

PROVIDER ADMINISTERED DRUGS – SITE OF CARE REVIEW GUIDELINES

Guideline Number: URG-9.10

Effective Date: April 1, 2019

[Instructions for Use](#) ⓘ

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Related Commercial Policies

- [Actemra® \(Tocilizumab\) Injection for Intravenous Infusion](#)
- [Alpha₁-Proteinase Inhibitors](#)
- [Benlysta® \(Belimumab\)](#)
- [Complement Inhibitors \(Soliris® & Ultomiris™\)](#)
- [Crysvita® \(Burosumab\)](#)
- [Entyvio® \(Vedolizumab\)](#)
- [Enzyme Replacement Therapy](#)
- [Exondys 51™ \(Eteplirsen\)](#)
- [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](#)
- [Trogarzo™ \(Ibalizumab\)](#)

Community Plan Policy

- [Provider Administered Drugs – Site of Care Review Guidelines](#)

COVERAGE RATIONALE

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):

1. 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:
 - a. 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**

- b. 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**
 - c. Outpatient treatment in the home or office setting presents a health risk due to a clinically significant physical or cognitive impairment; **or**
 - d. Difficulty establishing and maintaining patent vascular access
- or**
- 2. 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**
- 3. Initial infusion or re-initiation of therapy after more than 6 months.
- or**
- 4. 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).

Outpatient hospital facility-based infusion may be granted to initiate or re-initiate products for a short duration (e.g., 4 weeks).

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)
- Adagen[®] (Pegademase bovine)
- Aldurazyme[®] (Laronidase)
- Aralast NP[™] (A1-PI)
- Benlysta[®] (Belimumab)
- Cerezyme[®] (Imiglucerase)
- Crysvisa[®] (Burosumab)
- Elaprase[®] (Idursulfase)
- Elelyso[®] (Taliglucerase)
- Entyvio[®] (Vedolizumab)
- Exondys 51[™] (Eteplirsen)
- Fabrazyme[®] (Agalsidase beta)
- Glassia[™] (A1-PI)
- Ilaris[®] (Canakinumab)
- Ilumya[™] (Tildrakizumab-asmn)
- Inflectra[™] (Infliximab-dyyb)
- Kanuma[®] (Sebelipase alfa)
- Lumizyme[®] (Alglucosidase alfa)
- Mepsevii[™] (Vestronidase alfa-vjbk)
- Naglazyme[®] (Galsulfase)
- Ocrevus[™] (Ocrelizumab)
- Onpattro[™] (Patisiran)
- Orencia[®] (Abatacept)
- Prolastin[®]-C[™] (A1-PI)
- Radicava[™] (edaravone)
- Remicade[®] (Infliximab)
- Renflexis[™] (Infliximab-abda)
- Revcovi[™] (Elapegademase-lvlr)
- Simponi Aria[®] (Golimumab)
- Soliris[®] (Eculizumab)
- Trogarzo[™] (Ibalizumab)
- Vimizim[®] (Elosulfase alfa)
- VPRIV[®] (Velaglucerase)
- Zemaira[®] (A1-PI)

DEFINITIONS

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

BENEFIT CONSIDERATIONS

For self-funded plans with SPD language other than fully-insured Generic COC language, please refer to the member specific benefit plan document for coverage.

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 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.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 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."

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GUIDELINE HISTORY/REVISION INFORMATION

Date	Action/Description
04/01/2019	<ul style="list-style-type: none"> • Changed policy title; previously titled <i>Specialty Medication Administration – Site of Care Review Guidelines</i> • Reorganized policy template; simplified and relocated <i>Instructions for Use</i> and <i>Benefit Considerations</i> section • Updated list of related policies; added reference link to the policy titled <i>Revcovi™ (Elapegademase-Lvlr)</i> • Revised coverage rationale: <ul style="list-style-type: none"> ○ Modified criteria to indicate 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): <ul style="list-style-type: none"> ▪ 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: <ul style="list-style-type: none"> - 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 ▪ 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) ○ Added language to indicate: <ul style="list-style-type: none"> ▪ Outpatient hospital facility-based infusion may be granted to initiate or re-initiate products for a short duration (e.g., 4 weeks) ▪ 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 ○ Updated list of medications that require healthcare provider administration;

Date	Action/Description
	<ul style="list-style-type: none"> ○ added Revcovi™ (elapegedemase-IvIr) <ul style="list-style-type: none"> ○ Removed reference to the MCG™ Care Guidelines, 22nd edition, 2018, Home Infusion Therapy, CMT: CMT-0009(SR) • Updated supporting information to reflect the most current clinical evidence and references • Archived previous policy version URG-9.09

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.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Utilization Review Guidelines 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.