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† New criteria since previous publication
‡ Updated criteria since previous publication
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 Additional criteria may be developed from time to time and some may be withdrawn from use.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.
Changes at a glance

New criteria since previous publication:

- Anthim® (obiltoxaximab)
- Cabometyx® (cabozantinib)
- Cinqair® (reslizumab)
- Epclusa® (velpatasvir/sofosbuvir)
- Ocaliva® (obeticholic acid)
- Sprix® (ketorolac tromethamine)
- Taltz® (ixekizumab)
- Venetoclax® (venetoclax)
- Zynbryta® (dacalizumab)

Updated or modified criteria since previous publication:

- Forteo® – Clarified and updated step-therapy requirements with oral bisphosphonates
- Gleevec® – Added an exclusion criteria for use in idiopathic pulmonary fibrosis (IPF)
- Humira® – Added uveitis indication requirements
- Lupron® – Added utilization criteria for ovarian suppression in breast cancer
- Mekinist® – Corrected error in mutation requirement
- Prolia® – Clarified and updated step-therapy requirements with oral bisphosphonates
- Promacta® – Added indication for aplastic anemia
- Reclast® – Clarified and updated step-therapy requirements with oral bisphosphonates
- Revatio® – Added an exclusion criteria for use in idiopathic pulmonary fibrosis (IPF)
- Simponi® – Added Simponi® ARIA™ and restriction for inability to use self-injectable product
- Tafinlar® – Updated indication information
- Viekira Pak™, Viekira XR™ – Updated product formulation
**Abraxane® (paclitaxel)**

### FDA Approved Indication(s)
- Metastatic breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.
- Locally advanced or metastatic non-small cell lung cancer (NSCLC) as first-line treatment in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy.
- Metastatic adenocarcinoma of the pancreas as first-line treatment, in combination with gemcitabine.

### FDA Recommended Dose
- **Metastatic Breast Cancer**: 260 mg/m² intravenously over 30 minutes every 3 weeks.
- **NSCLC**: 100 mg/m² intravenously over 30 minutes on Days 1, 8, and 15 of each 21-day cycle; administer carboplatin on Day 1 of each 21-day cycle immediately after Abraxane®.
- **Adenocarcinoma of the Pancreas**: 125 mg/m² intravenously over 30-40 minutes on Days 1, 8 and 15 of each 28-day cycle; administer gemcitabine on Days 1, 8 and 15 of each 28-day cycle immediately after Abraxane®.
- Dose variation for hepatic impairment per AST and bilirubin levels per package insert.

### How Supplied
- 100 mg single use vial of lyophilized powder for suspension.

### Utilization Criteria
**For initial review:**
- Metastatic breast cancer
  - Must fail combination chemotherapy
  - OR
  - Relapse within 6 months of adjuvant chemotherapy
  - Chemotherapy must include regiment with anthracycline unless contraindicated.
- Locally advanced or metastatic non-small cell lung cancer
  - Used as first line therapy with carboplatin
  - Patient must not be candidate for surgery or radiation.
- Metastatic adenocarcinoma of the pancreas
  - Used as first line treatment in addition to gemcitabine.

**For continuation:**
- Patient must have a beneficial response to therapy without disease progression.

### Exclusion Criteria
- Baseline neutrophil counts of less than 1,500 cells/mm³ OR
- Baseline platelet count of less than 100,000 cells/mm³
- AST > 10x ULN
- Bilirubin > 5x ULN

### Required Medical Information
- Diagnosis
- Age
- Dose
- Body surface area (m²) OR height and weight
- Therapeutic history
- Baseline AST and Bilirubin levels
- Baseline CBC

### 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: Paclitaxel is a microtubule inhibitor that promotes the assembly of microtubules from tubulin dimers and stabilizes microtubules by preventing depolymerization
- Black Box Warning: Increased risk of neutropenia; do not administer to patients with baseline neutrophil counts < 1,500 cells/mm$^3$. Do not substitute for or with other paclitaxel formulations

**References**

*Last Reviewed November 9, 2015*
# 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 active polyarticular juvenile idiopathic arthritis in patients 2 years of age and older
- For the treatment of active systemic juvenile idiopathic arthritis in 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
- SubQ:
  - Less than 100 kg: 162 mg administered subcutaneously every other week, followed by an increase to every week based on clinical response
  - Greater than or equal to 100 kg: 162 mg administered subcutaneously every week

### Polyarticular juvenile idiopathic arthritis
- Less than 30 kg: 10 mg/kg IV every 4 weeks
- Greater than or equal to 30 kg: 8 mg/kg IV every 4 weeks

### Systemic juvenile idiopathic arthritis
- Less than 30 kg: 12 mg/kg IV every 2 weeks
- Greater than or equal to 30 kg: 8 mg/kg IV every 2 weeks

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

## Utilization Criteria

### For initial review:
- Patient has a documented negative TB test prior to initiation of therapy, AND
- Diagnosis of moderately to severely active rheumatoid arthritis, AND
  - Has tried and failed at least one non-biologic DMARD including methotrexate, AND
  - Member must use subcutaneous formulation of product, unless otherwise contraindicated or unable to self-administer, as detailed within supplied clinical documentation, AND
  - Has tried and failed at least two anti-TNF products, OR
  - Has tried and failed plan’s preferred biologic products, as applicable
- Diagnosis of active polyarticular juvenile idiopathic arthritis
  - Has tried and failed at least one non-biologic DMARD including methotrexate
- Diagnosis of active systemic juvenile idiopathic arthritis
  - Has tried and failed at least one corticosteroid or NSAID

### 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 an active infection, OR
- Concurrent use with other biologic DMARD therapies

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

### Age Restrictions
- Polyarticular Juvenile Idiopathic Arthritis or Systemic Juvenile Idiopathic Arthritis – 2 years of age and older
- Rheumatoid Arthritis – 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
# Adcetris® (brentuximab vedotin)

**FDA Approved Indication(s)**

- Hodgkin lymphoma after failure of autologous stem cell transplant (ASCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not ASCT candidates
- Systemic Anaplastic Large cell lymphoma after failure of at least one prior multi-agent chemotherapy regimen

**FDA Recommended Dose**

- 1.8 mg/kg administered only as an intravenous infusion over 30 minutes every 3 weeks.

**How Supplied**

- 50 mg single-use vial

**Utilization Criteria**

*For initial review:*

- Hodgkin lymphoma
  - Documented diagnosis of CD30+ Hodgkin lymphoma, AND
  - Documented failure of autologous stem cell transplant (ASCT), OR
  - Documented failure of at least two prior multi-agent chemotherapy regimens in patients who are not ASCT candidates
- Systemic Anaplastic Large cell lymphoma
  - Documented diagnosis of CD30+ anaplastic large cell lymphoma, AND
  - Documented failure of at least one prior multi-agent chemotherapy regimen

*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 exceeded 16 cycles of therapy

**Required Medical Information**

- Diagnosis
- Age
- Weight
- Treatment history
- 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: Brentuximab vedotin binds to CD30-expressing cells, followed by internalization of the drug complex and the release of monomethyl auristatin E (MMAE) via proteolytic cleavage. Binding of MMAE to tubulin disrupts the microtubule network within the cell, subsequently inducing cell cycle arrest and apoptotic death of the cells.
- Black Box Warning: Increased risk for contracting JC virus, resulting in progressive multifocal leukoencephalopathy (PML) and death
References


Last Reviewed November 10, 2015
**Adcirca® (tadalafil)**

<table>
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<th>FDA Approved Indication(s)</th>
<th>• To improve exercise ability in patients with pulmonary arterial hypertension (PAH) (WHO Group 1)</th>
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<td>FDA Recommended Dose</td>
<td>• 40 mg (two 20 mg tablets) taken once daily with or without food</td>
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<td>• 20 mg tablets</td>
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**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® and Afinitor® Disperz™ (everolimus)

## FDA Approved Indication(s)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afinitor®</td>
<td>For the treatment of postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer (Advanced HR+ BC) in combination with exemestane after failure of treatment with letrozole or anastrozole. For the treatment of progressive neuroendocrine tumors of pancreatic origin (PNET) that are unresectable, locally advanced or metastatic. For the treatment of advanced renal cell carcinoma (RCC) after treatment failure with sunitinib or sorafenib. For the treatment of renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.</td>
</tr>
<tr>
<td>Afinitor® and Afinitor® Disperz™</td>
<td>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.</td>
</tr>
</tbody>
</table>

## How Supplied

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afinitor® Tablets</td>
<td>2.5 mg, 5 mg, 7.5 mg, and 10 mg</td>
</tr>
<tr>
<td>Afinitor® Disperz™ (tablets for oral suspension)</td>
<td>2 mg, 3 mg, and 5 mg</td>
</tr>
</tbody>
</table>

## 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)

- 12

## 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

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) who have progressed on or are intolerant to crizotinib

**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, AND
- Member must have documentation of a previous treatment history with 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 >3x Upper Limit of Normal (ULN), OR
  - Total bilirubin >2x ULN in absence of cholestasis or hemolysis
- Presence of Interstitial Lung Disease (ILD)/Pneumonitis
- 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)**
- 12

**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**
Alimta® (pemetrexed disodium)

**FDA Approved Indication(s)**
- For the initial treatment of non-squamous, non-small cell lung cancer (NSCLC) in combination with cisplatin, as maintenance therapy, and after prior chemotherapy
- For the treatment of mesothelioma

**FDA Recommended Dose**
- 500 mg/m² administered as an intravenous infusion over 10 minutes on Day 1 of each 21-day cycle

**How Supplied**
- 100 mg or 500 mg vials

**Utilization Criteria**

*For initial review:*
- Non-squamous small cell lung cancer:
  - Must be used with cisplatin; OR
  - Must be used for maintenance therapy; OR
  - Must be used after a prior chemotherapy
- Mesothelioma:
  - Must be used with cisplatin

*For continuation (all indications):*
- Documentation of therapy efficacy and tolerability

**Exclusion Criteria**
- For the treatment of patients with squamous cell non-small cell lung cancer

**Required Medical Information**
- Diagnosis
- Height
- Weight

**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: Pemetrexed for injection is a folate analog metabolic inhibitor that exerts its action by disrupting folate-dependent metabolic processes essential for cell replication.
- Requires premedication and coadministration of folic acid and vitamin B 12 to reduce toxicity.

**References**
- Alimta® [package insert]. Indianapolis, IN: Lilly USA, LLC; September 2013.
## 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 other 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)**
- 12

**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 9, 2015*
**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), AND
- A baseline timed 25-foot walking test

For Continuation:
- The member must have a documented 10% or greater improvement from baseline in a timed 25-foot walking test

**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

**References**
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**
- The recommended dosage of Aralast NP® is 60 mg/kg body weight, administered at a rate not exceeding 0.08 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**

_Last Reviewed January 11, 2016_
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 CKD patients on dialysis:
  - 0.45 mcg/kg intravenously or subcutaneously weekly, OR
  - 0.75 mcg/kg intravenously or subcutaneously every 2 weeks
- Recommended starting dose for patients with CKD not on dialysis:
  - 0.45 mcg/kg intravenously or subcutaneously at 4 week intervals
- 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, 300, and 500 mcg/1 mL, and 150 mcg/0.75 mL
- Single-dose prefilled syringes: 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:
- Member has documented anemia associated with CKD
  - CKD on dialysis:
    - Hemoglobin (Hgb) level is less than 10 g/dL
  - 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; OR
- Member has documented anemia associated with cancer therapy, while currently treated with myelosuppressive chemotherapy, AND
  - 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

For Continuation of Coverage:
- CKD on dialysis:
  - Member has documented Hgb level equal to or less than 11 g/dL (on dialysis) or 10 g/dL (not on dialysis)

Exclusion Criteria
- Receiving myelosuppressive chemotherapy when the anticipated outcome is cure
- Used 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 the course of myelosuppressive chemotherapy

Required Medical Information
<table>
<thead>
<tr>
<th>Information Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td></td>
</tr>
<tr>
<td>Complete blood count</td>
<td></td>
</tr>
<tr>
<td>Concurrent medications</td>
<td></td>
</tr>
<tr>
<td>Age Restrictions</td>
<td>1 year of age and older</td>
</tr>
<tr>
<td>Prescriber Restrictions</td>
<td>Must be prescribed by a specialist in the disease being treated</td>
</tr>
<tr>
<td>Coverage Duration (months)</td>
<td>3</td>
</tr>
<tr>
<td>Quantity/Partial Fill Restrictions</td>
<td>30 day supply, no partial fill</td>
</tr>
<tr>
<td>Other Information</td>
<td>Mechanism of action: Darbepoetin alfa stimulates erythropoiesis by the same mechanism as endogenous erythropoietin</td>
</tr>
<tr>
<td></td>
<td>Black Box Warnings</td>
</tr>
<tr>
<td></td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>Cancer: Discontinue following completion of a chemotherapy course</td>
</tr>
<tr>
<td></td>
<td>Darbepoetin alfa has not been shown to improve quality of life, fatigue, or patient well-being in patients with cancer.</td>
</tr>
</tbody>
</table>

*Last Reviewed November 9, 2015*
# 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
- Terflunomide is a pyrimidine synthesis inhibitor
- Black Box Warning: Hepatotoxicity and Risk of Teratogenicity

## References

*Last Reviewed January 18, 2016*
Avastin® (bevacizumab)

FDA Approved Indication(s)

- Metastatic colorectal cancer (mCRC) in combination with 5-fluorouracil (5FU)-based chemotherapy for first- or second-line treatment.
- Metastatic colorectal cancer, with fluoropyrimidine/irinotecan or fluoropyrimidine/oxaliplatin based chemotherapy for second-line treatment in patients who have progressed on a first-line Avastin®-containing regimen.
- Non squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first-line treatment of unresectable, locally advanced, recurrent or metastatic disease.
- Glioblastoma, as a single agent, for those with progressive disease following prior therapy.
- Glioblastoma in combination with interferon alfa
- Metastatic renal cell carcinoma in combination with interferon alfa
- Cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic disease.
- Platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer in combination with paclitaxel, pegylated liposomal doxorubicin or topotecan for patients who received no more than 2 prior chemotherapy regimens

FDA Recommended Dose

- **Metastatic Colorectal Cancer (mCRC):**
  - 5 mg/kg intravenously (IV) every 2 weeks when used in combination with bolus IFL
  - 10 mg/kg IV every 2 weeks with FOLFOX4
  - 5 mg/kg IV every 2 weeks or 7.5 mg/kg IV every 3 weeks with fluoropyrimidine/irinotecan or fluoropyrimidine/oxaliplatin chemotherapy
- **Non-Squamous Non-Small Cell Lung Cancer (NSCLC):**
  - 15 mg/kg IV every 3 weeks in combination with carboplatin and paclitaxel
- **Glioblastoma:**
  - 10 mg/kg IV every 2 weeks
- **Metastatic Renal Cell Carcinoma (mRCC):**
  - 10 mg/kg IV every 2 weeks in combination with interferon alfa
- **Cervical Cancer:**
  - 15 mg/kg IV every 3 weeks with paclitaxel/cisplatin or paclitaxel/topotecan
- **Platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer**
  - 10 mg/kg every 2 weeks in combination with one of the following intravenous chemotherapy regimens: paclitaxel, pegylated liposomal doxorubicin, or topotecan
  - 15 mg/kg every 3 weeks in combination with topotecan

How Supplied

- 100 mg and 400 mg vials

Utilization Criteria

*For initial review:*

- **Metastatic Colorectal Cancer (mCRC)**
  - Patient must have clinically documented metastatic carcinoma of the colon or rectum, AND
  - Patient must have documented use in combination with intravenous 5-FU-based chemotherapy OR
  - Patient must have documented use in combination with fluoropyrimidine/irinotecan or fluoropyrimidine/oxaliplatin
- **Non-Squamous Non-Small Cell Lung Cancer (NSCLC)**
  - Patient must have clinically documented diagnosis of NSCLC, AND
  - Patient must have documented use in combination with carboplatin and paclitaxel
• **Glioblastoma**
  - Patient must have clinically documented diagnosis of glioblastoma, AND
  - Patient must have documentation of prior treatment failure

• **Metastatic Renal Cell Carcinoma (mRCC)**
  - Patient has a clinical diagnosis of metastatic renal cell carcinoma, AND
  - Patient must have documented use in combination with interferon alfa

• **Persistent, Recurrent, or Metastatic Carcinoma of the Cervix**
  - Patient must have clinically documented persistent, recurrent, or metastatic carcinoma of the cervix, AND
  - Patient must have documented use in combination with paclitaxel and cisplatin, OR
    - Patient must have documented use in combination with paclitaxel and topotecan

• **Platinum-Resistant, Recurrent Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer**
  - Patient must have clinically documented diagnosis of platinum-resistant, recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, AND
  - Patient must have documented use in combination with paclitaxel, pegylated liposomal doxorubicin or topotecan, AND
  - Patient must not have received more than 2 prior chemotherapy regimens, AND
  - Patient has not previously received bevacizumab

• **Platinum-Sensitive, Recurrent Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer**
  - Patient must have clinically documented diagnosis of platinum-sensitive, recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, AND
  - Patient must have documented use in combination with carboplatin and gemcitabine, AND
  - Patient has not previously received bevacizumab

• Utilization of bevacizumab for treatments of ocular conditions, such as macular edema (ME), may be considered per plan-specific policies

*For continuation:*
  - Review of therapy by an oncologist to confirm that the patient has not experienced progression of disease

**Exclusion Criteria**

• Patient has had major surgery within 28 days of therapy initiation

**Required Medical Information**

• **Diagnosis**
• **Age**
• **Weight**
• **Height**
• **Treatment history**
• **Concurrent medications**
• **Dose**

