# Prior Authorization Medications Requiring Review – Criteria for Use

The Medicare Part D formulary does not allow prior authorization or criteria restrictions on medications; this document applies to the Commercial, Triple Tier, and Multi-Choice formularies.

<table>
<thead>
<tr>
<th>Brand Name And/Or Therapeutic Class</th>
<th>Generic Name</th>
<th>J-Code</th>
<th>Medicare Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acthar® Corticotropin gel</td>
<td>J0800</td>
<td>Medicare Part D</td>
<td></td>
</tr>
<tr>
<td>Ampyra™ Dalfampridine</td>
<td></td>
<td>Medicare Part D</td>
<td></td>
</tr>
<tr>
<td>Arcalyst™ Rilonacept powder for solution</td>
<td>J3490</td>
<td>Medicare Part D</td>
<td></td>
</tr>
<tr>
<td>Berinert® Human C1 Inhibitor</td>
<td></td>
<td>Medicare Part D</td>
<td></td>
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<tr>
<td><strong>Botulinum Toxin:</strong></td>
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</tr>
<tr>
<td>Botox® (P)</td>
<td></td>
<td>J0585 (type A)</td>
<td>Medicare Part D</td>
</tr>
<tr>
<td>Myobloc® (N)</td>
<td></td>
<td>J0587 (type B)</td>
<td>Medicare Part D</td>
</tr>
<tr>
<td>Byetta® Exenatide SQ solution</td>
<td>J3490</td>
<td>Medicare Part D</td>
<td></td>
</tr>
<tr>
<td>Cinryze® Human C1 Inhibitor</td>
<td></td>
<td>Medicare Part B or D</td>
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</tr>
<tr>
<td>Gilneya™ Fingolimod</td>
<td></td>
<td>Medicare Part D</td>
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<tr>
<td><strong>Growth Hormones:</strong></td>
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<tr>
<td>Omnitrope® (P)</td>
<td></td>
<td>J2940-J2941</td>
<td>Medicare Part D</td>
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<tr>
<td>Genotropin® (N)</td>
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<tr>
<td>Humatrope® (N)</td>
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<tr>
<td>Norditropin® (N)</td>
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<tr>
<td>Nutropin AQ (N)</td>
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<tr>
<td>Saizen® (N)</td>
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<tr>
<td>Serostim® (N)</td>
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<tr>
<td>Zortive® (N)</td>
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<tr>
<td><strong>Hyaluronic Acid Derivatives:</strong></td>
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<tr>
<td>(viscosupplements):</td>
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<tr>
<td>Supartz® (P)</td>
<td></td>
<td>J7321-J7322</td>
<td>Medicare Part B</td>
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<tr>
<td>Synvisc® (2)</td>
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<td>Medicare Part D</td>
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<tr>
<td>Euflexxa® (N)</td>
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<tr>
<td>Hyalgan® (N)</td>
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<tr>
<td>Orthovisc® (N)</td>
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<tr>
<td>Synvisc-One® (N)</td>
<td></td>
<td>Medicare Part D</td>
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</tr>
<tr>
<td>Ilaris® Canakinumab</td>
<td></td>
<td>Medicare Part D</td>
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<tr>
<td>Januvia™ Sitagliptin</td>
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<td>Medicare Part D</td>
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<tr>
<td>Janumet™ Sitagliptin/metformin</td>
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<td>Medicare Part D</td>
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<tr>
<td>Kalbitor® Ecallantide</td>
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<td>Medicare Part D</td>
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<tr>
<td>Kombiglyze™ XR Saxagliptin/metformin extended-release</td>
<td>J3490</td>
<td>Medicare Part D</td>
<td></td>
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<tr>
<td>Kuvan™ Sapropterin tablets</td>
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<td>Medicare Part D</td>
<td></td>
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<tr>
<td>Mozobil™ Plerixafor injection</td>
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<td>Medicare Part D</td>
<td></td>
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<tr>
<td>Onglyza™ Saxagliptin</td>
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<td>Medicare Part D</td>
<td></td>
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<tr>
<td>Pradaxa® Dabigatran</td>
<td></td>
<td>Medicare Part D</td>
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<tr>
<td>Provenge® Sipuleucel-T</td>
<td>Q2043</td>
<td>Medicare Part B</td>
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<tr>
<td>Sabril® Vigabatrin</td>
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<td>Medicare Part D</td>
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<tr>
<td>Soliris® Eculizumab</td>
<td>J1300</td>
<td>Medicare Part B</td>
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<tr>
<td>Supprelin® LA Histrelin implant</td>
<td>J9226</td>
<td>Medicare Part D</td>
<td></td>
</tr>
<tr>
<td>Symlin® Pramlintide SQ solution</td>
<td>J3490</td>
<td>Medicare Part D</td>
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<tr>
<td>Tradjenta™ Liraglutide injection</td>
<td></td>
<td>Medicare Part D</td>
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</tr>
<tr>
<td>Tysabri® Natalizumab IV solution</td>
<td>J2323</td>
<td>Medicare Part B</td>
<td></td>
</tr>
<tr>
<td>Victoza® Liraglutide injection</td>
<td></td>
<td>Medicare Part D</td>
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<tr>
<td>Xgeva® Denosumab</td>
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<td>Medicare Part B</td>
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<tr>
<td>Xiaflex™ Collagenase clostridium histolyticum injection</td>
<td>J0775</td>
<td>Medicare Part B</td>
<td></td>
</tr>
<tr>
<td>Xolair® Omalizumab injectable</td>
<td>J2357</td>
<td>Medicare Part D</td>
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</tr>
</tbody>
</table>

P- Preferred  2-2nd line (if preferred failed)  NP- Non-preferred
### Medications Requiring Review – Criteria for Use

<table>
<thead>
<tr>
<th>Drug</th>
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</tr>
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</table>
| Acthar® - Corticotropin (gel) | Use of Acthar® is restricted to patients with a diagnosis of infantile spasms or adrenal insufficiency.  
- May be used in patients with MS on a case by case basis  
Ensure patient does not have any of the following diagnoses:  
- Congestive heart failure  
- Hypertension  
- Osteoporosis  
- Peptic Ulcer  
- Primary adrenocortical insufficiency or adrenocortical hyperactivity  
- Scleroderma  
- Hypersensitivity to porcine protein  
- Pancreatitis  
- Thromboembolic disorder  
Initial approval period: 3 months only for all indications |
| Ampyra™ - Dalfampridine | Candidates for treatment with dalfampridine should meet the following criteria:  
1. **Indications:** Dalfampridine (Ampyra™) extended release tablets should be reserved for treatment intended to improve walking capacity in ambulatory patients with multiple sclerosis (MS).  
**Dalfampridine is symptomatic treatment only and is not disease-modifying.**  
   a. Dalfampridine may be used for patients with any type of MS as categorized by clinical course, based upon clinical trials qualifying dalfampridine for approval.  
   b. Dalfampridine results were modest in published studies.  
      i. Only about 30% of clinical trial patients had an improvement in average walking speed of 20% or more (while about 10% of placebo-treated patients had the same level of improvement). To put this in perspective, an average 20% improvement in a timed walk over a 25-foot distance means on average the patient walked 25 feet 8 seconds if baseline was 10 seconds, or in 10 seconds if baseline was 12.5 seconds.  
      ii. In clinical trials, a response was defined as having an improvement in walking speed in more than half of the timed 25-foot walk tests. In two trials, 35% and 43% of patients met this standard for improvement (versus 8% and 9% of placebo-treated patients). In the minority of patients who achieved this response criteria, the improvements amounted to just under 2 seconds improvement over 25 feet, versus an 0.5 second improvement with placebo.  
      iii. These average improvements should be weighed against the risks of treatment – primarily the risk for seizures.  
   c. Dalfampridine clinical trials included only ambulatory patients. Therefore, efficacy and safety have not been tested in non-ambulatory patients.  
2. **Physical Therapy:** Physical therapy should be considered and appropriately used before exposing patients to dalfampridine  
3. **Response Assessment:** A response should become evident within two weeks. Patients should be given a trial of dalfampridine lasting from 30 to 60 days and then evaluated for response to determine whether to continue the drug. One objective indicator should be used, along with any subjective indicators, to assess response.  
   a. A useful objective assessment is the Timed 25-Foot Walk (T25FW) test. This was the test used in clinical trials qualifying dalfampridine for approval.  
      i. A baseline should be established at one or more visit after any possible physical therapy and before initiation of dalfampridine. |

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### Drug

**Prior authorization criteria**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Criteria</th>
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<tbody>
<tr>
<td>Arcalyst™ - Rilonacept</td>
<td><strong>A diagnosis of cryopyrin-associated periodic syndromes (CAPS) and all of the following criteria:</strong></td>
</tr>
<tr>
<td></td>
<td>1. Patient has documented laboratory evidence of a genetic mutation in the Cold-Induced Auto-inflammatory Syndrome 1 (CIAS1- sometimes referred to as the NLRP3).</td>
</tr>
<tr>
<td></td>
<td>2. There is clinical documentation that the patient is experiencing classic symptoms of CAPS in either criteria below:</td>
</tr>
<tr>
<td></td>
<td>a. Familial Cold Auto-Inflammatory Syndrome (FCAS) - recurrent episodes of rash, fever/chills, and joint pain following exposure to mild cold environment. (e.g. cool breeze, air conditioning) Symptoms generally last for up to 24 hours.</td>
</tr>
<tr>
<td></td>
<td>b. Muckle-Wells Syndrome (MWS) - chronic fever and rash sometimes exacerbated by generalized cold exposure. Episodes can last up to 2-3 days.</td>
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<tr>
<td></td>
<td>3. There is clinical documentation of significant functional impairment leading to limitations of activities of daily living (ADLs).</td>
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<tr>
<td></td>
<td>4. Failed, intolerant, or allergic to either of the following:</td>
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<tr>
<td></td>
<td>a. Prednisone</td>
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<td></td>
<td>b. Anakinra (Kineret®) injection</td>
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<tr>
<td></td>
<td>c. Canakinumab (Ilaris®) injection</td>
</tr>
</tbody>
</table>

**Reasons for non-coverage:**

- Concurrent use of live vaccines or tumor necrosis factor
- Chronic or active infections
- Untreated latent tuberculosis
- 11 years or younger

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Drug | Prior authorization criteria
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**Caution:**
- Increased risk of malignancies may occur

**Monitoring:**
- Improvement in signs and symptoms of cryopyrin-associated periodic syndromes (ie, fever, urticaria-like rash, arthralgia, myalgia, fatigue, and conjunctivitis)
- Lipid profiles; 2 to 3 months after initiation of therapy and periodically

**Dosing:**
- **Adult dose:** The recommended loading dose is 320 milligrams (mg) subcutaneously (SubQ) as 2 doses of 160 mg at 2 different sites. Followed by 160 mg SubQ once-weekly. Do not administer more than once weekly.
- **Pediatric dose:** The recommended loading dose is 4.4 milligrams/kilogram (mg/kg) subcutaneously (SubQ) (up to a maximum dose of 320 mg) as 1 or 2 injections with a maximum volume of 2 mL. If administered as 2 injections, then administer at 2 different sites. Followed by 2.2 mg/kg (up to a maximum dose of 160 mg) SubQ once weekly. Do not administer more than once weekly.

