of Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase; OR
- Patient has diagnosis of chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with documentation of resistance or intolerance to imatinib; OR
- Patient has diagnosis of Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with documentation of resistance or intolerance to prior therapy
- Pediatric patient has diagnosis of Ph+ CML or new diagnosis or Ph+ ALL

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Pregnancy
- History of QT prolongation
- Pre-existing myelosuppression

Required Medical Information
- Diagnosis
- Treatment history and concurrent medications
- Complete blood count with differential
- Liver function tests (AST, ALT, serum bilirubin)
**Age Restrictions**
- Ph+ CML in chronic phase: none
- Other indications: 1 year of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist or hematologist

**Coverage Duration (months)**
- 3 months (initial), 12 months (continuation)

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: Dasatinib inhibits kinases, including BCR-ABL, SRC family (SRC, LCK, YES, FYN), c-KIT, EPHA2, and PDGFRβ. Based on modeling studies, dasatinib is predicted to bind to multiple conformations of the ABL kinase.
- Warnings and precautions: Dasatinib treatment is associated with severe (grade 3 or 4) thrombocytopenia, neutropenia, and anemia; serious and fatal bleeding events; fluid retention; cardiac dysfunction; and may increase the risk of pulmonary arterial hypertension and QTc prolongation. Due to the potential for tumor lysis syndrome, maintain adequate hydration, correct uric acid levels prior to initiating therapy with dasatinib, and monitor electrolyte levels.

**References**
- Sprycel® [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; December 2018
Stelara® (ustekinumab)

FDA Approved Indication(s)
- Moderate to severe plaque psoriasis in members who are candidates for phototherapy or systemic therapy
- Active psoriatic arthritis, alone or in combination with methotrexate
- Moderately to severely active Crohn’s disease in members who have failed or were intolerant to treatment with immunomodulators, corticosteroids, or one or more tumor necrosis factor (TNF) blockers

FDA Recommended Dose
- Moderate to severe plaque psoriasis:
  - For Members weighing ≤100 kg (220 lbs), the recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks
  - For Members weighing >100 kg (220 lbs), the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks
- Active psoriatic arthritis:
  - 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks
  - For Members with coexistent moderate-to-severe plaque psoriasis weighing > 100 kg (220 lbs), the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks
- Crohn’s disease:
  - Weight-based intravenous induction dose:
    - | Body Weight of Patient | Dose |
    |------------------------|------|
    | 55 kg or less          | 260 mg |
    | More than 55 kg to 85 kg | 390 mg |
    | More than 85 kg        | 520 mg |
  - Subcutaneous maintenance dose of 90 mg administered 8 weeks after the initial intravenous dose, then every 8 weeks thereafter

How Supplied
- 45 mg/0.5 mL and 90 mg/1 mL prefilled syringes
- 45 mg/0.5 mL and 90 mg/1 mL vials

Utilization Criteria
For initial review:
- Member must have a documented negative TB test at baseline, AND
- Member has no active infection (including bacterial, fungal or viral), AND
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Plaque psoriasis/psoriatic arthritis
  - Documented failure of, intolerance or contraindication to, at least two traditional therapies (e.g., PUVA, UVB, methotrexate, or cyclosporine)
- Crohn’s disease
  - Prescriber is a gastroenterologist, AND
  - Member has tried and failed 2 or more of the following for at least 60 days:
    - Azathioprine
    - Balsalazide disodium
    - Budesonide
- Cyclosporine
- Mercaptopurine
- Mesalamine
- Methotrexate
- Osalazine sodium
- Prednisone
- Sulfasalazine

For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Member is currently receiving one or more biologic DMARD therapies

Required Medical Information
- Age
- Diagnosis
- Weight
- Treatment history
- Concurrent medications

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a dermatologist, rheumatologist, or gastroenterologist

Coverage Duration (months)
- 12 months

Quantity/Partial Fill Restrictions
- Plaque psoriasis/psoriatic arthritis: 30 day induction, 12 week maintenance
- Crohn’s disease: One-time intravenous induction dose, 8 week maintenance

Other Information
- Ustekinumab is a human IgG1κ monoclonal antibody that binds with high affinity and specificity to the p40 protein subunit used by both the interleukin (IL)-12 and IL-23 cytokines

References
### Stivarga® (regorafenib)

**FDA Approved Indication(s)**
- The treatment of locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) in patients who have been previously treated with imatinib and sunitinib
- The treatment of metastatic colorectal cancer (CRC) in patients who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF therapy, and an anti-EGFR therapy (if KRAS wild type)
- The treatment of hepatocellular carcinoma (HCC) in patients who have been previously treated with sorafenib

**FDA Recommended Dose**
- The recommended dose of regorafenib is 160 mg orally, once daily for the first 21 days of each 28-day cycle until disease progression or unacceptable toxicity.
- Regorafenib should be taken with a low-fat meal (< 30% fat).

**How Supplied**
- 40 mg tablets

### Utilization Criteria

**For initial review:**
- Diagnosis of metastatic colorectal cancer (CRC)
  - Previously treated with the following therapies:
    - Fluoropyrimidine-based chemotherapy (fluouracil, capecitabine)
    - Oxaliplatin-based chemotherapy
    - Irinotecan-based chemotherapy
    - Anti-VEGF therapy (bevacizumab, aflibercept)
    - Anti-EGFR therapy (panitumumab, cetuximab) if KRAS wild type mCRC
- Diagnosis of GIST
  - Patient is unable to undergo surgical removal of tumor, OR
  - Patient had disease progression to other parts of the body (metastatic), AND
  - Patient had previous treatment with both imatinib and sunitinib
- Diagnosis of HCC
  - Patient is not a transplant candidate, OR
  - Patient is unable to undergo surgical removal of tumor, OR
  - Patient had disease progression to other parts of the body (metastatic), AND
  - Patient had previous treatment with sorafenib

**For continuation:**
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

### Exclusion Criteria
- None

### Required Medical Information
- Diagnosis
- Age
- Dose
• Baseline liver function status (ALT, AST, serum bilirubin)
• Previous therapies

Age Restrictions
• 18 years of age and older

Prescriber Restrictions
• Must be prescribed by an oncologist

Coverage Duration (months)
• 12

Quantity/Partial Fill Restrictions
• None

Other Information
• Mechanism of action: Regorafenib is a small molecule inhibitor of multiple membrane-bound and intracellular kinases involved in normal cellular functions and in pathologic processes such as oncogenesis, tumor angiogenesis, and maintenance of the tumor microenvironment.
• Black Box Warning: Severe and sometimes fatal hepatotoxicity has been observed in clinical trials.

References

Last Reviewed August 11, 2017
# Strensiq™ (asfotase alfa)

**FDA-Approved Indication(s)**
- For the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP)

**FDA-Recommended Dose**
- 6 mg/kg per week administered subcutaneously as either:
  - 2 mg/kg three times per week, or
  - 1 mg/kg six times per week.
- The dose may be increased for lack of efficacy (e.g., no improvement in respiratory status, growth, or radiographic findings) up to 9 mg/kg per week administered subcutaneously as 3 mg/kg three times per week

**How Supplied**
- Available as 18 mg/0.45 mL, 28 mg/0.7 mL, 40 mg/mL, and 80 mg/0.8 mL

**Utilization Criteria**

*For initial review:*
- Member must have a diagnosis of perinatal/infantile or juvenile-onset HPP

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s provider

**Exclusion Criteria**
- None

**Required Medical Information**
- Age
- Diagnosis
- Dose

**Age Restrictions**
- Member must be less than 18 years old

**Prescriber Restrictions**
- Must be prescribed by a specialist experienced in the diagnosis and treatment of HPP

**Coverage Duration (months)**
- 12 months

**Quantity/Partial-Fill Restrictions**
- Dose optimization will be performed to minimize vial waste

**Other Information**
- Mechanism of action: HPP is caused by a deficiency in TNSALP enzyme activity, which leads to elevations in several TNSALP substrates, including inorganic pyrophosphate (PPI). Elevated extracellular levels of PPI block hydroxyapatite crystal growth which inhibits bone mineralization and causes an accumulation of unmineralized bone matrix which manifests as rickets and bone deformation in infants and children and as osteomalacia (softening of bones) once growth plates close, along with muscle weakness. Replacement of the TNSALP enzyme upon treatment reduces the enzyme substrate levels.
- Hypophosphatasia is a rare, autosomal disease that is associated with low levels of alkaline phosphatase in serum and bone and the development of osteomalacia and severe periodontal disease. Approximately 224 mutations of the TSALP have been identified. The severe forms are usually inherited as an autosomal recessive trait. The childhood and adult forms are autosomal
dominant traits with variable penetrance and clinical expression. The disease may present in the perinatal period, when it is lethal, and in infancy, where initial development appears normal. However, rachitic deformities develop by age six months, and approximately 50 percent of affected patients die during infancy. Hypophosphatasia may also develop during childhood, with premature loss of deciduous teeth, delayed walking, and waddling gait. Symptoms may improve spontaneously after puberty and recur later in life.

References

- Drezner, M. Epidemiology and etiology of osteomalacia. In: UpToDate, Snyder PJ (Ed), UpToDate, Waltham, MA. (Accessed on February 25, 2016.)
# Sutent® (sunitinib)

## FDA Approved Indication(s)
- For the treatment of gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib mesylate
- For the treatment of advanced renal cell carcinoma (RCC)
- For the adjuvant treatment of adult patients at high risk of recurrent RCC following nephrectomy
- For the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors (pNET) in patients with unresectable locally advanced or metastatic disease

## FDA Recommended Dose
- GIST and advanced RCC: 50 mg once daily for 4 weeks, followed by 2 weeks off
- Adjuvant treatment of RCC: 50 mg orally once daily for 4 weeks, followed by 2 weeks off for nine 6-week cycles
- pNET: 37.5 mg orally once daily

## How Supplied
- 12.5 mg, 25 mg, 37.5 mg and 50 mg capsules

## Utilization Criteria
**For initial review:**
- Member must have documentation of a diagnosis consistent with an FDA-approved indication, AND
- For with the treatment of GIST, member must have documentation of therapeutic trial of imatinib

**For continuation:**
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

## Exclusion Criteria
- Liver function tests >3x upper limit of normal
- Left ventricular ejection fraction (LVEF) below lower limit of normal

## Required Medical Information
- Diagnosis
- Age
- Dose
- Liver function tests (ALT, AST, bilirubin)
- Concurrent therapies
- LVEF

## Age Restrictions
- 18 years of age and older

## Prescriber Restrictions
- Must be prescribed by an oncologist

## Coverage Duration (months)
- 3 months (initial), 12 months (continuation)

## Quantity/Partial Fill Restrictions
- None

## Other Information
- Mechanism of action: Sunitinib is a small molecule that inhibits multiple receptor tyrosine kinases (RTKs), some of which are implicated in tumor growth, pathologic angiogenesis, and metastatic progression of cancer.
• Black Box Warning: Severe and fatal hepatotoxicity has been observed in clinical trials

References


Last Reviewed March 2, 2018
**Symdeko™ (tezacaftor/ivacaftor)**

**FDA Approved Indication(s)**
- For the treatment of cystic fibrosis (CF) in patients age 12 years and older who are homozygous for the F508del mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor
- If the patient’s genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

**FDA Recommended Dose**
- One Tezacaftor 100 mg/Ivacaftor 150 mg tablet taken orally in the morning and one Ivacaftor 150 mg in the evening, approximately 12 hours apart with fat-containing food.

**How Supplied**
- Tezacaftor 100 mg/Ivacaftor 150 mg tablets (yellow) and Ivacaftor 150 mg tablets (light blue); supplied in 56-count tablet carton containing a 4-week supply.

**Utilization Criteria**

*For initial review:*
- Member must have a diagnosis of cystic fibrosis with at least one of the following:
  - Documentation of two copies of the F508del mutation, OR
  - Documentation of one mutation responsive to tezacaftor/ivacaftor, AND
- Member is 12 years of age or older, AND
- Documentation of significant impairment of forced expiratory volume (FEV1), or presence of symptoms secondary to the decline in FEV1

*For continuation:*
- Documented clinical benefit, as evidenced by an improvement in FEV1, AND
- Member’s AST/ALT have remained within normal range

**Exclusion Criteria**
- Member has diagnosis of CF without the homozygous F508del mutation or mutation unresponsive to tezacaftor/ivacaftor

**Required Medical Information**
- Age
- Weight
- Concomitant medications
- Dose
- Documentation of mutation test results
- Baseline AST/ALT
- Forced expiratory volume (FEV1)

**Age Restrictions**
- 12 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a pulmonary specialist

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- None
Other Information

- Mechanism of action: Tezacaftor improves the conformation stability of F508del-CFTR, resulting in increased processing and trafficking of mature protein to the cell surface. Ivacaftor is a CFTR potentiator that facilitates increased chloride transport by potentiating the channel-open probability (or gating) of the CFTR protein at the cell surface.
- Black Box Warning: None
- Warnings and precautions: Elevated AST/ALT has occurred with treatment. Recommended to have a baseline ALT/AST and every 3 months during the first year of treatment, then yearly thereafter. Co-administration with CYP3A inducers is not recommended. Cataracts have been reported in pediatric patients. Baseline and periodic eye exams are recommended.