**Age Restrictions**

• 18 years of age and older

**Prescriber Restrictions**

• Must be prescribed by an oncologist

**Coverage Duration (months)**
### Quantity/Partial Fill Restrictions

- **None**

### Other Information

- **Mechanism of action:** Bevacizumab binds VEGF and prevents the interaction of VEGF to its receptors (Flt-1 and KDR) on the surface of endothelial cells. The interaction of VEGF with its receptors leads to endothelial cell proliferation and new blood vessel formation in in vitro models of angiogenesis. Administration of bevacizumab to xenotransplant models of colon cancer in nude (athymic) mice caused reduction of microvascular growth and inhibition of metastatic disease progression.
- **Black Box Warning:** Increased risk of gastrointestinal perforations, surgery and wound healing complications, and hemorrhage

### References

# Avonex® (interferon beta-1a)

## FDA Approved Indication(s)
- For the treatment of patients with relapsing forms of multiple sclerosis to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations

## FDA Recommended Dose
- 30 mcg injected intramuscularly once weekly

## How Supplied
- 30 mcg/0.5 mL prefilled syringe
- 30 mcg lyophilized powder vial
- 30 mcg / 0.5 mL 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 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
- 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 naïve with compensated liver disease in those ≥ 16 years of age: 0.5 mg 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
- Lamivudine-refractory or known lamivudine or telbivudine resistance substitutions in those ≥ 16 years of age: 1 mg once daily on an empty stomach
- Adults with decompensated liver disease: 1 mg once daily on an empty stomach
- Dose adjust for renal impairment (CrCl < 50 mL/min)

## How Supplied
- 0.5 mg and 1 mg 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
- Member must have 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:
- Entecavir should be discontinued after 12 months of persistently normal ALT levels and undetectable HBV DNA levels in HBeAg-positive adults without cirrhosis who seroconvert to anti-HBe
- For all others,
  - Member must have persistent low-level viremia (<2,000 IU/mL) on entecavir therapy, AND
  - Documentation of HBeAg-negative immune active CHB, OR
  - HBeAg positive with cirrhosis, in those 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

## Required Medical Information
- Diagnosis
- Age
- Weight (if <16 years of age)
- Dose
- Renal Function
- LFTs
- HBV status

## Age Restrictions
- 2 years of age
<table>
<thead>
<tr>
<th>Prescriber Restrictions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Must be prescribed by a gastroenterologist, hepatologist, or infectious disease specialist</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Coverage Duration (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 12 months</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quantity/Partial-Fill Restrictions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• None</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Information</th>
</tr>
</thead>
<tbody>
<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>
</tr>
<tr>
<td>• Black Box Warnings</td>
</tr>
<tr>
<td>o Severe acute exacerbations of hepatitis B have been documented after treatment discontinuation. Liver function should be monitored for several months after discontinuation.</td>
</tr>
<tr>
<td>o Patients co-infected with HIV should be receiving HAART in addition to entecavir.</td>
</tr>
<tr>
<td>o Lactic acidosis and hepatomegaly with steatosis (including fatal cases) have been reported in patients receiving nucleoside analogs.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>References</th>
</tr>
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*Last Reviewed January 27, 2016*
## Benlysta® (belimumab)

**FDA Approved Indication(s)**
- For the treatment of adult patients with active, autoantibody-positive, systemic lupus erythematosus who are receiving standard therapy

**FDA Recommended Dose**
- 10 mg/kg, infused over one hour, at two-week intervals for the first three doses and at four-week intervals thereafter

**How Supplied**
- 120 mg/5 mL and 400 mg/20 mL vials

**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**
- 18 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: Benlysta® is a BlyS-specific inhibitor that blocks the binding of soluble BlyS, a B-cell survival factor, to its receptors on B cells.

**References**
## Berinert® (human c1- esterase inhibitor) kit

### FDA Approved Indication(s)
- Berinert® is a plasma-derived C1 Esterase Inhibitor (Human) indicated 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:**
- Patient must have a confirmed diagnosis of hereditary angioedema

### Exclusion Criteria
- Not to be used for prophylactic therapy

### Required Medical Information
- Diagnosis
- Age
- 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

*Last Reviewed November 9, 2015*
**Betaseron® (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**

- 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

**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**

# Boniva® (ibandronate sodium)

## FDA Approved Indication(s)
- For the prevention or treatment of postmenopausal osteoporosis

## 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:
- Patient must be post-menopausal as confirmed by a physician
- Patient has a documented failure or intolerance to both alendronate and risedronate
- Patient has a documented T-score of ≤ -2.5

### 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
- 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

## References
- Boniva® [package insert]. San Francisco, CA: Genetech USA, Inc; April 2013

*Last Reviewed November 8, 2015*
**Bosulif® (bosutinib monohydrate)**

<table>
<thead>
<tr>
<th>FDA Approved Indication(s)</th>
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<tbody>
<tr>
<td>• For the treatment of chronic, accelerated or blast phase Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) with resistance or intolerance to prior therapy</td>
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<tr>
<th>FDA Recommended Dose</th>
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<tr>
<td>• 500 mg orally once daily with food</td>
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<tr>
<th>How Supplied</th>
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<tr>
<td>• 100 mg and 500 mg tablets</td>
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<tr>
<th>Utilization Criteria</th>
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<tr>
<td><strong>For initial review:</strong></td>
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<tr>
<td>• Member must have a diagnosis of chronic, accelerated, or blast phase Philadelphia chromosome-positive chronic myelogenous leukemia, AND</td>
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<tr>
<td>• Member must have tried and failed ≥ 2 of the following:</td>
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<tr>
<td>• Imatinib</td>
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<tr>
<td>• Dasatinib</td>
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<td>• Nilotinib</td>
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**Exclusion Criteria**

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<th>Required Medical Information</th>
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<tr>
<td>• Diagnosis</td>
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<td>• Age</td>
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<tr>
<td>• Dose</td>
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<tr>
<td>• Treatment history</td>
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<tr>
<th>Age Restrictions</th>
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<tr>
<td>• 18 years of age and older</td>
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<tr>
<th>Prescriber Restrictions</th>
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<tr>
<td>• Must be prescribed by an oncologist or hematologist</td>
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<tr>
<th>Coverage Duration (months)</th>
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<tr>
<td>• 12</td>
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<tr>
<th>Quantity/Partial Fill Restrictions</th>
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<tr>
<td>• 15 tablets for a 15 day supply for the first three months</td>
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<tr>
<th>Other Information</th>
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<tbody>
<tr>
<td>• Mechanism of action: Bosutinib is a tyrosine kinase inhibitor, targeting the Bcr-Abl kinase that promotes CML, as well as the Src-family kinases.</td>
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<tr>
<th>References</th>
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<tbody>
<tr>
<td>• Bosulif® [package insert]. New York, New York; Pfizer; September 2013.</td>
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*Last Reviewed November 9, 2015*
# Botox® (onabotulinum toxin a); Dysport® (botulinum toxin type a)

## FDA Approved Indication(s)

- 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.
- 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 or intolerance to anticholinergic medication.
- Prophylaxis of headaches in adult patients with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer).
- Treatment of upper limb spasticity in adult patients.
- Treatment of cervical dystonia in adult patients, to reduce the severity of abnormal head position and neck pain.
- Treatment of severe axillary hyperhidrosis that is inadequately managed by topical agents in adult patients.
- Treatment of blepharospasm and strabismus associated with dystonia in patients 12 years of age and older.

## 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 a 3-month interval. Exceptions are listed below.
  - Detrusor overactivity associated with a neurological condition – the maximum dose is 200 units per treatment no sooner than every 12 weeks.
  - OAB – the maximum dose is 100 units per treatment no sooner than every 12 weeks.
  - Blepharospasm – the cumulative dose in a 30-day period should not exceed 200 units.

## 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 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 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
- 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 month 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
- **Botox**® [package insert]. Irvine, CA: Allergan Pharmaceuticals; August 2015.
Cabometyx® (cabozantinib) †

FDA Approved Indication(s)
- For the treatment of patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy

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:
- Must have a diagnosis of RCC, previously treated with an anti-angiogenic 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 with treatment plan
- Previous 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
- Cabozantinib inhibits the tyrosine kinase activity of RET, MET, VEGFR-1, 2, and 3, KIT, TRKB, FLT-3, AXL, and TIE-2

References
### 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**
- Patient has diagnosis of unresectable locally advanced or metastatic medullary thyroid cancer

**Exclusion Criteria**

*For initial review:*
- Patient has congenital long QT syndrome
- Patient 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
- Age
- Dose
- Treatment history

**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**
**Carimune® (human immunoglobulin g)**

**FDA Approved Indication(s)**
- For the maintenance treatment of primary immunodeficiency (PID) and related disorders
- For the treatment of acute and chronic immune thrombocytopenic purpura (ITP)

**FDA Recommended Dose**
- 0.4 to 0.8 g/kg of body weight administered once every three to four weeks by intravenous infusion

**How Supplied**
- 3 g, 6 g, and 12 g single-use vials of lyophilized powder

**Utilization Criteria**

*For initial review:*
- For use in the treatment of PID and related disorders, in which there is sufficient evidence to support its use

*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**
- To be used for a non-FDA approved indication in which little or no supportive evidence can be found to support its use

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

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

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

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: Carimune® NF contains a broad spectrum of antibody specificities against bacterial, viral, parasitic, and mycoplasma antigens, that are capable of both opsonization and neutralization of microbes and toxin
- Black Box Warning: Increased risk of thrombosis, and renal dysfunction, including acute renal failure, osmotic nephrosis, and death

**References**

*Last Reviewed November 9, 2015*
# Cayston® (aztreonam)

## FDA Approved Indication(s)
- Cayston® is indicated to improve respirator 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
- Patient must have a diagnosis of CF with *Pseudomonas aeruginosa*
- Patient must have documentation of FEV₁ between 25% and 75% of predicted volume

## Exclusion Criteria
- Patient is currently receiving tobramycin

## Required Medical Information
- Diagnosis
- Age
- 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 December 20, 2015
Cimzia® (certolizumab pegol)

**FDA Approved Indication(s)**
- Reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy (CD)
- 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)

**FDA Recommended Dose**
- **CD**
  - 400 mg subcutaneously at weeks 0, 2 and 4
  - If response is documented, continue therapy at 400 mg every four weeks
- **RA, PsA, AS**
  - 400 mg subcutaneously at weeks 0, 2 and 4, followed by 200 mg every other week or 400 mg every four weeks

**How Supplied**
- Prefilled syringe starter kit
  - Six single-use prefilled syringes (PFS) containing 200 mg/1 mL of active product
- Prefilled syringe
  - Two single use PFS 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:*
- Member has a negative TB test, AND
- As applicable, member has tried and failed one or more of the plan’s preferred biologic therapies, AND
- **CD**
  - Prescriber is a gastroenterologist, AND
  - Patient has tried and failed 2 or more of the following:
    - Budesonide
    - Prednisone
    - Mesalamine
    - Mercaptopurine
    - Methotrexate
    - Azathioprine
    - Sulfasalazine
- **RA**
  - Prescriber is a rheumatologist, AND
  - Member must have tried and failed methotrexate for at least 30 days; OR
  - Tried and failed 2 or more of the following for at least 30 days use per agent:
    - Auranofin
    - Aurothioglucose
    - Azathioprine
    - Cyclosporine
    - Gold sodium thiomalate
    - Hydroxychloroquine
    - Leflunomide
### Penicillamine
- PsA
  - Prescriber is a dermatologist, AND
  - Member has tried and failed treatment with methotrexate
- AS
  - Prescriber is a rheumatologist, AND
  - Has tried and failed sulfasalazine in previous 6 months; OR
  - Was intolerant to sulfasalazine, COX-2 inhibitors, NSAIDs, or corticosteroids within the previous 6 months

**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

### 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: 12 months

### Quantity/Partial Fill Restrictions
- None

### Other Information
- Mechanism of action: Certolizumab pegol binds to human TNFα
- Black Box Warning: Risk of serious infections and malignancy

### References


Last Reviewed November 9, 2015
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/ microL, 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

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 month initial, 12 month 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. An alternative IL-5 antagonist is Nucala® (mepolizumab).
- 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


Last Reviewed April 20, 2016
# Cinryze® (human c1- esterase inhibitor)

## FDA Approved Indication(s)
- Cinryze® is a C1 esterase inhibitor indicated for routine prophylaxis against angioedema attacks in adolescent and adult patients with Hereditary Angioedema (HAE)

## FDA Recommended Dose
- 1,000 Units Cinryze® can be administered every 3 or 4 days for routine prophylaxis against angioedema attacks in HAE patients

## 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
- None

## Required Medical Information
- Diagnosis
- Age
- Dose

## Age Restrictions
- 16 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 10, 2015*
# 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
- 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 due to packaging

**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**

*Last Reviewed November 9, 2015*
# Copaxone®, Glatopa™ (glatiramer acetate)

## FDA Approved Indication(s)
- For the reduction of the frequency of relapses in patients with relapsing forms of Multiple Sclerosis

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

## How Supplied
- **Copaxone®, Glatopa™**: Single-use 20 mg/mL prefilled syringe
- **Copaxone®**: 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, AND
- The 40 mg formulation will only be considered medically necessary if the patient’s current physician supplies clinically-relevant documentation of injection-site intolerance, such as lipodystrophy

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

## Exclusion Criteria
- Patient is receiving other disease-modifying therapy (i.e., interferons, natalizumab, fingolimod, teriflunomide, or dimethyl fumarate)

## Required Medical Information
- Diagnosis of RRMS
- 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
- 30 day supply, no partial fill

## Other Information
- Immunomodulator; modifies immune processes thought to be responsible for the pathogenesis of MS

## References
### 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 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 an 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 January 18, 2016_
**Cotellic™ (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

**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

**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**

_Last Reviewed February 26, 2016_
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
- None

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 for the treatment of genotype 3 chronic hepatitis C virus (HCV)
- 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 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 tablets

Utilization Criteria
For initial review:
- Member must have a diagnosis of chronic HCV genotype 3 (GT3), 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 sofosbuvir therapy, AND
- Member must have evidence of stage 3 or greater fibrosis and/or compensated cirrhosis documented via a Metavir, Shear Wave Elastography (SWE) (transient elastography/Fibroscan, point-SWE, two-dimensional SWE), FibroTest, APRI, or equivalent test, OR Member has undergone liver transplant, OR
- Member has Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations, OR
- Member has proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis

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 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**
- 14 day supply limit per fill (two weekly cartons)

**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.

**References**

*Last Reviewed November 10, 2015*
Egrifta® (tesamorelin)

FDA Approved Indication(s)
- Reduction of excess abdominal fat in HIV-infected patients with lipodystrophy

FDA Recommended Dose
- 2 mg injected subcutaneously once a day.

How Supplied
- Single-use 2 mg powder vials

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.
- Patient must have HIV-associated lipodystrophy with excess abdominal fat.
  - Lipodystrophy defined as:
    - Men: waist circumference >= 95 cm (37.4 in); waist-to-hip ratio >= 0.94
    - Women: waist circumference >= 94 cm (37.0 in); waist-to-hip ratio >= 0.88
- Must provide baseline waist circumference.
- Must provide baseline lipid and TG levels
- Must not have an active malignancy

For continuation:
- Long-term cardiovascular (CV) safety and potential long-term CV benefit of tesamorelin have not been studied; therefore, careful consideration should be given to whether to continue therapy in patients who do not show a response to tesamorelin as measured by a reduction in visceral adipose tissue (VAT) by waist circumference or computed tomography (CT) scan. Studies did not cover.
- Must show improvement in waist circumference
- Must show improvement in lipid and TG levels

Exclusion Criteria
- Patients with disruption of the hypothalamic-pituitary axis due to hypophysectomy, hypopituitarism, pituitary tumor/surgery, head irradiation, or head trauma.
- Active malignancy
- Pregnancy

Required Medical Information
- Diagnosis
- Waist circumference
- Waist-to-hip ratio
- Lipid and TG levels
- Age
- Dose

Age Restrictions
- 18-65 years old

Prescriber Restrictions
- None

Coverage Duration (months)
- 6

Quantity/Partial Fill Restrictions
- None

Other Information
• Mechanism of action: tesamorelin binds and stimulates human GRF receptors with similar potency as the endogenous GRF. Growth Hormone-Releasing Factor (GRF), also known as growth hormone-releasing hormone (GHRH), is a hypothalamic peptide that acts on the pituitary somatotroph cells to stimulate the synthesis and pulsatile release of endogenous growth hormone (GH), which is both anabolic and lipolytic. GH exerts its effects by interacting with specific receptors on a variety of target cells, including chondrocytes, osteoblasts, myocytes, hepatocytes, and adipocytes, resulting in a host of pharmacodynamic effects. Some, but not all these effects, are primarily mediated by IGF-1 produced in the liver and in peripheral tissues.

• Black Box Warning: None

References


Last Reviewed November 9, 2015
# Enbrel® (etanercept)

## FDA Approved Indication(s)
- Rheumatoid Arthritis (RA)
- Polyarticular Juvenile Idiopathic Arthritis (JIA)
- Psoriatic Arthritis (PsA)
- Ankylosing Spondylitis (AS)
- Plaque Psoriasis (PsO)

## FDA Recommended Dose
- **RA, AS, PsA**
  - 50 mg per week
- **PSO**
  - 50 mg twice weekly starting does then 25 or 50 mg weekly
- **JIA**
  - 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
- 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 ≤ 50mg weekly
- **Psoriatic Arthritis/Ankylosing Spondylitis**
  - Prescriber is a rheumatologist, AND
  - Patient is intolerant to sulfasalazine, COX-2, NSAIDs, or corticosteroids, AND
  - Dose is ≤ 50mg 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
- 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 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**

*Last Reviewed November 9, 2015*
### 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:
  - a. Conventional therapy such as azathioprine, 6-mercaptopurine, methotrexate, or aminosalicylate; AND
  - b. 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

- Entyvio® [package insert]. Deerfield, IL: Takeda Pharmaceuticals America Inc; May 2014.

