Provider Administered Drugs – Site of Care

Guideline Number: URG-9.17
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Instructions for Use

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Coverage Rationale

See Benefit Considerations

This guideline 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; or
  - To initiate, re-initiate products for a short duration (e.g., 4 weeks)

  or
- Documentation (e.g., infusion records, medical records) of episodes of severe or potentially life-threatening adverse events (e.g., anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure) that have not been responsive to acetaminophen, steroids, diphenhydramine, fluids, infusion rate reductions, or other pre-medications, thereby increasing risk to the individual when administration is in the home or office setting; 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)
- Adakveo® (crizanlizumab-tmca)
- Aldurazyme® (laronidase)
- Aralast NP® (A1-PI)
- Avsola™ (infliximab-axxq)
- Benlysta® (belimumab)
- Cerezyme® (imiglucerase)
- Cimzia® (certolizumab pegol)
- Cinqair® (reslizumab)
- Crysvita® (burosumab-twza)
- Elaprase® (idursulfase)
- Elelyso® (taliglucerase)
- Entyvio® (vedolizumab)
- Exondys 51® (eteplirsen)
- Fabrazyme® (agalsidase beta)
- Fasenra® (benralizumab)
- Givlaari® (givosiran)
- Glassia® (A1-PI)
- Ilaris® (canakinumab)
- Ilumya™ (tildrakizumab-asmn)
- Inflectra® (infliximab-dyyb)
- Kanuma® (sebelipase alfa)
- Lumizyme® (alglucosidase alfa)
- Mepsevii™ (vestronidase alfa-vjbk)
- Naglazyme® (galsulfase)
- Nucala® (mepolizumab)
- Onpattro® (patisiran)
- Orencia® (abatacept)
- Prolastin®-C™ (A1-PI)
- Radicava® (edaravone)
- Reblozyl® (luspatercept-aamt)
- Remicade® (infliximab)
- Renflexis® (infliximab-abda)
- Revcovi® (elapegademase-lvlr)
- Simponi Aria® (golimumab)
- Soliris® (eculizumab)
- Stelara® (ustekinumab)
- Tepezza® (teprotumumab-trbw)
- Trogarzo® (ibalizumab-uiyk)
- Ultomiris® (ravulizumab-cwvz)
- Uplizna™ (inebilizumab-cdon)
- Viltepso™ (Viltolarsen)
- Vimizim® (elosulfase alfa)
- VPRIV® (velaglucerase)
- Vyepti™ (eptinezumab-jjmr)
- Vyondys 53™ (golodirsen)
- Zemaira® (A1-PI)

Documentation Requirements

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The documentation requirements outlined below are used to assess whether the member meets the clinical criteria for coverage but do not guarantee coverage of the service requested.

Specialty Medication	HCPCS Codes*	Required Clinical Information
Actemra® (tocilizumab)	J3262	Refer to Protocol titled Medical Record Requirements for Pre-Service Reviews for documentation requirements. Note: Once in the Medical Record Requirements for Pre-Service Reviews document, search for the medication name or applicable HCPCS code.
Adakveo® (crizanlizumab-tmca)	J0791	
Aldurazyme® (laronidase)	J1931	
Aralast NP® (A1-PI)	J0256	
Avsola™ (infliximab-axxq)	Q5121	
Benlysta® (belimumab)	J0490	
Cerezyme® (imiglucerase)	J1786	
Cimzia® (certolizumab pegol)	J0717	
Cinqair® (reslizumab)	J2786	
Crysvita® (burosumab-twza)	J0584	
Elaprase® (idursulfase)	J1743	
Elelyso® (taliglucerase)	J3060	
Entyvio® (vedolizumab)	J3380	
Exondys 51® (eteplirsen)	J1428	
Fabrazyme® (agalsidase beta)	J0180	
Fasenra® (benralizumab)	J0517	
Givlaari® (givosiran)	J0223	
Glassia® (A1-PI)	J0257	
Ilaris® (canakinumab)	J0638	
Ilumya™ (tildrakizumab-asmn)	J3245	
Inflectra® (infliximab-dyyb)	Q5103	
Kanuma® (sebelipase alfa)	J2840	
Lumizyme® (alglucosidase alfa)	J0221	
Mepsevii™ (vestronidase alfa-vjbk)	J3397	
Naglazyme® (galsulfase)	J1458	
Nucala® (mepolizumab)	J2182	
Onpattro™ (patisiran)	J0222	
Orencia® (abatacept)	J0129	
Prolastin®-C™ (A1-PI)	J0256	
Radicava® (edaravone)	J1301	
Reblozyl® (luspatercept-aamt)	J0896	
Remicade® (infliximab)	J1745	
Renflexis® (infliximab-abda)	Q5104	
Revcovi® (elapegademase-lvlr)	J3590	
Simponi Aria® (golimumab)	J1602	
Soliris® (eculizumab)	J1300	

Specialty Medication	HCPCS Codes*	Required Clinical Information
Stelara® (ustekinumab)	J3357, J3358	
Tepezza® (teprotumumab-trbw)	J3241, J3590	
Trogarzo® (ibalizumab-uiyk)	J1746	
Ultomiris® (ravulizumab-cwvz)	J1303	
Uplizna™ (inebilizumab-cdon)	C9399, J3590	
Viltepso® (Viltolarsen)	C9399, J3490, J3590	
Vimizim® (elosulfase alfa)	J1322	
VPRIV® (velaglucerase)	J3385	
Vyepti™ (eptinezumab-jjmr)	J3032, J3590	
Vyondys 53™ (golodirsen)	J1429	
Zemaira® (A1-PI)	J0256	