**Initial approval period:** 1 month

**Continued approval:** Up to 1 year based on physician documentation of disease stability and improvement.

**Berinert® - Human C1 Inhibitor**

**Candidates for acute attack treatment with human C1 inhibitor (Berinert®) should meet the following criteria:**

1. A diagnosis of Type I or Type II hereditary angioedema.
2. Prescriber must be an allergist.
3. Treatment of acute facial or abdominal facial attacks of HAE in adult or adolescent patients
4. Contraindications or inability to tolerate 17α-alkylated androgens (especially in females of child-bearing age), including hirsutism, menstrual irregularities, hepatic dysfunction, undiagnosed vaginal bleeding, porphyria, cardiac or renal disease, depression, muscle cramps and thrombosis. Patients with significant lipid abnormalities might also be considered.
5. Lack of response to currently available therapies such as 17α-alkylated androgens as evidenced by lack of symptom control.

**Reasons for non-coverage:**
- Routine prophylaxis against angioedema attacks in adolescent and adult patients with HAE
- Treatment for laryngeal attacks
- 12 years of age or younger

**Monitoring:**
- Symptomatic improvement
- Symptoms of hypersensitivity reaction during or after infusion
- Signs of thrombosis

**Consider long-term prophylaxis for patients with HAE who experience ≥one severe event per month or who are disabled more than five days per month OR if the patient has a history of previous airway compromise.**

Options include:
1. 17α-alkylated androgens (danazol, stanozolol if available, and oxandrolone): Generally

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<thead>
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<th>Drug</th>
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<tbody>
<tr>
<td></td>
<td>treatment of choice for long-term preventative treatment. Contraindications include pregnancy, breastfeeding, significantly impaired renal/ hepatic function, etc (refer to package insert for complete list). See Milan or Budapest Protocols for dosing recommendations. Use in children should be undertaken only with great caution.</td>
</tr>
<tr>
<td></td>
<td><strong>2. Antifibrinolytics (epsilon aminocaproic acid [Amicar]):</strong> Less effective than androgens. Often reserved for patients who do not tolerate or in whom anabolic androgens are contraindicated.</td>
</tr>
<tr>
<td></td>
<td><strong>3. Human C1 inhibitor (Cinryze®) replacement:</strong> May be necessary in patients in whom androgens are not effective (frequent angioedema attacks), not tolerated or contraindicated.</td>
</tr>
<tr>
<td></td>
<td>- Human C1 inhibitor prophylaxis is the safest prophylactic agent to use during pregnancy.</td>
</tr>
</tbody>
</table>

**Botulinum Toxins :**

**Preferred:**

**Botox® Type A Injections**

**Use of Botulinum Toxin for Chronic Migraine Headaches***

Patients must meet **ALL** of the criteria for coverage:

1. Migraine headaches for > 6 months and
2. Failure to improve with standard therapy**
3. Assessment and treatment of psychosomatic factors e.g stress, depression, and anxiety
4. Complete Neurological Evaluation
5. No contraindications e.g. infection in target muscle, neuromuscular disorder, or sensitivity to Botox A
6. Restricted to use by a neurologist trained to inject botulinum toxin

**Use of Botulinum Toxin for Cerebral Palsy***

Patient must meet **ALL** criteria for coverage:

1. Complete neurological evaluation
2. Failure to improve with standard therapy which includes dopaminergic medications (Sinemet®, Artane®), muscle relaxants (Lioresal®), and benzodiazepines (Valium).
3. Use limited to the muscles of the arms and legs.
4. No weakness, atrophy, or infection in the target muscle
5. No hypersensitivity to botulinum toxin or other component of the product
6. No evidence of pre-existing cardiovascular disease or dysphagia

**Use of Botulinum Toxin for Hyperhidrosis***

Patient must meet all criteria for coverage:

1. Receive recommendation from Dermatology after failed medical treatment with Drysol® and Robinul®.
2. Medical complications from hyperhidrosis including skin maceration with infection or dermatitis.
3. No history of neuromuscular disease.
4. No recent infection or malignancy in affected area.
5. No history of hyperthyroidism.

**Note:** The FDA has received reports of systemic adverse reactions including respiratory compromise and death following the use of Botulinum toxins types A (Botox®, Botox® Cosmetic) and B (Myobloc®) for both FDA-approved and unapproved uses. The reactions reported are suggestive of botulism, which occurs when Botulinum toxin spreads in the body beyond the site where it was injected. The most serious cases had outcomes that included hospitalization and death, and occurred mostly in children treated for cerebral palsy-associated limb spasticity. Consider these adverse events when reviewing requests.

*Consider Botulinum Toxin A (Botox®) before Botulinum Toxin B (Myobloc®)***

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**Note**: An adequate therapeutic trial of at least 3 classes of prophylactic medication (e.g. Beta Blockers, Antidepressants (tricyclics or SSRI’s), Periactin® (Cyproheptadine), Calcium Channel Blockers (Verapamil), Anticonvulsants (Valproic Acid, Topiramate), Triptans (e.g. Maxalt® to treat more than two migraines monthly) at the appropriate dose for 4 – 6 weeks each is required.

**Byetta® will be covered for current KP new start members who meet the following criteria:**

1. A diagnosis of type 2 diabetes mellitus **and**
2. Must be prescribed by Endocrinologist **and**
3. HgbA1c level 7%–9%, **and**
4. Failed to obtain adequate glycemic control on combination therapy with:
   a. Maximum tolerated doses of metformin (unless patient is not a candidate for metformin therapy) **and**
   b. Maximum tolerated doses of a sulfonylurea or a thiazolidinedione (unless the patient is not a candidate for either agent) **and**
   c. Maximum tolerated titration of insulin.
      i. Byetta may be initiated prior to insulin trial, in either of the following two conditions:
         1. Endocrinologist indicates hypoglycemia is uniquely undesirable, so unable to use insulin (e.g., in patients who have hazardous jobs) **OR**
         2. Endocrinologist indicates promotion of weight loss is a major consideration and this patient’s A1C is close to target (<8.0%)

**As outlined above, Byetta® is not a substitute for insulin in patients whose diabetes may benefit from insulin treatment**

**Reasons for non-coverage:**

- Type 1 diabetes mellitus
- Treatment of diabetic ketoacidosis
- Concurrent use with meglitinides (i.e. repaglinide, nateglinide), or alpha-glucosidase inhibitors (i.e. acarbose, miglitol)
- Pediatric patients (<18 years old)
- ESRD or severe renal impairment (CrCl < 30 mL/min)
- Patients with severe gastrointestinal disease (including gastroparesis)
- Diagnosis of pancreatitis, including hemorrhagic and necrotizing, prior to or after initiation of Byetta® (postmarketing cases, including fatalities, have been reported, therapy should be discontinued immediately).
- Prior history of a serious allergic reaction to Byetta® (i.e., anaphylaxis, angioedema, Stevens-Johnson syndrome, etc.)

**Use caution in the following patients:**

- Pregnant/nursing women (Pregnancy Category C)
- Concomitant use with pharmacologic agents known to affect renal function/hydration status/ and or patients experiencing nausea/vomiting/diarrhea with or without dehydration (i.e., ace-inhibitors, NSAIDS, diuretics)
- Concomitant use with a sulfonylurea (hypoglycemia)
- Concomitant use with warfarin (increased INR, sometimes with bleeding)
- Concomitant use with oral medications that require rapid gastric gastrointestinal absorption (Byetta® slows gastric emptying)
- Concomitant use with oral medications dependent on threshold concentrations for efficacy (i.e., contraceptives, antibiotics) – Patients should take drugs 1 hour prior to Byetta® injection

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<tr>
<td>• Concomitant use with medications requiring administration with food – Patients should take drug to be administered with a meal or snack when Byetta® is not being administered.</td>
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</tbody>
</table>

**Monitoring:**
- Renal function prior to initiation of Byetta® and periodically afterwards
- Hgba1c level
- Fasting and postprandial glucose
- Signs/symptoms of acute pancreatitis including unexplained, persistent, severe abdominal pain with or without vomiting

**Initial approval period:** 6 months

**Continued approval:** 1 year, based on review of compliance to therapy and documented improved glycemic control as evidenced by A1c lowering from pretreatment level to a1c goal <8%

**Byetta® will be covered for new members to KP already taking Byetta® who meet the following criteria:**

1. A diagnosis of type 2 diabetes mellitus **and**
2. Hgba1c level <8%

***Note:** New members to KP currently taking Byetta® upon enrollment whose diabetes is not controlled with Byetta® (i.e. – A1c> 8%) will need to meet the general criteria for KP new start members.

**Reasons for non-coverage:**
- Type 1 diabetes mellitus
- Treatment of diabetic ketoacidosis
- Concurrent use with meglitinides (i.e. repaglinide, nateglinide), or alpha-glucosidase inhibitors (i.e. acarbose, miglitol)
- Pediatric patients (<18 years old)
- ESRD or severe renal impairment (CrCl < 30 mL/min)
- Patients with severe gastrointestinal disease (including gastroparesis)
- Diagnosis of pancreatitis, including hemorrhagic and necrotizing, prior to or after initiation of Byetta® (postmarketing cases, including fatalities, have been reported, therapy should be discontinued immediately).
- Prior history of a serious allergic reaction to Byetta® (i.e., anaphylaxis, angioedema, Stevens-Johnson syndrome, etc.)

**Use caution in the following patients:**
- Pregnant/nursing women (Pregnancy Category C)
- Concomitant use with pharmacologic agents known to affect renal function/hydration status/and or patients experiencing nausea/vomiting/diarrhea with or without dehydration (i.e., ace-inhibitors, NSAIDS, diuretics)
- Concomitant use with a sulfonylurea (hypoglycemia)
- Concomitant use with warfarin (increased INR, sometimes with bleeding)
- Concomitant use with oral medications that require rapid gastric gastrointestinal absorption (Byetta® slows gastric emptying)
- Concomitant use with oral medications dependent on threshold concentrations for efficacy (i.e., contraceptives, antibiotics) – Patients should take drugs 1 hour prior to Byetta® injection
- Concomitant use with medications requiring administration with food – Patients should take drug to be administered with a meal or snack when Byetta® is not being administered.