_Last Reviewed November 9, 2015_
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
- 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, AND
- Member is considered to be within the highest priority population for treatment:
  - Member must have evidence of stage 3 or greater fibrosis and/or compensated cirrhosis documented via a Metavir, Shear Wave Elastography (SWE) (transient elastography/Fibroscan, point-SWE, two-dimensional SWE), FibroTest, APRI, or equivalent test, OR
  - Member has undergone liver transplant, OR
  - Member has Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations, OR
  - Member has proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis

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

Treatment experienced is considered Members with failed treatment with one of the following:
- Peginterferon alfa + ribavirin
- Protease inhibitor (i.e., telaprevir, boceprevir) + peginterferon alfa + ribavirin

Cirrhosis must be evidenced by one of the following:
- Metavir Stage F4
- Ishak score of 5 or 6
- Fibroscan score > 12.5 kPa
- FibroTest score > 0.75
- Aspartate aminotransferase platelet ratio index (APRI) ≥ 1

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)
- 12 weeks

### Quantity/Partial-Fill Restrictions
- 14 tablets for a 14 day supply

### Other Information
- Mechanism of action: Sofosbuvir is a nucleotide analog NS5B polymerase inhibitor. Velpatasvir is an inhibitor of the HCV NS5A protein.

### References

*Last Reviewed July 25, 2016*
### 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)**
- 6

**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**
# 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
  - a. No identifiable causes of Interstitial Lung Diseases, AND
  - b. 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
- Split fill (14 day increments)

**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
- Age
- Dose
- 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:**
- Patient has a diagnosis of relapsing multiple sclerosis
- Diagnosis has been confirmed by MRI

**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**
- Chronic progressive multiple sclerosis
- 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**
# Eylea® (aflibercept)

## FDA Approved Indication(s)
- Neurovascular age-related macular degeneration (AMD)
- Macular edema following ocular vein occlusion (RVO)
- Diabetic Macular Edema (DME)

## FDA Recommended Dose
- **AMD**: 2 mg administered every 4 weeks for the first 12 weeks followed by 2 mg once every 8 weeks
- **RVO**: 2 mg administered once every 4 weeks
- **DME**: 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:**
- Patient is diagnosed with an FDA-approved indication
- For AMD and DME: Must be intolerant to or have failed treatment with bevacizumab

**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
- Patients with ocular or periocular infections
- Patients with intraocular inflammation
- Hypersensitivity to aflibercept

## 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
- Coverage is limited to FDA-recommended dosing

## Other Information
- **Mechanism of action**: Aflibercept acts as a soluble decoy receptor that binds VEGF-A and PlGF, 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.

*Last Reviewed November 9, 2015*
## Faslodex® (fulvestrant)

### FDA Approved Indication(s)
- For the treatment of hormone receptor positive metastatic breast cancer in post-menopausal women with disease progression following anti-estrogen therapy

### FDA Recommended Dose
- 500 mg to be administered intramuscularly into the buttocks slowly (1 - 2 minutes per injection) as two 5 mL injections, one in each buttock, on days 1, 15, 29 and once monthly thereafter

### How Supplied
- 250 mg/5 mL vials

### Utilization Criteria
**For initial review:**
- Member must have a confirmed diagnosis of estrogen receptor positive metastatic breast cancer in postmenopausal women, AND
- Member must have a documented contraindication, treatment failure, or intolerance to one of the following: anastrozole, letrozole, or exemestane

**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
- Liver function status (AST, ALT, 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: Many breast cancers have estrogen receptors (ER) and the growth of these tumors can be stimulated by estrogen. Fulvestrant is an estrogen receptor antagonist that binds to the estrogen receptor in a competitive manner with affinity comparable to that of estradiol and downregulates the ER protein in human breast cancer cells.

### References
# Firazyr® (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)
- Patient must be having an attack associated with HAE (e.g., airway swelling, severe abdominal pain, facial swelling, painful facial distortion)

**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 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

*Last Reviewed November 9, 2015*
# 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
- BMD T-score ≤ -2.5, AND
- Tried and failed or is intolerant to at least one oral bisphosphonate, 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

### 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

## Exclusion Criteria
- Member has Paget’s disease, OR
- Member has received 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 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; August 2013.
# Gazyva® (obinutuzumab)

## FDA Approved Indication(s)
- For previously untreated chronic lymphocytic leukemia (CLL) in combination with chlorambucil

## FDA Recommended Dose
- 1000 mg, administered intravenously, with the exception of the first infusions in cycle 1, which are administered on day 1 (100 mg) and day 2 (900 mg)

## How Supplied
- 1000 mg/40 mL single use vials

## Utilization Criteria

### For initial review:
- Patient must be using chlorambucil in combination with obinutuzumab
- Patient must not have tried previous therapies before receiving obinutuzumab

### 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
- Therapeutic history

## Age Restrictions
- 18 years of age and over

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

## Coverage Duration (months)
- 12

## Quantity/Partial Fill Restrictions
- None

## Other Information
- Mechanism of action: Obinutuzumab is a monoclonal antibody that targets the CD20 antigen expressed on the surface of pre B- and mature B-lymphocytes. Upon binding to CD20, obinutuzumab mediates B-cell lysis through (1) engagement of immune effector cells, (2) by directly activating intracellular death signaling pathways and/or (3) activation of the complement cascade. The immune effector cell mechanisms include antibody-dependent cellular cytotoxicity and antibody-dependent cellular phagocytosis.
- Black Box Warning: Increased risk for hepatitis b virus (HBV) reactivation and progressive multifocal leukoencephalopathy

## References
Gilenya® (fingolimod)

FDA Approved Indication(s)
- To reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability in patients with relapsing forms of multiple sclerosis

FDA Recommended Dose
- One 0.5 mg capsule, once daily

How Supplied
- 0.5 mg 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
- Must have tried and failed all plan-specific step therapy requirements, as 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
- 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 la or Class III anti-arrhythmic drugs

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

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
- 30 day supply

Other Information
- Fingolimod is a sphingosine 1-phosphate receptor modulator
- 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 January 18, 2016*
# 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
- Adjunctive 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
  o Member shows no evidence of adverse drug reactions, AND
  o 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)

Required Medical Information
- Diagnosis, including phase or mutation status
- Age
- Dose
- 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
- 15 tablets for a 15 day supply for the first 6 fills

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 June 23, 2016
# 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>
<th>SHOX Deficiency</th>
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<tbody>
<tr>
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</table>

## 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

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
- Closed epiphyses
- 65 years of age and older
- Idiopathic Short Stature

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.
# 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
- **MS exacerbations**
  - 80-120 units 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

## How Supplied
- 5 mL multi dose vial

## Utilization Criteria

**For initial review:**
- Infantile Spasm (West Syndrome)
  - Patient is less than 2 years of age
- 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
- Other diagnosis
  - 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

**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**
- 2 years of age and older

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

**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**
Harvoni® (ledipasvir/sofosbuvir)

FDA Approved Indication(s)
- For the treatment of chronic hepatitis C (CHC, HCV) genotype 1 infection in adults.

FDA Recommended Dose
- One tablet orally, once daily

<table>
<thead>
<tr>
<th>Treatment Duration</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 weeks</td>
<td>Treatment naïve without cirrhosis (HCV RNA &lt; 6,000,000 IU/mL)</td>
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<tr>
<td>12 weeks</td>
<td>Treatment naïve with or without cirrhosis</td>
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<tr>
<td></td>
<td>Treatment experienced without cirrhosis</td>
</tr>
<tr>
<td>24 weeks</td>
<td>Treatment experienced with cirrhosis</td>
</tr>
</tbody>
</table>

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 genotype 1 (G1) with documented viral load collected within the previous three months, AND
- Member must be treatment naïve to sofosbuvir treatment, 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 is considered to be within the highest priority population for treatment:
  - Member must have evidence of stage 3 or greater fibrosis and/or compensated cirrhosis documented via a Metavir, Shear Wave Elastography (SWE) (transient elastography/Fibroscan, point-SWE, two-dimensional SWE), FibroTest, APRI, or equivalent test, OR
  - Member has undergone liver transplant, OR
  - Member has Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations, OR
  - Member has proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis

Coverage Duration:
- For coverage of 8 weeks of therapy, Member must meet all of the following criteria:
  - Is treatment naïve without cirrhosis
  - Has a documented HCV RNA of less than 6,000,000 IU/mL
- For coverage of 12 weeks of therapy, Member must meet one of the following criteria:
  - Has documented HCV RNA of greater than 6,000,000 IU/mL
  - Is treatment naïve with cirrhosis
  - Has been previously treated without documentation of cirrhosis
- For coverage of 24 weeks of therapy, a Member must have clinical documentation of cirrhosis and failure of previous therapy

\[a\] Estimates of test performance for advanced 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 0.67/0.063 : 0.95/0.51

\[b\] Treatment experienced is considered Members with failed treatment with one of the following:
- Peginterferon alfa + ribavirin
Protease inhibitor (i.e., telaprevir, boceprevir) + peginterferon alfa + ribavirin

Cirrhosis must be evidenced by one of the following:
- Metavir Stage F4
- Ishak score of 5 or 6
- Fibroscan score > 12.5 kPa
- FibroTest score > 0.75
- Aspartate aminotransferase platelet ratio index (APRI) ≥ 1

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
- Liver status
- 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)
- Coverage duration will depend on required duration of therapy

Quantity/Partial Fill Restrictions
- 14 tablets for a 14 day supply

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


Last Reviewed November 9, 2015
**Herceptin® (trastuzumab)**

**FDA-Approved Indication(s)**

- For adjuvant treatment of HER2-overexpressing node positive or node negative breast cancer as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel; with docetaxel and carboplatin; or as a single agent following multi-modality anthracycline-based therapy
- For the treatment of HER2-overexpressing metastatic breast cancer in combination with paclitaxel for first-line treatment, or as a single agent in patients who have received one or more chemotherapy regimens for metastatic disease
- For the treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma, in combination with cisplatin and capecitabine or 5-fluorouracil, in patients who have not received prior treatment for metastatic disease

**FDA-Recommended Dose**

- Adjuvant treatment of HER2-overexpressing breast cancer for a total of 52 weeks of therapy:
  - During and following paclitaxel, docetaxel, or docetaxel/carboplatin:
    - Initial dose of 4 mg/kg as a 90 minute IV infusion, then 2 mg/kg as a 30 minute IV infusion weekly during chemotherapy for the first 12 weeks (paclitaxel or docetaxel) or 18 weeks (docetaxel/carboplatin).
    - Continue with 6 mg/kg as a 30-90 minute IV infusion every three weeks starting one week after the last weekly dose of Herceptin.
  - As a single agent within three weeks of completion of multi-modality, anthracycline-based chemotherapy:
    - Initial dose of 8 mg/kg as a 90 minute IV infusion, then 6 mg/kg as a 30-90 minute IV infusion every three weeks
- Metastatic HER2-overexpressing breast cancer:
  - Initial dose of 4 mg/kg as a 90 minute IV infusion, then 2 mg/kg as a 30 minute IV infusion weekly until disease progression
- Metastatic HER2-overexpressing gastric cancer:
  - Initial dose of 8 mg/kg as a 90 minute IV infusion, then 6 mg/kg as a 30-90 minute IV infusion every three weeks until disease progression

**How Supplied**

- Multi-use vial containing 440 mg of lyophilized sterile powder for reconstitution with 20 mL Bacteriostatic Water for Injection. The final concentration is 21 mg/mL trastuzumab.

**Utilization Criteria**

*For initial review:*

- Member must have documentation of HER2 overexpression, as detected by an FDA-approved test, AND
- Adjuvant treatment of HER2-overexpressing breast cancer:
  - Used with doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel, OR
  - Used with docetaxel and carboplatin, OR
  - Used as a single agent following multi-modality anthracycline-based therapy
- Metastatic breast cancer:
  - Used in combination with paclitaxel for first-line treatment, OR
  - Used as a single agent in patients who have received one or more chemotherapy regimens for metastatic disease
- Metastatic gastric or gastroesophageal junction adenocarcinoma:
  - Member must not have received prior treatment for metastatic disease, AND
  - Used in combination with cisplatin and capecitabine or 5-fluorouracil

*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
- Weight
- Dose
- Therapeutic 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: trastuzumab is a mediator of antibody-dependent cellular cytotoxicity (ADCC) and inhibits the proliferation of human tumor cells that overexpress HER2
- Concurrent use with an anthracycline is associated with cardiac toxicity and should be avoided.
- Alternative dosing recommendation for trastuzumab in metastatic HER2-overexpressing gastric cancer is 6 mg/kg IV loading dose, then 4 mg/kg IV every 14 days per NCCN guidelines

**References**

*Last Reviewed February 8, 2016*
Hizentra® (human immunoglobulin g)

FDA Approved Indication(s)
- Indicated as replacement therapy for primary humoral immunodeficiency (PI) in adults and pediatric patients 2 years of age and older. This includes, but is not limited to, the humoral immune defect in congenital agammaglobulinemia, common variable immunodeficiency, X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies

FDA Recommended Dose
- Individualized based on the patient's clinical response to Hizentra therapy and serum immunoglobulin G (IgG) trough levels.

How Supplied
- 0.2 grams of protein per mL in 5 mL (1 g), 10 mL (2 g), 20 mL (4 g), and 50 mL (10 g) vials

Utilization Criteria
For initial review:
- Patient is diagnosed with one of the following primary humoral or combined immunodeficiencies:
  - X-linked agammaglobulinemia (Bruton’s agammaglobulinemia, congenital agammaglobulinemia)
  - SCID
  - Wiskott-Aldrich syndrome
  - X-linked or autosomal recessive hyper-IgM syndrome
  - Common variable immunodeficiency
  - Unspecified hypogammaglobulinemia

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
- Patients with hyperprolinemia (type I or II)
- IgA-deficient patients with antibodies against IgA and a history of hypersensitivity

Required Medical Information
- Diagnosis
- Age
- Dose

Age Restrictions
- 2 and older

Prescriber Restrictions
- Must be prescribed by an immunologist, allergist, or infectious disease specialist

Coverage Duration (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Hizentra supplies a broad spectrum of opsonizing and neutralizing IgG antibodies against a wide variety of bacterial and viral agents. The mechanism of action in PI has not been fully elucidated.
- Black Box Warning: Thrombosis

References
- Hizentra® [package insert]. Bern, Switzerland: CSL Behring AG; October 2013

Last Reviewed November 9, 2015
### 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 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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA, PsA, AS</td>
<td><strong>40 mg subcutaneously every other week</strong></td>
</tr>
<tr>
<td></td>
<td>For RA, dose may be increased to 40 mg every week</td>
</tr>
<tr>
<td>JIA</td>
<td><strong>22 – 33 lbs:</strong> 10 mg every other week</td>
</tr>
<tr>
<td></td>
<td><strong>33-66 lbs:</strong> 20 mg every other week</td>
</tr>
<tr>
<td></td>
<td><strong>Greater than 66 lbs:</strong> 40 mg every other week</td>
</tr>
<tr>
<td>Adult CD and UC</td>
<td><strong>Day 1:</strong> 160 mg day one or 80 mg per day for two consecutive days</td>
</tr>
<tr>
<td></td>
<td><strong>Day 15:</strong> 80 mg</td>
</tr>
<tr>
<td></td>
<td><strong>Day 29/Maintenance:</strong> 40 mg every other week</td>
</tr>
<tr>
<td>Pediatric CD</td>
<td><strong>37 – 88 lbs</strong></td>
</tr>
<tr>
<td></td>
<td>▪ <strong>Day 1:</strong> 80 mg</td>
</tr>
<tr>
<td></td>
<td>▪ <strong>Day 15:</strong> 40 mg</td>
</tr>
<tr>
<td></td>
<td>▪ <strong>Day 29/Maintenance:</strong> 40 mg every other week</td>
</tr>
<tr>
<td></td>
<td><strong>≥88 lbs</strong></td>
</tr>
<tr>
<td></td>
<td>▪ <strong>Day 1:</strong> 160 mg or 80 mg per day for two consecutive days</td>
</tr>
<tr>
<td></td>
<td>▪ <strong>Day 15:</strong> 40 mg</td>
</tr>
<tr>
<td></td>
<td>▪ <strong>Day 29/Maintenance:</strong> 40 mg every other week</td>
</tr>
</tbody>
</table>
- 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
  - 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, AND
    - 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 at least 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 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
  - 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:
- Review of therapy by the respective specialist confirms that the patient continues to have a beneficial response to therapy.
- For Ulcerative Colitis: Patient must have evidence of clinical remission by week 8 of adalimumab therapy

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 July 25, 2016
Hyaluronic Acid Derivatives, intra-articular

FDA-Approved Indication(s)

- Indicated for the treatment of pain in osteoarthritis of the knee in patients who failed non-pharmacologic therapy and simple analgesics

FDA-Recommended Dose and How Supplied

<table>
<thead>
<tr>
<th>Name</th>
<th>Description and Concentration</th>
<th>Volume</th>
<th>Dose per injection</th>
<th>Injections per Treatment cycle, given weekly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euflexxa®</td>
<td>Sodium hyaluronate 10 mg/mL</td>
<td>2 mL PFS</td>
<td>20 mg</td>
<td>3</td>
</tr>
<tr>
<td>Hyalgan®</td>
<td></td>
<td>2 mL PFS</td>
<td>20 mg</td>
<td>5</td>
</tr>
<tr>
<td>Supartz Fx™</td>
<td></td>
<td>2.5 mL PFS</td>
<td>25 mg</td>
<td>5</td>
</tr>
<tr>
<td>Monovisc™</td>
<td>Hyaluronan 22 mg/mL</td>
<td>4 mL PFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthovisc®</td>
<td>Hyaluronan 15 mg/mL</td>
<td>2 mL PFS</td>
<td>30 mg</td>
<td>3 or 4</td>
</tr>
<tr>
<td>Synvisc®</td>
<td>Hylan polymers A and B 8 mg/mL</td>
<td>2 mL PFS</td>
<td>16 mg</td>
<td>3</td>
</tr>
<tr>
<td>Synvisc-One®</td>
<td></td>
<td>6 mL PFS</td>
<td>48 mg</td>
<td>1</td>
</tr>
<tr>
<td>Gel-One®</td>
<td>Cross-linked hyaluronate 10 mg/mL</td>
<td>3 mL PFS</td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

Utilization Criteria

For initial review:
- Member must have a diagnosis of osteoarthritis of the knee, AND
- Documented failure of conservative, non-pharmacologic therapy (e.g., exercise program, weight loss (if applicable), physical therapy), AND
- Has tried and failed at least two simple analgesics (e.g., oral or topical NSAIDs, acetaminophen), AND
- Has tried and failed intra-articular corticosteroid injections

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
- The most recent treatment cycle was at least six months prior

Exclusion Criteria

- A known hypersensitivity to hyaluronic acid derivatives and/or their preparations
- Documented history of infections or skin disease in the area of the injection site

Required Medical Information

- Diagnosis
- Age
- Weight
- Dose
- Expected number of injections per cycle

Age Restrictions

- None

Prescriber Restrictions

- None

Coverage Duration (months)

- Six months
Quantity/Partial-Fill Restrictions

- None

Other Information

- Hyaluronan is found naturally in the body, particularly in the joints, and acts as a lubricant and helps to absorb shock.

