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
Medical

Referral Type
No

Authorization Required
(Does not apply to non-gatekeeper products)
No

Authorization Required
(Precertification always required for inpatient admission)
Yes, Home, Hospital Outpatient Facility

Precertification with Medical Director Review Required
Yes, Hospital Outpatient Facility

Applicable Site(s) of Service
(If site of service is not listed, Medical Director review is required)
Home, Office, Freestanding Ambulatory Infusion Suite (not associated with a hospital)

Special Considerations
Soliris does not require precertification however the site of service for Soliris infusion may require precertification. Refer to: Home Health Care and Specialty Medication Administration - Site of Care Review Guidelines.

1 Soliris does not require precertification however the site of service for Soliris infusion may require precertification. Refer to: Home Health Care and Specialty Medication Administration - Site of Care Review Guidelines.

2 New Jersey Small Members should refer to their Related Policies
- Acquired Rare Disease Drug Therapy Exception Process
- Experimental/Investigational Treatment
- Experimental/Investigational Treatment for NJ Plans
- Home Health Care
- Specialty Medication Administration - Site of Care Review Guidelines
Special Considerations

BENEFIT CONSIDERATIONS

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

Some Certificates of Coverage allow coverage of experimental/investigational treatments for life-threatening illnesses when certain conditions are met. Members should refer to their member specific benefit plan document for additional information.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the member specific benefit plan document or in the medical or drug policy.

Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the policy titled Acquired Rare Disease Drug Therapy Exception Process.

Requests for hospital outpatient facility infusion of Soliris require precertification with review by a Medical Director or their designee. Refer to the policy titled Specialty Medication Administration - Site of Care Review Guidelines.

Requests for home infusion of Soliris require pre-certification for the home care service (not for the Soliris itself). Refer to the policy titled Home Health Care.

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

The guidelines below provide indications for the drug Soliris (eculizumab).
Precertification is not required for the drug Soliris (eculizumab); however the site of service for the administration of Soliris may require precertification.

Soliris (eculizumab) is proven and medically necessary for the treatment of:
1. Atypical hemolytic uremic syndrome (aHUS)
2. Paroxysmal nocturnal hemoglobinuria (PNH)

Soliris is unproven and not medically necessary for treatment of Shiga toxin E. coli-related hemolytic uremic syndrome (STEC-HUS).

Site of Care Administration

Provider’s Office or Freestanding Ambulatory Infusion Suite (not associated with a hospital)
Administration of Soliris in a provider’s office or freestanding ambulatory infusion suite not associated with a hospital does not require precertification.

Home Administration
Administration of Soliris in the home requires pre-certification for the home care services (not for the Soliris itself). Refer to the policy titled Home Health Care.
Hospital Outpatient Facility

Administration of Soliris in a hospital outpatient facility (including any ambulatory infusion suite associated with the hospital) requires precertification with review by a Medical Director or their designee. Refer to the policy titled Specialty Medication Administration - Site of Care Review Guidelines.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Soliris (eculizumab) is a complement inhibitor indicated for:¹
- Treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.
- Treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

Limitations of Use:¹
- Soliris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

Use of Soliris is not recommended in these situations.

The use of Soliris increases a patient’s susceptibility to serious meningococcal infections (septicemia and/or meningitis). Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.¹
- Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.
- Immunize patients with a polyvalent meningococcal vaccine at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection.
- If urgent Soliris therapy is indicated in an unvaccinated patient, administer the meningococcal vaccine as soon as possible.
- Monitor patients for early signs of meningococcal infections and evaluate immediately if infection is suspected.
- Discontinue Soliris in patients who are undergoing treatment for serious meningococcal infections.

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS, prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747) or on the OneSource™ Safety Support website found at http://www.solirisrems.com/.¹,⁹

BACKGROUND

Eculizumab is a monoclonal antibody that binds with high affinity to compliment protein C5, which inhibits its cleavage to C5a and C5b and prevents the generation of the terminal complement complex C5b-9. In those patients with paroxysmal nocturnal hemoglobinuria (PNH), eculizumab inhibits terminal complement mediated intravascular hemolysis. In patients with atypical hemolytic uremic syndrome (aHUS), impairment in the regulation of complement activity leads to uncontrolled terminal complement activation, resulting in platelet activation, endothelial cell damage and thrombotic microangiopathy.¹-³

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 policy 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 may apply.