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| **Cinryze®**<br>- Human C1 Inhibitor solution | **Candidates for prophylaxis with human C1 inhibitor should meet the following criteria:**<br><br>1. A diagnosis of Type I or Type II hereditary angioedema.<br>2. Prescriber must be an allergist.<br>3. Contraindications or inability to tolerate 17α-alkylated androgens (especially in females of childbearing age), including hirsutism, menstrual irregularities, hepatic dysfunction, undiagnosed vaginal bleeding, porphyria, cardiac or renal disease, depression, muscle cramps and thrombosis. Patients with significant lipid abnormalities might also be considered.<br>4. Lack of response to currently available therapies such as 17α-alkylated androgens as evidenced by lack of symptom control.<br>5. Special circumstances may include use in pregnant females with hereditary angioedema (HAE). [Note: Studies in pregnant women have not been conducted and the effects on the fetus or on reproductive capacity are not definitively known. At this time, Cinryze® should be given to a pregnant woman only if clearly needed.]

**Reasons for non-coverage:**<br><br>• Treatment of angioedema acute attacks in adult and adolescent patients with HAE<br>• Under 9 years of age

**Monitoring:**<br><br>• Reduction in number, severity, and duration of swelling attacks<br>• Symptoms of hypersensitivity during or after infusion<br>• Signs of thrombosis

**Short-term Prophylaxis:**<br><br>1. **Minor Procedures:** Use of human C1 inhibitor is not required before minor manipulations if human C1 inhibitor is immediately available. As an alternative, danazol can be used in appropriate patients (starting at least 7 days before the procedure).<br>2. **Major Procedures or Intubation:** Consider the use of human C1 inhibitor for short-term prophylaxis to prevent attacks of angioedema when a patient with HAE has a planned exposure to a situation likely to trigger an attack, such as substantial dental work, invasive medical procedures, and surgical procedures.<br>   a. Doses of 500-1,500 units intravenously given one hour before the provoking event have been studied.<br>   b. Two doses of human C1 inhibitor should be available.<br>   c. Although there is limited data in the United States regarding the use of human C1 inhibitor in pregnancy, a set of international consensus guidelines state that human C1 inhibitor is the safest prophylactic agent to use during pregnancy.

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**Drug**

<table>
<thead>
<tr>
<th>Prior authorization criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term Prophylaxis: For patients with HAE who experience ≥ one severe event per month or who are disabled more than five days per month OR if the patient has a history of previous airway compromise, consider long-term prophylaxis. Options include:</td>
</tr>
<tr>
<td>1. <strong>17α-alkylated androgens (danazol, stanozolol if available, and oxandrolone):</strong> Generally treatment of choice for long-term preventative treatment. Contraindications include pregnancy, breastfeeding, significantly impaired renal/ hepatic function, etc (refer to package insert for complete list). See Milan or Budapest Protocols for dosing recommendations. Use in children should be undertaken only with great caution.</td>
</tr>
<tr>
<td>2. <strong>Antifibrinolytics (epsilon aminocaproic acid [Amicar®]):</strong> Less effective than androgens. Often reserved for patients who do not tolerate or in whom anabolic androgens are contraindicated.</td>
</tr>
<tr>
<td>3. <strong>Human C1 inhibitor replacement:</strong> May be necessary in patients in whom anrogens are not effective (frequent angioedema attacks), not tolerated or contraindicated.</td>
</tr>
<tr>
<td>a. Human C1 inhibitor prophylaxis is the safest prophylactic agent to use during pregnancy.</td>
</tr>
<tr>
<td><strong>Gilneya™ - Fingolimod</strong></td>
</tr>
</tbody>
</table>

**Guidelines for the Use of Fingolimod (Gilneya™) in the Treatment of Multiple Sclerosis**

**Inclusion Criteria**

1. Fingolimod (Gilneya™) should be reserved for treatment of relapsing forms of multiple sclerosis (MS).
   a. Considering potential risks from fingolimod therapy:
      i. Fingolimod should usually be reserved for use in patients who have had an inadequate response to other MS therapies (ie. Avonex®, Extavia® or Rebif®, and Copaxone®) or patients who are not able to tolerate other MS therapies.
      ii. Patients who are stable and well-controlled on other MS therapies should not be changed to fingolimod.
   b. Based upon evidence available at the time when these guidelines are being developed (02/2010):
      i. Use in primary progressive MS is not supported by clinical trial evidence.
      ii. Efficacy or safety for use of fingolimod beyond two years is not supported by clinical trial evidence.
2. Due to the possibility of increased risk of infections:
   a. Fingolimod should be used as monotherapy and not in combination with Avonex® (interferon beta-1a), other beta-interferons (Betaseron® or Rebif®, or glatiramer acetate (Copaxone®).
   b. Fingolimod should usually not be used in patients who are receiving chronic immunosuppressant therapy, who are receiving other immunomodulatory drugs, or are significantly immunocompromised for any reason.

**Dosage and Administration**

- Fingolimod is dosed at 0.5 mg orally once daily, with or without food. Doses higher than 0.5 mg daily are associated with minimal benefit and a higher risk of adverse events.
- All patients should be observed for six hours after the first dose is given, monitoring for signs and symptoms of bradycardia.

**Monitoring**

- All patients should be observed for six hours after the first dose is given, monitoring for signs and symptoms of bradycardia.
  o Patients at increased risk for bradycardia or bradyarrhythmia should have a baseline electrocardiogram (ECG) performed if an ECG has not been done in the previous 6 months.
  o Risk for development of bradycardia or heart block is considered to be increased in patient concurrently treated with beta blockers, calcium channel blockers, or antiarrhythmics (Class Ia or Class III) or in patients with “a low heart rate, history of syncope, sick sinus

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### Drug Prior authorization criteria

- Syndrome, 2nd degree or higher conduction block, ischemic heart disease, or congestive heart failure* according to Gilenya™ prescribing information. (Note: Class Ia antiarrhythmics include quinidine, procainamide, and disopyramide. Class III antiarrhythmics include amiodarone and sotalol.)
  - All Patients should have the following laboratory values completed within 6 months prior to initiating therapy: complete blood count (CBC), liver transaminase, and serum bilirubin
    - Patients should be monitored for any new signs or symptoms which might suggest PML. At the first such sign or symptom of PML, fingolimod treatment should be withheld immediately and diagnostic measures should be undertaken.
  - All Patients should have documented immunity to varicella zoster virus (chicken pox).
  - All patients should have a baseline ophthalmologic exam prior to initiation of fingolimod and at 3-4 months after treatment initiation.
  - For women of childbearing potential, patient agrees to use a form of contraception to prevent pregnancy during fingolimod treatment and for two months after discontinuation of fingolimod.

### Growth hormones:

- **Preferred:**
  - Omnitrope® cartridges for use in pen

- **Non-preferred:**
  - Gentropin®
  - Humatrope®
  - Norditropin®
  - Nutropin AQ®
  - Saizen®
  - Serostim®
  - Zortive®

**Note:** For all first time approvals, Omnitrope® is the first-line agent when growth hormone is indicated for pediatric growth hormone deficiency. Omnitrope® should be tried before approval is granted for other growth hormone agents.

**Criteria:**

1. A diagnosis Turner’s Syndrome that is confirmed by abnormal karyotype in female children greater than five years of age with appropriate timing and use of estrogen therapy; OR
2. Patients who have a diagnosis of classical growth hormone deficiency and who meet all the criteria below:
   - a. Height is consistently two standards deviation below mean for like age, pubertal maturation and gender over at least one year of serial measurements; **and**
   - b. Growth velocity that is less than the tenth percentile of normal for like age, pubertal maturation and gender over at least one year of serial measurements; **and**
   - c. Two provocative tests for growth hormones secretion with neither having a Peak > 10 ng/ml; OR

**Bone age determination within six months of the request, reflecting more than two standards deviations below that for like age and gender; with (c.) AND either (a.) or (b.), OR**

3. Pediatric patient with a diagnosis of ablation of the pituitary by surgery, tumor, or radiation, or infantile panhypopituitarism experiencing uncontrolled hypoglycemia while on adequate corticoid replacement.

4. Children with Prader-Willi Syndrome confirmed by appropriate genetic testing WITHOUT therapeutic contraindications: severe obesity or respiratory impairment.

5. Pre-pubertal children with chronic renal insufficiency, before renal transplant, providing: nutritional status optimized; metabolic abnormalities optimized; and steroid therapy minimized.

6. Patients who are small for gestational age and meet all the criteria below:
   - a. Patient is 2 years of age or older
   - b. Child was born small for gestational age, defined as birth weight and/or length at least two standard deviations below the mean for gestational age.
   - c. Child fails to manifest catch-up growth by two years of age, defined as height at least two standard deviations below the mean for age and sex.

**Note:** Bone age reflects the potential for the response to GH.

Height standard deviation score for chronologic age increase throughout all treatment years, but for bone age (BA) did not change significantly. Human GH treatment cannot make up a deficit in height prognosis already present at diagnosis, but prevents further loss of stature, which is why early diagnosis is important so that GH therapy can be instituted before significant height for BA deficit has occurred. (J

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**Discontinuation of treatment:**
Treatment with growth hormone will be discontinued if one or more of the following occurs:

1. Height velocity is not at or above the tenth percentile for like age, pubertal maturation and gender after one year of treatment (i.e. the treatment is not effective in achieving a significant increase in stature after one year of treatment).
   - a. Height velocity must be obtained by at least two measurements over a one-year period on stable HGH dosage;
2. Bone age is greater than or equal to 14 years of age for females and 16 years of age for males; or
3. The patient achieves a height that is within the 3rd percentile for normal adult height for the same sex

**Note:** Non-preferred growth hormone is only to be used when preferred (Omnitrope®) growth hormone has failed

<table>
<thead>
<tr>
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</tr>
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</table>
| Hyaluronic Acid Injection: | **Criteria for Use:** (bullet points below are all inclusive unless otherwise noted)  
1. Patient has clinically documented osteoarthritis of the knees (American College of Rheumatology criteria) confirmed by history, exam, x-ray, and synovial fluid analysis, and requested for use in knee
2. Failed or intolerant to nonpharmacological therapies (physical therapy, ice, weight loss, etc.)
3. Documented inadequate control of pain or intolerance to an adequate trial of acetaminophen (4Grams/day), NSAIDs, intraarticular corticosteroid injections, and other non-narcotic or narcotic analgesics
4. Efficacy of intra-articular corticosteroid injection lasting less than 6-8 weeks |
| Preferred: Supartz® (P) | Criteria for Continuation of Therapy:  
There are no data on repeated courses of therapy for Euflexxa® and Supartz®; there is no evidence of increased adverse drug events in repeated courses of therapy for Hyalgan®, Synvisc®, and Orthovisc® when separated by at least six months.  
**Note:** Supartz® is the preferred medication. Synvisc® may be approved if Supartz® is deemed ineffective or the patient has intolerance to Supartz®. |
| Non-preferred: Synvisc® (2nd Line) | Euflexxa® (N)  
Hyalgan® (N)  
Synvisc-One® (N)  
**Note:** Supartz® is the preferred medication. Synvisc® may be approved if Supartz® is deemed ineffective or the patient has intolerance to Supartz®.  