References

Ibrance™ (palbociclib)

FDA Approved Indication(s)
- For the treatment of post-menopausal women with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer as initial endocrine-based therapy for their metastatic disease, in combination with letrozole

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 bottles of 21 capsules

Utilization Criteria
For initial review:
- Patient has confirmed diagnosis of (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer
- The patient’s treatment plan contains concurrent letrozole

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 patient has previously been treated with endocrine-based therapy, such as tamoxifen, toremifene, letrozole, anastrozole, exemestane, or fulvestrant.

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

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) that is resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy
- For the treatment of Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL) that is resistant or intolerant to prior TKI therapy

FDA Recommended Dose
- 45 mg administered orally once daily

How Supplied
- 15 mg and 45 mg tablets

Utilization Criteria
For initial review:
- Diagnosis consist with FDA-approved indication
- No approvals pending re-introduction to market
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 (months)
- 12

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Ponatinib is a multi-kinase inhibitor.
- Black Box Warning: Increased risk for arterial thrombosis and hepatotoxicity

References

Last Reviewed November 9, 2015
### Imbruvica® (ibrutinib)

**FDA Approved Indication(s)**
- For the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy
- For the treatment of patients with chronic lymphocytic leukemia (CLL) who have received one prior therapy, and/or CLL with 17p deletion
- For the treatment of patients with Waldenström’s macroglobulinemia (WM)

**FDA Recommended Dose**
- MCL: 560 mg orally once daily
- CLL and WM: 420 mg orally once daily

**How Supplied**
- 140 mg capsules in 90-count and 120-count bottles

**Utilization Criteria**

*For initial review:*
- Patient must have a diagnosis of MCL, CLL, or WM, AND
- Patient must have received at least one prior therapy, including one of the following:
  - A chemotherapy regimen containing rituximab
  - Lenalidomide
  - 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
- 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**
- 60 capsules for a 15 day supply for the first six (6) fills

**Other Information**
- Mechanism of action: Ibrutinib is an inhibitor of Bruton’s tyrosine kinase (BTK)
- The safety and efficacy of ibrutinib was evaluated in an open-label, multi-center, single-arm study of patients with MCL. All patients (n=111) had received at least one prior treatment prior to ibrutinib, with a median number of three prior treatments per patient. The study’s primary endpoint was overall response rate, as assessed by the investigator. In this trial, overall response rate was 65.8%, with a median duration of response of 17.5 months.

**References**
• Imbruvica® [Package Insert]. Pharmacyclics, Inc: Sunnyvale, CA USA; January 2015.
• Rajkumar S. Treatment and prognosis of Waldenstrom macroglobulinemia. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed December 23, 2015.)
**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

References

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**

*Last Reviewed November 9, 2015*
# 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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hairy Cell Leukemia</strong></td>
<td>2 million IU/m2 administered intramuscularly or subcutaneously 3 times a week for up to 6 months</td>
</tr>
<tr>
<td></td>
<td>Patients with platelet counts of less than 50,000/mm3 should not be administered Intron A® intramuscularly, but instead by subcutaneous administration</td>
</tr>
<tr>
<td><strong>Malignant Melanoma</strong></td>
<td>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</td>
</tr>
<tr>
<td><strong>Follicular Lymphoma</strong></td>
<td>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</td>
</tr>
<tr>
<td><strong>AIDS related Kaposi’s Sarcoma</strong></td>
<td>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</td>
</tr>
<tr>
<td><strong>Condylomata Acuminata</strong></td>
<td>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</td>
</tr>
<tr>
<td><strong>Chronic HCV</strong></td>
<td>3 million IU three times a week administered subcutaneously or intramuscularly</td>
</tr>
<tr>
<td><strong>Chronic HBV</strong></td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>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</td>
</tr>
</tbody>
</table>

## 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
<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient has decompensated liver disease</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Required Medical Information</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td></td>
</tr>
<tr>
<td>Complete blood count with differential</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Age Restrictions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>For diagnosis of hairy cell leukemia, malignant melanoma, follicular lymphoma, AIDS related Kaposi's Sarcoma, and CML, patients must be &gt;18 years of age</td>
<td></td>
</tr>
<tr>
<td>For diagnosis of HBV, patient must be &gt; 1 year of age</td>
<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>Prescriber Restrictions</th>
<th></th>
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<tbody>
<tr>
<td>Must be prescribed by an oncologist or infectious disease specialist</td>
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<table>
<thead>
<tr>
<th>Coverage Duration (months)</th>
<th></th>
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<tbody>
<tr>
<td>12</td>
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<table>
<thead>
<tr>
<th>Quantity/Partial Fill Restrictions</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>None</td>
<td></td>
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<table>
<thead>
<tr>
<th>Other Information</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td></td>
</tr>
<tr>
<td>Black Box Warning: Alpha interferons may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders.</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>References</th>
<th></th>
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</thead>
</table>

*Last Reviewed November 9, 2015*
## IVIG (intravenous immunoglobulin)

### FDA-Approved Products and Indications

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Primary humoral immunodeficiency (PI)</th>
<th>Idiopathic thrombocytopenic purpura (ITP)</th>
<th>Chronic inflammatory demyelinating polyneuropathy (CIDP)</th>
<th>Kawasaki Syndrome</th>
<th>B-cell chronic lymphocytic leukemia (CLL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bivigam®</td>
<td>X</td>
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<tr>
<td>Carimune NF®</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Flebogamma®</td>
<td>X</td>
<td></td>
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<tr>
<td>Gammagard®</td>
<td>X</td>
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<tr>
<td>Gammagard S/D®</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
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<tr>
<td>Gammaked®</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td>Gamunex®</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Gammaplex®</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Hyqvia®</td>
<td>X</td>
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<td></td>
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<tr>
<td>Octagam®</td>
<td>X</td>
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<td></td>
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<tr>
<td>Privigen®</td>
<td>X</td>
<td>X</td>
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</tr>
</tbody>
</table>

#### 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:**
- **PI**
  - Documentation of diagnosis of common variable immunodeficiency (CVID), X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, severe combined immunodeficiencies, X-linked hyper-IgM syndrome, ataxia-telangiectasia, or DiGeorge syndrome
- **ITP**
  - For adults:
    - platelet count < 30 x10⁹/L
    - patient has tried a long course of corticosteroids (eg. prednisone for 21 days)
    - initial management: dose should initially be 1 g/kg as a one-time dose
  - For children:
    - must have signs of bleeding
    - Initial management: a single dose of 0.8 to 1 g/kg
- **For secondary ITP from chronic HCV infection**
  - Must have completed HCV antiviral therapy
- **For secondary ITP from HIV infection**
  - Must be currently on HIV antiviral therapy
- **CIDP**
  - For induction
    - Presence of disabling symptoms
    - The standard IVIg dosage is a loading dose of 2.0 gm/kg administered intravenously over
2–5 days, followed by 1 g/kg over 1 day every 3 weeks

- For continuation
  - Adequate response and toleration of side effects
- Kawasaki Syndrome
  - Diagnosis of Kawasaki syndrome and 4 days of fever
  - 2 g/kg in a single infusion with aspirin
- B-cell CLL
  - for prevention of bacterial infections in patients with hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell CLL
  - infusion of 400 mg/kg every 3 weeks
- Myasthenia Gravis
  - Short-term therapy
    - for sudden worsening of myasthenia gravis symptoms
    - for surgery preparation
    - adjuvant to minimize long-term side effects of oral immunosuppressive therapy
  - Chronic therapy
    - Intolerant to all other myasthenia gravis treatments
- Guillain-Barre Syndrome (GBS)
  - Non-ambulatory patients started within four weeks of the onset of neuropathic symptoms
  - For children with severe GBS
- Multifocal Motor Neuropathy
  - IVIg (2 g/kg (total cumulative dose) given over 2–5 days) should be the first-line treatment when disability is sufficiently severe to warrant treatment
  - Typical maintenance treatment regimens are 1 g/kg every 2–4 weeks or 2 g/kg every 1–2 months.

*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**
- Absolute IgA deficiency
- Hypersensitivity to immune globulin

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Weight
- Baseline Ig levels
- Baseline renal functioning

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

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

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- **Mechanism of action:** supplies a broad spectrum of opsonizing and neutralizing IgG antibodies against a wide variety of bacterial and viral agents.
- **Black box warning (varies with each product):**
  - Use of Immune Globulin Intravenous (IGIV) products, particularly those containing sucrose, has been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death
  - Thrombosis may occur with immune globulin (IGIV) products

### References
- Silvergled AJ. General Principles in the use of Immune Globulin. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on December 31, 2014.)
- Practice parameter for the diagnosis and management of primary immunodeficiency. American Academy of Allergy, Asthma & Immunology.
- Howard, J. Myasthenia gravis, a manual for the healthcare provider. Myasthenia Gravis Foundation of America Inc.
- Miller, Marc. Treatment of recurrent and resistant dermatomyositis and polymyositis in adults. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on December 31, 2014.)
- Hertl, M. Management of refractory pemphigus vulgaris and pemphigus foliaceus. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on December 31, 2014.)
# Jakafi® (ruxolitinib)

## FDA Approved Indication(s)
- 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 of hydroxyurea

## FDA Recommended Dose
- 5, 15, or 20 mg based on platelet count; see package insert

## How Supplied
- 5, 10, 15, 20, 25 mg tablets

## Utilization Criteria

### For initial review:
- Must be clinically diagnosed with primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis
- Jakafi is being used as monotherapy; patient not also receiving a TKI or immunomodulatory agents (lenalidomide, thalidomide)

### For continuation:
- Patient must have a documented 35% reduction in spleen volume as measured by CT or MRI (or 50% reduction in palpable spleen length) and a decrease in symptoms vs baseline

## Exclusion Criteria
- None

## Required Medical Information
- Diagnosis
- Age
- Dose

## Age Restrictions
- 18 and over

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

## Coverage Duration (months)
- 6

## Quantity/Partial Fill Restrictions
- 30 tablets for a 15 day supply for the first 6 fills

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

## References
# Jevtana® (cabazitaxel)

## FDA Approved Indication(s)
- For the treatment of patients with hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing treatment regimen

## FDA Recommended Dose
- 5 mg/m² administered every three weeks as a one-hour intravenous infusion in combination with oral prednisone 10 mg administered daily

## How Supplied
- 60 mg/1.5 mL single-use vial

## Utilization Criteria
### For initial review:
- Clinically diagnosed hormone refractory metastatic prostate cancer, AND
- Disease progression despite treatment with docetaxel, AND
- Neutrophil count must be greater than 1,500 cells/mm³

### For continuation:
- Patient responding to treatment without disease progression, AND
- Blood cell counts are being monitored frequently

## Exclusion Criteria
- Used as first-line therapy for the treatment of metastatic prostate cancer

## Required Medical Information
- Diagnosis
- Age
- Dose
- Treatment history
- Baseline liver function tests and renal 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: Cabazitaxel is a microtubule inhibitor which binds to tubulin and promotes its assembly into microtubules while simultaneously inhibiting disassembly, resulting in the inhibition of mitotic and interphase cellular functions.
- Black Box Warning: Neutropenic deaths have been reported. Obtain frequent blood counts to monitor for neutropenia. Do not administer if neutrophil counts are ≤1,500 cells/mm³. Severe hypersensitivity has been documented in patients.

## References

*Last Reviewed November 9, 2015*
## Kalbitor® (ecallantide)

<table>
<thead>
<tr>
<th><strong>FDA Approved Indication(s)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• For the treatment of acute attacks of hereditary angioedema (HAE) in patients 16 years of age and older</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>FDA Recommended Dose</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• 30 mg (3 mL) administered subcutaneously in three 10 mg (1 mL) injections</td>
</tr>
<tr>
<td>• An additional 30 mg may be administered following 24 hours of initial dose and insufficient clinical improvement</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>How Supplied</strong></th>
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</thead>
<tbody>
<tr>
<td>• Each carton contains three single-use 10 mg/1 mL vials</td>
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</tbody>
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<table>
<thead>
<tr>
<th><strong>Utilization Criteria</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For initial review:</strong></td>
</tr>
<tr>
<td>• Patient must have documented diagnosis of HAE, as confirmed by serum complement factor testing or family history of HAE</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Exclusion Criteria</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patient has a history of anaphylactic response to ecallantide administration</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Required Medical Information</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Diagnosis</td>
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<tr>
<td>• Concurrent medications</td>
</tr>
<tr>
<td>• Treatment history</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Age Restrictions</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Must be 16 years of age and older</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Prescriber Restrictions</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Must be prescribed by an allergist or hematologist</td>
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<table>
<thead>
<tr>
<th><strong>Coverage Duration (months)</strong></th>
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<tbody>
<tr>
<td>• 1 month</td>
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<table>
<thead>
<tr>
<th><strong>Quantity/Partial Fill Restrictions</strong></th>
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</thead>
<tbody>
<tr>
<td>• Patient will be able to fill for 60 mg (6 mL) per authorization</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Other Information</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• 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.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>References</strong></th>
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</thead>
</table>

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

FDA Approved Indication(s)

- For the treatment of cystic fibrosis (CF) in patients age 6 years and older who have one of the following mutations in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R
- 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 150 mg tablet taken orally every 12 hours (300 mg total daily dose) with fat-containing food
- See package insert for dose modification recommendations

How Supplied

- 150 mg tablets

Utilization Criteria

For initial review:

- Member must have a diagnosis of cystic fibrosis, AND
- Presence of G551D mutation in the CFTR gene as detected by an FDA-cleared 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

- Documentation of homozygous F508del mutations in the CFTR gene,

Required Medical Information

- Diagnosis
- Copy of mutational test results
- Age
- Dose

Age Restrictions

- 6 years and older

Prescriber Restrictions

- Must be prescribed by a pulmonary specialist

Coverage Duration (months)

- 12

Quantity/Partial Fill Restrictions

- 28 tablets for 14 days for the first 6 fills

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


Last Reviewed November 9, 2015
**Keytruda® (pembrolizumab)**

### Approved Indication(s)
- Treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor

### FDA Recommended Dose
- 2 mg/kg administered as an intravenous infusion over 30 minutes every three weeks until disease progression or unacceptable toxicity

### How Supplied
- 50 mg single use vials

### Utilization Criteria
**For initial review:**
- Patient must have a diagnosis of unresectable or metastatic melanoma, AND
- Patient must have tried and failed ipilimumab, AND
- If patient is BRAF V600 mutation positive, must have tried and failed one BRAF inhibitor such as vemurafenib, dabrafenib, or trametinib

**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 upper limit of normal (ULN) or total bilirubin >1.5x ULN
- Inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks
- Persistent Grade 2 or 3 adverse reactions that do not recover to Grade 0-1 within 12 weeks after last dose
- Pregnancy (Category D)

### Required Medical Information
- Diagnosis
- Dose
- Treatment history
- Concomitant medications
- BRAF V600 mutation status
- Baseline thyroid function tests
- Baseline liver function tests (AST, ALT, bilirubin)

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

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

### Coverage Duration (months)
- Three months
- Continuation of approval will require documented assessment of tolerability

### Quantity/Partial Fill Restrictions
- None

### Other Information
- Discontinue pembrolizumab if AST/ALT increases by ≥50% relative to baseline and lasts for at least 1 week
- Mechanism of action: a monoclonal antibody, which binds to human programmed death receptor-1 (PD-1)
1), resulting in an anti-tumor immune response. By binding to PD-1, pembrolizumab blocks its interactions and allows for inhibition of active T-cell proliferation and cytokine production.

