PROVIDER ADMINISTERED DRUGS – SITE OF CARE

Policy Number: PHARMACY 276.23 T2
Effective Date: July 1, 2019

Table of Contents

<table>
<thead>
<tr>
<th>Conditions of Coverage</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONDITIONS OF COVERAGE</td>
<td>1</td>
</tr>
<tr>
<td>COVERAGE RATIONALE</td>
<td>2</td>
</tr>
<tr>
<td>DEFINITIONS</td>
<td>3</td>
</tr>
<tr>
<td>CLINICAL EVIDENCE</td>
<td>3</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>4</td>
</tr>
<tr>
<td>POLICY HISTORY/REVISION INFORMATION</td>
<td>5</td>
</tr>
<tr>
<td>INSTRUCTIONS FOR USE</td>
<td>5</td>
</tr>
</tbody>
</table>

Related Policies

- Actemra® (Tocilizumab) Injection for Intravenous Infusion
- Alpha-1-Proteinase Inhibitors
- Benlysta® (Belimumab)
- Complement Inhibitors (Soliris® & Ultomiris™)
- Crysvita® (Burosumab)
- Drug Coverage Guidelines
- Entyvio® (Vedolizumab)
- Enzyme Replacement Therapy
- Exondys 51™ (Eteplirsen)
- Home Health Care
- Ilaris® (Canakinumab)
- Ilumya™ (Tildrakizumab-Asmn)
- Infliximab (Remicade®, Inflectra™, Renflexis™)
- Intravenous Enzyme Replacement Therapy (ERT) for Gaucher Disease
- Ocrevus™ (Ocrelizumab)
- Onpattro™ (Patisiran)
- Orencia® (Abatacept) Injection for Intravenous Infusion
- Radicava™ (Edaravone)
- Simponi Aria® (Golimumab) Injection for Intravenous Infusion
- Specialty Pharmacy for Certain Specialty Medications Administered in an Outpatient Hospital Setting
- Trogarzo™ (Ibalizumab-Uiyk)

CONDITIONS OF COVERAGE

<table>
<thead>
<tr>
<th>Applicable Lines of Business/Products</th>
<th>This policy applies to Oxford Commercial plan membership.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefit Type</td>
<td>General Benefits Package</td>
</tr>
<tr>
<td>Referral Required</td>
<td>No</td>
</tr>
<tr>
<td>(Does not apply to non-gatekeeper products)</td>
<td></td>
</tr>
<tr>
<td>Authorization Required</td>
<td>Yes&lt;sup&gt;1,2,3&lt;/sup&gt;</td>
</tr>
<tr>
<td>(Precertification always required for inpatient admission)</td>
<td></td>
</tr>
<tr>
<td>Precertification with Medical Director Review Required</td>
<td>Yes&lt;sup&gt;1,2,3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Applicable Site(s) of Service</td>
<td>Hospital Outpatient Facility&lt;sup&gt;1,2,3&lt;/sup&gt;</td>
</tr>
<tr>
<td>(If site of service is not listed, Medical Director review is required)</td>
<td></td>
</tr>
</tbody>
</table>
Special Considerations

- Fabrazyme® (Agalsidase beta)
- Glassia™ (A1-PI)
- Ilaris® (Canakinumab)
- Ilumya™ (Tildrakizumab-asmn)
- Inflectra™ (Infliximab-dyyb)
- Kanuma® (Sebelipase alfa)
- Lumizyme® (Aglucosidase alfa)
- Mepservii® (Vestronidase alfa-vjbk)
- Naglazyme® (Galsulfase)
- Ocrevus™ (Ocrelizumab)
- Onpattro™ (Patisiran)
- Orenica® (Abatacept)

**COVERAGE RATIONALE**

This policy addresses the criteria for consideration of allowing hospital outpatient facility specialty medication infusion services. This includes claim submission for hospital based services with the following CMS/AMA Place of Service codes:

- 19 Off-Campus - Outpatient Hospital; and
- 22 On-Campus - Outpatient Hospital

Alternative sites of care, such as non-hospital outpatient infusion, physician office, ambulatory infusion or home infusion services are well accepted places of service for medication infusion therapy. If an individual does not meet criteria for outpatient hospital facility infusion, alternative sites of care may be used.