Ilaris® - Canakinumab  
A diagnosis of cryopyrin-associated periodic syndromes (CAPS) and all of the following criteria:  
1. Patient has documented laboratory evidence of a genetic mutation in the Cold-Induced Auto-inflammatory Syndrome 1 (CIAS1- sometimes referred to as the NLRP3).  
2. There is clinical documentation that the patient is experiencing classic symptoms of CAPS in either criteria below:  
   a. Familial Cold Auto-Inflammatory Syndrome (FCAS): recurrent episodes of rash, fever/chills, and joint pain following exposure to mild cold environment. (e.g. cool breeze, air conditioning) Symptoms generally last for up to 24 hours.  
   b. Muckle-Wells Syndrome (MWS): chronic fever and rash sometimes exacerbated by generalized cold exposure. Episodes can last up to 2-3 days.  

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<tbody>
<tr>
<td></td>
<td>3. There is clinical documentation of significant functional impairment leading to limitations of activities of daily living (ADLs).</td>
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<td></td>
<td>4. Failed, intolerant, or allergic to either of the following:</td>
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<tr>
<td></td>
<td>a. Prednisone</td>
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<td></td>
<td>b. Anakinra (Kineret®) injection</td>
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<tr>
<td><strong>Reasons for non-coverage:</strong></td>
<td>• Concurrent use of immunosuppressive therapy</td>
</tr>
<tr>
<td></td>
<td>• Chronic, active, or recurrent infections</td>
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<tr>
<td></td>
<td>• Untreated latent tuberculosis</td>
</tr>
<tr>
<td></td>
<td>• Under 4 years of age</td>
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<tr>
<td><strong>Caution:</strong></td>
<td>• Concurrent use with live vaccines not recommended</td>
</tr>
<tr>
<td></td>
<td>• Increased risk of malignancies may occur</td>
</tr>
<tr>
<td></td>
<td>• Infections, serious (mostly upper respiratory tract) have been reported; discontinue if serious infection develops</td>
</tr>
<tr>
<td><strong>Monitoring:</strong></td>
<td>• Serum C reactive protein and serum amyloid A levels periodically</td>
</tr>
<tr>
<td></td>
<td>• Improvement in signs and symptoms of cryopyrin-associated periodic syndromes (ie, fever, urticaria-like rash, arthralgia, myalgia, fatigue, and conjunctivitis)</td>
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<tr>
<td></td>
<td>• Latent tuberculosis test prior to initiating therapy</td>
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<tr>
<td><strong>Dosing:</strong></td>
<td>• The recommended dose of Ilaris® is 150 mg for CAPS patients with body weight greater than 40kg.</td>
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<td>• For CAPS patients with body weight between 15 kg and 40 kg, the recommended dose is 2mg/kg.</td>
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<td>• For children 15 to 40 kg with an inadequate response, the dose can be increased to 3mg/kg.</td>
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<td></td>
<td>• Ilaris is administered every 8 weeks as a single dose via subcutaneous injection.</td>
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<tr>
<td><strong>Initial approval period:</strong></td>
<td>1 month</td>
</tr>
<tr>
<td><strong>Continued approval:</strong></td>
<td>Up to 1 year based on physician documentation of disease stability and improvement.</td>
</tr>
<tr>
<td><strong>Januvia™/-Sitagliptin</strong></td>
<td>Januvia™/ Janumet™ will be covered for current KP new start members who meet the following criteria:</td>
</tr>
<tr>
<td></td>
<td>1. A diagnosis of type 2 diabetes mellitus and</td>
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<tr>
<td></td>
<td>2. Must be prescribed by an Endocrinologist and</td>
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<tr>
<td></td>
<td>3. HgbA1c level 7%–9%, and</td>
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<td></td>
<td>4. Failed to obtain adequate glycemic control on combination therapy with:</td>
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<tr>
<td></td>
<td>a. Maximum tolerated doses of metformin monotherapy (unless patient is not a candidate for metformin therapy) and</td>
</tr>
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<td></td>
<td>b. Maximum tolerated doses of a sulfonylurea or a thiazolidinedione (unless the patient is not a candidate for either agent) and</td>
</tr>
<tr>
<td></td>
<td>c. Maximum tolerated titration of insulin.</td>
</tr>
<tr>
<td></td>
<td>i. Januvia™/Janumet™ may be initiated prior to insulin trial, in either of the following two conditions:</td>
</tr>
<tr>
<td></td>
<td>1. Endocrinologist indicates hypoglycemia is uniquely undesirable, so</td>
</tr>
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**Drug** | **Prior authorization criteria**
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| | unable to use insulin (e.g., in patients who have hazardous jobs) OR 2. Endocrinologist indicates promotion of weight loss is a major consideration and this patient's A1C is close to target (< 8.0%) |

**As outlined above, Januvia™/Janumet™ are not substitutes for insulin in patients whose diabetes control may benefit from insulin therapy**

**Reasons for non-coverage:**
- Type 1 diabetes mellitus
- Treatment of diabetic ketoacidosis
- Concurrent use with insulin
- Pediatric patients (<18 years old)
- Prior history of a serious allergic reaction to sitagliptin (i.e., anaphylaxis, angioedema, Stevens-Johnson syndrome, etc.)
- Severe hepatic insufficiency (Child-Pugh score >9)

**Use caution in the following patients:**
- ESRD requiring hemodialysis or peritoneal dialysis
- Pregnant/nursing women
- Concomitant use with a sulfonylurea due to increased risk of hypoglycemia
- History of pancreatitis

**Monitoring:**
- Renal function prior to initiation of Januvia™/Janumet™ and periodically afterwards
- HgbA1c level
- Serum glucose level
- Development of pancreatitis after initiation or dose increases

**Initial approval period:** 6 months

**Continued approval:** 1 year, based on review of compliance to therapy and documented improved glycemic control as evidenced by A1c lowering from pretreatment level to a1c goal <8%

**Januvia™/Janumet™ will be covered for new members to KP already taking Januvia™/Janumet™ who meet the following criteria:**

1. A diagnosis of type 2 diabetes mellitus and 2. HgbA1c level <8%

*****Note: New members to KP currently taking Januvia™/Janumet™ upon enrollment whose diabetes is not controlled with Januvia™/Janumet™ (i.e., A1c > 8%) will need to meet the general criteria for KP new start members.**

**Reasons for non-coverage:**
- Type 1 diabetes mellitus
- Treatment of diabetic ketoacidosis
- Concurrent use with insulin
- Pediatric patients (<18 years old)
- Prior history of a serious allergic reaction to sitagliptin (i.e., anaphylaxis, angioedema, Stevens-Johnson syndrome, etc.)
- Severe hepatic insufficiency (Child-Pugh score >9)

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<td><strong>Initial approval period:</strong></td>
<td>6 months</td>
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<td><strong>Continued approval:</strong></td>
<td>1 year, based on review of compliance to therapy and documented improved glycemic control as evidenced by A1c lowering from pretreatment level to a1c goal &lt;8%</td>
</tr>
</tbody>
</table>

**Kalbitor® - Ecallantide**

**Candidates for acute attack treatment with encallantide should meet the following criteria:**

1. A diagnosis of Type I or Type II hereditary angioedema.
2. Prescriber must be an allergist.
3. Contraindications or inability to tolerate 17α-alkylated androgens (especially in females of childbearing age), including hirsutism, menstrual irregularities, hepatic dysfunction, undiagnosed vaginal bleeding, porphyria, cardiac or renal disease, depression, muscle cramps and thrombosis. Patients with significant lipid abnormalities might also be considered.
4. Lack of response to currently available therapies such as 17α-alkylated androgens as evidenced by lack of symptom control.
5. Lack of response to Berinert®

**Reasons for non-coverage:**

- Routine prophylaxis against angioedema attacks in adolescent and adult patients with HAE
- Under 16 years of age

**Monitoring:**

- Symptomatic improvement
- Symptoms of hypersensitivity reaction during or after infusion

**Consider long-term prophylaxis for patients with HAE who experience ≥ one severe event per month or who are disabled more than five days per month OR if the patient has a history of previous airway compromise.**

**Options include:**

1. 17α-alkylated androgens (danazol, stanozolol if available, and oxandrolone): Generally treatment of choice for long-term preventative treatment. Contraindications include pregnancy, breastfeeding, significantly impaired renal/hepatic function, etc (refer to package insert for complete list). See Milan or Budapest Protocols for dosing recommendations. Use in children should be undertaken only with great caution.
2. Antifibrinolytics (epsilon aminocaproic acid [Amicar]): Less effective than androgens. Often reserved for patients who do not tolerate or in whom anabolic androgens are contraindicated.
3. Human C1 inhibitor (Cinryze®) replacement: May be necessary in patients in whom androgens are not effective (frequent angioedema attacks), not tolerated or contraindicated.
   a. Human C1 inhibitor prophylaxis is the safest prophylactic agent to use during

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<tr>
<td><em>Kombiglyze™ XR</em>&lt;br&gt;-Saxagliptin and metformin extended-release</td>
<td>See Onglyza™ and Kombiglyze™ XR below.</td>
</tr>
</tbody>
</table>
| *Kuvan™*<br>- Sapropterin tablets | Patients must meet all criteria for coverage for use of Kuvan™ for Phenylketonuria:  
1. Absence of the following medications:  
a. Medications known to inhibit folate metabolism (eg, methotrexate)  
b. Nitric oxide-mediated vasorelaxation medications (eg sildenafil, vardenafil, tadalafil)  
c. Levodopa  
2. Currently following a phenylalanine restricted diet |
| *Mozobil™*<br>- Plerixafor injection | **Mozobil™ will be covered in members over the age of 18 years who meet the following criteria:**  
1. A diagnosis of non-Hodgkin’s lymphoma or multiple myeloma  
2. Patient also prescribed a granulocyte-colony stimulating factor  
3. Failed mobilization with standard doses of granulocyte-colony stimulating factor alone (Mozobil™ is not considered first-line therapy)  
4. Decreasing CD 34+ count  

**Mozobil™ will not be covered for members in the following categories:**  
1. Patients with leukemia  
2. Pediatric patients  

**Dosing and Administration:**  
- 0.24 mg/kg (actual body weight) subQ approximately 11 hr prior to initiation of apheresis for up to 4 consecutive days; administer granulocyte-colony stimulating factor (G-CSF) 10 mcg/kg via subQ bolus or continuous infusion once daily in the morning for 4 days prior to the first evening dose of plerixafor, and on each day prior to apheresis; **MAX dose of 40 mg/day**  
- Mozobil™ is administered by subcutaneous injection.  