References


Last Reviewed April 3, 2018
Synagis® (palivizumab)

FDA Approved Indication(s)
- For the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in children at high-risk of RSV disease

FDA Recommended Dose
- 15 mg/kg intramuscularly monthly throughout RSV season

How Supplied
- 50 mg/0.5 mL and 100 mg/1 mL single-dose solution vials

Utilization Criteria
- Preterm infants without chronic lung disease (CLD) of prematurity or congenital heart disease (CHD)
  - Child < 12 months of age at start of RSV season*, born before 29 weeks, 0 days gestation
- Preterm infants with CLD
  - Child < 12 months of age at start of RSV season*, born before 32 weeks, 0 days gestation, and requires >21% oxygen for at least the first 28 days after birth, OR
  - Child between 12 to < 24 months of age at start of RSV season*, born before 32 weeks, 0 days gestation, who required >21% oxygen for their first 28 days of life, and require medical support with at least one of the following during the 6 months prior to start of RSV season*:
    - Chronic systemic corticosteroid therapy
    - Bronchodilator therapy
    - Supplemental oxygen
- Infants with CHD
  - Child < 12 months of age at start of RSV season*, with CHD, including those with acyanotic heart disease who are receiving medication to control congestive heart failure and will require cardiac surgical procedures, or have moderate to severe pulmonary hypertension, OR
  - Child < 24 months of age at start of RSV season who is to undergo cardiac transplantation during the RSV season
- Infants with other qualifying conditions
  - Child < 12 months of age at start of RSV season*, with neuromuscular disease or congenital anomaly that impairs the ability to clear secretions from the upper airway, OR
  - Child < 12 months of age at start of RSV season*, with cystic fibrosis and clinical evidence of CLD and/or nutritional compromise, OR
  - Child < 24 months of age at start of RSV season*, with cystic fibrosis with severe lung disease or are under the 10th percentile in weight, OR
  - Child < 24 months of age at start of RSV season*, who are severely immune-compromised

*RSV season to begin November 1 of the year, unless otherwise warranted by regional RSV data.

Exclusion Criteria
- Children who do not meet inclusion criteria, but have the following conditions, should generally not receive RSV prophylaxis therapy:
  - Infants and children with hemodynamically insignificant heart disease
  - Infants and children with lesions adequately corrected by surgery
  - Infants with mild cardiomyopathy
  - Infants with Down syndrome
• Children who have experienced RSV infection in the current season
• Children >12 months of age

Required Medical Information

• Diagnosis
• Gestational age
• Date of birth
• Current Weight
• Birth Weight
• Risk factors
• Dose
• Prescriber specialty
• Previous Synagis® administration
• Anticipated start date of Synagis®

Age Restrictions

• See utilization criteria above

Prescriber Restrictions

• None

Coverage Duration (months)

• 5 months, or until end of RSV season per region

Quantity/Partial Fill Restrictions

• 5 months/5 doses at 15 mg/kg

Dispensed Quantity (5% fill margin)

• Dose of ≤52.5 mg = Dispense one 50 mg vial
• Dose 52.5-105 mg = Dispense one 100 mg vial
• Dose 106-157.5 mg = Dispense one 100 mg and one 50 mg vial
• Dose 157.5-210 mg = Dispense two 100 mg vials
• Dose >210 mg = Dispense two 100 mg vials and one 50 mg vial

References

• Synagis® [Package Insert]. MedImmune, LLC. Gaithersburg, MD. March 2014.
• Committee on Infectious Diseases, Bronchiolitis Guidelines Committee. Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. Pediatrics. Published online July 28, 2014.
Syprine® (trientine)

FDA Approved Indication(s)
- For the treatment of the treatment of patients with Wilson's disease who are intolerant of penicillamine

FDA Recommended Dose
- Initial dose: 500-750 mg/day for pediatric patients and 750-1250 mg/day for adults given in divided doses two, three or four times daily
- Max dose: 2000 mg/day for adults or 1500 mg/day for pediatric patients age 12 or under

How Supplied
- 250 mg capsules

Utilization Criteria
For initial review:
- Member must have a documented diagnosis of Wilson’s disease, as confirmed by at least one of the following; AND
- Member must have tried and failed a penicillamine product

For continuation:
- Member must have documentation of treatment response, as verified per progress notes

Exclusion Criteria
- Pregnancy, unless risk/benefit has been assessed and documented by the provider

Required Medical Information
- Diagnosis
- Current medication list
- Therapeutic history
- Pregnancy status

Age Restrictions
- None

Prescriber Restrictions
- Must be prescribed by a hepatologist or a physician who specializes in the treatment of inherited metabolic disorders

Coverage Duration (months)
- 6 months initially, 12 months thereafter

Quantity/Partial Fill Restrictions
- Maximum of 240 capsules per 30 day period

Other Information
- Wilson’s disease (hepatolenticular degeneration) is an autosomal inherited metabolic defect resulting in an inability to maintain a near-zero balance of copper. The resultant levels of copper causes neurologic and hepatic disease.
- Syprine® is a copper chelating agent that works to reduce the copper levels seen in Wilson’s disease.

References
- Syprine® (trientine) [prescribing information]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; December 2016.

Last Reviewed May 24, 2017
Tafinlar® (dabrafenib)

FDA Approved Indication(s)

- Indicated as a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test
- Indicated in combination with trametinib for:
  - The treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test
  - The adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection
  - The treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test
  - The treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options

FDA Recommended Dose

- 150 mg orally twice daily, taken at least 1 hour before or 2 hours after a meal

How Supplied

- 50 mg and 75 mg capsules

Utilization Criteria

For initial review:

Unresectable or Metastatic Melanoma:

- Member must have documentation of BRAF V600E mutation, as detected by an FDA-approved test, AND
  - Medication is being used as a single agent, OR
- Member has documentation of BRAF V600E or V600K mutation, as detected by an FDA-approved test, AND
  - Medication is being used in combination with trametinib

Resectable Melanoma:

- Member must have documentation of BRAF V600E or V600K mutation, as detected by an FDA-approved test, AND
- Documentation of lymph node involvement, AND
- Medication is being used as adjuvant treatment after complete resection in combination with trametinib

NSCLC:

- Member must have documentation of BRAF V600E mutation, as detected by an FDA-approved test, AND
- Medication is being used in combination with trametinib

Locally Advanced or Metastatic ATC:

- Member has documentation of BRAF V600E mutation, as detected by an FDA-approved test, AND
- Medication is being used in combination with trametinib, AND
- Prescriber confirms no satisfactory locoregional treatment options are available

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Presence of wild-type BRAF melanoma, wild-type BRAF NSCLC, or wild-type BRAF ATC

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Concurrent medications
- BRAF V600E or V600K mutation status

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration (months)**
- 3 months (initial), 12 months (continuation)

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: dabrafenib is an inhibitor of some mutated forms of BRAF kinases. Dabrafenib and trametinib target two different kinases in the RAS/RAF/MEK/ERK pathway. Use of dabrafenib and trametinib in combination resulted in greater growth inhibition of BRAF V600 mutation-positive melanoma cell lines in vitro and prolonged inhibition of tumor growth in BRAF V600 mutation positive melanoma xenografts compared with either drug alone.
- Warnings and precautions: New primary cutaneous and non-cutaneous malignancies, hemorrhage, cardiomyopathy, uveitis, serious febrile reactions, and serious skin toxicity can occur when dabrafenib is administered as a single agent or when used with trametinib.

**References**

*Last Reviewed June 18, 2018*
**Tagrisso™ (osimertinib)**

**FDA Approved Indication(s)**
- For the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test
- For the treatment of patients with metastatic EGFR T790M mutation-positive NSCLC, as detected by an FDA-approved test, whose disease has progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy

**FDA Recommended Dose**
- 80 mg orally once daily

**How Supplied**
- 40 mg and 80 mg tablets

**Utilization Criteria**

*For initial review:*
- Member has documentation of metastatic non-small cell lung cancer, **AND**
- Confirmation of EGFR exon 19 deletion or exon 21 L858R mutation, as detected by an FDA-approved test, **AND**
  - Medication is being used as first-line treatment; **OR**
  - Confirmation of EGFR T790M mutation, as detected by an FDA-approved test, **AND**
    - Documentation of progression on or after prior systemic therapy with a TKI (erlotinib, afatinib, gefitinib)

*For continuation:*
- Provider must confirm that the patient has not experienced progression of disease

**Exclusion Criteria**
- Patients who have diagnosed cardiomyopathy or who have a left ventricular ejection fraction (LVEF) < 40%
- Patients who have diagnosed interstitial lung disease (ILD) or pneumonitis

**Required Medical Information**
- Age
- Concurrent medications
- Diagnosis
- EGFR mutation testing
- Dose
- Treatment history

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration (months)**
- 3 months (initial), 12 months (continuation)

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
• Mechanism of action: osimertinib is a kinase inhibitor that binds irreversibly to certain mutant forms of EGFR (T790M, L858R, and exon 19 deletion) at approximately 9-fold lower concentrations than wild type. In cultured cells and animal tumor implantation models, osimertinib exhibited anti-tumor activity against NSCLC lines harboring EGFR-mutations (T790M/L858R, L858R, T790M/exon 19 deletion, and exon 19 deletion) and, to lesser extent, wild-type EGFR amplifications.

• Overall objective response rates (ORR) for two studies in 201 and 210 patients were 57% and 61%, respectively. Ongoing responses ranged from 1.1 to 5.6 months after median follow-up of 4.2 months for study 1 and 4.0 months for study 2.

• Despite initial responses to EGFR TKIs, the majority of patients will have disease progression within 1 to 2 years after treatment initiation from acquired resistance. Approximately 60% of acquired resistance cases are attributed to additional EGFR mutation, EGFR T790M.

References

• Tagrisso™ [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; April 2018.


## Takhzyro™ (lanadelumab-flyo)†

### FDA Approved Indication(s)
- For the prevention of hereditary angioedema (HAE) attacks in patients 12 years of age and older

### FDA Recommended Dose
- 300 mg subcutaneous injection every 2 weeks
- Dosing interval of every 4 weeks may be considered if member is well-controlled (e.g., attack free) for more than 6 months

### How Supplied
- 300 mg/2 ml single-dose vials

### Utilization Criteria

**For initial review:**
- Member must have a confirmed diagnosis of hereditary angioedema, where diagnosis is based on evidence of a normal C1 level and a low C4 level (C4 less than 14 mg/dL; normal range 14 to 40 mg/dL, or C4 below the lower limit of normal as defined by the laboratory performing the test), AND
- Member must not be on a medication known to cause drug-induced angioedema, such as an ACE inhibitor, estrogen replacement therapy, or hormone contraceptives, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

**For continuation:**
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

### Exclusion Criteria
- Concurrently receiving other agents for the prevention of HAE attacks

### Required Medical Information
- Diagnosis
- Recent chart notes with a treatment history, plan and assessment for care

### Age Restrictions
- 12 years of age and older

### Prescriber Restrictions
- Must be prescribed by an allergist or immunologist

### Coverage Duration (months)
- 6 months initial, 12 months continuation

### Quantity/Partial Fill Restrictions
- None

### Other Information
- Mechanism of action: Lanadelumab-flyo is a fully human monoclonal antibody that binds plasma kallikrein and decreases its activity to control excess bradykinin generation in patients with HAE.

### References

*Last Reviewed November 8, 2018*
Taltz™ (ixekizumab)‡

**FDA-Approved Indication(s)**
- For the treatment of moderate-to-severe plaque psoriasis (PsO) in adults who are candidates for systemic therapy or phototherapy
- For the treatment of active psoriatic arthritis (PsA) in adults

**FDA-Recommended Dose**
- **Plaque psoriasis**
  - 160 mg (two 80 mg subcutaneous injections) at week 0, then 80 mg every two weeks for the first 12 weeks (3 months), then 80 mg every 4 weeks thereafter
- **Psoriatic arthritis**
  - 160 mg (two 80 mg subcutaneous injections) at week 0, then 80 mg every 4 weeks
  - For patients with coexistent moderate-to-severe plaque psoriasis, use dosing regimen for plaque psoriasis

**How Supplied**
- 80 mg single-dose autoinjector
- 80 mg single-dose prefilled syringe

**Utilization Criteria**

*For initial review:*
- Member must have a diagnosis of moderate-to-severe plaque psoriasis or active psoriatic arthritis, AND
- Documented negative tuberculosis (TB) test at baseline, AND
- Member must have failed, or did not tolerate, a 3-month trial of at least one conventional or non-biologic disease modifying therapy, such as methotrexate, cyclosporine, PUVA or UVB, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable

*For continuation:*
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- None

**Required Medical Information**
- Diagnosis, including documentation of disease severity and body surface area (BSA) coverage
- Age
- Dose
- Treatment history

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a dermatologist

**Coverage Duration (months)**
- 3 months (initial), 12 months (continuation)

**Quantity/Partial-Fill Restrictions**
Ixekizumab is a human interleukin-17A antagonist. Alternative interleukin (IL) inhibitors used in the management of psoriasis include Cosentyx® (secukinumab, an IL-17A inhibitor), and Stelara® (ustekinumab, an IL-23 inhibitor).

In the three clinical trials that brought the drug to market, the percent of subjects who achieved a Psoriasis Area and Severity Index (PASI)-75 score ranged from 87-90% by week 12 of therapy.

In clinical trials, Crohn’s disease and ulcerative colitis, including exacerbations, occurred at greater frequency in the ixekizumab group than the placebo group during the 12-week, placebo-controlled period. Patients with pre-existing Crohn’s disease or ulcerative colitis may benefit from biologic therapy that does not work within the IL-17 immunopathogenesis.