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<th>HCPCS Code</th>
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<td>J1300</td>
<td>Injection, eculizumab, 10 mg</td>
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<tr>
<th>ICD-10 Diagnosis Code</th>
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<td>Hemolytic-uremic syndrome</td>
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<tr>
<td>D59.5</td>
<td>Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]</td>
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</table>
Proven/Medically Necessary Uses

Atypical Hemolytic Uremic Syndrome (aHUS)
Eculizumab is indicated for the treatment of atypical hemolytic uremic syndrome (aHUS).¹

Paroxysmal Nocturnal Hemoglobinuria (PNH)
Eculizumab is indicated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH).¹

Hillmen et al evaluated the long-term safety and efficacy of continuous administration of eculizumab in 195 patients with paroxysmal nocturnal hemoglobininuria (PNH) over 66 months.² Patients previously enrolled in the Phase II pilot study and its extensions, the Phase III TRIUMPH (Transfusion Reduction Efficacy and Safety Clinical Investigation, a Randomized, Multicenter, Double-Blind, Placebo-Controlled, Using Eculizumab in Paroxysmal Nocturnal Hemoglobininuria) study (NCT00122330), or the Phase III SHEPHERD (Safety in Hemolytic PNH Patients Treated With Eculizumab: A Multi-Center Open-Label Research Design) study (NCT00130000) were eligible to participate. All patients had a minimum of 10% PNH red blood cells at enrolment in the parent trials and were vaccinated with a meningococcal vaccine at least 14 days prior to the first eculizumab infusion in the parent studies. Efficacy assessments were performed at least every 2 weeks from the time of initiation of eculizumab therapy in the parent study. Efficacy endpoints included patient survival degree of hemolysis, thrombotic events (TE), mean change from baseline in hemoglobin and the number of units of transfused packed red blood cells (PRBCs) administered. Assessments of renal function were performed over the duration of the study by determining the CKD stage using formulas for estimated glomerular filtration rate (GFR). Safety was assessed through monitoring of adverse events (AEs), clinical laboratory tests and vital signs. Four patient deaths were reported, all unrelated to treatment, resulting in a 3-year survival estimate of 97.6%. All patients showed a reduction in lactate dehydrogenase levels, which was sustained over the course of treatment (median reduction of 86.9% at 36 months). Incidence of TEs decreased by 81.8%, with 96.4% of patients remaining free of TEs. Researchers observed a time-dependent improvement in renal function: 93.1% of patients exhibited improvement or stabilization in CKD score at 36 months. Transfusion independence increased by 90.0% from baseline, with the number of red blood cell units transfused decreasing by 54.7%. The median treatment duration was 30.3 months with a maximum duration of 66 months. Eculizumab was well tolerated, with no evidence of cumulative toxicity and a decreasing occurrence of adverse events over time. Very few patients discontinued treatment. Researchers concluded that long-term treatment with eculizumab resulted in sustained improvement in patient outcomes by rapidly reducing hemolysis and significantly reducing the frequency of severe and life-threatening morbidities, such as TEs and CKD, and thus, improving patient survival.

Unproven/Not Medically Necessary Use
Eculizumab is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).³ While the few studies available demonstrate possible efficacy of eculizumab in treating Shiga toxin E. coli-related hemolytic uremic syndrome,³⁴ further studies are warranted to demonstrate that it is both safe and effective for this indication.

REFERENCES

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare Pharmacy Clinical Pharmacy Program that was researched, developed and approved by the UnitedHealth Group National Pharmacy & Therapeutics Committee [2016D0049D]

## POLICY HISTORY/REVISION INFORMATION

<table>
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<tr>
<th>Date</th>
<th>Action/Description</th>
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| 02/01/2017 | • Removed language pertaining to New Jersey (NJ) Individual Plans (*NJ individual benefit plans transitioned to UnitedHealthcare Oxford Navigate effective Jan. 1, 2017*)  
• Archived previous policy version PHARMACY 277.5 T2 |