**Monitoring:**  
- Caution should be used in the following groups  
  o Patient with moderate/severe renal impairment (CrCl<50mL/min)  
  o Pregnant or nursing mothers  
- Monitor white blood cell counts during plerixafor use. Exercise clinical judgment when administering plerixafor to patients with peripheral blood neutrophil counts higher than 50,000/mcL  
- Monitor platelet counts in all patients who receive plerixafor and then undergo apheresis.  
- Monitor renal function  
- Peripheral blood CD 34+ cell count (cells/mcL)  
- Signs and symptoms of splenic enlargement (left upper abdominal pain and/or scapular or shoulder pain) and possible rupture  

**Initial approval period:** Approved for up to 4 doses (1 dose per day/) for up to 4 consecutive days  

**Note:** Transplant specialist at Northside Hospital Blood and Bone Marrow unit states Mozobil™ has been used successfully for Hodgkin’s lymphoma, evidence review is pending.  

*Onglyza™*<br>-Saxagliptin | **Onglyza™/Kombiglyze™ XR will be covered for current KP new start members who meet the following criteria:**  

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</table>
| **Kombiglyze™ XR**<br>-Saxagliptin and metformin extended-release | 1. A diagnosis of type 2 diabetes mellitus and<br>2. Must be prescribed by an endocrinologist and<br>3. HbA1c level 7%–9%, and<br>4. Failed to obtain adequate glycemic control on combination therapy with:<br>   a. Maximum tolerated doses of metformin monotherapy (unless patient is not a candidate for metformin therapy) and<br>   b. Maximum tolerated doses of a sulfonylurea or a thiazolidinedione (unless the patient is not a candidate for either agent) and<br>   c. Maximum tolerated titration of insulin.<br>      i. Onglyza™/Kombiglyze™ XR may be initiated prior to insulin trial, in either of the following two conditions:<br>         1. Endocrinologist indicates hypoglycemia is uniquely undesirable, so unable to use insulin (e.g., in patients who have hazardous jobs) OR<br         2. Endocrinologist indicates promotion of weight loss is a major consideration and this patient's A1C is close to target (<_8.0%)<br>5. Unable to tolerate or inadequate response to Januvia™<br>

**As outlined above, Onglyza™/Kombiglyze™ XR is not a substitute for insulin in patients whose diabetes control may benefit from insulin therapy**

**Reasons for non-coverage:**<br>• Type 1 diabetes mellitus<br>• Treatment of diabetic ketoacidosis<br>• Concurrent use with insulin<br>• Pediatric patients (<18 years old)<br>• Prior history of a serious allergic reaction to saxagliptin (i.e. anaphylaxis, angioedema, Stevens-Johnson syndrome, etc.)

**Use caution in the following patients:**<br>• Renal impairment, moderate, severe, or end-stage renal disease requiring hemodialysis (CrCl of 50 mL/min or less); dosage adjustment may be required; monitoring recommended<br>• Pregnant/nursing women<br>• Concomitant use with a sulfonylurea due to increased risk of hypoglycemia

**Monitoring:**<br>• Renal function prior to initiation of Onglyza™/Kombiglyze™ XR and periodically afterwards<br>• HbA1c level<br>• Serum glucose level

**Initial approval period:** 6 months

**Continued approval:** 1 year, based on review of compliance to therapy and documented improved glycemic control as evidenced by A1C lowering from pretreatment level to a1c goal <8%

**Onglyza™/Kombiglyze™ XR will be covered for new members to KP already taking Onglyza™/Kombiglyze™ XR who meet the following criteria:**

1. A diagnosis of type 2 diabetes mellitus<br>2. HbA1c level <8%,
3. Unable to tolerate or inadequate response to Januvia™
***Note: New members to KP currently taking Onglyza™/Kombiglyze™ XR upon enrollment whose diabetes is not controlled with Onglyza™/Kombiglyze™ XR (i.e. – A1c> 8%) will need to meet the general criteria for KP new start members.

Reasons for non-coverage:
- Type 1 diabetes mellitus
- Treatment of diabetic ketoacidosis
- Concurrent use of insulin
- Pediatric patients (<18 years old)
- Prior history of a serious allergic reaction to saxagliptin (i.e. anaphylaxis, angioedema, Stevens-Johnson syndrome, etc.)

Use caution in the following patients:
- Renal impairment, moderate, severe, or end-stage renal disease requiring hemodialysis (CrCl of 50 mL/min or less); dosage adjustment may be required; monitoring recommended
- Pregnant/nursing women
- Concomitant use with a sulfonylurea due to increased risk of hypoglycemia

Monitoring:
- Renal function prior to initiation of Onglyza™/Kombiglyze™ XR and periodically afterwards
- HgbA1c level
- Serum glucose level

Initial approval period: 6 months

Continued approval: 1 year, based on review of compliance to therapy and documented improved glycemic control as evidenced by A1c lowering from pretreatment level to a1c goal <8%

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**Pradaxa® - Dabigatran**

**Inclusion Criteria**

All of the following must apply:
- Diagnosis of irreversible atrial fibrillation
- CHADS2 Score ≥ 1, identified as an anticoagulation candidate (ASA not an option) AND
  - Uninterrupted warfarin therapy has been tried for at least 22 weeks
  - Patient time in therapeutic range (TTR) < 54%
- CHADS2 score ≥ 2 AND
  - Uninterrupted warfarin therapy has been tried for at least 22 weeks
  - Patient TTR < 54%

**Calculation of CHADS2 Score**

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>H</td>
<td>Hypertension*</td>
</tr>
<tr>
<td>A</td>
<td>Age ≥ 75 years</td>
</tr>
<tr>
<td>D</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>S2</td>
<td>Prior Stroke or TIA</td>
</tr>
</tbody>
</table>

* Hypertension: blood pressure consistently above 140/90 mmHg or treated hypertension on medication

**Exclusion Criteria**

Excluded if any of the following are present:
- CHADS2 Score = 0
- Patient TTR ≥ 67%
Because the Medicare Part D formulary does not allow prior authorization or criteria restrictions on medications, this document applies to the Commercial, Triple Tier, and Multi-Choice formularies.

**Drug Prior authorization criteria**

- History of heart valve disorder
- Severe, disabling stroke within the previous 6 months
- Stroke within the previous 14 days
- At an increased risk for bleeding
- CrCl < 30 mL/min
- Active liver disease
- Active infective endocarditis
- Anemia or thrombocytopenia
- Malignancy
- Reversible causes of atrial fibrillation
- Pregnancy
- Women of childbearing potential who refuse to use a form of contraception
- Contraindication to warfarin treatment
- Anemia or Thrombocytopenia
- Need for anticoagulant treatment of disorders other than atrial fibrillation

CHA DS score or CHAD S2 score is a clinical prediction rule for estimating the risk of stroke in patients with non-rheumatic atrial fibrillation (AF), a common and serious heart arrhythmia associated with thromboembolic stroke. It is used to determine whether or not treatment is required with anticoagulation therapy or antiplatelet therapy,[1] since AF can cause stasis of blood in the upper heart chambers, leading to the formation of a mural thrombus that can dislodge into the blood flow, reach the brain, cut off blood supply to the brain, and cause a stroke. A high CHAD S2 score corresponds to a greater risk of stroke, while a low CHAD S2 score corresponds to a lower risk of stroke. The CHAD S2 score was validated by a study of nonrheumatic atrial fibrillation patients aged 65 to 95 who were not prescribed the anticoagulant warfarin.[2]

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**Provenge® - Sipuleucel-T**

**Guidelines for the Use of Provenge® in the Treatment of Adneocarcinoma of the Prostate**

Prescriber should be enrolled in the Dendreon ON Call Program: (877) 556-3737. Representatives can be reached at (877) 336-3736 to answer general questions, Monday-Friday from 8:00a-8:00pm (ET) and 24 hours per day in the event of a product related health emergency

**Inclusion Criteria (ALL of the following must apply):**

1. Histological documentation of adenocarcinoma of the prostate without evidence of neuroendocrine or small cell features
2. Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1
3. Must have Progressive androgen independent prostate cancer.
   a. Current (i.e., within past 6 months) and continuing evidence of disease progression while on medical castration or after surgical castration demonstrated by:
      i. PSA progression OR
      ii. progression of measurable disease OR
      iii. progression of non-measurable disease
4. Must have metastatic disease as evidenced by:
   a. soft tissue metastases on CT of abdomen/pelvis within 6 months
   b. bony metastases on bone scan within 6 months
   c. no known lung, liver, or brain metastases, malignant pleural effusions, or malignant ascites
5. Life expectancy of at least 6 months
6. No Anti-androgen withdrawal response; defined as a > 25% drop in PSA following discontinuation of a non-steroidal anti-androgen
   a. Patients are eligible once PSA rises above the nadir observed after anti-androgen discontinuation.
   b. For verification, PSA should be obtained shortly prior to anti-androgen discontinuation.

Subsequently, a PSA must be obtained > 4 weeks (flutamide) or > 6 weeks (bicalutamide, nilutamide) following anti-androgen discontinuation and prior to Provenge.