References

**Tarceva® (erlotinib hydrochloride)**

**FDA Approved Indication(s)**
- Non-small cell lung cancer (NSCLC)
  - First-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test
  - Maintenance treatment of patients with locally advanced or metastatic non-small cell lung cancer whose disease has not progressed after four cycles of platinum-based first-line chemotherapy
  - Treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of at least one prior chemotherapy regimen
- Pancreatic cancer
  - In combination with gemcitabine for the first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer

**FDA Recommended Dose**
- **NSCLC**
  - 150 mg once daily
- **Pancreatic Cancer**
  - 100 mg once daily in combination with gemcitabine
  - Note: 150 mg once daily frequently used in practice when toxicity is not problematic

**How Supplied**
- 25, 100, 150 mg tablets

**Utilization Criteria**

*For initial review:*
- **NSCLC**
  - First-line therapy
    - Metastatic disease, AND
    - EGFR positive mutations present
  - Non-first-line therapy
    - Locally advanced or metastatic disease, AND
    - Disease has not progressed after four cycles of platinum-based chemotherapy, OR
    - Patient has tried and failed at least one previous chemotherapy regimen
- **Pancreatic cancer**
  - Diagnosis of advanced, unresectable, or metastatic pancreatic cancer, AND
  - Gemcitabine being used concurrently

*For continuation:*
- Provider must confirm that the patient has not experienced progression of disease

**Exclusion Criteria**
- None

**Required Medical Information**
- Age
- Concurrent medications
- Diagnosis
- Dose
- Treatment history
**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: Erlotinib reversibly inhibits the kinase activity of EGFR, preventing autophosphorylation of tyrosine residues associated with the receptor and thereby inhibiting further downstream signaling

**References**
**Targretin® (bexarotene)**

**FDA Approved Indication(s)**
- For the treatment of cutaneous manifestations of cutaneous T-cell lymphoma (CTCL) in patients who are refractory to at least one prior systemic therapy (capsules)
- For the topical treatment of cutaneous lesions in patients with CTCL (Stage IA and IB) who have refractory or persistent disease after other therapies or who have not tolerated other therapies (gel)

**FDA Recommended Dose**
- Capsules: 300 mg/m² once daily
- Gel: Applied topically once every other day, increased in weekly intervals to a max of four times daily, based on tolerance to therapy

**How Supplied**
- 75 mg capsules
- 1% gel

**Utilization Criteria**

*For initial review:*
- Diagnosis of cutaneous manifestations of cutaneous T-cell lymphoma
- Documentation of previous failed therapies

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Pregnancy
- Liver function tests ≥ 3x ULN

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Height and weight
- Baseline lipid levels, liver function tests, and complete blood counts with differential

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- Weight based dosing

**Other Information**
- Mechanism of action: Bexarotene inhibits the growth in vitro of some tumor cell lines of hematopoietic and squamous cell origin
- Black Box Warning: Bexarotene is a member of the retinoid class of drugs that is associated with birth defects in humans. Bexarotene is pregnancy Category X and must not be administered to pregnant woman.
References

- Targretin® 1% gel [Package Insert]. Woodcliff Lake, NJ: Eisai Inc; February 2014.
Tasigna® (nilotinib)

FDA Approved Indication(s)
- For the treatment of newly diagnosed adult patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP)
- For the treatment of chronic phase and accelerated phase (AP) Ph+ CML in adult patients resistant to or intolerant to prior therapy that included imatinib

FDA Recommended Dose
- Newly diagnosed Ph+ CML: 300 mg orally, twice daily
- Resistant or intolerant Ph+ CML: 400 mg orally, twice daily

How Supplied
- 150 mg and 200 mg capsules

Utilization Criteria
For initial review:
- Patient has diagnosis of CP Ph+ CML; OR
- Patient has a diagnosis of AP Ph+ CML and has tried and failed treatment with imatinib

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Pregnancy, OR
- History of QT prolongation, OR
- Untreated hypokalemia and/or hypomagnesemia, OR
- Concurrent use of drugs known to prolong the QT interval and strong CYP3A4 inhibitors

Required Medical Information
- Diagnosis
- Age
- Dose
- Treatment history
- Concurrent medications
- Complete blood count with differential
- Liver function tests (AST, ALT, serum bilirubin)

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Nilotinib is an inhibitor of the BCR-ABL kinase. Nilotinib binds to and stabilizes the inactive conformation of the kinase domain of ABL protein.
- Black Box Warning:
• Nilotinib prolongs the QT interval; monitoring for hypokalemia and hypomagnesemia is required throughout therapy
• Sudden deaths have been reported in patients receiving nilotinib. Do not administer nilotinib to patients with hypokalemia, hypomagnesemia, or long QT syndrome.
• Avoid concomitant drugs known to prolong QT interval and strong CYP3A4 inhibitors

References

**Tecfidera® (dimethyl fumarate)**

**FDA Approved Indication(s)**
- For the treatment of patients with relapsing forms of multiple sclerosis

**FDA Recommended Dose**
- Starting dose: 120 mg orally twice daily for 7 days
- Maintenance dose: 240 mg orally twice daily

**How Supplied**
- 30-day starter pack
  - 7-day bottle of 120 mg capsules, quantity 14
  - 23-day bottle of 240 mg capsules, quantity 46
- 120 mg capsules
  - 7-day bottle of 14 capsules
- 240 mg capsules
  - 30-day bottle of 60 capsules

**Utilization Criteria**

*For initial review:*
- Must have diagnosis of relapsing form of multiple sclerosis (RRMS, SPMS, PRMS), AND
- Must have a baseline complete blood count, serum aminotransferase, alkaline phosphatase, and total bilirubin levels prior to treatment, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

*For continuation:*
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Must have a documented benefit to therapy, as assessed by a neurologist or other qualified provider

**Exclusion Criteria**
- Receiving other concurrent disease modifying therapies

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Therapeutic history

**Age Restrictions**
- Must be 18 years of age or older

**Prescriber Restrictions**
- Must be prescribed by a neurologist

**Coverage Duration (months)**
- 12 months

**Quantity/Partial Fill Restrictions**
- None

**References**
Technivie® (paritaprevir/ritonavir/ombitasvir)

FDA-Approved Indication(s):
• For use in combination with ribavirin (RBV) for the treatment of patients with genotype 4 (GT4) chronic hepatitis C virus (HCV) infection who do not have cirrhosis.
• Limitation of use: Paritaprevir/ritonavir/ombitasvir is not recommended for the use in patients with moderate hepatic impairment (Child-Pugh B)

FDA-Recommended Dose
• Two tablets taken orally once daily with a meal, used in combination with weight-based ribavirin for 12 weeks

How Supplied
• Tablets containing 12.5 mg ombitasvir, 75 mg paritaprevir, and 50 mg ritonavir

Utilization Criteria

For initial review:
• Member must have a diagnosis of chronic HCV genotype 4 (GT4), with a documented viral load collected within the previous three months, AND
• Physician must attest to the patient’s ability and dedication to remain adherent to the entire course of therapy, AND
• Physician must confirm that alcohol and illicit substance abuse is absent for the previous six months, or patient is currently seeing an addiction specialist, AND
• Member must receive concurrent ribavirin therapy, AND
• If member is HIV co-infected, member must be concurrently receiving suppressive antiretroviral therapy
• Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

Exclusion Criteria
• Concurrent use with sofosbuvir, simeprevir or ledipasvir/sofosbuvir, OR
• Concurrent use with medications highly dependent on CYP3A4 for clearance, OR
• Concurrent use of ethinyl estradiol containing medications, OR
• Moderate to severe hepatic impairment (Child-Pugh B or C), OR
• Decompensated cirrhosis, OR
• Coverage may be revoked if patient is non-adherent through the first two months of therapy, as evidenced by claim records or verbal confirmation of poor adherence

Required Medical Information
• Age
• Diagnosis including genotype
• Viral load
• Dose and duration of therapy
• Concurrent medications
• Treatment history
• Fibrosis stage

Age Restrictions
• Must be 18 years of age or older

Prescriber Restrictions
• Must be prescribed by a gastroenterologist, hepatologist, or infectious disease specialist
Coverage Duration (months)

- 3 months

Quantity/Partial Fill Restrictions

- None

Other Information

- Mechanism of action: Ombitasvir is an NS5B polymerase inhibitor, paritaprevir is a NS3/4A protease inhibitor, and ritonavir is utilized to increase peak and trough plasma concentrations of ombitasvir and paritaprevir.
- Ritonavir can induce protease inhibitor resistance in HIV positive members who are not currently receiving suppressive anti-retroviral therapy

References


Last Reviewed January 28, 2019
**Temodar® (temozolomide)**

**FDA Approved Indication(s)**
- Newly diagnosed glioblastoma multiforme
- Refractory anaplastic astrocytoma

**FDA Recommended Dose**
- Glioblastoma multiforme
  - 75 mg/m² daily for 42 days concomitant with focal radiotherapy (60 Gy administered in 30 fractions) followed by maintenance Temodar (150 mg/m² daily for 5 days every 28 days) for 6 cycles beginning 4 weeks after the concomitant phase
  - Dosing may be increased or decreased based on tolerability; See package insert
- Anaplastic astrocytoma
  - 150 mg/m² for 5 days every 28 days
  - Dosing may be increased or decreased based on tolerability; See package insert

**How Supplied**
- 5, 20, 100, 140, 180, 250 mg capsules
- 100 mg powder for injection

**Utilization Criteria**

For *initial review*:
- Newly diagnosed glioblastoma multiforme (GBM)
  - Used concomitantly with radiotherapy and then as maintenance treatment
- Diagnosis of refractory anaplastic astrocytoma
  - (i.e., patients who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine)
- Diagnosis of advanced metastatic melanoma (NCCN category 2A)
  - Has tried and failed NCCN preferred agents
  - Dosing: 200 mg/m² for 5 days every 28 days

For *continuation*:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- None

**Required Medical Information**
- Diagnosis
- Age
- Dose

**Age Restrictions**
- 3 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
• Mechanism of action: Temozolomide is not directly active but undergoes rapid nonenzymatic conversion at physiologic pH to the reactive compound 5-(3-methyltriazen-1-yl)-imidazole-4-carboxamide (MTIC). The cytotoxicity of MTIC is thought to be primarily due to alkylation of DNA. Alkylation (methylation) occurs mainly at the O6 and N7 positions of guanine.

• Black Box Warning: None

References

• Temodar® [package insert]. White House Station, NJ: Schering Corporation; October 2014.
# Thalomid® (thalidomide)

## FDA Approved Indication(s)
- Multiple Myeloma (MM)
- Erythema Nodosum Leprosum (ENL)

## FDA Recommended Dose
- **Multiple Myeloma**: 200 mg once daily
- **Erythema Nodosum Leprosum**: 100 to 400 mg daily

## How Supplied
- 50 mg, 100 mg, 150 mg, and 200 mg oral capsules

## Utilization Criteria

### For initial review:
- **Erythema nodosum leprosum**
  - Patient has a clinical diagnosis of ENL
- **Multiple Myeloma**
  - Patient has a clinical diagnosis of MM that is refractory to other chemotherapeutic regimens; OR
  - Clinically newly diagnosed multiple myeloma when used in conjunction with dexamethasone
- Must be administered in compliance with all of the terms outlined in the S.T.E.P.S. REMS program

### For continuation:
- Women of childbearing age must have pregnancy testing done once weekly during the first 4 weeks of treatment and then once every 4 weeks if the menstrual cycle is regular and once every 2 weeks if the menstrual cycle is irregular and the results must be negative each time

## Exclusion Criteria
- Pregnancy

## Required Medical Information
- Diagnosis
- Age
- Dose
- Previous therapeutic history
- Complete blood count (CBC) with differential

## Age Restrictions
- 12 years of age and older

## Prescriber Restrictions
- Must be prescribed by an oncologist registered with the S.T.E.P.S. REMS program

## Coverage Duration (months)
- 12

## Quantity/Partial Fill Restrictions
- None

## Other Information
Mechanism of action: Available data from in vitro studies and clinical trials suggest that the immunologic effects of this compound can vary substantially under different conditions, but may be related to suppression of excessive tumor necrosis factor-alpha (TNF-α) production and down-modulation of selected cell surface adhesion molecules involved in leukocyte migration.

Black Box Warning: Increased risk of severe embryo-fetal toxicity and venous thromboembolism.

References

**Tibsovo® (ivosidenib)†**

**FDA Approved Indication(s)**
- For the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test

**FDA Recommended Dose**
- 500 mg taken orally once daily
- See prescribing information for dose modifications

**How Supplied**
- 250 mg tablets

**Utilization Criteria**
*For initial review:*
- Member must have documentation of relapsed or refractory AML, AND
- Documentation of a susceptible isocitrate dehydrogenase-1 (IDH1) mutation, as detected by an FDA-approved test
  - IDH1 mutation test should be done at the time of relapse

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Pregnancy
- Concomitant use of itraconazole or ketoconazole

**Required Medical Information**
- Age
- Diagnosis
- Therapeutic history
- IDH1 mutation testing

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist or hematologist

**Coverage Duration (months)**
- 3 months (initial); 12 months (continuation)

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: Ivosidenib is a small molecule inhibitor that targets the mutant isocitrate dehydrogenase 1 (IDH1) enzyme. Susceptible IDH1 mutations are defined as those leading to increased levels of 2-hydroxyglutarate (2-HG) in the leukemia cells and where efficacy is predicted by 1) clinically meaningful remissions with the recommended dose of ivosidenib and/or 2) inhibition of mutant IDH1 enzymatic activity at concentrations of ivosidenib sustainable at the recommended dosage according to validated methods. The most common of such mutations are R132H and R132C substitutions.
- Black Box Warning: Patients treated with ivosidenib have experienced symptoms of differentiation syndrome, which can be fatal if not treated. Symptoms may include fever, dyspnea, hypoxia,
pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, hypotension, and hepatic, renal, or multi-organ dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

- **Warnings and Precautions:** Concomitant use of ivosidenib with drugs known to prolong the QTc interval and CYP3A4 inhibitors may increase the risk of QTc interval prolongation. Monitor patients taking ivosidenib for onset of new signs or symptoms of motor and/or sensory neuropathy such as unilateral or bilateral weakness, sensory alterations, paresthesias, or difficulty breathing. Permanently discontinue TIBSOVO in patients who are diagnosed with Guillain-Barré syndrome.