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
- RA
  - A treatment course of methotrexate was ineffective after at least a 6-12 week treatment course unless contraindicated or not tolerated
  - Patient has tried and failed a 12 week treatment course of, or was intolerant to, adalimumab and etanercept
- **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
## 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
- Patient has tried and failed or is intolerant to allopurinol and febuxostat

**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
- 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 has had an inadequate response to two or more drugs indicated for the treatment of MS, 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:**
- 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

<table>
<thead>
<tr>
<th>Letairis® (ambrisentan)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDA Approved Indication(s)</strong></td>
</tr>
<tr>
<td>- For the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability and delay clinical worsening</td>
</tr>
<tr>
<td><strong>FDA Recommended Dose</strong></td>
</tr>
<tr>
<td>- 5 mg orally, once daily; may increase to 10 mg orally once daily as tolerated</td>
</tr>
<tr>
<td><strong>How Supplied</strong></td>
</tr>
<tr>
<td>- 5 mg and 10 mg tablets</td>
</tr>
<tr>
<td><strong>Utilization Criteria</strong></td>
</tr>
<tr>
<td><strong>For initial review:</strong></td>
</tr>
<tr>
<td>- 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)</td>
</tr>
<tr>
<td>- Patient must have tried and failed a calcium channel blocker therapy</td>
</tr>
<tr>
<td>- Patient must have tried and failed, or have a contraindication to, a short acting vasodilator (i.e., sildenafil)</td>
</tr>
<tr>
<td><strong>For continuation:</strong></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>- Pregnancy</td>
</tr>
<tr>
<td><strong>Required Medical Information</strong></td>
</tr>
<tr>
<td>- Diagnosis</td>
</tr>
<tr>
<td>- Age</td>
</tr>
<tr>
<td>- Dose</td>
</tr>
<tr>
<td>- Sex</td>
</tr>
<tr>
<td>- Baseline liver function tests (ALT, AST, bilirubin)</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 a pulmonologist or cardiologist</td>
</tr>
<tr>
<td><strong>Coverage Duration (months)</strong></td>
</tr>
<tr>
<td>- 12</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: 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.</td>
</tr>
<tr>
<td>- Black Box Warning: Pregnancy Category X; embryo-fetal toxicity</td>
</tr>
<tr>
<td><strong>References</strong></td>
</tr>
<tr>
<td>- Hopkins W, Rubin L. “Treatment of Pulmonary Hypertension in Adults.” In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2013.</td>
</tr>
</tbody>
</table>

*Last Reviewed December 11, 2015*
# 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:**
- Patient must have one of the listed FDA approved indications

**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
- 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)
- 3

## Quantity/Partial Fill Restrictions
- None

## Other Information
- Black Box Warning: None

## References

Last Reviewed November 9, 2015
Lucentis® (ranibizumab)

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

**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**: 0.3 mg (0.05 mL of 6 mg/mL solution) is recommended to be administered by intravitreal injection once a month

**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 and DME: Must be intolerant to or failed treatment with bevacizumab

*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**
- 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

- Arroyo JG. Age-related macular degeneration: Treatment and prevention. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on January 1, 2015.)

Last Reviewed November 9, 2015
# 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® 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:
- **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
  - **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

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
- Breast feeding, OR
- Undiagnosed abnormal vaginal bleeding

Required Medical Information
- Diagnosis
- Age
- Dose
- Treatment history (Endometriosis and uterine leiomyoma)

Age Restrictions
- 2-12 for central precocious puberty
- 18 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 and CPP

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. Animal and human studies indicate that after an initial stimulation, chronic administration of leuprolide acetate results in suppression of testicular and ovarian steroidogenesis.

References
# 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
- 250 mg intramuscularly once weekly (every 7 days) beginning between 16 weeks, 0 days and 20 weeks, 6 days of gestation, and continuing through 36 weeks, 6 days of gestation

## How Supplied
- 5 mL multi-dose vial containing 1250 mg hydroxyprogesterone caproate

## 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
- Multiple gestations
- Other risk factors for preterm birth, including the following:
  - Cigarette smoking or substance abuse
  - Uncontrolled hypertension
  - Abnormal cervix or uterus
  - History of miscarriage
  - Infection during pregnancy

## 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. (Accessed December 28, 2015.)

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_Last Reviewed December 30, 2015_
Mekinist® (trametinib)  

**FDA Approved Indication(s)**
- For the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test
- 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

**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, 1 mg, and 2 mg capsules

**Utilization Criteria**

*For initial review:*
- Must have diagnosis of unresectable or metastatic melanoma, AND
- Must have documentation of BRAF V600E or V600K mutation in metastatic melanoma tumor tissue, 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**
- Previous treatment with vemurafenib or dabrafenib

**Required Medical Information**
- Diagnosis
- Age
- Dose
- BRAF V600E and BRAF V600K mutation status

**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**
- 30 day supply
- 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

**References**
**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

*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**
- 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*
Neulasta® (pegfilgrastim)

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

FDA Recommended Dose
- Subcutaneous injection of 6 mg administered once per chemotherapy cycle in adults. Do not administer Neulasta between 14 days before and 24 hours after administration of cytotoxic chemotherapy.

How Supplied
- 6 mg/0.6 mL prefilled syringe
- 6 mg/0.6 mL On-Body Injector for Neulasta (Neulasta Delivery Kit)

Utilization Criteria

For initial review:
- All uses: Prescriber must be an oncologist or hematologist, 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
    - Liver dysfunction, most notably elevated bilirubin
    - 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 Neulasta 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 Neulasta 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
    - 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
- 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

*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

### 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)
- 6

### Quantity/Partial Fill Restrictions
- 2 injections per 28 days

### Common Chemotherapy Regimens with ≥20% Risk of Febrile Neutropenia
- Acute Lymphoblastic Leukemia (ALL)
  - ALL induction regimens
- Bladder Cancer
  - MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)(neoadjuvant, adjuvant, metastatic)
- Breast Cancer
  - Docetaxel + trastuzumab (metastatic or relapsed)
  - Dose-dense AC followed by T (doxorubicin, cyclophosphamide, paclitaxel) (adjuvant)
  - TAC (docetaxel, doxorubicin, cyclophosphamide, paclitaxel)(adjuvant)
- Esophageal and Gastric Cancers
  - Docetaxel/cisplatin/fluorouracil
- Hodgkin Lymphoma
- **BEACOPP** (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
- **Kidney Cancer**
  - Doxorubicin/gemcitabine
- **Non-Hodgkin’s Lymphomas**
  - ICE (ifosfamide, carboplatin, etoposide) (DLBCL, PTCL, 2\textsuperscript{nd} line, salvage)
  - RICE (rituximab, ifosfamide, carboplatin, etoposide)
  - CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) +/- rituximab
  - MINE (mesna, ifosfamide, novantrone, etoposide)(DLBCL, PTCL, 2\textsuperscript{nd} line, refractory)
  - DHAP (dexamethasone, cisplatin, cytarabine)(peripheral T-cell lymphomas, diffuse large B-cell lymphoma, 2\textsuperscript{nd} line)
  - ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine)(DLBCL, TPCL, 2\textsuperscript{nd} line recurrent)
  - HyperCVAD + rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone + rituximab)
- **Melanoma**
  - Dacarbazine-based combo (dacarbazine, cisplatin, vinblastine)(advanced, metastatic, or recurrent)
  - Dacarbazine-based combination with IL-2, interferon alfa (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa) (advanced, metastatic, or recurrent)
- **Ovarian Cancer**
  - Topotecan
  - Paclitaxel
  - 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 every 21 days
  - CMF classic (cyclophosphamide, methotrexate, fluorouracil) (adjuvant)
  - AC (doxorubicin, cyclophosphamide) + sequential docetaxel (adjuvant) (taxane portion only)
  - AC + sequential docetaxel + trastuzumab (adjuvant)
  - FEC (fluorouracil, epirubicin, cyclophosphamide) + Paclitaxel every 21 days (metastatic or relapsed)
  - Paclitaxel every 21 days (metastatic or relapsed)
  - TC (docetaxel, cyclophosphamide)
- **Cervical Cancer**
  - Cisplatin/topetecan (recurrent or metastatic)
- Paclitaxel/cisplatin
- Topetecan (recurrent or metastatic)
- Irinotecan (recurrent or metastatic)

### Colorectal Cancer
- FOLFOX (fluorouracil, leucovorin, oxaliplatin)

### Esophageal and Gastric Cancers
- Irinotecan/cisplatin
- Epirubicin/cisplatin/5-fluorouracil
- Epirubicin/cisplatin/capecitabine

### Multiple Myeloma
- DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)
- DT-PACE + bortezomib (VTD-PACE)

### Non-Hodgkin’s Lymphomas
- EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) (AIDS-related NHL, Burkitt Lymphoma, recurrent)
- EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + IT chemotherapy (AIDS-related NHL, DLBCL, recurrent)
- GDP (gemcitabine, dexamethasone, cisplatin, (DLBCL, PTCL, 2nd line)
- GDP (gemcitabine, dexamethasone, cisplatin) + rituximab (DLBCL, 2nd line)
- FMR (fluorouracil, mitoxantrone, rituximab)
- R-CHOP (cyclophosphamide, doxorubicin/mitoxantrone, vincristine, prednisone, rituximab)

### Non-Small Cell Lung Cancer
- Cisplatin/paclitaxel (adjuvant, advanced/metastatic)
- Cisplatin/vinorelbine (adjuvant, advanced/metastatic)
- Cisplatin/docetaxel (adjuvant, advanced/metastatic)
- Cisplatin/etoposide (adjuvant, advanced/metastatic)
- Carboplatin/paclitaxel (adjuvant, advanced/metastatic)
- Docetaxel (advanced/metastatic)

### Ovarian Cancer
- Carboplatin/docetaxel

### Pancreatic Cancer
- FOLFIRINOX

### Prostate Cancer
- Cabazitaxel

### Small Cell Lung Cancer
- Etoposide/carboplatin

### Testicular Cancer
- Etoposide/cisplatin

### Uterine Sarcoma
- Docetaxel (advanced/metastatic)

### 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

Last Reviewed November 9, 2015
# 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 (eg, 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 Neupogen following BMT is 10 mcg/kg/day given as an IV infusion of 4 or 24 hours, or as a continuous 24-hour SC infusion. For patients receiving BMT, the first dose of Neupogen 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 Neupogen for the mobilization of PBPC is 10 mcg/kg/day. It is recommended that Neupogen be given for at least 4 days before the first leukapheresis procedure and continued until the last leukapheresis.
- Chronic neutropenia
  - Congenital Neutropenia: 6 mcg/kg every day
  - Idiopathic neutropenia: 5 mcg/kg every day
  - 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
  - 5mcg/kg/day. Doses may be increased in increments of 5 mcg/kg for each chemotherapy cycle, according to the duration and severity of the ANC nadir. Neupogen should be administered no earlier than 24 hours after the administration of cytotoxic chemotherapy. Neupogen should not be administered in the period 24 hours before the administration of chemotherapy. Neupogen 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. Neupogen administration should continue until the ANC remains greater than 1,000/mm³ for 3 consecutive CBCs or exceeds 10,000/mm³

How Supplied

- Neupogen®
<table>
<thead>
<tr>
<th><strong>Vial</strong></th>
<th>300 mcg/mL, 1 mL vial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>300 mcg/mL, 1.6 mL vial (480 mcg/1.6 mL)</td>
</tr>
<tr>
<td><strong>Prefilled syringe</strong></td>
<td>600 mcg/mL (300 mcg/0.5 mL)</td>
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<tr>
<td></td>
<td>600 mcg/mL (480 mcg/0.8 mL)</td>
</tr>
<tr>
<td><strong>Granix™</strong></td>
<td><strong>Prefilled syringe</strong></td>
</tr>
<tr>
<td></td>
<td>600 mcg/mL (300 mcg/0.5 mL)</td>
</tr>
<tr>
<td></td>
<td>600 mcg/mL (480 mcg/0.8 mL)</td>
</tr>
</tbody>
</table>

**Utilization Criteria**

*For initial review:*

- **Primary prophylaxis**
  - Patient must be receiving a myelosuppressive chemotherapy regimen associated with a \( \geq 20\% \) risk of febrile neutropenia (See below for list of recognized regimens)
  - Patient may have \( \geq 10\% \) 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
    - Poor renal function
    - Liver dysfunction, most notably elevated bilirubin
    - 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 Neupogen 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
  - \( \text{ANC} \leq 1 \times 10^9/L \)
  - Patient is receiving Neupogen 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 Neupogen 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**
  - Must have one of the following:
    - Age greater than 65 years
    - Being hospitalized at the time of the development of fever
    - 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
- 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

**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)
  - ALL induction regimens
- Bladder Cancer
  - MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)(neoadjuvant, adjuvant, metastatic)
- Breast Cancer
  - Docetaxel + trastuzumab (metastatic or relapsed)
  - Dose-dense AC followed by T (doxorubicin, cyclophosphamide, paclitaxel) (adjuvant)
  - TAC (docetaxel, doxorubicin, cyclophosphamide, paclitaxel)
- Esophageal and Gastric Cancers
  - Docetaxel/cisplatin/fluorouracil
- Hodgkin Lymphoma
  - BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
- **Kidney Cancer**
  - Doxorubicin/gemcitabine

- **Non-Hodgkin’s Lymphomas**
  - CFAR (cyclophosphamide, fludarabine, alemtuzumab, rituximab) (CLL with del, relapsed/refractory)
  - ICE (ifosfamide, carboplatin, etoposide) (DLBCL, PTCL, 2nd line, salvage)
  - RICE (rituximab, ifosfamide, carboplatin, etoposide)
  - CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) +/- rituximab
  - MINE (mesna, ifosfamide, novantrone, etoposide)(DLBCL, PTCL, 2nd line, refractory)
  - DHAP (dexamethasone, cisplatin, cytarabine)(peripheral T-cell lymphomas, diffuse large B-cell lymphoma, 2nd line)
  - ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine)(DLBCL, TPCL, 2nd line recurrent)
  - HyperCVAD + rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone + rituximab)

- **Melanoma**
  - Dacarbazine-based combo (dacarbazine, cisplatin, vinblastine)(advanced, metastatic, or recurrent)
  - Dacarbazine-based combination with IL-2, interferon alfa (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa) (advanced, metastatic, or recurrent)

- **Myelodysplastic Syndromes**
  - Antithymocyte globulin, rabbit/cyclosporine

- **Ovarian Cancer**
  - Topotecan
  - Paclitaxel
  - 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 every 21 days
  - CMF classic (cyclophosphamide, methotrexate, fluorouracil) (adjuvant)
  - AC (doxorubicin, cyclophosphamide) + sequential docetaxel (adjuvant) (taxane portion only)
  - AC + sequential docetaxel + trastuzumab (adjuvant)
  - FEC (fluorouracil, epirubicin, cyclophosphamide) + Paclitaxel every 21 days (metastatic or relapsed)
  - TC (docetaxel, cyclophosphamide)

- **Cervical Cancer**
<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Treatment Options</th>
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| Colorectal Cancer | - Cisplatin/topotecan (recurrent or metastatic)  
- Paclitaxel/cisplatin  
- Topotecan (recurrent or metastatic)  
- Irinotecan (recurrent or metastatic) |
| Esophageal and Gastric Cancers | - Cisplatin/topotecan  
- Paclitaxel/cisplatin  
- Topotecan (recurrent or metastatic)  
- Irinotecan (recurrent or metastatic) |
| Hodgkin Lymphoma | - FOLFOX (fluorouracil, leucovorin, oxaliplatin)  
- STAN FOLFOX (fluorouracil, leucovorin, vinblastine, dacarbazine)  
- Stanford V (mechlorethamine, doxorubicin, vinblastine, bleomycin, etoposide, prednisone) |
| Multiple Myeloma | - DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)  
- DT-PACE + bortezomib (VTD-PACE) |
| Non-Hodgkin’s Lymphomas | - EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) (AIDS-related NHL, Burkitt Lymphoma, recurrent)  
- EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + IT chemotherapy (AIDS-related NHL, DLBCL, recurrent)  
- ACOD (modified CHOP-doxorubicin, cyclophosphamide, vincristine, and prednisone)  
- GDP (gemcitabine, dexamethasone, cisplatin, (DLBCL, PTCL, 2nd line)  
- GDP (gemcitabine, dexamethasone, cisplatin) + rituximab (DLBCL, 2nd line)  
- FMRT (fludarabine, mitoxantrone, rituximab)  
- R-CHOP (cyclophosphamide, doxorubicin/mitoxantrone, vincristine, prednisone, rituximab) |
| Non-Small Cell Lung Cancer | - Cisplatin/paclitaxel (adjuvant, advanced/metastatic)  
- Cisplatin/vinorelbine (adjuvant, advanced/metastatic)  
- Cisplatin/docetaxel (adjuvant, advanced/metastatic)  
- Cisplatin/irinotecan (advanced/metastatic)  
- Cisplatin/etoposide (adjuvant, advanced/metastatic)  
- Carboplatin/paclitaxel (adjuvant, advanced/metastatic)  
- Docetaxel (advanced/metastatic) |
| Ovarian Cancer | - Carboplatin/docetaxel |
| Pancreatic Cancer | - Cabazitaxel |
| Small Cell Lung Cancer | - Etoposide/carboplatin |
| Testicular Cancer | - Etoposide/cisplatin |
| Uterine Sarcoma | - Docetaxel (advanced/metastatic) |

**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.
- **Black Box Warning: Splenic rupture**

**References**

- Granix™ [package insert], North Wales, PA; Teva Pharmaceuticals. December 2014.
Nexavar® (sorafenib)

FDA Approved Indication(s)
- Unresectable hepatocellular Carcinoma
- Advanced Renal Cell Carcinoma
- Differentiated Thyroid Carcinoma

FDA Recommended Dose
- 400 mg (2 x 200 mg tablets) twice daily
- See package insert for dose modification recommendations

How Supplied
- 200 mg tablet

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
- None

Required Medical Information
- Diagnosis
- Age
- Dose

Age Restrictions
- 18 and over

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 3

Quantity/Partial Fill Restrictions
- 60 tablets for 15 days supply for the first 6 fills

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-β). 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 relapsing/refractory multiple myeloma, AND
- 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
- Must have a documented benefit to therapy, as assessed by the member’s 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/mm$^3$
- Member has an absolute neutrophil count (ANC) less than 500/mm$^3$
- 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.
- Multiple Myeloma, or Kahler’s disease, is a type of cancer that develops in the plasma cells of the
bone marrow. This form of hematologic malignancy is the third most common in the United States after lymphoma and leukemia. The lifetime risk of diagnosis with multiple myeloma in the United States is 1 in 143 (0.7%). When this cancer causes hyper-proliferation of the body’s normal plasma cells, increased bone destruction and abnormal production of antibodies is seen. This in turn can lead to consequences such as renal failure, anemia, spinal cord compression, nerve damage, infection, hyperviscosity of the blood, and light chain amyloidosis. The exact etiology of this cancer is still unknown; however, several theories have been established regarding the role of hereditary and acquired genetic mutations in the development of this disease.