**For code descriptions, see the Applicable Codes section.*

Definitions

Site of Care: Choice for physical location of infusion administration. Sites of Care include hospital inpatient, hospital outpatient, physician office, ambulatory infusion suite, or home-based setting.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this guideline does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
C9399	Unclassified drugs or biologicals
J0129	Injection, abatacept, 10 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self administered)
J0180	Injection, agalsidase beta, 1 mg
J0221	Injection, alglucosidase alfa, (Lumizyme), 10 mg
J0222	Injection, patisiran, 0.1 mg
J0223	Injection, givosiran, 0.5 mg
J0256	Injection, alpha 1-proteinase inhibitor (human), not otherwise specified, 10 mg
J0257	Injection, alpha 1 proteinase inhibitor (human), (Glassia), 10 mg
J0490	Injection, belimumab, 10 mg
J0517	Injection, benralizumab, 1 mg
J0584	Injection, burosumab-twza, 1 mg
J0638	Injection, canakinumab, 1 mg
J0717	Injection, certolizumab pegol, 1 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered)
J0791	Injection, crizanlizumab-tmca, 5 mg
J0896	Injection, luspatercept-aamt, 0.25 mg
J1300	Injection, eculizumab, 10 mg

HCPCS Code	Description
J1301	Injection, edaravone, 1 mg
J1303	Injection, ravulizumab-cwvz, 10 mg
J1322	Injection, elosulfase alfa, 1 mg
J1428	Injection, eteplirsen, 10 mg
J1429	Injection, golodirsen, 10 mg
J1458	Injection, galsulfase, 1 mg
J1602	Injection, golimumab, 1 mg, for intravenous use
J1743	Injection, idursulfase, 1 mg
J1745	Injection, infliximab, excludes biosimilar, 10 mg
J1746	Injection, ibalizumab-uiyk, 10 mg
J1786	Injection, imiglucerase, 10 units
J1931	Injection, laronidase, 0.1 mg
J2182	Injection, mepolizumab, 1 mg
J2786	Injection, reslizumab, 1 mg
J2840	Injection, sebelipase alfa, 1 mg
J3032	Injection, eptinezumab-jjmr, 1 mg
J3060	Injection, taliglucerase alfa, 10 units
J3241	Injection, teprotumumab-trbw, 10 mg
J3245	Injection, tildrakizumab, 1 mg
J3262	Injection, tocilizumab, 1 mg
J3357	Ustekinumab, for subcutaneous injection, 1 mg
J3358	Ustekinumab, for intravenous injection, 1 mg
J3380	Injection, vedolizumab, 1 mg
J3385	Injection, velaglucerase alfa, 100 units
J3397	Injection, vestronidase alfa-vjbk, 1 mg
J3490	Unclassified drugs
J3590	Unclassified biologics
Q5103	Injection, infliximab-dyyb, biosimilar, (Inflectra), 10 mg
Q5104	Injection, infliximab-abda, biosimilar, (Renflexis), 10 mg
Q5121	Injection, infliximab-axxq, biosimilar, (avsola), 10 mg

Benefit Considerations

This guideline applies to members who have medical necessity language in their Certificate of Coverage (COC) or Summary Plan Document with benefits available for health care services if medically necessary and have been approved for the requested medication clinical use.

This guideline applies to UnitedHealthcare Commercial plans. This guideline does not apply to Medicare or Medicaid plans.

Clinical Evidence

Home infusion as a place of service is well established and accepted by physicians. A 2010 home infusion provider survey by the National Home Infusion Association reported providing 1.24 million therapies to approximately 829,000 patients, including 129,071 infusion therapies of specialty medications.

In a trial evaluating patients with paroxysmal nocturnal hemoglobinuria, after initial 2-5 doses of eculizumab (Soliris), 79 patients received continued infusion with every 14 days in the home setting for the duration of the study – 1-98 months, mean duration of 39 months. The survival of patients treated with eculizumab was not different from age- and sex-matched normal controls (P = .46) but was significantly better than 30 similar patients managed before eculizumab (P = .030). Three patients on eculizumab, all over 50 years old, died of causes unrelated to PNH. Twenty-one patients (27%) had a thrombosis before starting eculizumab (5.6 events per 100 patient-years) compared with 2 thromboses on eculizumab (0.8 events per 100 patient-years; P < .001). Twenty-one patients with no previous thrombosis discontinued warfarin on eculizumab with no thrombotic sequelae. Forty of 61 (66%) patients on eculizumab for more than 12 months achieved transfusion independence. The 12-month mean transfusion requirement reduced from 19.3 units before eculizumab to 5.0 units in the most recent 12 months on eculizumab (P < .001). Eculizumab dramatically alters the natural course of PNH, reducing symptoms and disease complications as well as improving survival to a similar level to that of the general population.

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 authrors 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.7 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 homecare 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 setting 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 naïve, 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 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."

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Guideline History/Revision Information

Date	Summary of Changes
01/01/2021	**Coverage Rationale** • Revised list of specialty medications requiring healthcare provider administration; added: o Uplizna™ (inebilizumab-cdon) o Viltepso® (Viltolarsen) **Documentation Requirements** • Updated list of specialty medications with associated documentation requirements; added: o Uplizna™ (inebilizumab-cdon) o Viltepso® (Viltolarsen) **Applicable Codes** • Added HCPCS codes C9399 and J3490 **Supporting Information** • Archived previous policy version URG-9.16

Instructions for Use

This Utilization Review Guideline provides assistance in interpreting UnitedHealthcare 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 guideline, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Utilization Review Guideline is provided for informational purposes. It does not constitute medical advice.

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