**Outpatient hospital facility-based intravenous medication infusion is medically necessary for individuals who meet at least ONE of the following criteria** (submission of medical records is required):

- Documentation that the individual is medically unstable for administration of the prescribed medication at the alternative sites of care as determined by any of the following:
  - The individual’s complex medical status or therapy requires enhanced monitoring and potential intervention above and beyond the capabilities of the office or home infusion setting; or
  - The individual’s documented history of a significant comorbidity (e.g., cardiopulmonary disorder) or fluid overload status that precludes treatment at an alternative Site Of Care; or
  - Outpatient treatment in the home or office setting presents a health risk due to a clinically significant physical or cognitive impairment; or
  - Difficulty establishing and maintaining patent vascular access
  - To initiate, re-initiate products for a short duration (e.g., 4 weeks) or
  - Initial infusion or re-initiation of therapy after more than 6 months; or
  - Homecare or infusion provider has deemed that the individual, home caregiver, or home environment is not suitable for home infusion therapy (if the prescriber cannot infuse in the office setting).

**Ongoing outpatient hospital facility-based infusion duration of therapy will be no more than 6 months to allow for reassessment of the individual’s ability to receive therapy at an alternative Site Of Care.**

This policy applies to these specialty medications that require healthcare provider administration:

- Actemra® (Tocilizumab)
- Aldurazyme® (Laronidase)
- AraLast NP™ (A1-PI)
- Benlysta® (Belimumab)
- Cerazyme® (Imiglucerase)
- Crysvirta® (Burosumab)
- Elaprase® (Idursulfase)
- Elelyso® (Taliiglucerase)
- Entyvio® (Vedolizumab)
- Exondys 51™ (Eteplirsen)
- Fabrazyme® (Agalsidase beta)
- Glassia™ (A1-PI)
- Ilaris® (Canakinumab)
- Ilumya™ (Tildrakizumab-asmn)
- Inflectra™ (Infliximab-dyyb)
- Kanuma® (Sebelipase alfa)
- Lumizyme® (Aglucosidase alfa)
- Mepservii® (Vestronidase alfa-vjbk)
- Naglazyme® (Galsulfase)
- Ocrevus™ (Ocrelizumab)
- Onpattro™ (Patisiran)
- Orenica® (Abatacept)
UnitedHealthcare

Provider Administered Drugs

receive treatment in various care settings.
The American Academy of Allergy Asthma and Immunology has published guidelines for the suitability of patients to

therapy is generally considered safe and effective, exhibiting few and usually

of belimumab is currently available, indicating the appropriateness of home administration. Alpha

velaglucerase have been demonstrated to be infused

Infusions of enzyme replacement therapies including agalsidase, elosulfase, galsulfase, iduronidase, idursulfase, vela
glucerase have been shown to be safely infused in the community setting. A chart review of 3161 patients who

received a combined 20,976 infusions in community clinics was conducted to evaluate safety across all types of

patients. Infliximab infusions are safe in the community setting. Severe ADRs were rare. A total of 524 (2.5% of all

infusions) acute ADRs in 353 patients (11.2%) were recorded. Most reactions (i.e., ADRs) were mild \( n=263 \) (50.2%, 1.3% of all infusions) or moderate \( n=233 \) (44.5%, 1.1% of all infusions). Twenty-eight reactions (5.3%, 0.1% of all infusions) were severe. Emergency medical services were called to transport patients to hospital for seven of the severe reactions, of which none required admission. As per pre-established medical directives adrenaline was administered three times. The authors concluded that infliximab infusions are safe in the community setting. Severe ADRs were rare. None required active physician intervention; nurses were able to treat all reactions by following standardized medical directives. 

Infliximab has been shown to be safely infused in the community setting. A chart review of 3161 patients who

received a combined 20,976 infusions in community clinics was conducted to evaluate safety across all types of

patients. Infliximab infusions are safe in the community setting. Severe ADRs were rare. A total of 524 (2.5% of all

infusions) acute ADRs in 353 patients (11.2%) were recorded. Most reactions (i.e., ADRs) were mild \( n=263 \) (50.2%, 1.3% of all infusions) or moderate \( n=233 \) (44.5%, 1.1% of all infusions). Twenty-eight reactions (5.3%, 0.1% of all infusions) were severe. Emergency medical services were called to transport patients to hospital for seven of the severe reactions, of which none required admission. As per pre-established medical directives adrenaline was administered three times. The authors concluded that infliximab infusions are safe in the community setting. Severe ADRs were rare. None required active physician intervention; nurses were able to treat all reactions by following standardized medical directives. 