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**References**


_Last Reviewed October 25, 2018_
Tobramycin for inhalation (Bethkis®, Kitabis Pak®, Tobi®, and Tobi® Podhaler™)

FDA Approved Indication(s)
• For the management of *Pseudomonas aeruginosa* infection in patients with cystic fibrosis

FDA Recommended Dose
• Bethkis®: 300 mg via inhalation twice daily for 28 days followed by 28 days off drug
• Kitabis Pak®: 300 mg via inhalation twice daily for 28 days followed by 28 days off drug
• Tobi® for inhalation: 300 mg via inhalation twice daily for 28 days followed by 28 days off drug
• Tobi® Podhaler™: Four 28 mg capsules twice daily for 28 days followed by 28 days off drug

How Supplied
• Bethkis®: 300 mg/4 mL single-dose ampules for nebulization
• Kitabis Pak®: 300 mg/5 mL single-dose ampules for nebulization + PARI LC® Plus reusable Nebulizer
• Tobi® for inhalation: 300 mg/5 mL single-dose ampules for nebulization
• Tobi® Podhaler™: 28 mg capsules for use in Podhaler™ device

Utilization Criteria
For initial review:
• Member has a confirmed diagnosis of cystic fibrosis, AND
• Member has suspected or confirmed diagnosis of *Pseudomonas aeruginosa* lung infection, AND
• Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

For continuation:
• Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
• Patient has a known hypersensitivity to aminoglycosides

Required Medical Information
• Diagnosis
• Dose
• Documentation of *Pseudomonas aeruginosa* infection

Age Restrictions
• 6 years of age and older

Prescriber Restrictions
• Must be prescribed by a pediatrician or infectious disease specialist

Coverage Duration (months)
• 12

Quantity/Partial Fill Restrictions
• 28 day supply every 56 days

Other Information
• Mechanism of action: Tobramycin is an aminoglycoside antibiotic with activity against *Pseudomonas aeruginosa*
• Safety and efficacy have not been demonstrated in patients under the age of 6 years, patients with 
FEV1 <25% or >75% predicted, or patients colonized with *Burkholderia cepacia*

**References**

• Mogayzel PJ Jr, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic 
Tremfya® (guselkumab)

FDA Approved Indication(s)

- For the treatment of adult patients with moderate-to-severe plaque psoriasis (PsO) who are candidates for systemic therapy or phototherapy

FDA Recommended Dose

- 100 mg subcutaneously at week 0, 4, and every 8 weeks thereafter

How Supplied

- Single-dose 100 mg/mL prefilled syringe

Utilization Criteria

For initial review:

- Member must have a documented diagnosis of moderate to severe plaque psoriasis, AND
  - Documentation of a negative TB test AND
  - Documentation of psoriasis involving at least 10% body surface area (BSA), OR
  - Documentation of psoriatic lesions affecting the hands, feet, or genital area leading to disability or impact on quality of life, AND
- Member must have had a previous trial of at least one or more forms of preferred conventional or non-biologic therapies, such as PUVA (Phototherapy Ultraviolet Light A), UVB (Ultraviolet Light B), acitretin, methotrexate, or cyclosporine, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable

For continuation:

- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Member must have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria

- The member is receiving additional biologic therapies OR apremilast

Required Medical Information

- Diagnosis
- Body surface area (BSA) coverage percentage
- Treatment history
- Concurrent medications

Age Restrictions

- 18 years of age and older

Prescriber Restrictions

- Must be prescribed by a dermatologist

Coverage Duration (months)

- 12 months

Quantity/Partial Fill Restrictions

- Quantity Limits: 1 prefilled syringe (100 mg) every 8 weeks, after initial dose

Other Information

Warnings and precautions: Tuselkumab may increase the risk of infection. Members should be up to date on all immunizations prior to start of therapy. No live vaccines should be administered to the patient during treatment.

References

# Tykerb® (lapatinib)

## FDA Approved Indication(s)
- For the treatment of advanced, HER2+ breast cancer, in combination with capecitabine, in patients who have received prior anthracycline, taxane, and trastuzumab therapy.
- For the treatment of HR+ HER2+ metastatic breast cancer in post-menopausal women, in combination with letrozole, for whom hormonal therapy is indicated.

## FDA Recommended Dose
- HER2+ metastatic breast cancer in combination with capecitabine
  - 1,250 mg orally (5 tablets) once daily on days 1-21 of a 28 day cycle
- HR+ HER2+ metastatic breast cancer in combination with letrozole
  - 1,500 mg orally (6 tablets) once daily

## How Supplied
- 250 mg tablets

## Utilization Criteria
### For initial review:
- HER2+ metastatic breast cancer in combination with capecitabine
  - Has received prior therapy including anthracycline, taxane, and trastuzumab
- HR+ HER2+ metastatic breast cancer used in combination with an aromatase inhibitor
  - Patient is post-menopausal as documented by provider

### For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

## Exclusion Criteria
- Patient has severe pulmonary symptoms
- Patient has history of prolonged QT intervals and/or arrhythmia
- Pregnancy

## Required Medical Information
- Diagnosis
- Age
- Dose
- Baseline left ventricular ejection fraction (LVEF)
- Baseline liver function tests (ALT, AST, serum bilirubin)

## Age Restrictions
- 18 years of age and older

## Prescriber Restrictions
- Must be prescribed by an oncologist

## Coverage Duration (months)
- 12

## Quantity/Partial Fill Restrictions
- 30 day supply

## Other Information
- Mechanism of action: Lapatinib is a kinase inhibitor of the intracellular tyrosine kinase domains of both Epidermal Growth Factor Receptor (EGFR) and Human Epidermal Receptor Type 2 (HER2) receptors
• Black Box Warning: Severe hepatotoxicity has been observed in clinical trials

References


Last Reviewed November 9, 2015
**Tymlos® (abaloparatide)**

**FDA Approved Indication(s)**
- For the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy

**FDA Recommended Dose**
- 80 mcg subcutaneously once daily

**How Supplied**
- 3120 mcg/1.56 mL (2000 mcg/mL) multi-dose pre-filled pen

**Utilization Criteria**

*For initial review:*
- Member must be female with postmenopausal osteoporosis, AND
- Member is at high risk for fracture, AND
- Member is currently receiving supplemental calcium and vitamin D unless contraindicated, AND
- Bone mineral density (BMD) T-score ≤ -2.5 and > -5.0 at the lumbar spine or hip, AND
- Member has tried at least one oral bisphosphonate for at least 3 – 6 months and failed, OR
- Member is intolerant or has a contraindication to at least one oral bisphosphonate as evidenced by documentation in provider notes, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

*For continuation:*
- Benefit of therapy evidenced by BMD, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s prescriber

**Exclusion Criteria**
- Member is at risk for osteosarcoma, OR
- Member has Paget’s disease, OR
- Member has unexplained elevations of alkaline phosphatase, OR
- Member has open epiphyses, bone metastases or a history of skeletal malignancies, OR
- Member has received prior bone radiation, OR
- Member has received abaloparatide or parathyroid hormone analogs (e.g., teriparatide) for more than 24 months

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Concurrent medications
- Treatment history

**Age Restrictions**
- 18 and older

**Prescriber Restrictions**
- None

**Coverage Duration (months)**
• 12
• 24-month total max

Quantity/Partial Fill Restrictions
• None

Other Information
• Mechanism of action: Endogenous 34-amino acid parathyroid hormone (PTH) is the primary regulator of calcium and phosphate metabolism in bone and kidney.
• Black Box Warning: Potential risk of osteosarcoma

References
• Tymlos® (abaloparatide) [prescribing information]. Waltham, MA: Radius Health Incorporated; April 2017.
• Redbook Online®. Truven Health Analytics LLC Micromedex Solutions; July 2017.
**Tysabri® (natalizumab)**

**FDA Approved Indication(s)**
- Multiple Sclerosis (MS)
- Crohn’s Disease (CD)

**FDA Recommended Dose**
- 300 mg infused over one hour every four weeks

**How Supplied**
- 300 mg/15 mL in a sterile, single-use vial

**Utilization Criteria**

*For initial review:*
All indications:
- Natalizumab will be used as monotherapy, AND
- Physician and patient are registered with the TOUCH® Program, AND

**Multiple Sclerosis**
- Member has a diagnosis of MS, AND
- Member must have tried and failed two or more preferred agents for the treatment of MS, as evidenced by continued clinical relapse or worsening of the disease. Clinical relapse is defined as one of the following while at steady state on therapy:
  - Member experiences at least one relapse within the past 12 months
  - Member continues to have CNS lesion progression as measured by MRI

**Crohn’s Disease**
- Member has a diagnosis of moderate to severe CD, AND
- Member has tried and failed at least 1 conventional therapy, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable

*For continuation:*
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Member is receiving concurrent immunosuppressants or a TNF-α inhibitor

**Required Medical Information**
- Diagnosis
- Concurrent medications
- Age
- Dose
- Treatment history

**Age Restrictions**
- 18 years of age or older

**Prescriber Restrictions**
- Must be prescribed by a neurologist or gastroenterologist

**Coverage Duration (months)**
- 12
Quantity/Partial Fill Restrictions

- None

Other Information

- Mechanism of action: alpha-4 integrin inhibitor
- Black Box Warning: Progressive Multifocal Leuкоencephalopathy
- Solution must be prepared no longer than 8 hours prior to administration

References

Uptravi® (selexipag)

FDA-Approved Indication(s)
• Treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH

FDA-Recommended Dose
• Starting dose is 200 micrograms (mcg) given twice daily
• For patients with moderate hepatic impairment (Child-Pugh class B), the starting dose is 200 mcg once daily.

How Supplied
• Supplied as film coated round tablets in bottles of 60 or 120 tablets
• Available in tablet strengths of 200, 400, 600, 800, 1000, 1200, 1400, and 1600 mcg

Utilization Criteria
For initial review:
• Member must have a confirmed diagnosis of PAH (WHO Group I), AND
• WHO functional class II-IV, AND
• Patient must have tried and failed, or have a contraindication to, a calcium channel blocker therapy; AND
• Patient must have tried and failed, or have a contraindication to, a short acting vasodilator (i.e., sildenafil)

For continuation:
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
• Documented diagnosis of pulmonary veno-occlusive disease (PVOD)
• Severe hepatic impairment (Child-Pugh class C)

Required Medical Information
• Age
• Diagnosis
• Dose
• WHO Functional class
• Treatment history

Age Restrictions
• Member must be 18 years of age and older

Prescriber Restrictions
• Must be prescribed by a pulmonologist or cardiologist

Coverage Duration (months)
• 12

Quantity/Partial-Fill Restrictions
• None

Other Information
• Mechanism of action: Selexipag is an oral prostacyclin receptor (IP receptor) agonist that is structurally distinct from prostacyclin. Selexipag is hydrolyzed by carboxylesterase 1 to yield its active metabolite, which is approximately 37-fold as potent as selexipag. Selexipag and the active
metabolite are selective for the IP receptor versus other prostanoid receptors (EP1-4, DP, FP and TP).

References


• Hopkins W, Rubin L. “Treatment of Pulmonary Hypertension in Adults.” In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, January 2016.
Vemlidy® (tenofovir alafenamide)†

FDA Approved Indication(s)
- For the treatment of chronic hepatitis B virus (HBV) infection in adults with compensated liver disease

FDA Recommended Dose
- 25 mg taken orally once daily with food

How Supplied
- 25 mg tablet

Utilization Criteria
For initial review:
- Member must have a diagnosis of chronic hepatitis B virus (HBV) infection, AND
- Must have documentation of negative HIV test prior to initiating therapy, AND
- Prescriber is a gastroenterologist, hepatologist, or infectious disease specialist, AND
- Member is at least 18 years of age, AND
- Member has tried and failed, or intolerant or resistant to, lamivudine monotherapy, UNLESS
  - Member is resistant to telbivudine or entecavir

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Treatment is being prescribed for HIV infection

Required Medical Information
- Diagnosis
- Age
- Therapeutic history
- Renal function
- Liver Function Tests
- HBV status

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a gastroenterologist, hepatologist, or infectious disease specialist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: inhibits reverse transcriptase and incorporates into viral DNA, resulting in DNA chain termination (nucleotide reverse transcriptase inhibitor)
- Warnings and Precautions:
  - Severe acute exacerbations of hepatitis B have been documented after treatment discontinuation. Liver function should be monitored for several months after discontinuation.
  - Patients co-infected with HIV should be receiving HAART in addition to entecavir.
- Lactic acidosis and hepatomegaly with steatosis (including fatal cases) have been reported in patients receiving nucleoside analogs.

