UnitedHealthcare Community Plan

UnitedHealthcare® Community Plan

SOLIRIS® (ECULIZUMAB)- ARIZONA

Policy Number: CS2017D0049A **Effective Date**: October 1, 2017

Table of Contents **Page**

Commercial Policy

- Soliris® (Eculizumab)

INSTRUCTIONS FOR USE

This Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced. The terms of the federal, state or contractual requirements for benefit plan coverage may differ greatly from the standard benefit plan upon which this Drug Policy is based. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage supersedes this Drug Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the contractual requirements for benefit plan coverage prior to use of this Drug Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Drug Policy 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. 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.

BENEFIT CONSIDERATIONS

Before using this policy, please check the federal, state or contractual requirements for benefit coverage.

COVERAGE RATIONALE

Soliris (eculizumab) is proven and medically necessary for treatment of:

1. Atypical hemolytic uremic syndrome (aHUS)[1]
2. Paroxysmal nocturnal hemoglobinuria (PNH)[1]

Authorization will be issued for 12 months.

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

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/.[1,3]

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 federal, state or contractual requirements 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 Coverage Determination Guidelines may apply.

HCPCS Code	Description
J1300	Injection, eculizumab, 10 mg

ICD-10 Diagnosis Code	Description
D59.3	Hemolytic-uremic syndrome
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]

CLINICAL EVIDENCE

Proven

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 hemoglobinuria (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 Hemoglobinuria) 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). The incidence of reported 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

Eculizumab is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).[1] While the few studies available demonstrate possible efficacy of eculizumab in treating Shiga toxin E. coli-related hemolytic uremic syndrome,[4-6] further studies are warranted to demonstrate that it is both safe and effective for this indication.

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) that specifically address eculizumab (Soliris™). Local Coverage Determinations (LCDs) exist; see the LCDs for Drugs and Biologicals, Coverage of, for Label and Off-Label Uses.

Medicare may cover outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. See the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals at https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/bp102c15.pdf.
(Accessed March 29, 2016)

REFERENCES

1. Soliris® [package insert]. Cheshire, CT: Alexion Pharmaceuticals, Inc.; January 2016.
2. Hillmen P, Muus P, Röth A, et al. Long-term safety and efficacy of sustained eculizumab treatment in patients with paroxysmal nocturnal haemoglobinuria. *Br J Haematol*. 2013 Apr 25.
3. OneSource™ Safety Support. Available at: http://www.solirisrems.com/. Accessed June 18, 2015.
4. Lapeyraque AL, Malina M, Fremeaux-Bacchi V, et al. Eculizumab in severe Shiga-toxin-associated HUS. *N Engl J Med*. 2011 Jun 30;364(26):2561-3.
5. Kielstein JT, Beutel G, Fleig S, et al. Best supportive care and therapeutic plasma exchange with or without eculizumab in Shiga-toxin-producing E. coli O104:H4 induced haemolytic-uraemic syndrome: an analysis of the German STEC-HUS registry. *Nephrol Dial Transplant*. 2012 Oct;27(10):3807-15.
6. Delmas Y, Vendrely B, Clouzeau B, et al. Outbreak of Escherichia coli O104:H4 haemolytic uraemic syndrome in France: outcome with eculizumab. *Nephrol Dial Transplant*. 2014 Mar;29(3):565-72.

POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
10/01/2017	• New policy. This policy applies to only the Arizona line of business.