

SPECIALTY MEDICATION ADMINISTRATION – SITE OF CARE REVIEW GUIDELINES

Policy Number: PHARMACY 276.21 T2

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- | Related Policies |
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| • Actemra® (Tocilizumab) Injection for Intravenous Infusion |
| • Alpha₁-Proteinase Inhibitors |
| • Benlysta® (Belimumab) |
| • Crysvita® (Burosumab) |
| • 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 |
| • Soliris® (Eculizumab) |
| • Specialty Pharmacy for Certain Specialty Medications Administered in an Outpatient Hospital Setting |
| • Trogarzo™ (Ibalizumab-Uiyk) |

INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting Oxford benefit plans. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members. Oxford reserves the right, in its sole discretion, 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.

When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Clinical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Clinical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Clinical Policy. Other Policies may apply.

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

CONDITIONS OF COVERAGE

Applicable Lines of Business/Products	This policy applies to Oxford Commercial plan membership.
Benefit Type	General Benefits Package
Referral Required (Does not apply to non-gatekeeper products)	No
Authorization Required (Precertification always required for inpatient admission)	Yes ^{1,2}
Precertification with Medical Director Review Required	Yes ²
Applicable Site(s) of Service (If site of service is not listed, Medical Director review is required)	Hospital Outpatient Facility ³
Special Considerations	<p>¹Providers must call Oxford's Medical Management to obtain precertification for administration of any drug listed in this policy in a hospital outpatient facility.</p> <p>²Requests for hospital outpatient facility infusion of any drug listed in this policy require review by a Medical Director or their designee.</p> <p>³Participating hospitals are required to purchase Actemra[®] (tocilizumab), Entyvio[®] (vedolizumab), Infliximab (Remicade[®], Inflectra[™], Renflexis[™]), Ocrevus[™] (ocrelizumab), Orencia[®] (abatacept), and Simponi Aria[®] (golimumab) from the BriovaRx Specialty Pharmacy when the medication is administered in an outpatient hospital setting; refer to the policy titled Specialty Pharmacy for Certain Specialty Medications Administered in an Outpatient Hospital Setting for additional information.</p>

BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

Essential Health Benefits for Individual and Small Group

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits ("EHBs"). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

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 any of the following criteria (submission of medical records detailing at least **one** of the following criteria is required):

- Medically unstable based upon submitted clinical history; or
- Initial medication infusion of or re-initiation after more than 6 months following discontinuation of therapy; or

- Previous experience of a severe adverse event following infusion. Examples include but are not limited to anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure; or
- Continuing experience of adverse events that cannot be mitigated by pre-medications or infusion rate adjustments; or
- Physically and/or cognitively impaired and no home caregiver available; or
- Difficulty establishing and maintaining patent vascular access; or
- Homecare or infusion provider has deemed that the individual, home caregiver, or home environment is not suitable for home infusion therapy.

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)
- Crysvita[®] (burosumab-twza)
- 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-vjkb)
- Naglazyme[®] (galsulfase)
- Ocrevus[™] (ocrelizumab)
- Onpattro[™] (Patisiran)
- Orencia[®] (abatacept)
- Prolastin[®]-C[™] (A₁-PI)
- Radicava[™] (edaravone)
- Remicade[®] (infliximab)
- Renflexis[™] (infliximab-abda)
- Simponi Aria[®] (golimumab)
- Soliris[®] (eculizumab)
- Trogarzo[™] (ibalizumab)
- Vimizim[®] (elosulfase alfa)
- VPRIV[®] (velaglucerase)
- Zemaira[®] (A₁-PI)

For medical necessity clinical coverage criteria, see MCG[™] Care Guidelines, 22nd edition, 2018, Home Infusion Therapy, CMT: CMT-0009(SR).

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.⁹

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.

MCG[™] Care Guidelines, 22nd edition, 2018, Home Infusion Therapy, CMT: CMT-0009(SR) addresses criteria for home infusion therapy. Clinical patient characteristics for home suitability include: clinical stability, no need for close observation or daily nurse care, and reliable venous access. Additional criteria for home environment, infusion plan and patient ability to participate in care are summarized.²

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."

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-9.09]

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
01/01/2019	<ul style="list-style-type: none"> • Updated list of related policies; added reference link to the policy titled: <ul style="list-style-type: none"> ○ Ilumya™ (Tildrakizumab-Asmn) ○ Onpattro™ (Patisiran) • Revised coverage rationale: <ul style="list-style-type: none"> ○ Replaced reference(s) to: <ul style="list-style-type: none"> ▪ "Patient" with "individual" ▪ "Members" with "individuals" ○ Updated list of applicable specialty medications that require healthcare provider administration; added Ilumya™ (Tildrakizumab-asmn) and Onpattro™ (Patisiran) ○ Modified language to clarify the listed MCG™ Care Guidelines should be referenced for medical necessity <i>clinical coverage</i> criteria

Date	Action/Description
	<ul style="list-style-type: none">• Updated supporting information to reflect the most current references• Archived previous policy version PHARMACY 276.20 T2