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<table>
<thead>
<tr>
<th>Drug</th>
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</tr>
</thead>
</table>
| 7. | Testosterone < 50 ng/dL achieved via medical or surgical castration  
   a. Medical Castration (Lupron or Zoladex) has occurred and has been continued for at least 3 months OR  
   b. Surgical (orchiectomy) castration must have occurred at least 3 months prior |
| 8. | No known pathologic long-bone fractures, imminent pathologic long-bone fracture (cortical erosion on radiography > 50%) or spinal cord compression. |
| 9. | No requirement for systemic immunosuppressive therapy (e.g. corticosteroids) for any reason |
| 10. | None of the following may occur within 28 days prior to Provenge®:  
   a. Surgery  
   b. External beam radiation therapy  
   c. Treatment with chemotherapy  
   d. Treatment with other investigational products  
   e. Treatment with other systemic therapy for prostate cancer (except for medication castration with Lupron® or Zoladex®)  
   f. Treatment with 5-α-reductase inhibitors (e.g., finasteride [Proscar®], dutasteride [Avodart®])  
   g. Treatment with high dose calcitriol [1,25(OH)2VitD] (i.e., > 0.5 µg/day)  
   h. Treatment with ketoconazole  
   i. Treatment with PC-SPES (or PC-SPEC) or Saw Palmetto  
   j. Treatment with megestrol acetate (Megace®), diethylstilbesterol (DES), or cyproterone acetate  
   k. Treatment with non-steroidal antiandrogens (e.g., flutamide, nilutamide or bicalutamide)  
   l. No change (initiation or discontinuation) in bisphosphonate therapy  
   m. No systemic corticosteroids  
   i. Use of inhaled, intranasal, intra-articular, and topical steroids is acceptable, as is a short course (i.e., < 1 day) of corticosteroids to prevent a reaction to the IV contrast used for CT scans  
   n. No use of narcotics for cancer related pain  
   o. Average weekly pain score of ≥ 4 (measured by the Visual Analogue Scale (VAS)) 14 days prior to treatment initiation |
| 11. | The following lab values must be demonstrated prior to therapy initiation:  
   a. White blood cell (WBC) > 2,500 cells/µL  
   b. Neutrophils > 1,000 cells/µL  
   c. Platelets > 100,000 cells/µL  
   d. Hemoglobin (HgB) > 9.0 g/dL  
   e. Creatinine < 2.0 mg/dL  
   f. Total Bilirubin < 2 x upper limit of normal (ULN)  
   g. Aspartate transferase (AST) < 2.5 x ULN  
   h. Alanine transferase (ALT) < 2.5 x ULN  
   i. Serum PSA > 5.0 ng/mL |

Notes:

a. **PSA Progression**: Two consecutive PSA values, at least 14 days apart, each > 5.0 ng/mL and > 50% above the minimum PSA observed during castration therapy or above the pre-treatment value if there was no response.

b. **Measurable disease**: > 50% increase in the sum of the cross products of all measurable lesions or the development of any new lesions. The change will be measured against the best response to castration therapy or against the pre-castration measurements if there was no response.

c. **Non-measurable disease**:  
   o **Soft tissue disease**: The appearance of 1 or more new lesions, and/or unequivocal worsening of non measurable disease when compared to imaging

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<table>
<thead>
<tr>
<th>Drug</th>
<th>Prior authorization criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sabril® - Vigabatrin</td>
<td><strong>Criteria For Use:</strong> A diagnosis of infantile spasms or refractory complex partial seizures and must meet all criteria under the appropriate diagnosis below.</td>
</tr>
<tr>
<td></td>
<td><strong>Infantile Spasms</strong></td>
</tr>
<tr>
<td></td>
<td>1. Prescribed by a neurologist</td>
</tr>
<tr>
<td></td>
<td>2. Between the ages of 1 month to 2 years old.</td>
</tr>
<tr>
<td></td>
<td>3. Potential benefit must outweigh the potential risk of vision loss.</td>
</tr>
<tr>
<td></td>
<td>4. Must have vision tested to the extent possible depending on the age of the child at baseline before beginning treatment and at least every 3 months.</td>
</tr>
<tr>
<td></td>
<td><strong>Refractory Complex Partial Seizures</strong></td>
</tr>
<tr>
<td></td>
<td>1. Prescribed by a neurologist.</td>
</tr>
<tr>
<td></td>
<td>2. 18 years of age or older.</td>
</tr>
<tr>
<td></td>
<td>3. Tried and failed at least 2 other anticonvulsant agents.</td>
</tr>
<tr>
<td></td>
<td>4. Vigabatrin used as adjunct therapy.</td>
</tr>
<tr>
<td></td>
<td>5. Potential benefit must outweigh the potential risk of vision loss.</td>
</tr>
<tr>
<td></td>
<td>6. Must have vision tested at baseline before beginning treatment and at least every 3 months.</td>
</tr>
</tbody>
</table>

**Caution:**
- Peripheral visual field defect, the risk increases with higher doses and longer duration.
- Should not be used with other drugs associated with serious adverse ophthalmic effects such as retinopathy or glaucoma unless the benefit outweighs the risk.
- Renal impairment: CrCl greater than 50 to 80 mL/min, decrease dose by 25%; CrCl greater than 30 to 50 mL/min, decrease dose by 50%; CrCl greater than 10 to 30 mL/min, decrease dose by 75%

**Monitoring:**
- Vision must be tested at baseline and every 3 months
- Worsening of depression, suicidal ideation, and abnormal changes in behavior

**Special considerations:**
- FDA mandated Risk Evaluation and Mitigation Strategies (REMS) associated with Sabril®.
- The medication is shipped directly to the patient.
- Available only through a special restricted distribution program called SHARE, by calling 1-888-45-SHARE.
- Only prescribers and pharmacies registered with SHARE may prescribe and distribute Sabril®.
- For infants the medication is usually taken for 6-9 months. Dosage is often reduced at this point to see if symptoms re-emerge. If so, the dosage is increased to previous levels.
- Upon discontinuation, tapering of dose recommended

**Dosing:**
- Infantile Spasms: Initial, 50 mg/kg/day ORALLY in 2 divided doses; titrate by 25 to 50 mg/kg/day increments every 3 days up to a MAX of 150 mg/kg/day

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<table>
<thead>
<tr>
<th>Drug</th>
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</tr>
</thead>
</table>
| **Refractory Complex Partial Seizures** | - Adjunct therapy: initial, 500 mg ORALLY twice daily; titrate total daily dose in 500-mg increments at weekly intervals to a MAX dose of 1500 mg twice daily  
  **Initial Approval period:** 3 months  
  **Continued approval:**  
  - Approval renewed every 3 months for Refractory Complex Partial Seizures  
    - Must provide updates on eye exams upon renewal.  
    - Must show a substantial clinical benefit within 3 months of starting treatment in order to continue therapy.  
  - Approval must be granted after 1 month of therapy then renewed every 3 months thereafter  
    - Must provide updates on eye exams every 3 months.  
    - Must show a substantial clinical benefit within 2-4 weeks of starting treatment in order to continue therapy.  |

**Soliris®**  
- Eculizumab

**Guidelines for the use of eculizumab (Soliris®)**

**Inclusion Criteria:**
1. A documented diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) AND  
2. Must be prescribed by a hematologist or oncologist AND  
3. Must be ≥ 18 years of age AND  
4. Must be vaccinated with a quadrivalent meningococcal vaccine at least 2 weeks before the first dose of eculizumab is administered (patients should be revaccinated according to medical guidelines or vaccine labeling) AND  
5. Must be transfusion dependent requiring at least 4 RBC transfusions in the past 12 months AND  
6. Hemoglobin levels are < 9 mg/dl in the presence of symptoms OR < 7 mg/dl without symptoms

**Reasons for non-coverage:**
- Hypersensitivity to eculizumab or any of its components  
- Unresolved serious *Neisseria meningitidis* infection  
- Not currently vaccinated against *Neisseria meningitidis* infection.

**Caution:**
- Use with caution in patients with systemic infections since eculizumab blocks complement, making patients more susceptible to infections  
- Administration may result in infusion reactions such as hypersensitivity or anaphylaxis

**Monitoring:**
- Patients should be monitored for infusion reactions.  
- Monitor patients for 8 weeks after discontinuation of

**Dosing:**
- Weeks 1 through 4: 600 mg intravenously every 7 days  
- Week 5: 900 mg intravenously 7 days after the last dose  
- Week 6 through 52: 900 mg intravenously every 14 days  
- After the first year, eculizumab is dosed at 900 mg intravenously every 14 days

**Initial approval period:** 1 year  
**Continued approval:**  
Up to 1 year based on physician documentation of the following:

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### Drug Prior authorization criteria

- Patient is showing improvement in disease stability based on the following:
- Patient is tolerating therapy without an adverse effects

**Supprelin® LA - Histrelin implant**

Patients must meet all criteria for coverage for use of Supprelin® LA for Central Precocious Puberty:

1. Failed, intolerant, or allergic to Lupron Depot®
2. 2 years or older

**Symlin® - Pramlintide**

Symlin® is covered for members who meet the following criteria:

1. Prescriber must be an Endocrinologist
2. **Type 1 diabetics**
   a. Using both basal insulin and short-acting insulin, **AND**
   b. Requires three or more insulin injections daily, **OR**
   c. Using an insulin pump
3. **Type 2 diabetics**
   a. Receiving maximum tolerated doses of metformin, unless the patient is not a candidate for metformin therapy, and
   b. Using both basal insulin and short-acting insulin, **AND**
   c. Requires three or more insulin injections daily, **OR**
   d. Using an insulin pump **AND**
   e. Failure to achieve adequate glycemic control despite individualized insulin management, defined as:
      i. A1C level is greater than 7% and less than 9%, **or**
      ii. Marked day-to-day variability in glucose levels (based on review of self-monitoring blood glucose levels)

### Reasons for Non-Coverage:

Symlin® is **not covered** for patients meeting any of the following criteria:

- Poor compliance with current insulin regimen
- Poor compliance with prescribed self-blood glucose monitoring
- An A1C greater than 9%
- Recurrent severe hypoglycemia requiring assistance during the previous 6 months
- Presence of hypoglycemia unawareness
- Confirmed diagnosis of gastroparesis
- Need for medications that stimulate GI motility
- Pediatric patients (less than 18 years of age)
- Concurrent use with other oral antidiabetic medications (except metformin and sulfonylureas) or drugs that alter gastrointestinal motility

**Initial approval period:** 6 months

**Continued approval:** 1 year, based on review of compliance to therapy and documented improved glycemic control as evidenced by A1C lowering from pretreatment level

**Tradjenta™ - Linagliptin**

Tradjenta™ will be covered for current KP new start members who meet the following criteria:

1. A diagnosis of type 2 diabetes mellitus **and**
2. Must be prescribed by an endocrinologist **and**
3. HgbA1c level 7%–9%, **and**
4. Failed to obtain adequate glycemic control on combination therapy with:
   a. Maximum tolerated doses of metformin monotherapy (unless patient is not a candidate for metformin therapy) **and**
   b. Maximum tolerated doses of a sulfonylurea or a thiazolidinedione (unless the patient is