**References**

**Venclexta™ (venetoclax)**

**FDA-Approved Indication(s)**
- For the treatment of patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), with or without 17p deletion, who have received at least one prior therapy

**FDA-Recommended Dose**
- Venetoclax should be initiated via a five-week ramp-up schedule to gradually reduce tumor burden (debulk) and decrease the risk of tumor lysis syndrome (TLS)

<table>
<thead>
<tr>
<th>Week</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily Dose</td>
<td>20 mg</td>
<td>50 mg</td>
<td>100 mg</td>
<td>200 mg</td>
<td>400 mg</td>
</tr>
</tbody>
</table>

- Venetoclax is administered orally once daily
  - As monotherapy: until disease progression or unacceptable toxicity is observed
  - In combination with rituximab: for 24 months from cycle 1, day 1 of rituximab

**How Supplied**
- 10, 50, and 100 mg tablets; the first four weeks of therapy are available in a starter pack

**Utilization Criteria**

*For initial review:*
- Member must have a diagnosis of CLL or SLL, AND
- Member must have progressed on, or had intolerance to, at least one prior therapy, AND
- Member must receive appropriate tumor lysis syndrome (TLS) prophylaxis and monitoring based on tumor burden, as indicated in progress notes

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Concomitant use with strong CYP3A inhibitors at initiation and during ramp-up phase
- Member is pregnant, is planning to become pregnant, or is lactating
- Member has pre-existing neutropenia

**Required Medical Information**
- Diagnosis
- Treatment history
- Concomitant medications

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a hematologist or oncologist

**Coverage Duration (months)**
- 3 months (initial), 12 months (continuation)

**Quantity/Partial-Fill Restrictions**
- None

**Other Information**
- Venetoclax is a selective and orally bioavailable small-molecule inhibitor of BCL-2, an anti-apoptotic protein. Overexpression of BCL-2 has been demonstrated in CLL cells where it mediates tumor cell
survival and has been associated with resistance to chemotherapeutics. Venetoclax helps restore the process of apoptosis by binding directly to the BCL-2 protein, thereby displacing pro-apoptotic proteins.

- Venetoclax can cause rapid reduction in tumor and thus an increased risk for tumor lysis syndrome (TLS). Assessment of risk should be performed before starting treatment. Patients should be premedicated with anti-hyperuricemics and adequate hydration.

**References**


*Last Reviewed June 25, 2018*
Verzenio™ (abemaciclib)†

FDA Approved Indication(s)

- For the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer, in combination with an aromatase inhibitor as initial endocrine-based therapy
- For the treatment of women with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy, in combination with fulvestrant
- For the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting as monotherapy

FDA Recommended Dose

- In combination with fulvestrant or an aromatase inhibitor: 150 mg orally twice daily
  - Refer to the full prescribing information for the recommended dose of fulvestrant or aromatase inhibitor being used
  - Pre/perimenopausal women treated with abemaciclib plus fulvestrant should be treated with a gonadotropin-releasing hormone agonist according to current clinical practice standards
- Monotherapy: 200 mg orally twice daily
  - Refer to prescribing information for dose modifications

How Supplied

- 50 mg, 100 mg, 150 mg, and 200 mg tablets
- Supplied in 7-day dose packs containing 14 tablets

Utilization Criteria

For initial review:
- Member has a confirmed diagnosis of HR-positive, HER2-negative advanced or metastatic breast cancer, AND
  - Medication is being used as initial endocrine-based therapy, in combination with an aromatase inhibitor; OR
  - Member has documentation of disease progression following endocrine therapy and medication is being used in combination with fulvestrant; OR
- Member has documentation HR-positive, HER2-negative metastatic breast cancer, AND
  - Member has documentation of disease progression following endocrine therapy and prior chemotherapy, AND
  - Medication is being used as monotherapy

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria

- None

Required Medical Information

- Diagnosis
- Age
- Dose
- Treatment history
- CBC and liver function tests
**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration (months)**
- 3 months (initial); 12 months (continuation)

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: Abemaciclib is an inhibitor of cyclin-dependent kinase (CDK) 4 and 6, which are downstream of signaling pathways which lead to cellular proliferation. Abemaciclib has been shown to reduce cellular proliferation of estrogen receptor (ER)-positive breast cancer cell lines.
- Warnings and precautions:
  - Diarrhea was reported in up to 90% of patients treated with abemaciclib, including Grade 3 diarrhea in up to 20%. Patients should be instructed to start antidiarrheal therapy at the first sign of loose stools and notify healthcare provider for appropriate follow up. For Grade 3 or 4 diarrhea, or diarrhea that requires hospitalization, discontinue abemaciclib until toxicity resolves to ≤Grade 1, and then resume at the next lower dose.
  - Monitor complete blood counts and liver function tests (LFTs) prior to the start of abemaciclib therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia, persistent or recurrent Grade 2 hepatic transaminase elevation, or Grade 3 or 4 hepatic transaminase elevation.

**References**
Viekira Pak™, Viekira XR™ (ombitasvir, paritaprevir, ritonavir, dasabuvir)

FDA Approved Indication(s)
- For the treatment of chronic hepatitis C (CHC, HCV) genotype 1 infection in adults with or without concurrent ribavirin therapy
- Limitation of Use: Not recommended for use in patients with decompensated liver disease

FDA Recommended Dose
- Viekira Pak™: Two ombitasvir (12.5 mg), paritaprevir (75 mg), ritonavir (50 mg) tablets once in the morning and one dasabuvir (250 mg) tablet twice daily (morning and evening), with a meal
- Viekira XR™: Three tablets by mouth once daily, with a meal

<table>
<thead>
<tr>
<th>Duration</th>
<th>Ribavirin</th>
<th>Genotype</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 weeks</td>
<td>Yes</td>
<td>1a</td>
<td>Without cirrhosis</td>
</tr>
<tr>
<td>24 weeks</td>
<td>Yes</td>
<td>1a</td>
<td>With compensated cirrhosis (Child-Pugh A)</td>
</tr>
<tr>
<td>12 weeks</td>
<td>No</td>
<td>1b</td>
<td>With or without compensated cirrhosis (Child-Pugh A)</td>
</tr>
</tbody>
</table>

How Supplied
- Viekira Pak™: Ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg combination tablets and dasabuvir 250 mg tablets supplied in a monthly carton for a total of 28 days of therapy
- Viekira XR™: Ombitasvir, paritaprevir, ritonavir, dasabuvir 8.33/50/33.33/200 mg fixed-dose combination, extended-release tablet

Utilization Criteria
For initial review:
- Member must have a diagnosis of chronic HCV genotype 1 (G1) with subtype, with a documented viral load collected within the previous three months, AND
- Physician must attest to the patient’s ability and dedication to remain adherent to the entire course of therapy, AND
- Physician must confirm that alcohol and illicit substance abuse is absent for the previous six months, or patient is currently seeing an addiction specialist, AND
- Member must receive concurrent ribavirin therapy if genotype 1a (with or without cirrhosis), AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

 Estimates of test performance for advance fibrosis: cirrhosis (specificity/sensitivity)
- FibroTest 0.93/0.70 : 0.87/0.41
- Fibroscan® 0.96/0.45 : 0.93/0.39
- ALT 0.79/0.78 : 0.78/0.08
- Biopsy 0.67/.063 : 0.95/0.51

Exclusion Criteria
- Concurrent use with sofosbuvir, simeprivir, or ledipasvir/sofosbuvir, OR
- Concurrent use with medications highly dependent on CYP3A4 for clearance, strong inducers of CYP3A4 or CYP2C8, or strong inhibitors of CYP2C8, OR
- Moderate to severe hepatic impairment (Child-Pugh B or C), OR
- Decompensated cirrhosis, OR
• Coverage may be revoked if patient is non-adherent through the first two months of therapy, as evidenced by claim records or verbal confirmation of poor adherence

Required Medical Information
• All documentation required to support the utilization and exclusion criteria for coverage

Age Restrictions
• Must be 18 years of age and older

Prescriber Restrictions
• Must be prescribed by a gastroenterologist, hepatologist, or infectious disease specialist

Coverage Duration (months)
• Genotype 1a without cirrhosis, Genotype 1b with or without cirrhosis – 3 months
• Genotype 1a with cirrhosis – 6 months

Quantity/Partial Fill Restrictions
• None

Other Information
• Mechanism of action: Ombitasvir is an NS5B polymerase inhibitor, paritaprevir is a NS3/4A protease inhibitor, dasabuvir is a non-nucleoside NS5B polymerase inhibitor, and ritonavir is a protease inhibitor.

• Cross-resistance is expected among NS5A inhibitors, NS3/4A protease inhibitors, and nonnucleoside NS5B-palm inhibitors by class. Dasabuvir retained full activity against HCV replicons containing a single NS5B S282T substitution, which is associated with resistance to nucleos(t)ide analogue NS5B polymerase inhibitors.

References
• Viekira XR™ [Package Insert]. Chicago, IL: Abbvie, Inc.; November 2018.

Last Reviewed January 28, 2019
**Vivitrol® (naltrexone for extended-release injectable suspension)**

**FDA Approved Indication(s)**
- For the treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiation of treatment
- For the prevention of relapse to opioid dependence, following opioid detoxification

**FDA Recommended Dose**
- 380 mg intramuscularly every four weeks

**How Supplied**
- 380 mg vial of naltrexone, packaged with one vial of 4 mL diluent

**Utilization Criteria**

For initial review:
- For all conditions, the member must have a diagnosis consistent with FDA-labeling, AND
- For alcohol dependence:
  - The member must be able to abstain from alcohol in an outpatient setting prior to initiation of treatment, AND
  - The member must have documented adherence issues with daily oral naltrexone
- For the prevention of relapse to opioid dependence following detoxification:
  - The member must have successfully completed an opioid detoxification program, AND
  - Must be opioid-free for at least 10 days prior to initiating treatment with naltrexone

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- The member is currently receiving opioid analgesics
- Current physiologic opioid dependence
- Acute opioid withdrawal
- Positive urine screen for opioids
- Acute hepatitis or liver failure

**Required Medical Information**
- Age
- Dose
- Concurrent medications
- Comprehensive metabolic panel (CMP)

**Age Restrictions**
- 18 years of age or older

**Prescriber Restrictions**
- Must be prescribed by an addiction medicine specialist

**Coverage Duration (months)**
- 12

**Quantity/Partial-Fill Restrictions**
- None

**Other Information**
• Mechanism of action: Naltrexone is an opioid antagonist with highest affinity for the mu opioid receptor.
• Naltrexone causes precipitation of opioid withdrawal. An opioid-free duration of a minimum of 7-10 days is recommended for patients to avoid precipitation of opioid withdrawal that may be severe enough to require hospitalization.
• Following naltrexone treatment opioid tolerance is reduced from pretreatment baseline, and patients are vulnerable to potentially fatal overdose at the end of a dosing interval, after missing a dose, or after discontinuing naltrexone treatment.

References
• Johnson, BA. Pharmacotherapy for alcohol use disorder. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed January 6, 2016.
• Strain, E. Pharmacotherapy for opioid use disorder. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed January 6, 2016.
Vizimpro® (dacomitinib)†

FDA Approved Indication(s)
- First-line treatment of metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations

FDA Recommended Dose
- 45 mg orally once daily until disease progression or unacceptable toxicity
- See prescribing information for dose modifications

How Supplied
- 15 mg, 30 mg, and 45 mg tablets x 30-count bottles

Utilization Criteria

For initial review:
- Member has confirmation of metastatic non-small cell lung cancer, AND
- Confirmation of EGFR exon 19 deletion or exon 21 L858R mutation, as detected by an FDA-approved test

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Pregnancy
- Confirmation of interstitial lung disease (ILD)
- Concurrent use with proton pump inhibitors or CYP2D6 substrates

Required Medical Information
- Age
- Diagnosis
- Treatment history
- EGFR mutation testing
- Concurrent medications
- Dose

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 3 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Irreversibly inhibits EGFR family kinase activity (EGFR/HER1, HER2, and HER4) and certain EGFR activating mutations (exon 19 deletion or the exon 21 L858R substitution mutation)
- Warnings and Precautions: Severe and fatal interstitial lung disease (ILD)/pneumonitis occurred in patients treated with dacomitinib. Monitor patients for pulmonary symptoms and withhold treatment in patients who present with worsening of respiratory symptoms which may be indicative of ILD (e.g., dyspnea, cough, and fever). Permanently discontinue treatment if ILD is confirmed.
Diarrhea occurred in 86% of treated patients, with Grade 3 or 4 diarrhea reported in 11% of patients. Withhold dacomitinib for persistent Grade 2 or any Grade 3 or 4 dermatologic adverse reaction until recovery to less than or equal to Grade 1 severity.

References

- Vizimpro (dacomitinib) [prescribing information]. New York, NY: Pfizer Labs; September 2018.