- 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

Nucala® (mepolizumab)

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

**FDA Recommended Dose**
- 100 mg injected subcutaneously once every 4 weeks

**How Supplied**
- 100 mg single-dose 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 more oral 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 ≥ 150 microL, 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

**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 and pulmonary function results

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

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

**Coverage Duration (months)**
- 6 initial, 12 month 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), UpToDate, Waltham, MA. Accessed December 24, 2015.
# 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:
- Used for an FDA-approved indication, AND
- Member must have documented inadequate response to UDCA, OR
- Member must have clinical documentation that patient is unable to tolerate UDCA, AND
- Alkaline phosphatase, serum transaminases and total bilirubin levels collected prior to treatment.

### 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**

# 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)
- 12 months

## Quantity/Partial Fill Restrictions
- Split fill (30 capsules per 60 day supply)

## 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
o 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
- Member is considered to be within the highest priority population for treatment:
  - Member must have evidence of stage 3 or greater fibrosis and/or compensated cirrhosis documented via a Metavir, Shear Wave Elastography (SWE) (transient elastography/Fibroscan, point-SWE, two-dimensional SWE), FibroTest, APRI, or equivalent test, AND
  - Member has undergone liver transplant, OR
  - Member has Type 2 or 3 essential mixed cyroglobulinemia with end-organ manifestations, OR
  - Member has proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis, AND,
- Patient must be simultaneously receiving peginterferon alfa and ribavirin (PR), OR
- Member is concurrently receiving sofosbuvir
- Utilization with sofosbuvir for patients with genotype 1 will be allowed only under the condition that the patient meets all utilization criteria for sofosbuvir 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

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

Estimates of test performance for advanced 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
- Have a contraindication related to PR regimens, OR
- Patient has a diagnosis of HCV with NS3 Q80K polymorphism, OR
- Have previously received simeprevir, boceprevir or telaprevir therapy, OR
- 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
- 14 capsules for 14 days

Other Information
- Mechanism of action: Simeprevir is a direct-acting antiviral (DAA) and inhibits the HCV NS3/4A protease.
- Place in therapy:
  - Simeprevir in combination with sofosbuvir with or without ribavirin is considered first line in treatment naïve patients with HCV genotype 1a or 1b infection
  - Simeprevir in combination with peginterferon alfa and ribavirin is no longer recommended for treatment naïve patients with HCV genotype 1.

References
Opdivo® (nivolumab)

FDA Approved Indication(s)
- For the treatment of unresectable or metastatic, BRAF V600 mutation-positive melanoma with disease progression following treatment with ipilimumab and a BRAF inhibitor
- For the treatment of BRAF V600 wild-type, unresectable or metastatic melanoma, as a single agent or in combination with ipilimumab
- For the treatment of patients with metastatic squamous non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy
- For the treatment of patients with advanced renal cell carcinoma (RCC) who have received prior antiangiogenic therapy

FDA Recommended Dose
- Melanoma, NSCLC, RCC:
  - 3 mg/kg every two weeks, administered via infusion
- Melanoma (used in combination with ipilimumab):
  - 1 mg/kg every three weeks for 4 doses, followed by 3 mg/kg every two weeks, administered via infusion

How Supplied
- 10 mg/mL (40 mg/4 mL, 100 mg/10 mL) single-use vials

Utilization Criteria
For initial review:
- For the treatment of unresectable or metastatic melanoma:
  - If BRAF V600 mutation positive, documentation of disease progression following ipilimumab and a BRAF inhibitor (i.e. vemurafenib or dabrafenib)
- For the treatment of NSCLC:
  - Documentation of progression following erlotinib, afatinib, or docetaxel
- For the treatment of RCC:
  - Documentation of disease progression following bevacizumab, sunitinib, sorafenib, axitinib, or pazopanib

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, including confirmatory genetic testing as applicable
- Treatment history
- Dose
- Pertinent labs, including baseline CBC

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- Must be prescribed by an oncologist

Coverage Duration (months)
- 6 months

Quantity/Partial Fill Restrictions
- None
Other Information

- Mechanism of action: Nivolumab binds the PD-1 ligands, PD-L1 and PD-L2, to the PD-1 receptor found on T cells, thus inhibiting T-cell proliferation and cytokine production.
- Approval for was granted via accelerated approval, and confirmatory clinical trials are on-going.

References


Last Reviewed January 22, 2016
# Orencia® (abatacept)

## FDA Approved Indication(s)
- Adult Rheumatoid Arthritis (RA)
- Juvenile Idiopathic Arthritis (JIA)

## FDA Recommended Dose
- **Adult RA:**
  - Subcutaneous injection: 125 mg once weekly with or without loading intravenous infusion
  - Initial infusion on day one based on weight, followed by one 125 mg subcutaneous injection with 24 hours, followed by 125 subcutaneous once a week
    - Less than 60 kg: 500 mg (2 vials)
    - 60 to 100 kg: 750 mg (3 vials)
    - 100+ kg: 1000 mg (4 vials)
  - Loading dose is not mandatory for all patients
- **Juvenile Idiopathic Arthritis:**
  - If less than 75 kg, administer 10 mg/kg
  - Patients weighing greater than 75 kg should be dosed based on adult recommendations

## How Supplied
- 250 mg/15 mL vial for intravenous infusion
- 125 mg/1 mL prefilled glass syringe

## 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 has documented failure of, or intolerance to at least two anti-TNF therapies, OR
- Member has documented failure of, or intolerance to, their plan’s preferred biologic product(s), AND
- For adult members, 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
- 6 years or older

## Prescriber Restrictions
- Must be prescribed by a rheumatologist

## Coverage Duration (months)
### 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
# Orkambi™ (lumacaftor/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 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
- Two tablets (each containing lumacaftor 200 mg/ivacaftor 125 mg) taken orally every 12 hours with fat-containing food

## How Supplied
- 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 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

## 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
- 12 years of age and older

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

## Coverage Duration (months)
- 12

## Quantity/Partial Fill Restrictions
- 56 tablets for 14-day supply for the first six fills

## 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 10, 2015*
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:

<table>
<thead>
<tr>
<th>Day</th>
<th>AM</th>
<th>PM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>10mg</td>
<td></td>
</tr>
<tr>
<td>Day 2</td>
<td>10mg</td>
<td>10mg</td>
</tr>
<tr>
<td>Day 3</td>
<td>10mg</td>
<td>20mg</td>
</tr>
<tr>
<td>Day 4</td>
<td>20mg</td>
<td>20mg</td>
</tr>
<tr>
<td>Day 5</td>
<td>20mg</td>
<td>30mg</td>
</tr>
</tbody>
</table>

- 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
- 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 at least two anti-TNF products, OR
- Has tried and failed all preferred biologic products, as 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
- 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


*Last Reviewed November 9, 2015*
# 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

## 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-infected 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 naïve 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 November 9, 2015_
Pegintron® (peginterferon alfa-2b)

FDA Approved Indication(s)
- For the treatment of chronic hepatitis C (CHC/HCV) in patients with compensated liver disease

FDA Recommended Dose
- Adult patients: 1.5 mcg/kg/week
- Pediatric patients: 60 mcg/m²/week

How Supplied
- 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

Utilization Criteria
For initial review:
- Patient has diagnosis of HCV with detectable viral load
- Patient is naïve to interferon-based therapy
- Patient must have tried and failed an interferon-free HCV regimen
- Approval is for 48 weeks (Genotypes 1) 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

Exclusion Criteria
- Patient has hepatic decompensation (Child-Pugh score ≥ 6) with cirrhosis before treatment

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

Age Restrictions
- 3 years of age and older

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

Coverage Duration (months)
- 12, pending patient-specific factors as noted above

Quantity/Partial Fill Restrictions
- None

Other Information
- Mechanism of action: Pegylated recombinant human interferon alfa-2b 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 November 9, 2015
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
- Diagnosis has been confirmed by MRI

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-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)
- 12 months

Quantity/Partial Fill Restrictions
- None

Other Information
- The mechanism of action of interferon therapy in the treatment of MS is currently unknown

References
**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.

*Last Reviewed November 10, 2015*
# 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 (CVD), in combination with diet and maximally tolerated statin therapy

## FDA-Recommended Dose
- 75 mg subcutaneous injection, dosed every two weeks
- If response to treatment is inadequate, dosage may be increased to a maximum dosage of 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 documentation of heterozygous or homozygous Familial Hypercholesterolemia (FH), confirmed through genetic testing of LDL receptor mutation(s), AND
- Member must have tried and failed six-month therapies of both high-intensity atorvastatin (80 mg) and rosuvastatin (40 mg) therapies\(^1\), unless otherwise contraindicated\(^2\), AND
- Member has tried and failed at least one non-statin hyperlipidemia add-on therapy after failure of high-intensity statin therapy\(^3\), AND
- Member must have documentation of baseline fasting LDL-C levels of greater than 100 mg/dL if currently on high-intensity statin therapy, OR greater than 190 mg/dL if intolerant to high-intensity statin therapy plus non-statin therapy.

\(^1\)Statin intolerance is defined as:
- Statin Induced myopathy, with documented CPK values greater than 10 times the upper limit of normal (ULN), AND
- Return of myopathy when reinstated on alternative statin, OR
- Statin-induced hepatitis, with all other causes of hepatitis ruled out, AND 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:
- Active liver disease, as defined by ALT and AST of three times the upper limit of normal (ULN), documented on two or more occasions
- 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:**
- At week eight: Member must have documentation of a 50% or greater reduction in LDL-C levels by week eight of therapy
- At month twelve: Member must have documentation of continuously suppressed fasting lipid 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**
- 18 years of age and older

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

**Coverage Duration (months)**
- 2 months (initial), 12 (continued)

**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.
- The effect of PCSK9 inhibitors on cardiovascular morbidity and mortality has not yet been determined.

**References**
**Procrit® (epoetin alfa)**

**FDA Approved Indication(s)**
- For the treatment of anemia due to Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis
- For the treatment of anemia due to zidovudine in HIV-infected patients
- For the treatment of anemia in patients with non-myeloid malignancies, where anemia is due to the effects of concomitant myelosuppressive chemotherapy and upon initiation, there is a minimum of two additional months of planned chemotherapy
- 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 3 times weekly (adults) and 50 Units/kg 3 times weekly (children on dialysis)
  - Individualize maintenance dose
  - Intravenous route recommended for patients on hemodialysis
- **Zidovudine-treated HIV-infected Patients:** 100 Units/kg 3 times weekly
- **Cancer Patients on Chemotherapy:** 40,000 Units weekly or 150 Units/kg 3 times weekly (adults); 600 Units/kg intravenously weekly (children ≥ 5 years)
- **Surgery Patients:** 300 Units/kg per day daily for 15 days or 600 Units/kg weekly

**How Supplied**
- 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

**Utilization Criteria**
*For initial review:*
- For all indications:
  - Other causes of anemia have been ruled out or corrected, AND
  - Anemia must be documented with Hct <30% and Hgb < 10 gm/dL
- **Myelosuppressive Chemotherapy**
  - Member has non-myeloid malignancy, AND
  - Chemotherapy is anticipated to last at least 2 months, AND
  - Chemotherapy is not intended for cure
- **Perisurgery:**
  - Member must also receive concurrent DVT prophylaxis therapy

*For continuation:*
- Benefit as evidenced by increase in hemoglobin, 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 cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure
- Patients undergoing cardiac or vascular surgery
- Patient has uncontrolled hypertension

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

**Age Restrictions**
- None

**Prescriber Restrictions**
- Must be prescribed by an oncologist or hematologist
- For patients with cancer receiving myelosuppressive chemotherapy, prescriber must be enrolled in the ESA APPRISE Oncology Program

**Coverage Duration (months)**

**Initial Coverage:**
- CKD: 3 months (12 weeks)
- HIV treatment with zidovudine: 2 months (8 weeks)
- Myelosuppressive chemotherapy: 2 months (8 weeks)
- Perisurgery: 1 month (4 weeks)

**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 November 9, 2015*
# 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
- 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
- member

## 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, AND
  - BMD T-score ≤ -2.5, AND
  - Has tried and failed or is intolerant to at least one oral bisphosphonate
- 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 must be corrected prior to initiating therapy
- 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**
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.)
# 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, AND
- Patient must have a baseline forced vital capacity (FVC) of ≥ 40% of predicted

**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 forced vital capacity (FVC)
- 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 November 10, 2015
# 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.
### 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

*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**
- 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

**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**
# 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

- 5 mg/year

## Other Information

- Mechanism of action: Reclast® 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. January 2015.
**Remicade® (infliximab)**

### 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 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:**
  - For reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 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 and Pediatric 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

- **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
- For all disease states: Member must have a negative TB test, AND
- Rheumatoid Arthritis
  - Prescriber is a rheumatologist, AND
  - Member is concurrently receiving methotrexate, AND
  - Has tried methotrexate in previous 6 months, OR
  - Has tried and failed methotrexate and two other disease modifying anti-rheumatic therapies (DMARDs) in the previous 3 months
- Ankylosing spondylitis
  - Prescriber is a rheumatologist, AND
  - Has tried and failed sulfasalazine in previous 6 months; OR
  - Was intolerant to sulfasalazine, COX-2 inhibitors, NSAIDs, or corticosteroids within the previous 6 months
- Plaque psoriasis
  - Prescriber is a dermatologist, AND
  - Has greater than 10% BSA involvement, or affected area includes palms, soles, head, neck, or genitalia, AND
  - Has tried and failed ≥ 1 topical agents in previous 6 months, AND
  - Intolerant to topical agents, topical immunomodulators, systemic therapy, or phototherapy
- Psoriatic arthritis
  - Member is intolerant to sulfasalazine, COX-2, NSAIDs, or corticosteroids
- Crohn’s disease/Ulcerative colitis
  - Prescriber is a gastroenterologist, AND
  - Member is 6 years of age or older, AND
  - Member has tried and failed ≥ 2 conventional therapies (corticosteroids, 5-ASA agents, immunosuppressant) for at least 30 days, AND
  - Disease is steroid dependent

**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 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)

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Treatment history
- TB test with date
- Concurrent medications

**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® (evolocumab)

FDA-Approved Indication(s)
- For the additional lowering of low density lipoprotein cholesterol (LDL-C) in adults with homozygous familial hypercholesterolemia (HoFH), heterozygous familial hypercholesterolemia (HeFH), or clinical atherosclerotic cardiovascular disease (CVD), in combination with diet and maximally tolerated statin therapy

FDA-Recommended Dose
- HeFH, CVD: 420 mg subcutaneous injection once monthly, or 140 mg subcutaneous injection every two weeks
- HoFH: 420 mg subcutaneous injection once monthly

How Supplied
- 140 mg/mL single-use prefilled syringe or single-use prefilled SureClick® autoinjector

Utilization Criteria

For initial coverage:
- Member must have documentation of heterozygous or homozygous Familial Hypercholesterolemia (FH), confirmed through genetic testing of LDL receptor mutation(s), AND
- Member must have tried and failed six-month therapies of both high-intensity atorvastatin (80 mg) and rosvustatin (40 mg) therapies1, unless otherwise contraindicated2, AND
- Member has tried and failed at least one non-statin hyperlipidemia add-on therapy after failure of high-intensity statin therapy3, AND
- Member must have documentation of baseline fasting lipid levels of greater than 100 mg/dL if currently on high-intensity statin therapy, OR greater than 190 mg/dL if intolerant to high-intensity statin therapy plus non-statin therapy.

1Statin intolerance is defined as:
- Statin Induced myopathy, with documented CPK values greater than 10 times the upper limit of normal (ULN), AND
- Return of myopathy when reinstated on alternative statin, OR
- Statin-induced hepatitis, with all other causes of hepatitis ruled out, AND 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

2Accepted contradictions to both atorvastatin and rosvustatin:
- Active liver disease, as defined by ALT and AST of three times the upper limit of normal (ULN), documented on two or more occasions
- Pregnancy
- Nursing Mothers
- Documentation of rhabdomyolysis, confirmed by medical records and the documentation of CPK levels 10 times the upper limit of normal

3Accepted Non-Statin Therapies:
- Cholestyramine
- Colestipol
- Colesevelam
- Fenofibrate
- Niacin
- Ezetimibe
- Lomitapide
- Mipomersen
For continuation of coverage:

- At week eight: Member must have documentation of a 50% or greater reduction in LDL-C levels by week eight of therapy
- At month twelve: Member must have documentation of continuously suppressed fasting lipid 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

- 18 years of age and older

Prescriber Restrictions

- Must be prescribed by a cardiologist

Coverage Duration (months)

- 2 months (initial), 12 (continued)

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.
- The effect of PCSK9 inhibitors on cardiovascular morbidity and mortality has not yet been determined.