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<table>
<thead>
<tr>
<th>Drug</th>
<th>Prior authorization criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>not a candidate for either agent) and</td>
</tr>
<tr>
<td></td>
<td>c. Maximum tolerated titration of insulin.</td>
</tr>
<tr>
<td></td>
<td>i. Tradjenta™ may be initiated prior to insulin trial, in either of the following two conditions:</td>
</tr>
<tr>
<td></td>
<td>1. Endocrinologist indicates hypoglycemia is uniquely undesirable, so unable to use insulin (e.g., in patients who have hazardous jobs) OR</td>
</tr>
<tr>
<td></td>
<td>2. Endocrinologist indicates promotion of weight loss is a major consideration and this patient's A1C is close to target (&lt;_8.0%)</td>
</tr>
<tr>
<td></td>
<td>5. Unable to tolerate or inadequate response to Januvia™</td>
</tr>
<tr>
<td></td>
<td>** As outlined above, Tradjenta™ is not a substitute for insulin in patients whose diabetes control may benefit from insulin therapy</td>
</tr>
</tbody>
</table>

**Reasons for non-coverage:**
- Type 1 diabetes mellitus
- Treatment of diabetic ketoacidosis
- Concurrent use of insulin
- Pediatric patients (<18 years old)
- Prior history of a serious allergic reaction to linagliptin (i.e. urticaria, angioedema, or bronchial hyperreactivity)

**Use caution in the following patients:**
- Pregnant/nursing women
- Concomitant use with a sulfonylurea due to increased risk of hypoglycemia

**Monitoring:**
- HgbA1c level
- Serum glucose level

**Initial approval period:** 6 months

**Continued approval:** 1 year, based on review of compliance to therapy and documented improved glycemic control as evidenced by A1C lowering from pretreatment level to a1c goal <8%

**Tradjenta™ will be covered for new members to KP already taking Tradjenta™ who meet the following criteria:**

1. A diagnosis of type 2 diabetes mellitus
2. HgbA1c level <8%
3. Unable to tolerate or inadequate response to Januvia™

***Note: New members to KP currently taking Tradjenta™ upon enrollment whose diabetes is not controlled with Tradjenta™ (i.e. – A1c> 8%) will need to meet the general criteria for KP new start members.

**Reasons for non-coverage:**
- Type 1 diabetes mellitus
- Treatment of diabetic ketoacidosis
- Concurrent use of insulin
- Pediatric patients (<18 years old)
- Prior history of a serious allergic reaction to linagliptin (i.e. urticaria, angioedema, or bronchial hyperreactivity)

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**Drug** | **Prior authorization criteria**
--- | ---

**hyperreactivity)**

**Use caution in the following patients:**
- Pregnant/nursing women
- Concomitant use with a sulfonylurea due to increased risk of hypoglycemia

**Monitoring:**
- HgbA1c level
- Serum glucose level

**Initial approval period:** 6 months

**Continued approval:** 1 year, based on review of compliance to therapy and documented improved glycemic control as evidenced by A1c lowering from pretreatment level to a1c goal <8%

| **Tysabri®** | Kaiser Permanente will utilize the manufacturer sponsored TOUCH program first (ensure patients meet the requirement) followed by these Kaiser Georgia criteria for natalizumab (Tysabri®).

**Guidelines for the Use of Natalizumab (Tysabri®) in the Treatment of Multiple Sclerosis**

**Inclusion Criteria:**
1. Natalizumab (Tysabri®) should be reserved for treatment of relapsing forms of multiple sclerosis (MS).
   a. Considering potential risks from natalizumab therapy, including the risk of progressive multifocal leukoencephalopathy (PML):
      i. Natalizumab should usually be reserved for use in patients who have had an inadequate response to other MS therapies or patients who are not able to tolerate other MS therapies.
      ii. Patients who are stable and well-controlled on other MS therapies should not be changed to natalizumab.
   b. Based upon evidence available at the time when these guidelines are being developed (09/2006):
      i. Use in primary progressive MS is not supported by clinical trial evidence.
      ii. Efficacy or safety for use of natalizumab beyond two years is not supported by clinical trial evidence.
2. Due to the possibility of increased risk for PML or other infections:
   a. Natalizumab should be used as monotherapy and not in combination with Avonex® (interferon beta-1a), other beta-interferons (Betaseron® or Rebif®), or glatiramer acetate (Copaxone®).
   b. Natalizumab should usually not be used in patients who are receiving chronic immunosuppressant therapy, who are receiving other immunomodulatory drugs, or are significantly immunocompromised for any reason.

**Dosage and Administration:**
- Natalizumab should be administered to multiple sclerosis patients once every 4 weeks in a dose of 300 mg diluted in 100 ml Normal Saline given intravenously over about one hour. Natalizumab should NOT be given as a bolus or push.
- Natalizumab should only be administered in an infusion center with adequate facilities for treating a hypersensitivity or infusion-related reaction.

**Monitoring:**
- During the infusion and for at least one hour after completion of the infusion of natalizumab,

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patients should be observed for signs and symptoms of hypersensitivity or infusion-related reactions.

- The natalizumab infusion must be stopped immediately, and the physician should be consulted immediately, if signs or symptoms related to a hypersensitivity reaction are seen. These may include urticaria, dizziness, fever, rash, rigors, pruritis, nausea, flushing, hypotension, dyspnea, or chest pain.

- Patients should have a recent MRI brain scan prior to initiation of natalizumab treatment. This MRI may be helpful in differentiating MS symptoms from PML, should PML be suspected.

- Patients should be monitored for any new signs or symptoms which might suggest PML. At the first such sign or symptom of PML, natalizumab treatment should be withheld immediately and diagnostic measures should be undertaken.

<table>
<thead>
<tr>
<th>Drug</th>
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</tr>
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<tbody>
<tr>
<td><strong>Victoza®</strong></td>
<td><strong>Victoza® will be covered for current KP new start members who meet the following criteria:</strong></td>
</tr>
<tr>
<td>- Liraglutide</td>
<td>1. A diagnosis of type 2 diabetes mellitus and</td>
</tr>
<tr>
<td></td>
<td>2. Must be prescribed by an Endocrinologist and</td>
</tr>
<tr>
<td></td>
<td>3. HgbA1c level 7%–9%, and</td>
</tr>
<tr>
<td></td>
<td>4. Failed to obtain adequate glycemic control on combination therapy with:</td>
</tr>
<tr>
<td></td>
<td>a. Maximum tolerated doses of metformin (unless patient is not a candidate for metformin therapy) and</td>
</tr>
<tr>
<td></td>
<td>b. Maximum tolerated doses of a sulfonylurea or a thiazolidinedione (unless the patient is not a candidate for either agent) and</td>
</tr>
<tr>
<td></td>
<td>c. Maximum tolerated titration of insulin.</td>
</tr>
<tr>
<td></td>
<td>i. Victoza® may be initiated prior to insulin trial, in either of the following two conditions:</td>
</tr>
<tr>
<td></td>
<td>1. Endocrinologist indicates hypoglycemia is uniquely undesirable, so unable to use insulin (e.g., in patients who have hazardous jobs) OR</td>
</tr>
<tr>
<td></td>
<td>2. Endocrinologist indicates promotion of weight loss is a major consideration and this patients A1C is close to target (&lt;_8.0%)</td>
</tr>
</tbody>
</table>

**As outlined above, Victoza® and Byetta® are not substitutes for insulin in patients whose diabetes may benefit from insulin treatment**

**Reasons for non-coverage:**

- Type 1 diabetes mellitus
- Treatment of diabetic ketoacidosis
- Concurrent use with meglitinitides (i.e. repaglinide, nateglinide), or alpha-glucosidase inhibitors (i.e. acarbose, miglitol)
- Pediatric patients (<18 years old)
- ESRD or severe renal impairment (CrCl < 30 mL/min)
- Patients with severe gastrointestinal disease (including gastroparesis)
- Diagnosis of pancreatitis, including hemorrhagic and necrotizing, prior to or after initiation of Byetta® (postmarketing cases, including fatalities, have been reported, therapy should be discontinued immediately).
- Prior history of a serious allergic reaction to Byetta® (i.e., anaphylaxis, angioedema, Stevens-Johnson syndrome, etc.)

**Use caution in the following patients:**

- Pregnant/nursing women (Pregnancy Category C)
- Concomitant use with pharmacologic agents known to affect renal function/hydration status/ and or patients experiencing nausea/vomiting/diarrhea with or without dehydration (i.e., ace-inhibitors, NSAIDS, diuretics)

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</thead>
<tbody>
<tr>
<td></td>
<td>• Concomitant use with a sulfonylurea (hypoglycemia)</td>
</tr>
<tr>
<td></td>
<td>• Concomitant use with warfarin (increased INR, sometimes with bleeding)</td>
</tr>
<tr>
<td></td>
<td>• Concomitant use with oral medications that require rapid gastric gastrointestinal absorption (Byetta® slows gastric emptying)</td>
</tr>
<tr>
<td></td>
<td>• Concomitant use with oral medications dependent on threshold concentrations for efficacy (i.e., contraceptives, antibiotics) – Patients should take drugs 1 hour prior to Byetta® injection</td>
</tr>
<tr>
<td></td>
<td>• Concomitant use with medications requiring administration with food – Patients should take drug to be administered with a meal or snack when Byetta® is not being administered.</td>
</tr>
</tbody>
</table>

**Monitoring:**
- Renal function prior to initiation of Byetta® and periodically afterwards
- HgA1c level
- Fasting and postprandial glucose
- Signs/symptoms of acute pancreatitis including unexplained, persistent, severe abdominal pain with or without vomiting

**Initial approval period:** 6 months

**Continued approval:** 1 year, based on review of compliance to therapy and documented improved glycemic control as evidenced by A1c lowering from pretreatment level to a1c goal <8%

**Victoza® will be covered for new members to KP already taking Victoza® who meet the following criteria:**

1. A diagnosis of type 2 diabetes mellitus **and**
2. HgA1c level <8%
3. Unable to tolerate Byetta®

***Note: New members to KP currently taking Victoza® upon enrollment whose diabetes is not controlled with Victoza® (i.e. – A1c > 8%) will need to meet the general criteria for KP new start members.***

**Reasons for non-coverage:**
- Type 1 diabetes mellitus
- Treatment of diabetic ketoacidosis
- Concurrent use with meglitinides (i.e. repaglinide, nateglinide), or alpha-glucosidase inhibitors (i.e. acarbose, miglitol)
- Pediatric patients (<18 years old)
- ESRD or severe renal impairment (CrCl < 30 mL/min)
- Patients with severe gastrointestinal disease (including gastroparesis)
- Diagnosis of pancreatitis, including hemorrhagic and necrotizing, prior to or after initiation of Byetta® (postmarketing cases, including fatalities, have been reported, therapy should be discontinued immediately).
- Prior history of a serious allergic reaction to Byetta® (i.e., anaphylaxis, angioedema, Stevens-Johnson syndrome, etc.)