Last Reviewed October 21, 2018
## Vosevi™ (sofosbuvir/velpatasvir/voxilaprevir)

### FDA-Approved Indication(s)
- For the treatment of adult patients with chronic hepatitis C (HCV) without cirrhosis or with compensated cirrhosis (Child-Pugh A), and:
  - For genotypes 1-6, who have been previously treated with an HCV regimen containing an NS5A inhibitor
  - For genotypes 1a or 3, who have been previously treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor

### FDA-Recommended Dose
- Dosed as one tablet daily (400 mg sofosbuvir, 100 mg velpatasvir, 100 mg voxilaprevir) for 12 weeks

### How Supplied
- Bottles of 28 tablets

### Utilization Criteria
*For initial review:*
- Member must have a diagnosis of chronic HCV with documented genotype and viral load collected within the previous three months, AND
- Physician must attest to the member’s ability and dedication to remain adherent to the entire course of therapy, AND
- Physician must confirm that alcohol and illicit substance abuse is absent for the previous six months, or member is currently seeing an addiction specialist, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

### Exclusion Criteria
- Member has documentation of decompensated cirrhosis (Child-Pugh B, C), OR
- Member has documentation of severe renal impairment (GFR < 30)

### Required Medical Information
- Dose and duration of therapy
- HCV genotype and subtype
- HCV treatment history
- Baseline ALT
- Current renal function (GFR)

### Age Restrictions
- 18 years of age or older

### Prescriber Restrictions
• Must be prescribed by a gastroenterologist, hepatologist, or infectious disease specialist

**Coverage Duration (months)**

• 12 weeks

**Quantity/Partial-Fill Restrictions**

• 28 days supply

**Other Information**

• Mechanism of action: Direct-acting antiviral (DAA) NS5B polymerase inhibitor (sofosbuvir), NS5A inhibitor (velpatasvir), NS3/4A protease inhibitor (voxilaprevir)

**References**


**Votrient® (pazopanib hydrochloride)**

**FDA Approved Indication(s)**
- For the treatment of advanced renal cell carcinoma (RCC)
- For the treatment of soft tissue sarcoma (STS) in patients who have received prior chemotherapy

**FDA Recommended Dose**
- 800 mg orally once daily without food

**How Supplied**
- 200 mg tablets

**Utilization Criteria**

*For initial review:*
- Patient has a diagnosis of renal cell carcinoma or soft tissue sarcoma with documentation of prior chemotherapy

*For continuation:*
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Patient has severe hepatic impairment (ALT, AST 3x ULN)
- Pregnancy

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Previous therapies
- Liver function (ALT, AST, serum bilirubin)

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration (months)**
- 3 months (initial), 12 months (continuation)

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: Pazopanib is a multi-tyrosine kinase inhibitor of vascular endothelial growth factor receptor (VEGFR)-1, VEGFR-2, VEGFR-3, platelet-derived growth factor receptor (PDGFR)-α and -β, fibroblast growth factor receptor (FGFR)-1 and -3, cytokine receptor (Kit), interleukin-2 receptor inducible T-cell kinase (Itk), leukocyte-specific protein tyrosine kinase (Lck), and transmembrane glycoprotein receptor tyrosine kinase (c-Fms).
- Black Box Warning: Increased risk of severe and fatal hepatotoxicity

**References**

Last Reviewed August 1, 2018
### Xalkori® (crizotinib)

**FDA Approved Indication(s)**

- For the first-line treatment of anaplastic lymphoma kinase (ALK)-positive metastatic or ROS1-positive non-small cell lung cancer (NSCLC)

**FDA Recommended Dose**

- 250 mg twice daily
- Reduced dose for hepatic function, QTc interval, symptomatic bradycardia per package insert

**How Supplied**

- 250 mg capsules

**Utilization Criteria**

*For initial review:*

- Member must have a diagnosis of ALK-positive or ROS1-positive metastatic NSCLC

*For continuation:*

- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**

- Severe hepatic dysfunction (ALT or AST >3xULN; total bilirubin >1.5xULN in absence of cholestasis or hemolysis)
- Presence of interstitial lung disease or pneumonitis
- QTc > 500msec with Torsades de pointes or polymorphic ventricular tachycardia or serious arrhythmia or life threatening bradycardia with/without concomitant medications

**Required Medical Information**

- Diagnosis
- Dose
- Concomitant medications
- Liver function tests

**Age Restrictions**

- 18 years of age and older

**Prescriber Restrictions**

- Must be prescribed by an oncologist

**Coverage Duration (months)**

- 6 months (initial), 12 months (continuation)

**Quantity/Partial Fill Restrictions**

- None

**Other Information**

- Mechanism of action: Crizotinib is an inhibitor of receptor tyrosine kinases including ALK and other genes. Translocations can affect the ALK gene resulting in the expression of oncogenic fusion proteins which results in activation and dysregulation of the gene's expression and signaling which can contribute to increased cell proliferation and survival in tumors expressing these proteins.
- Black Box Warning: None

**References**

Xeljanz®, Xeljanz® XR (tofacitinib citrate)

**FDA Approved Indication(s)**
- For the treatment of adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to methotrexate, as monotherapy or in combination with methotrexate or other nonbiologic disease-modifying antirheumatic drugs (DMARDs)
- For the treatment of adults with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to methotrexate or other disease-modifying antirheumatic drugs (DMARDs)
- For the treatment of adults with moderately to severely active ulcerative colitis (UC)

**FDA Recommended Dose**
- RA, PsA: 5 mg twice daily or 11 mg once daily
- UC: 10 mg twice daily for at least 8 weeks; then 5 or 10 mg twice daily
  - Discontinue after 16 weeks of 10 mg twice daily, if adequate therapeutic benefit is not achieved.
- See prescribing information for dose adjustments in renal/hepatic impairment

**How Supplied**
- Xeljanz®: 5 mg and 10 mg tablets
- Xeljanz® XR: 11 mg tablets

**Utilization Criteria**

*For initial review:*
For all conditions:
- The member must have a negative TB test prior to initiating therapy, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- UC:
  - Prescriber is a gastroenterologist, AND
  - Member must have documented failure, intolerance, or contraindication to ≥ 2 conventional therapies (e.g., corticosteroids, 5-ASA agents, immunosuppressants, immunomodulators)
- RA/PsA:
  - Prescriber is a rheumatologist, AND
  - Member must have failed a trial of, or is intolerant to, methotrexate monotherapy or at least one non-biologic DMARD for at least 6-12 weeks

*For continuation:*
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Review of therapy by a specialist confirms that there is a continued beneficial response to therapy, AND
- Member’s liver function and complete blood count have remained within normal range
- For ulcerative colitis: member must have evidence of therapeutic benefit by week 16.

**Exclusion Criteria**
- The member is using or planning to use tofacitinib in combination with biologic DMARDs, biologic therapies for the treatment of UC, or potent immunosuppressants (e.g., azathioprine or cyclosporine), OR
- Severe hepatic impairment, OR
• Absolute lymphocyte count < 500 cells/mm³, OR
• Absolute neutrophil count (ANC) < 1000 cells/mm³, OR
• Hemoglobin < 9 g/dL

**Required Medical Information**

• Diagnosis
• Concurrent medications
• Liver function tests (AST, ALT)
• Complete blood count
• Date of last negative tuberculosis skin test

**Age Restrictions**

• 18 years of age and older

**Prescriber Restrictions**

• Must be prescribed by a rheumatologist or gastroenterologist

**Coverage Duration (months)**

• UC: 4 months (initial), 12 months (continuation)
• RA, PsA: 12 months

**Quantity/Partial Fill Restrictions**

• 10 mg tablet limited to diagnosis of UC
• 11 mg tablet limited to diagnosis of RA/PsA

**Other Information**

• Mechanism of action: Tofacitinib is a Janus kinase (JAK) inhibitor
• Black Box Warning: Patients treated with tofacitinib are at increased risk for developing serious infections that may lead to hospitalization or death, and lymphoma and other malignancies have been observed in patients treated with tofacitinib.

**References**


*Last Reviewed June 22, 2018*
### Xeloda® (capecitabine)

#### FDA Approved Indication(s)
- For the adjuvant treatment of patients with Dukes’ C colon cancer
- As first-line monotherapy for the treatment of metastatic colon cancer, when treatment with fluoropyrimidine therapy alone is preferred
- For the treatment of metastatic breast cancer:
  - In combination with docetaxel, after failure of prior anthracycline-containing therapy
  - As monotherapy in patients resistant to both paclitaxel and anthracycline-containing regimens

#### FDA Recommended Dose
- Monotherapy: 1250 mg/m² twice daily orally for 2 weeks followed by a one week rest period in 3-week cycles
- In combination with docetaxel: 1250 mg/m² twice daily for 2 weeks followed by a 7-day rest period, combined with docetaxel at 75 mg/m² as a 1-hour IV infusion every 3 weeks

#### How Supplied
- 150 mg and 500 mg tablets

#### Utilization Criteria

1. **For initial review:**
   - For use in patients who meet FDA-approved indications

2. **For continuation:**
   - Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

#### Exclusion Criteria
- Patient has dihydropyrimidine dehydrogenase (DPD) deficiency, OR
- Patient has severe renal impairment (CrCl < 30 mL/min), OR
- Member is requesting the branded formulation of product

#### Required Medical Information
- Diagnosis
- Age
- Dose and frequency
- Patient height and weight
- Renal function (CrCl)
- Treatment history

#### Age Restrictions
- 18 years of age and older

#### Prescriber Restrictions
- Must be prescribed by an oncologist

#### Coverage Duration (months)
- 12

#### Quantity/Partial Fill Restrictions
- 30 day supply

#### Other Information
• Mechanism of action: Enzymes convert capecitabine to 5-fluorouracil (5-FU) \textit{in vivo}. Both normal and tumor cells metabolize 5-FU to metabolites which cause cell injury and cellular death.

• Black Box Warning: Patients receiving warfarin must monitor anticoagulation response frequently while on therapy due to an increased risk of bleeding and death.

• For dosing, BSA (m$^2$) = ( [Height(in) x Weight(lbs)] / 3131)$^{\frac{1}{2}}$

References

• Xeloda$^\circledR$ [package insert]. South San Francisco, CA: Genentech USA, Inc; October 2014.

Last Reviewed November 9, 2015
### Xeomin® (incobotulinumtoxina)

**FDA Approved Indications**
- For the treatment of adult patients with:
  - Upper limb spasticity
  - Cervical dystonia, in both botulinum toxin-naive and previously treated patients
  - Blepharospasm previously treated with onabotulinumtoxinA
- For the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients

**FDA Recommended Dose**
- Upper limb spasticity: Up to 400 units per treatment no sooner than every 12 weeks
- Cervical dystonia: 120 units per treatment
- Blepharospasm: 1.25-2.5 units per injection site, up to a maximum dose of 35 units per eye, given no more frequently than every 12 weeks
- Glabellar lines: 20 units per treatment divided into 5 equal IM injections of 4 units each

**How Supplied**
- 50 unit, 100 unit, and 200 unit single-use vials of lyophilized powder

**Utilization Criteria**
- For initial review:
  - Used for the treatment of upper limb spasticity, cervical dystonia, or blepharospasm
  - The indicated diagnosis (including any applicable labs and/or tests) and medication usage must be supported by documentation from the patient’s medical records
  - Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable
- For continuation:
  - Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable, AND
  - Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Used for the treatment of glabellar lines

**Required Medical Information**
- Diagnosis
- Age
- Dose

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by a provider skilled in the treatment of neurologic conditions, such as neurologist, otolaryngologist, ophthalmologist, physical therapist, or physiatrist

**Coverage Duration (months)**
- Initial coverage may be limited to 6 months to establish efficacy
- 12 month continuation

**Quantity/Partial Fill Restrictions**
• Upper limb spasticity: 400 units every 12 weeks
• Cervical dystonia: 120 Units every 12 weeks
• Blepharospasm: 70 Units every 12 weeks

Other Information
• Mechanism of action: incobotulinumtoxina blocks cholinergic transmission at the neuromuscular junction by inhibiting the release of acetylcholine from peripheral cholinergic nerve endings.
• Black Box Warning: Risk of distant spread of toxin effect, leading to symptoms consistent with botulinum toxicity

References
• Xeomin® [package insert]. Greensboro, NC: Merz Pharmaceuticals, LLC; December 2017.
**Xermelo® (telotristat ethyl)**

**FDA-Approved Indication(s):**
- For the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy.

**FDA-Recommended Dose**
- 250 mg three times daily

**How Supplied**
- 250 mg tablets; each monthly case contains four weekly boxes. Each weekly box contains seven daily dose packs

**Utilization Criteria**

*For initial review:*
- Member must have a diagnosis of carcinoid syndrome diarrhea, AND
- Member must have tried and failed three months of treatment with a somatostatin analog such as octreotide, lanreotide, or pasireotide. Failure is defined as continued uncontrolled diarrhea (i.e. ≥4 bowel movements daily).
- Member must be using Xermelo® concomitantly with a somatostatin analog

*For continuation:*
- Member must have documentation of treatment response, as verified by their specialist provider.

**Exclusion Criteria**
- Documentation of severe constipation or severe persistent or worsening abdominal pain while on therapy

**Required Medical Information**
- Diagnosis
- Concurrent medications
- Treatment history

**Age Restrictions**
- Must be 18 years of age or older

**Prescriber Restrictions**
- Must be prescribed by an oncologist or gastroenterologist

**Coverage Duration (months)**
- 4 Months initial; 12 months continuation

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Carcinoid syndrome is the term applied to a constellation of symptoms that are associated with elevations in serum serotonin, or its metabolite urinary 5-hydroxyindoleacetic acid (5-HIAA), secreted by some carcinoid tumors. Two of the most common manifestations are flushing and diarrhea.
- Telotristat is an oral tryptophan hydroxylase inhibitor that is thought to work in carcinoid syndrome by inhibiting the rate limiting step in the conversion of the amino acid tryptophan to serotonin.

**References**
Xiaflex™ (collagenase clostridium histolyticum)

**FDA-Approved Indication(s):**
- For the treatment of adult patients with Dupuytren’s contracture with a palpable cord
- For the treatment of adult men with Peyronie’s disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy

**FDA-Recommended Dose**
- Dupuytren’s contracture: 0.58 mg into target area per treatment cycle, up to three times per cord at approximately four week intervals.
- Peyronie’s disease: 0.58 mg into target area. One treatment cycle consists of two injection procedures; each cycle may be repeated at six week intervals.