Ten children were enrolled in the home infusion program if they were compliant with hospital-based infliximab infusions and other medications, had no adverse events during hospital-based infliximab infusions, were in remission and had access to experienced pediatric home care nursing. The children received 59 home infusions with a dose range of 7.5 to 10 mg/kg/dose. Home infusions ranged from 2 to 5 hours. Since infusions could be performed any day of the week, school absenteeism was decreased. The average patient satisfaction rating for home infusions was 9 on a scale from 1 to 10 (10 = most satisfied). Three patients experienced difficulty with IV access requiring multiple attempts, but all were able to receive their infusions. One infusion was stopped because of arm pain above the IV site. This patient had his next infusion in the hospital before returning to the home infusion program. No severe adverse events (palpitations, blood pressure instability, hyperemia, respiratory symptoms) occurred during home infusions. In the carefully selected patients, infliximab infusions administered at home were safe and are cost-effective. Patients and families preferred home infusions, since time missed from school and work was reduced.

Several studies have demonstrated the safety of infusing a variety of infused medications in the home setting. Infusions of enzyme replacement therapies including agalsidase, elosulfase, galsulfase, iduronidase, idursulfase, velaglucerase have been demonstrated to be infused safely in the home. In addition, a self-administered formulation of belimumab is currently available, indicating the appropriateness of home administration. Alpha-1-antitrypsin therapy is generally considered safe and effective, exhibiting few and usually well tolerated side effects.

**Professional Societies**

**American Academy of Allergy Asthma and Immunology**
The American Academy of Allergy Asthma and Immunology has published guidelines for the suitability of patients to receive treatment in various care settings including clinical characteristics of patients needing a high level of care in the
hospital outpatient facility which includes patient characteristics: previous serious infusion reaction such as anaphylaxis, seizure, myocardial infarction, or renal failure, immune globulin therapy naive, continual experience of moderate or serious infusion related adverse reactions, physical or cognitive impairment.

**Hunter Syndrome European Expert Council**
European recommendations for the diagnosis and multidisciplinary management of a rare disease published an article reviewing the collective experiences with agalsidase beta home infusion therapy and outlines how safe, patient-centered homecare can be organized in enzyme replacement therapy for patients with Fabry disease. Criteria include that "Patients must have received ERT in hospital for 3-6 months; if patients have previously had IRRs, they must be under control with premedication, and they must not have had an IRR in the 2-8 weeks before homecare is approved and premedication must be given. If a patient has significant respiratory disease (%FVC, 40% or less; or evidence of serious obstructive airway disease), homecare may not be suitable."

**Agency for Healthcare Research and Quality (AHRQ)**
The Agency for Healthcare Research and Quality (AHRQ) publication on Enzyme Replacement Therapy states, “Home infusion of ERT was initially studied in patients with type I Gaucher disease. It has been reported as an option for patients with Fabry disease, MPS I, and MPS II, and MPS VI. However, patients with infantile Pompe disease may not be able to transfer to home care because of an increased risk for serious adverse events during an infusion. In general, the outcomes measured in these studies and the follow-up durations were similar to those reported by disease in the clinical studies summarized under Guiding Question 3. Safety was the main focus of most home infusion studies, as the patients had already been receiving ERT in a more controlled setting.”

**REFERENCES**
The foregoing Oxford policy has been adapted from an existing UnitedHealthcare national policy that was researched, developed and approved by UnitedHealthcare Medical Technology Assessment Committee. [URG-9.11]


American Academy of Allergy Asthma and Immunology. Guidelines for the site of care for administration of IGIV therapy. December 2011.


Centers for Medicare & Medicaid Services: Place of service code set. .


### POLICY HISTORY/REVISION INFORMATION

<table>
<thead>
<tr>
<th>Date</th>
<th>Action/Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>07/01/2019</td>
<td><strong>Title Change</strong></td>
</tr>
<tr>
<td></td>
<td>Previously titled Provider Administered Drugs – Site of Care Review Guidelines</td>
</tr>
<tr>
<td></td>
<td><strong>Coverage Rationale</strong></td>
</tr>
<tr>
<td></td>
<td>Simplified content</td>
</tr>
<tr>
<td></td>
<td>Revised list of specialty medications that require healthcare provider administration:</td>
</tr>
<tr>
<td></td>
<td>o Added Ultomiris™ (ravulizumab-cwvz)</td>
</tr>
<tr>
<td></td>
<td>o Removed Adagen® (pegademase bovine)</td>
</tr>
<tr>
<td></td>
<td><strong>Supporting Information</strong></td>
</tr>
<tr>
<td></td>
<td>Archived previous policy version PHARMACY 276.22 T2</td>
</tr>
</tbody>
</table>

### INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting UnitedHealthcare Oxford standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare Oxford reserves the right to modify its Policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice.

The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Oxford Clinical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.