References

- Scott R. Evolocumab, Endocrinologic and Metabolic Drugs Advisory Committee. FDA. 2015.
**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


*Last Reviewed June 23, 2016*
# Revlimid® (lenalidomide)

## FDA Approved Indication(s)
- Multiple myeloma (MM), in combination with dexamethasone, in patients who have received at least one prior therapy
- 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
- Not indicated and not recommended for the treatment of patients with chronic lymphocytic leukemia (CLL) outside of controlled clinical trials

## FDA Recommended Dose
- **Multiple Myeloma and Mantle Cell Lymphoma**
  - 25 mg once daily on Days 1-21 of repeated 28-day cycles
- **Myelodysplastic Syndromes**
  - 10 mg once daily

## How Supplied
- 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg capsules

## Utilization Criteria
**For initial review:**
- Physician must be registered with the REVLIMID REMS™ program and follow all procedures related to ordering and monitoring a patient receiving lenalidomide, AND
- **Multiple myeloma**
  - Patient has tried at least one prior chemotherapy, AND
  - Used in combination with dexamethasone or melphalan and prednisone, AND
  - Used as maintenance following response to either stem cell transplant or primary induction therapy
- **Myelodysplastic syndromes**
  - Member has transfusion dependent anemia or symptomatic anemia with clinically significant cytopenias, AND
  - Diagnosis associated with a deletion 5q cytogenic abnormality, AND
  - Member has tried or is intolerant to erythropoiesis-stimulating agents (ESAs) such as erythropoietin or darbepoeitin
- **Mantle cell lymphoma**
  - Patient 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
- **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
## 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
- Age
- Dose
- 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**
- Copegus®[Package Insert], Hoffmann-La Roche Inc.: South San Francisco, CA; 2013.
**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) in adult patients in combination with glucocorticoids

**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 Rituxan maintenance eight weeks following completion of Rituxan in combination with chemotherapy. Administer Rituxan as a single-agent every 8 weeks for 12 doses
  - Non-progressing, Low-Grade, CD20-Positive, B-cell NHL, after first-line 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
  - Diffuse Large B-Cell NHL
    - 375 mg/m²: administer on Day 1 of each cycle of chemotherapy for up to 8 infusions
    - In combination with Zevalin®
      - 250 mg/m²: administer as intravenous infusion on day 1, 7, 8, and 9 of therapy
- **CLL:**
  - 375 mg/m² for the first cycle; 500 mg/m² in cycles two through six
- **RA:**
  - Two-1000 mg intravenous infusions spaced two weeks apart
  - Maintenance infusions may be administered every 24 weeks 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 single-use vials
- 500 mg/50 mL single-use vials

**Utilization Criteria**
*For initial review:*
- Patient has a diagnosis consistent with an FDA-approved indication
- For RA:
  - Prescriber is a rheumatologist, AND,
  - Member is 18 years of age or older, AND
  - Member is receiving concurrent methotrexate therapy, unless otherwise contraindicated or not tolerated, AND
  - Member has documented treatment failure of two previous TNF therapies
- **For CLL:**
  - Prescriber is an oncologist or hematologist, AND
  - Member has documented treatment failure with a first-line therapy
- **For GPA, MPA:**
  - Member is at least 18 years of age or older, AND
  - Member has documented treatment failure or intolerance to methotrexate and azathioprine, AND,
  - Member is concurrently receiving glucocorticoids
- **NHL**
  - Prescriber is an oncologist or hematologist

**For continuation:**
- 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 has not received a rituximab infusion in the previous 16 weeks

**Exclusion Criteria**
- Member has active infection
- Therapy to be used in combination with other DMARD therapy

**Required Medical Information**
- Diagnosis
- Age
- Dose
- Height and Weight
- Previous treatment history
- Treatment plan
- Concurrent medications

**Age Restrictions**
- None

**Prescriber Restrictions**
- Must be prescribed by an oncologist/hematologist or rheumatologist

**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**
- National Comprehensive Cancer Network (NCCN), Clinical Practice Guidelines in Oncology. Non-


Last Reviewed November 10, 2015
# 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)

## 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 protease 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
### 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
- Amifostine (> 300 mg/m²)
- Arsenic trioxide
- Azacitidine
- Bendamustine
- Busulfan
- Carboplatin
- Carmustine
- Cisplatin
- Clofarabine
- Cyclophosphamide
- Cytarabine (> 200 mg/m²)
- Dacarbazine
- Dactinomycin
- Daunorubicin
- Doxorubicin
- Epirubicin
- Idarubicin
- Ifosfamide
- Interferon alfa (≥ 10 million IU/m²)
- Irinotecan
- Mechlorethamine
- 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
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


Last Reviewed November 16, 2015
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 < 20 kg/m²) 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/m²); 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


Last Reviewed November 9, 2015
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
- Rheumatoid Arthritis:
  - Member is receiving methotrexate concomitantly, AND
  - Member has documented failure of, or intolerance to adalimumab and etanercept, AND
  - Coverage of infused formulation requires documented intolerance to, or inability to safely administer, self-injectable product
- Psoriatic Arthritis and Ankylosing Spondylitis:
  - Member has documented failure of, or intolerance to both adalimumab and etanercept
- Moderate to severe Ulcerative colitis:
  - Member has documented failure of >1 non-biologic DMARD therapy (i.e. aminosalicylates, corticosteroids, azathioprine, or 6-mercaptopurine), AND
  - Member has documented failure or intolerance to adalimumab

*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 alternative biologic DMARD therapy

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

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

**Prescriber Restrictions**
- Must be prescribed by a gastroenterologist or rheumatologist

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- None

**Other Information**
- Mechanism of action: Golimumab is a human monoclonal antibody that binds to both the soluble and transmembrane bioactive forms of human TNFα.
- Black Box Warning: Serious infections, including TB, bacterial sepsis, and opportunistic infections, and malignancy

**References**

_Last Reviewed June 14, 2016_
**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 be naïve to sofosbuvir treatment
- Member must have a diagnosis of HCV genotype 1-6 with documented viral load collected within the previous three months, AND
- Member is considered to be within the highest priority population for treatment:
  - Member must have evidence of stage 3 or greater fibrosis and/or compensated cirrhosis documented via a Metavir, Shear Wave Elastography (SWE) (transient elastography/Fibroscan, point-SWE, two-dimensional SWE), FibroTest, APRI, or equivalent test,* OR Member has undergone liver transplant, OR
  - Member has Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations, OR
  - Member has proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis; 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

**For Extended Therapy:**
- Member has had a documented response to therapy based upon viral load, AND
- Member has remained adherent throughout therapy

\(^a\) 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**
- 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**
- 14 tablets for a 14 day supply

**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 NSSA resistant mutations.

**References**

Last Reviewed November 9, 2015
Sprix® (ketorolac tromethamine, nasal spray)

FDA-Approved Indication(s)
- For the short term management (up to 5 days) of moderate to moderately severe pain that requires analgesia at the opioid level

FDA-Recommended Dose
- For patients < 65 years of age:
  - 31.5 mg (one 15.75 mg spray in each nostril) every 6 to 8 hours
  - Maximum daily dose: 126 mg (four doses)
- For patients ≥ 65 years of age, patients with renal impairment, and adult patients less than 50 kg:
  - 15.75 mg (one 15.75 mg spray in one nostril) every 6 to 8 hours
  - Maximum daily dose: 63 mg (four doses)

How Supplied
- Single-day preservative-free spray bottles, containing 8 sprays for a total of 126 mg of ketorolac tromethamine

Utilization Criteria
For initial review and continuation:
- Member must have a diagnosis of moderate to moderately severe pain, AND
- Member is being treated for acute pain, with a treatment duration of ≤ 5 days, AND
- Member is not eligible or a candidate for opioid-based treatment, AND
- Member has tried and failed oral, systemic NSAIDs, OR
- Member is unable to swallow, has dysphagia, esophagitis, mucositis, or uncontrollable nausea/vomiting

Exclusion Criteria
- Medication is being used in the setting of coronary artery bypass graft (CABG) surgery, OR
- Medication is being used as a prophylactic analgesic before major surgery, OR
- Medication is being used concomitantly with probenecid, pentoxifylline, other forms of ketorolac or other NSAIDs, OR
- Total duration of use of ketorolac tromethamine nasal spray alone or sequentially with other formulations of ketorolac (IM/IV or oral) exceeds 5 days

Required Medical Information
- Weight
- Diagnosis
- Treatment history
- Creatinine clearance (CrCl)

Age Restrictions
- 18 years of age and older

Prescriber Restrictions
- None

Coverage Duration (months)
- 1

Quantity/Partial-Fill Restrictions
- None

Other Information
- Mechanism of action: Ketorolac is a non-steroidal anti-inflammatory (NSAID) that inhibits cyclooxygenase (COX-1 and COX-2), resulting in the reduced synthesis of prostaglandins, thromboxanes, and prostacyclin. Ketorolac has analgesic, anti-inflammatory, and antipyretic properties.
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*Last Reviewed July 27, 2016*
# Sprycel® (dasatinib)

## FDA Approved Indication(s)
- For the treatment of adults with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase
- For the treatment of adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib
- For the treatment of adults with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy

## FDA Recommended Dose
- Chronic phase CML: 100 mg once daily
- Accelerated phase CML, myeloid or lymphoid blast phase CML, or Ph+ ALL: 140 mg once daily

## 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

### 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

## Required Medical Information
- Diagnosis
- Treatment history and 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 months

## Quantity/Partial Fill Restrictions
- 15 tablets for 15 day supply for the first 6 fills

## 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.
References


Last Reviewed November 9, 2015
### 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

**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

**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
- Documented failure of, intolerance or contraindication to, at least two traditional therapies (e.g., PUVA, UVB, methotrexate, or cyclosporine), AND
- Member has documented failure of, or intolerance to, at least two anti-TNF therapies, OR
- Member has documented failure of the plan’s preferred biologics

*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 currently receiving one or more biologic DMARD therapies

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

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

**Prescriber Restrictions**
- Must be prescribed by a dermatologist and/or rheumatologist

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

**Quantity/Partial Fill Restrictions**
- 30 day induction, 12 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)

#### 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.
- Stivarga 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 (fluorouracil, 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 must try and fail adequate treatment trials of both imatinib and sunitinib

**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
- 15 tablets for a 15 day supply for the first three months of therapy

#### 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

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
- None

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 malate)

#### FDA Approved Indication(s)
- For the treatment of gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to Gleevec® (imatinib mesylate)
- For the treatment of advanced renal cell carcinoma (RCC)
- 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 RCC: 50 mg once daily for 4 weeks, followed by 2 weeks off
- pNET: 37.5 mg orally once daily

#### How Supplied
- 12.5 mg, 25 mg, and 50 mg capsules

#### Utilization Criteria
**For initial review:**
- Patient has clinically documented diagnosis of GIST, RCC, or pNET
- For patients with GIST, 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)
- 12

#### Quantity/Partial Fill Restrictions
- 14 capsule for 14 day supply

#### 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
**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
  - 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
  - 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
  - Child < 12 months of age at start of RSV season*, with cystic fibrosis and clinical evidence of CLD and/or nutritional compromise
  - 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
  - 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

**Tafinlar® (dabrafenib)**

**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
- In combination with trametinib, is indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test

**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:*
- Must have diagnosis of unresectable or metastatic melanoma, AND
- If used as a single agent:
  - Must have documentation of BRAF V600E mutation in metastatic melanoma tumor tissue, as detected by an FDA-approved test, OR
- If used in combination with trametinib:
  - Must have documentation of BRAF V600E or V600K mutation in metastatic melanoma tumor tissue, 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
- Age
- Dose
- BRAF V600E or V600K mutation status

**AgeRestrictions**
- 18 years of age and older

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

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

**Quantity/Partial Fill Restrictions**
- Partial fill medication, 14 day supply for the first three months, followed by 30 day supply

**Other Information**
- Mechanism of action: Mutated-BRAF kinase inhibitor

**References**
# Taltz™ (ixekizumab) †

<table>
<thead>
<tr>
<th><strong>FDA-Approved Indication(s)</strong></th>
<th>For the treatment of moderate-to-severe plaque psoriasis (PsO) in adults who are candidates for systemic therapy or phototherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDA-Recommended Dose</strong></td>
<td>• 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</td>
</tr>
</tbody>
</table>
| **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, 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 failed, or did not tolerate, at least 1 anti-Tumor Necrosis Factor (TNF) agent, such as infliximab, etanercept, or adalimumab, OR  
• Member must have failed plan-preferred biologic agents, as 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, 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)** | Three month initial, 12 month continuation |
| **Quantity/Partial-Fill Restrictions** | None |
| **Other Information** | • 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

- Taltz™ [package insert]. Indianapolis, IN: Eli Lilly; March 2016
## Tagrisso™ (osimertinib)

### FDA Approved Indication(s)
- Treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, who have progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy

### FDA Recommended Dose
- 80 mg orally once daily

### How Supplied
- 40, 80 mg tablets

### Utilization Criteria

**For initial review:**
- Confirmation of the T790M mutation in tumor specimens through an FDA-approved test (e.g., cobas® EGFR mutation test used in clinical trials)
- Patients must have progressed on prior systemic therapy, including treatment with either erlotinib, afatinib, or 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
- 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
- 15 tablets for a 15 day supply

### 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.
- NCCN Guidelines have recommended osimertinib as subsequent therapy for patients with EGFR TKI therapy in the 2016 update.
- 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

**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**
- 15 tablets for a 15 day supply

**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**

_Last Reviewed November 9, 2015_
# 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/m\(^2\) 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 \(\geq 3x\) 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**
- 56 tablets for 14 day supply for the first 6 fills

**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

<table>
<thead>
<tr>
<th>References</th>
</tr>
</thead>
</table>
### Tecfidera® (dimethyl fumerate)

**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, AND
- Must have tried and failed all plan-specific step therapy requirements, as applicable

*For continuation:*
- 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**
- 30 day supply

**References**

Last Reviewed January 18, 2016
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
- Member is considered to be within the highest priority population for treatment:
  - Member must have evidence of stage 3 or greater fibrosis and/or compensated cirrhosis documented via a Metavir, Shear Wave Elastography (SWE) (transient elastography/Fibroscan, point-SWE, two-dimensional SWE), FibroTest, APRI, or equivalent test, OR
  - Member has undergone liver transplant, OR
  - Member has Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations, OR
  - Member has proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis
  - If member is HIV co-infected, member must be concurrently receiving suppressive antiretroviral therapy

*a 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, 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
• 14 day supply limit per fill (two weekly cartons)

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
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

### 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


Last Reviewed November 9, 2015
# Tobi® and Tobi® Podhaler™ (tobramycin)

## FDA Approved Indication(s)
- For the management of *Pseudomonas aeruginosa* infection in patients with cystic fibrosis

## FDA Recommended Dose
- Tobi® for inhalation: 300 mg via inhalation twice daily for 28 days
- Tobi® Podhaler™: Four 28 mg capsules twice daily for 28 days

## How Supplied
- 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:
- Patient has diagnosis of cystic fibrosis, AND
- Patient has suspected or confirmed diagnosis of *Pseudomonas aeruginosa* lung infection, AND
- Patient has tried and failed generic inhaled tobramycin formulations

### 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 a known hypersensitivity to aminoglycosides

## Required Medical Information
- Diagnosis
- Age
- 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*

## 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
- 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*
# 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 has tried and failed at least 1 disease-modifying therapy
- Crohn’s Disease
  - Patient has a diagnosis of moderate to severe CD, AND
  - Member has tried and failed at least 1 conventional therapies, AND
  - Member has tried and failed at least two anti-TNF therapies, OR
  - Member has tried and failed their plan’s preferred biologics

*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 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 Leukoencephalopathy
• Solution must be prepared no longer than 8 hours prior to administration

References

• Olek M. Treatment of relapsing-remitting multiple sclerosis in adults. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed July 17, 2015.)
**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**
hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J 2016; 37:67.

Hopkins W, Rubin L. “Treatment of Pulmonary Hypertension in Adults.” In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, January 2016.
**Vectibix™ (panitumumab)**

**FDA Approved Indication(s)**
- For the treatment of for the treatment of metastatic colorectal carcinoma (mCRC) with disease progression on or following fluoropyrimidine, oxaliplatin, and irinotecan chemotherapy regimens

**FDA Recommended Dose**
- 6 mg/kg, administered as an intravenous infusion over 60-90 minutes, every 14 days

**How Supplied**
- 20 mg/mL (5 mL, 10 mL, and 20 mL) single-use vials

**Utilization Criteria**

*For initial review:*
- Patient has clinically diagnosed metastatic colorectal carcinoma
- Patient had disease progression on or following fluoropyrimidine, oxaliplatin, and irinotecan containing chemotherapy regimens

*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 KRAS mutation-positive mCRC, or if KRAS mCRC status is unknown

**Required Medical Information**
- Diagnosis
- Age
- Weight
- Dose
- Previous chemotherapy regimens
- KRAS mCRC status

**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: Panitumumab binds specifically to EGFR on both normal and tumor cells, and competitively inhibits the binding of ligands for EGFR
- Black Box Warning: Dermatologic toxicities and severe/fatal infusion reactions were observed in clinical trials

**References**
**Venclexta™ (venetoclax)†**

**FDA-Approved Indication(s)**
- For the treatment of patients with chronic lymphocytic leukemia (CLL) with 17p deletion who have received at least one prior therapy (i.e., relapsed/refractory CLL)

**FDA-Recommended Dose**
- Venetoclax is administered orally, once daily, until disease progression or unacceptable toxicity is observed
- Venetoclax should be initiated via a five-week ramp-up schedule (below) to reduce tumor burden and the risk of tumor lysis syndrome (TLS)

<table>
<thead>
<tr>
<th>Week</th>
<th>Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20 mg</td>
</tr>
<tr>
<td>2</td>
<td>50 mg</td>
</tr>
<tr>
<td>3</td>
<td>100 mg</td>
</tr>
<tr>
<td>4</td>
<td>200 mg</td>
</tr>
<tr>
<td>5+</td>
<td>400 mg</td>
</tr>
</tbody>
</table>

**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, AND
- Member must have documentation of the 17p deletion, as detected by an FDA approved test, AND
- Member must have progressed on, or had intolerance to, at least one prior CLL therapy (See: “Other Information” below), 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
- Member is pregnant, is planning to become pregnant, or is lactating
- Member has pre-existing neutropenia

**Required Medical Information**
- Diagnosis, with documentation of the 17p deletion
- 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, followed by 12 months continuation

**Quantity/Partial-Fill Restrictions**
- 30 tablets for a 30 day supply

**Other Information**
- Venetoclax is an orally available 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.
- Venetoclax’s approval was granted under an “accelerated approval” process based on preliminary overall response rate data. Continued approval for this indication is contingent upon verification and description of clinical benefit in a confirmatory trial.
- National Comprehensive Cancer Network (NCCN) recognized line therapies for CLL with del(17p) include:
  - Ibrutinib
  - High-dose methylprednisolone (HDMP) with rituximab
  - Fludarabine, cyclophosphamide, and rituximab (FCR)
  - Fludarabine and rituximab (FR)
  - Obinutuzumab and chlorambucil
  - Alemtuzumab +/- rituximab

References


Last Reviewed June 2, 2016
**Vidaza® (azacitidine)**

**FDA Approved Indication(s)**
- For the treatment of patients with the following FAB myelodysplastic syndrome (MDS) subtypes:
  - Refractory anemia (RA) or refractory anemia with ringed sideroblasts (RARS) (if accompanied by neutropenia or thrombocytopenia or requiring transfusions)
  - Refractory anemia with excess blasts (RAEB)
  - Refractory anemia with excess blasts in transformation (RAEB-T)
  - Chronic myelomonocytic leukemia (CMMoL)

**FDA Recommended Dose**
- First treatment cycle
  - 75 mg/m² subcutaneously or intravenously, daily for 7 days
- Subsequent treatment cycles
  - If no beneficial effect is seen after 2 treatment cycles and if no toxicity other than nausea and vomiting has occurred, may increase dose to 100 mg/m²

**How Supplied**
- 100 mg single-use vial

**Utilization Criteria**
*For initial review:*
- Clinically diagnosed MDS as defined under indications

*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 advanced malignant hepatic tumors
- Patient is pregnant or planning to father a child

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

**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: Vidaza® is a pyrimidine nucleoside analog of cytidine. It is believed to exert its antineoplastic effects by causing hypomethylation of DNA and direct cytotoxicity on abnormal hematopoietic cells in the bone marrow.