**How Supplied**
- 0.9 mg/3 mL (0.3 mg/mL) solution in a single-dose glass vial

**Utilization Criteria**

For initial review:
- Dupuytren’s contracture:
  - Member must have documentation of flexion deformities ≥ 20 degrees at the metacarpophalangeal (MCP) or proximal interphalangeal (PIP) joints, AND
  - Must have documentation of a palpable cord
- Peyronie’s disease:
  - Member must have a palpable plaque with curvature deformity of at least 30 degrees at the start of therapy, AND
  - Member must have tried and failed a series of verapamil injections

**Exclusion Criteria**
- Treatment of Peyronie’s plaques that involve the penile urethra

**Required Medical Information**
- Diagnosis
- Treatment history

**Age Restrictions**
- Must be 18 years of age or older

**Prescriber Restrictions**
- If prescribing for Dupuytren’s contracture, prescriber must be experienced in injection procedures of the hand and in the treatment of Dupuytren’s contracture
- If prescribing for Peyronie’s disease, prescriber must be a urologist certified with the Xiaflex® REMS program by enrolling and completing training in the administration of Xiaflex® treatment

**Coverage Duration (months)**
- 3 Months

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Black Box Warnings: Corporal rupture (penile fracture) was reported as an adverse reaction in 5 of 1044 (0.5%) treated patients in clinical studies. In other treated patients (9 of 1044; 0.9%), other severe penile injury has been reported. Severe penile hematoma was also reported as an adverse reaction in 39 of 1044 (3.7%) treated patients.
• Injection into collagen-containing structures such as tendons or ligaments of the hand may result in damage to those structures and possible permanent injury such as tendon rupture or ligament damage. Therefore, injection should only be administered into the collagen cord with a MP or PIP joint contracture, and care should be taken to avoid injecting into tendons, nerves, blood vessels, or other collagen-containing structures of the hand.

References

• Xiaflex™ (collagenase clostridium histolyticum) [prescribing information]. Malvern, PA: Endo Pharmaceuticals; December 2016.

Last Reviewed May 2, 2018
Xolair® (omalizumab)

FDA Approved Indication(s)

- Moderate to severe persistent asthma in patients 6 years of age and older with a positive skin test, or in vitro reactivity to a perennial aeroallergen, with symptoms that are inadequately controlled with inhaled corticosteroids.
- Chronic idiopathic urticaria in adults and adolescents (12 years of age and above) who remain symptomatic despite H1 antihistamine treatment.

FDA Recommended Dose

- Asthma: 75 to 375 mg subcutaneous, dosed every 2 or 4 weeks
- Chronic Idiopathic Urticaria: 150 or 300 mg subcutaneous, dosed every 4 weeks

How Supplied

- 150 mg/5 mL single-use vial

Utilization Criteria

For initial review:

- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Asthma
  - Member must have a diagnosis of severe persistent asthma, AND
  - Member must have an inadequate response to a three-month course of inhaled corticosteroids, long-acting beta2-agonists, and montelukast, AND
  - Member must have documented history of severe attacks leading to either hospitalization or use of oral corticosteroids, AND
  - Member must have a baseline serum IgE level between 30 IU/mL and 700 IU/mL, AND
  - Member is currently receiving long-acting beta2-agonist, inhaled corticosteroid therapy, and short-acting beta2-agonist as rescue therapy, unless otherwise contraindicated
- Chronic idiopathic urticaria
  - Member must have a diagnosis of chronic idiopathic urticaria, AND
  - Member must be considered refractory to monotherapy with treatment failure after max-dose second generation antihistamine, H2-antagonist, leukotriene receptor antagonist, and first-generation antihistamine

For continuation:

- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable, AND
- Member must have a documented clinical response to therapy

Exclusion Criteria

- Planned use for the treatment of other allergic conditions

Required Medical Information

- Diagnosis
- Weight
- Previous and concurrent therapies
- Baseline spirometry results
- Serum IgE (for treatment of asthma)

Age Restrictions

- 6 years of age and older for asthma, 12 years of age and older for chronic idiopathic urticaria

Prescriber Restrictions
Must be prescribed by a pulmonologist, allergist, or immunologist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Omalizumab inhibits the binding of IgE to the high-affinity IgE receptor on the surface of mast cells and basophils.
- Black Box Warning: Anaphylaxis has been reported to occur after administration of Xolair.

References

Xospata® (gilteritinib)

FDA Approved Indication(s)
- Relapsed or refractory acute myeloid leukemia (AML) with an FMS-like tyrosine kinase 3 (FLT3) mutation detected by an FDA-approved test

FDA Recommended Dose
- 120 mg one time daily for a minimum of 6 months as response may be delayed

How Supplied
- Bottles of 90 tablets

Utilization Criteria

For initial review:
- Member has a confirmed diagnosis of relapsed or refractory acute myeloid leukemia with an FMS-like tyrosine kinase 3 (FLT3) mutation detected by an FDA-approved test

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- None

Required Medical Information
- Diagnosis
- Age
- Treatment history
- FLT3 test results

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a hematologist or oncologist
**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action:
- Black Box Warning: Patients treated with Xospata have experienced Differentiation Syndrome. Symptoms include fever, dyspnea, hypoxia, pulmonary infiltrates, pleural or pericardial effusion, rapid weight gain or peripheral edema, hypotension or renal dysfunction. Treat patients with corticosteroid therapy and hemodynamic monitoring if Differentiation Syndrome is suspected.

**References**
**Xtandi® (enzalutamide)**

**FDA Approved Indication(s)**
- For the treatment of patients with castration-resistant prostate cancer

**FDA Recommended Dose**
- 160 mg (four 40 mg capsules) orally once daily, with or without food
- See prescribing information for dose modifications
- Patients receiving enzalutamide should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy

**How Supplied**
- 40 mg capsules

**Utilization Criteria**

For initial review:
- Member must have a diagnosis of an FDA-approved indication, AND
- Member is concurrently receiving a gonadotropin-releasing hormone (GnRH) analog, OR
- Member has documentation of a bilateral orchiectomy

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

**Exclusion Criteria**
- Concurrent treatment with Zytiga® (abiraterone)

**Required Medical Information**
- Diagnosis
- Age
- Dose

**Age Restrictions**
- 18 years of age and older

**Prescriber Restrictions**
- Must be prescribed by an oncologist

**Coverage Duration (months)**
- 3 months (initial), 12 months (continuation)

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- **Mechanism of action:** Enzalutamide is an androgen receptor inhibitor that acts on different steps in the androgen receptor signaling pathway. Enzalutamide has been shown to competitively inhibit androgen binding to androgen receptors and inhibit androgen receptor nuclear translocation and interaction with DNA.
- **Warnings and precautions:** Enzalutamide can cause fetal harm and potential loss of pregnancy. Advise patients of the risk of developing a seizure while receiving enzalutamide and of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others. Enzalutamide should be permanently discontinued in patients who develop a seizure during treatment. Posterior reversible encephalopathy syndrome (PRES) has been reported in patients receiving enzalutamide.

**References**

Last Reviewed July 18, 2018
Xyrem® (sodium oxybate)

FDA Approved Indication(s)

• For the treatment of cataplexy in narcolepsy
• For the treatment of excessive daytime sleepiness in narcolepsy

FDA Recommended Dose

• Recommended starting dose of 4.5 grams per night, administered as two equal doses: 2.25 g at bedtime and 2.25 g 2.5-4 hours later. Increase dose by 1.5 g per night at weekly intervals (split as 0.75 g for each dose) to the effective dose range of 6 g-9 g per night

<table>
<thead>
<tr>
<th>Patient’s Total Nightly Dose</th>
<th>Take at Bedtime</th>
<th>Take 2.5-4 Hours Later</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.5 g</td>
<td>2.25 g</td>
<td>2.25 g</td>
</tr>
<tr>
<td>6 g</td>
<td>3 g</td>
<td>3 g</td>
</tr>
<tr>
<td>7.5 g</td>
<td>3.75 g</td>
<td>3.75 g</td>
</tr>
<tr>
<td>9 g</td>
<td>4.5 g</td>
<td>4.5 g</td>
</tr>
</tbody>
</table>

• Hepatic Impairment: recommended starting dose of 2.25 g per night, administered as two equal doses: ~1.13 g at bedtime and ~1.13 g 2.5-4 hours later
• See package insert for dose adjustment with divalproex sodium

How Supplied

• Oral solution (500mg/mL)

Utilization Criteria

For initial review:

• Member and prescriber must be enrolled in the Xyrem® REMS Program, AND
• Prescriber must confirm that alcohol and illicit substance abuse is absent, AND
• For the treatment of cataplexy in narcolepsy,
  • Member must have a confirmed diagnosis of narcolepsy with cataplexy, AND
  • Member must have a documented inadequate response to at least three medications used for narcolepsy with cataplexy from independent medication classes (modafinil, armodafinil, a tricyclic antidepressant [e.g. amitriptyline, desipramine, imipramine, etc.], a selective serotonin reuptake inhibitor [e.g. fluoxetine, sertraline, paroxetine, etc.], or venlafaxine). Documented trials of each medication must be at least three months in duration.
• For the treatment of narcolepsy with excessive daytime sleepiness,
  • Member must have a confirmed diagnosis of narcolepsy with excessive daytime sleepiness, AND
  • Member must have a documented inadequate response to at least three CNS stimulant medications used for narcolepsy with excessive daytime sleepiness (e.g., modafinil, armodafinil, methylphenidate, dextroamphetamine, or amphetamine/dextroamphetamine). Documented trials of each medication must be at least three months in duration.

For Continuation:

• Confirmation that Xyrem® use has resulted in either a reduction in cataplexy symptoms or a reduction in excessive daytime sleepiness symptoms as assessed and documented by the member’s specialist provider

Exclusion Criteria

• Concomitant treatment with CNS depressants (e.g. ethanol, sedative hypnotics, anxiolytics, barbiturates, benzodiazepines, opioid analgesics, etc.)
• Diagnosed succinic semialdehyde dehydrogenase deficiency

Required Medical Information
Current medication list
Substance abuse attestation
Treatment history

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by a neurologist and sleep specialist

Coverage Duration
- 3 months for initial approval
- 12 months maintenance following documented reduction of cataplexy attacks or excessive daytime sleepiness

Quantity/Partial Fill Restrictions
- Quantity limit of 540 mL per 30 day supply (9 g/day is max FDA-labeled dose); maximum 30 day supply per fill

Other Information
- Xyrem® is a Schedule III controlled substance.
- Mechanism of Action: Xyrem® is a CNS depressant. The mechanism of action of Xyrem® in the treatment of narcolepsy is unknown, however, it is hypothesized that the therapeutic effects are mediated through GABA<sub>B</sub> actions. Sodium oxybate is the sodium salt of gamma hydroxybutyrate (GHB).
- Most patients in the clinical trials received concurrent therapy with a CNS stimulant (>70% of subjects in clinical trials were receiving concurrent treatment with CNS stimulants).
- Benefit/risk of use should be assessed in patients with sleep apnea, compromised respiratory function (asthma, COPD, etc.), or a disease state necessitating sodium restrictive diet (Xyrem® formulation contains a significant amount of sodium – see package insert).
- AWP as of 3/29/17: $4,744.76 per 180mL bottle (patient may use up to 3 bottles per month).

References
# Zejula® (niraparib)

## FDA Approved Indication(s)
- For the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

## FDA Recommended Dose
- 300 mg (three 100 mg capsules) by mouth once daily

## How Supplied
- 100 mg capsules

## Utilization Criteria

### For initial review:
- Member must have a documented diagnosis of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer; AND
- Member must have a start date no later than 8 weeks after their most recent platinum-containing regimen

### For continuation:
- Member must have documentation of treatment response, as verified per progress notes

## Exclusion Criteria
- None

## Required Medical Information
- Diagnosis
- Current medication list
- Therapeutic history (date of platinum therapy discontinuation)
- Complete blood count (CBC)

## Age Restrictions
- 18 years of age and older

## Prescriber Restrictions
- Must be prescribed by an oncologist

## Coverage Duration (months)
- 12 months

## Quantity/Partial Fill Restrictions
- None

## Other Information
- Mechanism of action: Niraparib is a poly ADP-ribose polymerase (PARP) inhibitor that blocks an enzyme involved in repairing damaged DNA. By blocking PARP, DNA inside the cancerous cells accumulates damage, slowing tumor growth and leading to cell death.

## References

*Last Reviewed May 23, 2017*
Zelboraf® (vemurafenib)

FDA Approved Indication(s)
- For the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation, as detected by an FDA-approved test
- For the treatment of patients with Erdheim-Chester Disease (ECD) with BRAF V600 mutation

FDA Recommended Dose
- 960 mg (four 240 mg tablets) orally every 12 hours

How Supplied
- 240 mg tablet

Utilization Criteria

For initial review:
- Member must have documentation of a diagnosis consistent with an FDA-approved indication, AND
- Must have documentation of BRAF V600E or V600 mutation, as detected by an FDA-approved test

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Presence of wild-type BRAF melanoma

Required Medical Information
- Diagnosis
- Confirmation of BRAF V600E or BRAF V600 mutation
- Age
- Dose

Age Restrictions
- 18 years and over

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 3 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Vemurafenib is a low molecular weight, orally available inhibitor of some mutated forms of BRAF serine-threonine kinase, including BRAF V600E. Vemurafenib also inhibits other kinases in vitro such as CRAF, ARAF, wild-type BRAF, SRMS, ACK1, MAP4K5, and FGR at similar concentrations. Some mutations in the BRAF gene including V600E result in constitutively activated BRAF proteins, which can cause cell proliferation in the absence of growth factors that would normally be required for proliferation. Vemurafenib has anti-tumor effects in cellular and animal models of melanomas with mutated BRAF V600E.