**Use caution in the following patients:**
- Pregnant/nursing women (Pregnancy Category C)
- Concomitant use with pharmacologic agents known to affect renal function/hydration status/ and or patients experiencing nausea/vomiting/diarrhea with or without dehydration (i.e., ace-inhibitors, NSAIDS, diuretics)

*Because the Medicare Part D formulary does not allow prior authorization or criteria restrictions on medications, this document applies to the Commercial, Triple Tier, and Multi-Choice formularies.*

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Because the Medicare Part D formulary does not allow prior authorization or criteria restrictions on medications, this document applies to the Commercial, Triple Tier, and Multi-Choice formularies.

Drug | Prior authorization criteria
--- | ---
| • Concomitant use with a sulfonylurea (hypoglycemia)  
• Concomitant use with warfarin (increased INR, sometimes with bleeding)  
• Concomitant use with oral medications that require rapid gastric gastrointestinal absorption (Byetta® slows gastric emptying)  
• Concomitant use with oral medications dependent on threshold concentrations for efficacy (i.e., contraceptives, antibiotics) – Patients should take drugs 1 hour prior to Byetta® injection  
• Concomitant use with medications requiring administration with food – Patients should take drug to be administered with a meal or snack when Byetta® is not being administered.

**Monitoring:**

- Renal function periodically
- HgbA1c level
- Fasting and postprandial glucose
- Signs/symptoms of acute pancreatitis including unexplained, persistent, severe abdominal pain with or without vomiting

**Initial approval period:** 6 months

**Continued approval:** 1 year, based on review of compliance to therapy and documented improved glycemic control as evidenced by A1c lowering from pretreatment level to A1c goal <8%

| **Xgeva™**  
- **Denosumab** |
| **Xgeva™ will be covered for KP members who meet the following criteria:** |
| 1. Patient must have of one of the following:  
  d. A diagnosis of bone metastases and advanced breast or prostate cancer **OR**  
  e. A diagnosis of bone metastases from solid tumors (other than breast or prostate cancer)  
 2. A therapeutic trial and clinical failure with pamidronate **OR** zoledronic acid (Zometa®) **AND**  
  a. Clinical failure defined as development of new skeletal related event (SRE) while receiving treatment with pamidronate or zoledronic acid for at least 3 months  
 3. Must be prescribed by an hematologist or oncologist **AND**  
 4. Calcium levels have been checked and any pre-existing hypocalcemia has been corrected **AND**  
 5. Patient has had a baseline dental exam prior to initiating denosumab therapy

**Reasons for non-coverage:**

- Treatment of skeletal-related events in patients with multiple myeloma
- Renal impairment (CrCl of 30 ml/min or less) or end-stage renal disease requiring hemodialysis
- Hypocalcemia
- Pediatric patients (<18 years old)
- Non-FDA approved indications

**Use caution in the following patients:**

- Pregnant/nursing women

**Dosing:**

- Inject 120 mg subcutaneously every four weeks
- Medication **MUST** be given by a health care professional

**Monitoring:**

- Serum calcium prior to therapy initiation and periodically. Adequately supplement all patients with calcium and vitamin D
- Symptoms of osteonecrosis of the jaw

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<table>
<thead>
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<tr>
<td><strong>Xiflex™</strong>&lt;br&gt;Collagenase&lt;br&gt;Clostridium Histolticum</td>
<td>Guidelines for the Use of Xiaflex™ in the Treatment of Duputren’s Contractures&lt;br&gt;<em>Xiflex™ is only available through the Xiaflex™ Experience Program</em>&lt;br&gt;&lt;br&gt;<strong>Inclusion Criteria (ALL of the following must apply):</strong>&lt;br&gt;1. Documented diagnosis of Dupuytren’s contracture with a palpable cord AND&lt;br&gt;2. Must be prescribed and administered by a hand surgeon, plastic surgeon, orthopedic surgeon or rheumatologist AND&lt;br&gt;3. Documentation of training in Xiaflex™ injections must be provided by the prescriber AND&lt;br&gt;4. A positive “table top test” – defined as the inability to simultaneously place the affected finger and palm flat against a table top AND&lt;br&gt;5. Documented contracture of at least 40 degrees flexion for a metacarpophalangeal joint contracture or at least 20 degrees flexion for a proximal interphalangeal joint contracture AND&lt;br&gt;6. Documentation that the flexion deformity results in functional limitations AND&lt;br&gt;7. Must be 18 years of age or older AND&lt;br&gt;8. Must not have had surgery on the primary joint within the past 90 days AND&lt;br&gt;9. Xiaflex™ will only be used on one cord at a time&lt;br&gt;   a. Treatment of each cord should be undertaken in sequential order with only one cord receiving Xiaflex™ at a time&lt;br&gt;&lt;br&gt;<strong>Dosage and Administration</strong>&lt;br&gt;• The dose for Xiaflex™ is 0.58 mg per injection into a palpable cord with a contracture of a metacarpophalangeal (MP) joint or a proximal interphalangeal (PIP) joint, according to the injection procedure&lt;br&gt;• Finger extension procedures may be performed approximately 24 hours after the injection in the event the cord has not spontaneously ruptured&lt;br&gt;&lt;br&gt;<strong>Use caution in the following patients:</strong>&lt;br&gt;• Caution is advised in those receiving anticoagulation therapy, with the exception of low-dose aspirin (maximum 150 mg/day).&lt;br&gt;&lt;br&gt;<strong>Monitoring:</strong>&lt;br&gt;• Patient must follow-up with provider within 24 hours following an injection for finger extension procedure&lt;br&gt;&lt;br&gt;<strong>Initial approval:</strong> 3 months&lt;br&gt;&lt;br&gt;<strong>Continued approval:</strong>&lt;br&gt;• Injection may be repeated up to a maximum of 3 sessions for cord at 4 week intervals if reduction in primary joint contracture is not 0-5 degrees of full extension&lt;br&gt;• Patient must follow-up within 24 hours following an injection for finger extension procedure if a contracture persists in order to qualify for more injections&lt;br&gt;&lt;br&gt;<strong>Xolair®</strong>&lt;br&gt;Omalizumab injectable</td>
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**Drug Prior authorization criteria**

1. Specific IgE by skin PRICK test or CAP RAT to perennial antigens that must correlate with patients clinical history, **AND**
2. Determination of atopic status by Kaiser Permanente allergist
3. Baseline total IgE serum level from 30-700 int. units/mL
4. Reversible airway obstruction as documented by:
   a. Response to inhaled short-acting beta agonists (eg, FEV1 reversibility of = 12% with at least a 200 mL increase in FEV1) within 30 minutes after administration of albuterol (90-180 mcg), or
   b. Positive exercise or methacholine challenge, or
   c. Positive response (at least a 15% increase in FEV1 with at least a 200 mL increase in FEV1) after a course of treatment (eg, inhaled or systemic corticosteroids)
5. Baseline FEV1 = 40% and <80% of predicted despite appropriate treatment
6. Patients in any of the following drug therapy categories might be considered for omalizumab:
   a. Patients receiving high-dose inhaled corticosteroid (ICS) plus long-acting beta-agonist (LABA) [eg, Advair® 500/50 twice daily] with poor asthma control as defined by an Asthma Control Test (ACT) score of ≤15 or who experience significant complications which could be related to frequent courses of oral corticosteroids or the high dose ICS (eg, cataracts, fractures, or diabetes)
   b. Patients who do not tolerate LABA and are receiving high-dose ICS with concomitant leukotriene modifier with poor asthma control as defined by an ACT score of ≤15 or who experience significant complications which could be related to frequent courses of oral corticosteroids or the high dose ICS (eg, cataracts, fractures, or diabetes)
   c. Note regarding patients on maintenance oral corticosteroids: In a pre-approval clinical trial including asthmatic subjects requiring oral corticosteroids, exacerbations were not decreased and oral corticosteroid use was not reduced among omalizumab-treated patients compared with a placebo group.
7. 12-64 years of age. [Note: Clinical trial experience in patients ≥65 years of age has been too limited to determine whether they respond differently from younger patients. However, FDA reviewers noted a trend towards higher rates of adverse events in older patients.]
8. Careful re-evaluation of trigger avoidance measures (pets, dust mites, foods, pollen, smoke exposure, etc) and control of comorbid factors (allergy, sinusitis, GERD, anxiety disorder, panic disorder, vocal chord dysfunction, etc) to determine if these measures can decrease the need to initiate omalizumab therapy.
9. Careful re-evaluation of medication use and compliance prior to initiation of omalizumab which includes the following:
   a. Prescriber review of anti-inflammatory (AI) ratio and refill history
   b. Prescriber review of inhaler and spacer technique
   c. Patient-completed Asthma Control Test (ACT) prior to omalizumab initiation
10. Prior to initiation of omalizumab - due to the risk of malignancies - a candidate for omalizumab treatment should have a dermatologic evaluation to screen for pre-existing skin cancer and should have undergone age/gender appropriate cancer screening procedures as recommended by Kaiser Permanente.

**Exclusion Criteria:**

- History of adverse reaction to omalizumab or any of its
- History of or high risk for cancer (See Adverse Events section of these Guidelines.)
- Pregnancy (If patient becomes pregnant during therapy, omalizumab should be discontinued.)
- Primary or secondary immunodeficiency and patients who are HIV-positive.
- Patients with major autoimmune diseases (eg, lupus erythematosus, rheumatoid arthritis, et al)
- Patients with significant systemic diseases.

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<td></td>
<td>• Concomitant use of allergen immunotherapy with omalizumab, a combination which has not been evaluated in clinical trials.</td>
</tr>
<tr>
<td></td>
<td>• Allergic bronchopulmonary aspergillosis.</td>
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<td>• Smokers</td>
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**Monitoring:**

- If omalizumab therapy is judged to be successful at four months, plan to continue treatment for up to one year.
  - Omalizumab therapy should be discontinued after one year.
  - Reevaluate asthma control at one, three, and six month intervals or as necessary.
  - If asthma control deteriorates during reevaluation, consider restarting omalizumab therapy.
  - Serum total IgE levels measured less than one year following discontinuation of omalizumab may not reflect steady state free IgE levels and should not be used to reassess the dosing regimen. Use serum IgE levels from pretreatment prior to initial dosing of omalizumab.

**Note:** Xolair® should only be authorized for 6 months. Patients must be re-evaluated for coverage determination every 6 months.

***See QRM for the entire Guideline for the use of omalizumab***

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