**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

Duration | Ribavirin | Genotype | Population
--- | --- | --- | ---
12 weeks | Yes | 1a | Without cirrhosis
24 weeks | Yes | 1a | With compensated cirrhosis (Child-Pugh A)
12 weeks | No | 1b | With or without compensated cirrhosis (Child-Pugh A)

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
- Member is considered to be within the highest priority population for treatment:
  - Member must have evidence of stage 3 or greater fibrosis and/or compensated cirrhosis documented via a Metavir, Shear Wave Elastography (SWE) (transient elastography/Fibroscan®, point-SWE, two-dimensional SWE), FibroTest, APRI, or equivalent test,a ORMember has undergone liver transplant, OR
  - Member has Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations, OR
  - Member has proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis; 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)

Exclusion Criteria

- 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

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• Concurrent use with sofosbuvir, simeprevir, 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
• 14 day supply limit per fill (two weekly cartons)

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
# 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.
**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)

**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)**
- 12

**Quantity/Partial Fill Restrictions**
- 60 tablets for a 15 day supply

**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**
# Xalkori® (crizotinib)

## FDA Approved Indication(s)
- Non-small cell lung cancer
  - First-line treatment for anaplastic lymphoma kinase (ALK)-positive metastatic 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 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)
- 12

## Quantity/Partial Fill Restrictions
- 15 day partial fill for 6 months

## 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® (tofacitinib citrate)**

**FDA Approved Indication(s)**
- For the treatment of adults with moderately to severe rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate, with or without concurrent non-biologic DMARD therapy

**FDA Recommended Dose**
- 5 mg twice daily

**How Supplied**
- 5 mg tablets

**Utilization Criteria**

*For initial review:*
- The member is diagnosed with moderately or severely active rheumatoid arthritis, **AND**
- The member has a documented negative TB test, **AND**
- The member has failed a trial of, or is intolerant to, methotrexate, **AND**
- The member is not using more than 2 tablets per day, **AND**
- The member has failed or is intolerant to at least 2 anti-TNF products, **OR**
- The member has tried and failed plan's preferred biologic products, as applicable

*For continuation:*
- Review of therapy by a rheumatologist confirms that there is a continued beneficial response to therapy, **AND**
- Member’s liver function and complete blood count have remained within normal range

**Exclusion Criteria**
- The member is using or planning to use tofacitinib in combination with biologic DMARDs or potent immunosuppressants (e.g., azathioprine or cyclosporine)

**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

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- 30 day supply, no restrictions

**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 November 9, 2015
# 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
### For initial review:
- For use in patients who meet FDA-approved indications

### 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)

## 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) *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, $\text{BSA (m²)} = (\frac{\text{Height (in)} \times \text{Weight (lbs)}}{3131})^{\frac{1}{2}}$
References


Last Reviewed November 9, 2015
**Xeomin® (incobotulinumtoxina)**

**FDA Approved Indication(s)**
- For the treatment of adults with cervical dystonia, to decrease the severity of abnormal head position and neck pain in both botulinum toxin-naïve and previously treated patients
- For the treatment of blepharospasm in adults 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**
- Cervical dystonia: 120 Units per treatment
- Blepharospasm: 1.25-2.5 Units per injection site
- Glabellar lines: 20 Units per treatment

**How Supplied**
- 50 Unit and 100 Unit single-use vials of lyophilized powder

**Utilization Criteria**

*For initial review:*
- Used for the treatment of 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.

*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 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 dermatologist, neurologist, or ophthalmologist

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- Cervical dystonia: 120 Units every 12 weeks
- Blepharospasm: 70 Units every 12 weeks

**Other Information**
- Mechanism of action: Xeomin® 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**

_Last Reviewed November 10, 2015_
# Xgeva® (denosumab)

**FDA Approved Indication(s)**
- Prevention of skeletal-related events in patients with bone metastases from solid tumors
- Treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity
- Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy
- Limitation of use: Denosumab is not indicated for the prevention of skeletal-related events in patients with multiple myeloma

**FDA Recommended Dose**
- Bone Metastasis from solid tumors
  - 120 mg administered as a subcutaneous injection every four weeks
- Giant cell tumor of bone
  - 120 mg administered every four weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy
- Hypercalcemia of malignancy
  - 120 mg every 4 weeks with additional 120 mg doses on days 8 and 15 of the first month of therapy

**How Supplied**
- 120 mg/ 1.7 mL (70 mg/mL) single-use vial

**Utilization Criteria**

*For initial review:*
- Member is receiving concurrent calcium and vitamin D supplement, unless contraindicated or not tolerated, AND
- For prevention of skeletal related events and giant cell tumor of bone:
  - Confirmation of bone metastases
- For hypercalcemia of malignancy:
  - Member has tried and failed IV bisphosphonate therapy

*For continuation:*
- Member has not experienced disease progression, 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 prevention of skeletal-related events in members with multiple myeloma, OR
- Pre-existing hypocalcemia, OR
- Member is concurrently receiving other denosumab therapy (Prolia®)

**Required Medical Information**
- Diagnosis
- Serum calcium levels
- Documentation of a baseline oral examination
- Concurrent medications
- 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
- Members with giant cell tumor of bone may receive three vials (360 mg) for the first month of therapy

**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, their precursors, and osteoclast-like giant cells.

**References**

*Last Reviewed November 9, 2015*
Xolair® (omalizumab)

**FDA Approved Indication(s)**
- Moderate to severe persistent asthma in patients 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**
- 150 to 375 mg subcutaneous, dosed every 2 or 4 weeks

**How Supplied**
- 150 mg/5 mL single-use vial

**Utilization Criteria**
*For initial review:*
- **Asthma**
  - Patient must have a diagnosis of severe persistent asthma, AND
  - Patient must have an inadequate response to a three-month course of inhaled corticosteroids, long-acting beta₂-agonists, and montelukast, AND
  - Patient must have documented history of severe attacks leading to either hospitalization or use of oral corticosteroids, AND
  - Baseline serum IgE level between 30 IU/mL and 700 IU/mL, AND
  - Patient is currently receiving long-acting beta₂-agonist, inhaled corticosteroid therapy, and short-acting beta₂-agonist as rescue therapy, unless otherwise contraindicated
- **Chronic idiopathic urticarial**
  - Patient must have a diagnosis of chronic idiopathic urticarial, AND
  - Patient 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:*
- Patient must have a documented clinical response to therapy

**Exclusion Criteria**
- Planned use for the treatment of other allergic conditions

**Required Medical Information**
- Diagnosis
- Age
- Weight
- Previous and concurrent therapies
- Baseline spirometry results
- Serum IgE (for treatment of asthma)

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

**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

## Xtandi® (enzalutamide)

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

### FDA Recommended Dose
- 160 mg (four 40 mg capsules) orally once daily

### How Supplied
- 40 mg capsules

### Utilization Criteria

#### For initial review:
- Member must have a diagnosis of mCRPC

#### 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)
- 12 months

### Quantity/Partial Fill Restrictions
- 14 day supply for the first 3 months, followed by 30 day supplies thereafter

### Other Information
- Mechanism of action: androgen receptor inhibitor

### References

*Last Reviewed November 9, 2015*
**Zelboraf® (vemurafenib)**

**FDA Approved Indication(s)**
- For the treatment of unresectable or metastatic melanoma with BRAF V600E mutation, as detected by an FDA-approved test

**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 a diagnosis of BRAF V600E mutation-positive metastatic melanoma

*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 mutation
- Age
- Dose

**Age Restrictions**
- 18 and over

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

**Coverage Duration (months)**
- 12

**Quantity/Partial Fill Restrictions**
- 120 tablets for 15 day supply for the first 6 fills

**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
- Black Box Warning: None

**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></td>
<td></td>
</tr>
<tr>
<td>Treatment-naïve or PegIFN/RBV-experienced</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without baseline NS5A polymorphisms*</td>
<td>No</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1b</td>
<td></td>
<td></td>
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<tr>
<td>Treatment-naïve or PegIFN/RBV-experienced</td>
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<tr>
<td>Genotype 4</td>
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<td>Treatment-naïve</td>
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<tr>
<td>Genotype 1a or 1b</td>
<td>+ RBV</td>
<td>12 weeks</td>
</tr>
<tr>
<td>PegIFN/RBV/PI-experienced†</td>
<td></td>
<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>
</tr>
<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 telprevir

**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 is considered to be within the highest priority population for treatment:
  - Member must have evidence of stage 3 or greater fibrosis and/or compensated cirrhosis documented via a Metavir, transient elastography/Fibroscan, FibroTest, APRI, or equivalent test, OR
  - Member has undergone liver transplant, OR
  - Member has Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations, OR
  - Member has proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis

**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
  - Liver status

**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**
- 14 tablets for a 14 day supply

**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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced breast cancer</td>
<td>3.6 mg/28 day supply</td>
</tr>
<tr>
<td>Endometrial thinning</td>
<td>3.6 mg/28 day supply</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>3.6 mg/28 day supply</td>
</tr>
<tr>
<td>Prostatic carcinoma</td>
<td>3.6 mg/28 day supply</td>
</tr>
<tr>
<td>Stage B2 to C prostatic carcinoma</td>
<td>3.6 mg/28 day supply</td>
</tr>
<tr>
<td></td>
<td>10.8 mg/84 day supply</td>
</tr>
</tbody>
</table>

### 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

**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 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
# 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
- 60 capsules for 15 day supply

## 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*
Zometa® (zoledronic acid)

FDA Approved Indication(s)
- For the treatment of hypercalcemia and malignancy
- For the treatment of patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy. Prostate cancer should have progressed after treatment with at least one hormonal therapy.

FDA Recommended Dose
- Treatment of Hypercalcemia of Malignancy
  - 4 mg as a single-use intravenous (IV) infusion over no less than 15 minutes.
  - 4 mg as retreatment after a minimum of 7 days.
  - Dose adjustments are not necessary in treating patients for hypercalcemia of malignancy presenting with mild-to-moderate renal impairment prior to initiation of therapy (serum creatinine less than 400 micromol/L or 4.5 mg/dL)
- Treatment of Multiple Myeloma and Bone Metastasis from Solid Tumors
  - 4 mg as a single-use IV infusion over no less than 15 minutes every 3-4 weeks for patients with creatinine clearance (CrCl) of greater than 60 mL/min
  - Dose adjustment as follows:

<table>
<thead>
<tr>
<th>CrCl</th>
<th>Recommended Dose Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 to 60 mL/min</td>
<td>Reduce dose to 3.5 mg</td>
</tr>
<tr>
<td>40 to 49 mL/min</td>
<td>Reduce dose to 3.3 mg</td>
</tr>
<tr>
<td>30 to 39 mL/min</td>
<td>Reduce dose to 3 mg</td>
</tr>
<tr>
<td>&lt;30 mL/min</td>
<td>Use not recommended</td>
</tr>
</tbody>
</table>

How Supplied
- 4 mg/100 mL single-use ready-to-use bottle
- 4 mg/5 mL single-use vial of concentrate

Utilization Criteria
For Initial Reviews:
- Member has a diagnosis consistent with FDA-approved indications for use, AND
- For hypercalcemia of malignancy
  - Member has albumin-corrected calcium (cCa) of greater than or equal to 12 mg/dL [3.0 mmol/L] using the formula: cCa in mg/dL = Ca in mg/dL + 0.8 (4.0 g/dL – patient albumin [g/dL])
- For multiple myeloma and bone metastasis from solid tumors:
  - Member is receiving standard antineoplastic therapy AND
  - Member also receiving calcium 500 mg and 400 international units (IU) of vitamin D daily

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
- CrCl < 30 mL/min, OR
- Doses greater than 4 mg, OR
- Pre-existing hypocalcemia or other disturbances of mineral metabolism, OR
- Treatment of hypercalcemia associated with hyperparathyroidism or other nontumor-related conditions, OR
- Member is receiving other IV bisphosphonate therapy (pamidronate oribandronate), OR
- Member is receiving other zoledronic acid therapy (Reclast®)

### Required Medical Information
- Diagnosis
- Age
- Dose
- Treatment history
- Concurrent medications
- Creatinine Clearance (CrCl)
- Corrected calcium (for treatment of hypercalcemia of malignancy)

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

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

### Coverage Duration (months)
- 12

### Quantity/Partial Fill Restrictions
- None

### Other Information
- Mechanism of action: zoledronic acid is a bisphosphonate and acts primarily on bone. It is an inhibitor of osteoclast-mediated bone resorption.
- Zoledronic acid has equivalent benefits to IV pamidronate in decreasing pain and bone-related complications, improving performance status, and preserving quality of life in patients with Durie-Salmon stage III multiple myeloma at least one lytic lesion.
- Among bisphosphonates (zoledronic acid, pamidronate, and ibandronate), the National Comprehensive Cancer Network (NCCN) Multiple Myeloma Panel Members prefer zoledronic acid for the treatment of hypercalcemia.

### References
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 <0.5Gi/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

- 30 tablets for a 15 day supply

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.
  o Inhibition of chemotaxis and adhesion, and reduced cell viability.

References

**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**

*Last Reviewed November 10, 2015*
Zynbryta™ (daclizumab) †

FDA Approved Indication(s)

- For the treatment of adult patients with relapsing forms of multiple sclerosis (MS); because of its safety profile, the use of Zynbryta™ should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS

FDA Recommended Dose

- 150 mg administered subcutaneously once monthly (may be self-administered)

How Supplied

- Supplied in a single-dose prefilled syringe providing 1 mL of 150 mg/mL of daclizumab

Utilization Criteria

For initial review:

- Member has a diagnosis of relapsing multiple sclerosis, AND
- Member has had an inadequate response to two or more drugs indicated for the treatment of MS, AND
- Member has a negative TB test prior to initiating therapy, AND
- Serum transaminases and total bilirubin levels collected prior to treatment, AND
- Requirements of the Zynbryta™ REMS program are met

For continuation:

- Confirmation that the member continues to have a beneficial response to therapy as assessed and documented by the member’s specialist provider
- Clinical documentation of member’s most recent liver function tests

Exclusion Criteria

- Members with pre-existing hepatic disease or hepatic impairment, including ALT or AST at least 2 times the upper limit of normal
- Members with a history to daclizumab or any other component of the formulation

Required Medical Information

- Diagnosis
- Age
- Dose
- TB test
- Treatment history
- Pertinent labs

Age Restrictions

- 18 years of age and older

Prescriber Restrictions

- Must be prescribed by a neurologist

Coverage Duration (months)

- 3 months initially, 12 months thereafter

Quantity/Partial Fill Restrictions

- None

Other Information

- Mechanism of action: The precise mechanism by which Zynbryta™ exerts therapeutic effects in MS is unknown but is presumed to involve modulation of interleukin-2 mediated activation of lymphocytes through binding to CD25, a subunit of the high-affinity IL-2 receptor.
- Black box warnings:
  - Zynbryta™ can cause severe liver injury, including life-threatening events, liver failure, and
autoimmune hepatitis. Obtain transaminase and bilirubin levels before initiation of Zynbryta™. Monitor and evaluate transaminase and bilirubin levels monthly and up to 6 months after the last dose.

- Zynbryta™ is contraindicated in patients with pre-existing hepatic disease or hepatic impairment.
- Immune-mediated disorders including skin reactions, lymphadenopathy, non-infectious colitis, and other immune-mediated disorders can occur with Zynbryta™

- In a clinical trial comparing Zynbryta™ to Avonex® in 1,841 patients, Zynbryta™ had a statistically significant effect on the annualized relapse rate (0.216 vs. 0.393, relative reduction of 45%, p < 0.001) and on the number of new or newly enlarging T2 hyperintense lesions (4.31 vs. 9.44, relative reduction of 54%, p < 0.0001).
- In a placebo-controlled trial with Zynbryta™ as an active comparator, Zynbryta™ had statistically significant effect on the annualized relapse rate, the proportion of patients relapse free, the number of new T1 Gd-enhancing lesions, and the number of new or newly enlarging T2 hyperintense lesions.

### References


Last Reviewed June 10, 2016
# Zytiga® (abiraterone)

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

**FDA Recommended Dose**
- 1,000 mg (four 250 mg tablets) orally once daily on an empty stomach, in combination with 5 mg oral prednisone twice daily

**How Supplied**
- 250 mg tablets

**Utilization Criteria**

*For initial review:*
- Patient is receiving concurrent prednisone 5 mg orally twice daily (or equivalent) unless there is a contraindication.
- Baseline ALT, AST, and bilirubin tests 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

**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)**
- 12 months

**Quantity/Partial Fill Restrictions**
- 14 day supply for the first 3 months, followed by 30 day supplies thereafter

**Other Information**
- Mechanism of action: CYP17 inhibitor

**References**

*Last Reviewed November 10, 2015*