References
Zepatier™ (elbasvir/grazoprevir)

**FDA-Approved Indication(s)**

- For the treatment of chronic hepatitis C virus (HCV) genotypes 1 and 4 infection in adults with or without cirrhosis

**FDA-Recommended Dose**

- One tablet by mouth once daily, with or without ribavirin (see indications below)

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Ribavirin (RBV)</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1a</td>
<td>No</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Treatment-naïve or PegIFN/RBV-experienced</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without baseline NS5A polymorphisms*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genotype 1b</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment-naïve or PegIFN/RBV-experienced</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genotype 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment-naïve</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genotype 1a or 1b</td>
<td>+ RBV</td>
<td>12 weeks</td>
</tr>
<tr>
<td>PegIFN/RBV/PI-experienced</td>
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<td></td>
</tr>
<tr>
<td>Genotype 1a</td>
<td>+ RBV</td>
<td>16 weeks</td>
</tr>
<tr>
<td>Treatment-naïve or PegIFN/RBV-experienced</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With baseline NS5A polymorphisms</td>
<td></td>
<td></td>
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<tr>
<td>Genotype 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PegIFN/RBV-experienced</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- *polymorphisms at amino acid positions 28, 30, 31, or 93
- *PI: HCV NS3/4A protease inhibitor: boceprevir, simeprevir, or teleprevir

**How Supplied**

- Tablet containing 50 mg elbasvir and 100 mg grazoprevir in a carton containing two 14-count dose packs (28 tablets total)

**Utilization Criteria**

*For initial review:*

- Member must have a diagnosis of HCV genotype 1 or 4, AND
- If genotype 1a, documentation of testing for the NS5A resistance-associated polymorphism, AND
- Must be given with RBV if required per the chart above, AND
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable

**Exclusion Criteria**

- Moderate or severe hepatic impairment (Child-Pugh B or C).
- OATP1B1/3 inhibitors, strong CYP3A inducers and inhibitors, and efavirenz
- If taken with RBV, the contraindications to RBV apply.

**Required Medical Information**

- Age
- Dose and duration of therapy
- Diagnosis
- HCV Genotype, subtype, and documentation of NS5A polymorphism if applicable
- HCV treatment history
- Current medication list
- Baseline ALT

**Age Restrictions**
- Must be 18 years of age or older

**Prescriber Restrictions**
- Must be prescribed by a gastroenterologist, hepatologist, or infectious disease specialist

**Coverage Duration (months)**
- Total coverage duration will depend on required duration of therapy with a maximum of 16 weeks

**Quantity/Partial-Fill Restrictions**
- None

**Other Information**
- Both ingredients are direct-acting antiviral agents, with non-overlapping resistance profiles, that target different steps in the replication cycle. Elbasvir is a HCV NS5A inhibitor and grazoprevir is a HCV NS3/4A protease inhibitor.
- Asymptomatic elevations in ALT were observed in the clinical trial. Therefore, hepatic laboratory testing should be done (at a minimum) at baseline, treatment week 8, and treatment week 12 for those receiving 16 weeks of therapy.

**References**
Zoladex® (goserelin acetate)

FDA Approved Indication(s)
- Use in combination with flutamide for the management of locally confined carcinoma of the prostate
- Palliative treatment of advanced carcinoma of the prostate
- The management of endometriosis
- Use as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding
- Use in the palliative treatment of advanced breast cancer in pre- and perimenopausal women

FDA Recommended Dose
- Advanced breast cancer
  - 3.6 mg/28 day supply
- Endometrial thinning
  - 3.6 mg/28 day supply
- Endometriosis
  - 3.6 mg/28 day supply
- Prostatic carcinoma
  - 3.6 mg/28 day supply or 10.8 mg/84 day supply
- Stage B2 to C prostatic carcinoma
  - 3.6 mg/28 day supply or 10.8 mg/84 day supply

How Supplied
- 3.6 mg and 10.8 mg subcutaneous implants

Utilization Criteria

For initial review:
- Member must have a diagnosis consistent with an FDA-approved indication
- Member must have documented failure of, or intolerance to, their plan’s preferred product(s), as applicable
- Gender Dysphoria in Adolescents
  - The member meets DSM-V or ICD-10 criteria for the diagnosis of gender identity disorder, AND
  - The adolescent has experienced puberty to at least Tanner stage 2, AND
  - Documentation that the adolescent has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed), AND
  - Any co-existing psychological, medical, or social problems that could interfere with treatment have been addressed and member has adequate psychological and social support for treatment, AND
  - Member has given informed consent to begin treatment
    - If the adolescent has not reached the age of medical consent, the parent(s)/legal guardian(s) have consented to the treatment, AND
  - Prescriber is an endocrinologist

For continuation:
- Member must have documented failure of, or intolerance to, their plan’s preferred biologic product(s), as applicable
• Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
• None

Required Medical Information
• Diagnosis
• Age
• Dose

Age Restrictions
• 18 years of age and older

Prescriber Restrictions
• Must be prescribed by an oncologist

Coverage Duration (months)
• 12

Quantity/Partial Fill Restrictions
• None

Other Information
• Mechanism of action: Zoladex® is a synthetic decapeptide analogue of GnRH. It acts as an inhibitor of pituitary gonadotropin secretion when administered in the biodegradable formulation.

References
• World Professional Association for Transgender Health. Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People. V7. Available at www.wpath.org

Last Reviewed August 18, 2017

Zolgensma (onasemnogene abeparvovec-xioi)

FDA Approved Indication(s)
• For the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with two mutations in the survival motor neuron 1 (SMN1) gene.

FDA Recommended Dose
• Zolgensma is a single-dose intravenous infusion
• The recommended dose of Zolgensma is 1.1 x 10^{14} vector genomes per kilogram (vg/kg) of body weight
• See package insert for dosing chart

How Supplied
• Customized kits to meet dosing requirements for each patient
• Each kit contains 2 to 9-10 mL vials of Zolgensma with a fill volume of either 5.5 mL or 8.3 mL, depending upon dose and one alcohol wipe per vial
• Vial nominal concentration is 2 x 10^{13} vg/mL
• Shipped frozen; store in refrigerator up to 14 days

Utilization Criteria
Initial review:
- For member with spinal muscular atrophy (SMA) in patients less than 2 years of age who meet ALL the following:
  - Confirmed diagnosis of SMA type I via:
    - Bi-allelic SMN1 deletions or variants, AND
    - Two copies of SMN2 gene, AND
    - Absence of c.859G>C modification in exon 7 of the SMN2 gene
  - Patient is not on permanent ventilation (tracheostomy or respiratory assistance for 16 or more hours per day [including noninvasive ventilatory support] continuously for 14 or more days in the absence of acute reversible illness. Excludes perioperative ventilation)
  - Documented test confirming anti-adeno-associated virus serotype 9 (AAV9) antibody titer less than or equal to 1:50
  - Member not previously treated with gene replacement therapy for SMA
  - Concomitant therapy of systemic corticosteroids equivalent to oral prednisolone 1 milligram per kilogram of body weight per day (mg/kg/day) for a total of 30 days

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Advanced SMA (complete paralysis of limbs, permanent ventilator-dependence)
- Previous gene therapy or concomitant
- Active viral infection

Required Medical Information
- Diagnosis
- Weight
- Baseline anti-AAV9 antibody testing
- AST, ALT, total bilirubin, prothrombin time, platelets, troponin-1
- Therapeutic history
- Medication list

Age Restrictions
- 2 years of age and younger

Prescriber Restrictions
- Must be prescribed by a neurologist specializing in SMA

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: recombinant AAV9-based gene therapy that delivers a copy of the gene encoding the human SMN protein
- Black Box Warning: Acute Serious Liver Injury; prior to starting therapy evaluate liver function and for at least 3 months after infusion

References
- Finkel RS, Mercuri E, Meyer OH, et.al. Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics. Neuromuscular Disorders. March 2018;28(3):197-207
Zolinza® (vorinostat)

FDA Approved Indication(s)
- For the treatment of cutaneous manifestations in patients with cutaneous T-cell lymphoma (CTCL) who have progressive, persistent or recurrent disease on or following two systemic therapies

FDA Recommended Dose
- 400 mg orally once daily, with food

How Supplied
- 100 mg capsules

Utilization Criteria

For initial review:
- Member must have a diagnosis of cutaneous T-cell lymphoma (CTCL), AND
- Documentation of two separate previous systemic therapies

For continuation:
- Member must have a clinical response to treatment within 3 to 6 months of beginning treatment.
  - If a response is seen, therapy will be approved each time for an additional 3 months

Exclusion Criteria
- Lack of clinical response after 6 months of treatment

Required Medical Information
- Diagnosis
- Age
- Dose
- Liver function status (ALT, AST, bilirubin)
- Therapeutic history and previous therapies

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- Three (3) months

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Vorinostat inhibits the enzymatic activity of select histone deacetylases. The antineoplastic effect of vorinostat is yet to be fully described.

References

Last Reviewed November 10, 2015
Zydelig™ (idelalisib)

FDA Approved Indication(s)
- Relapsed Chronic Lymphocytic Leukemia (CLL)
  - For use in combination with rituximab in patients for whom rituximab alone would be considered appropriate therapy
- Relapsed Follicular B-cell non-Hodgkin Lymphoma
  - In patients who have received at least two prior systemic therapies
- Relapsed small lymphocytic lymphoma (SLL)
  - In patients who have received at least two prior systemic therapies

FDA Recommended Dose
- 150 mg twice daily
- Withhold medication and dose adjustments for ALT/AST >5-20 x ULN, bilirubin >3-10 x ULN, severe diarrhea (≥7 stools over baseline) or hospitalization, neutropenia (ANC <0.5 Gi/L), thrombocytopenia (platelets <25 Gi/L) per package insert recommendations.

How Supplied
- 100 mg or 150 mg as 60 film-coated tablets per bottle

Utilization Criteria
For initial review:
- Member must have a diagnosis consistent with an FDA-approved indication
For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- ALT/AST >20x ULN
- Bilirubin >10x ULN
- Pregnancy

Required Medical Information
- Diagnosis
- Age
- Dose
- Treatment history
- Concurrent medications

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 12 months

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Inhibitor of PI3Kδ kinase, which is expressed in both normal and malignant B-cells.
• Induces apoptosis and inhibits proliferation in cell lines derived from malignant B-cells and in primary tumor cells.
• Inhibits several cell signaling pathways, including B-cell receptor (BCR) signaling and the CXCR4 and CXCR5 signaling, which are involved in trafficking and homing of B-cells to the lymph nodes and bone marrow.
• Inhibition of chemotaxis and adhesion, and reduced cell viability.

References


Last Reviewed November 9, 2015
Zykadia™ (ceritinib)

FDA Approved Indication(s)
- Treatment for anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to Xalkori® (crizotinib)

FDA Recommended Dose
- 750 mg once daily

How Supplied
- 150 mg capsules

Utilization Criteria

For initial review:
- Member must have a diagnosis of ALK-positive metastatic NSCLC with a previous treatment history of crizotinib

For continuation:
- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria
- Severe hepatic dysfunction (ALT or AST >3xULN; total bilirubin >2xULN in absence of cholestasis or hemolysis)
- Presence of interstitial lung disease or pneumonitis
- QTc > 500msec with Torsades de pointes or polymorphic ventricular tachycardia or serious arrhythmia or life threatening bradycardia with/without concomitant medications
- Uncontrollable persistent hyperglycemia

Required Medical Information
- Diagnosis
- Dose
- Concomitant and previous therapies
- Liver function tests

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Ceritinib is a kinase inhibitor against ALK. Ceritinib inhibits the ALK-mediated phosphorylation of the downstream signaling protein STAT3, and proliferation of ALK-dependent cancer cells.
- Black Box Warning: None

References
Zytiga® (abiraterone)

FDA Approved Indication(s)

- In combination with prednisone for the treatment of patients with:
  - Metastatic castration-resistant prostate cancer (mCRPC)
  - Metastatic high-risk castration-sensitive prostate cancer

FDA Recommended Dose

- Metastatic castration-resistant prostate cancer:
  - 1,000 mg (two 500 mg tablets or four 250 mg tablets) orally once daily with prednisone 5 mg twice daily
- Metastatic castration-sensitive prostate cancer:
  - 1,000 mg (two 500 mg tablets or four 250 mg tablets) orally once daily with prednisone 5 mg once daily

How Supplied

- 250 mg tablets, 500 mg tablets

Utilization Criteria

For initial review:

- Member has documentation of an FDA-approved indication, AND
- Member is receiving concurrent prednisone 5 mg orally twice daily or once daily based on indication (or equivalent), unless contraindicated, AND
- Baseline ALT, AST, and bilirubin tests are monitored prior to treatment initiation
  - Patients with a Child-Pugh B score should only receive 250 mg once daily

For continuation:

- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider

Exclusion Criteria

- Concurrent treatment with enzalutamide
- Pregnancy

Required Medical Information

- Diagnosis
- Dose
- Liver function status with liver enzyme levels

Age Restrictions

- 18 years of age and older

Prescriber Restrictions

- Must be prescribed by an oncologist

Coverage Duration (months)

- 3 months (initial), 12 months (continuation)

Quantity/Partial Fill Restrictions

- None

Other Information

- Mechanism of action: CYP17 inhibitor

References


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