Eculizumab (Soliris®)

**Description of Procedure or Service**

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare clonal hematopoietic stem cell disorder clinically characterized by chronic complement-mediated hemolysis, thrombosis, and bone marrow failure. Thrombosis, the major cause of death in PNH, is observed in approximately 40% of patients. The symptoms associated with this disorder, including fatigue, pain, esophageal spasm, and erectile dysfunction, are often severe and disabling.

Hemolytic-uremic syndrome (HUS) is characterized by hemolytic anemia, thrombocytopenia, and renal failure caused by platelet thrombi in the microcirculation of the kidney and other organs. Typical (acquired) HUS is triggered by infectious agents such as strains of E. coli (Stx-E. coli) that produce powerful Shiga-like exotoxins, whereas atypical HUS (aHUS) can be genetic, acquired, or idiopathic (of unknown cause). Onset of atypical HUS ranges from prenatal to adulthood. Individuals with genetic atypical HUS frequently experience relapse even after complete recovery following the presenting episode. Sixty percent of genetic aHUS progresses to end-stage renal disease (ESRD).

On March 16, 2007, Eculizumab (Soliris®; Alexion Pharmaceuticals, Inc. Cheshire, CT), a humanized monoclonal antibody that binds to the human C5 complement protein, received accelerated approval by the U.S. Food and Drug Administration for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.

On September 23, 2011 the U.S. Food and Drug Administration (FDA) approved Eculizumab (Soliris®) for the treatment of all pediatric and adult patients with atypical hemolytic uremic syndrome (aHUS).

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

**Related Policies:**
Place of Service for Medical Infusion

**Policy**

BCBSNC will provide coverage for Eculizumab (Soliris®) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.
Eculizumab (Soliris®)

Benefits Application
This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Eculizumab (Soliris®) is covered
Eculizumab may be considered medically necessary as a treatment for Paroxysmal Nocturnal Hemoglobinuria (PNH) when the following clinical criteria are met:

- The member has a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH); **AND**
- The member is transfusion-dependent (i.e., has at least 1 transfusion in the 24 months prior to initiation of eculizumab due to documented hemoglobin less than 7 g/dL in persons without anemic symptoms or less than 9 g/dL in persons with symptoms from anemia) prior to initiation of eculizumab treatment; **OR** the member has a documented history of major adverse vascular events from thromboembolism; **AND**
- The member has been administered a meningococcal vaccine at least two weeks prior to initiation of eculizumab therapy; **AND**
- The member is re-vaccinated according to current medical guidelines for vaccine use while on eculizumab therapy.

Eculizumab may be considered medically necessary as a treatment for Atypical Hemolytic Uremic Syndrome (aHUS) when the following clinical criteria are met:

- The member has a diagnosis of Atypical Hemolytic Uremic Syndrome (aHUS); **AND**
- The member has been administered a meningococcal vaccine at least two weeks prior to initiation of eculizumab therapy; **AND**
- The member is revaccinated according to current medical guidelines for vaccine use while on eculizumab therapy.

When Eculizumab (Soliris®) is not covered
Use of Eculizumab as a treatment of conditions other than aHUS or PNH is considered investigational.

Use of Eculizumab as treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS) is considered investigational.

Continued use of Eculizumab as a treatment of PNH is considered not medically necessary when transfusion requirements are not significantly reduced.

Continued use of Eculizumab as a treatment of PNH is considered not medically necessary when thromboembolism events persist despite treatment.

Policy Guidelines

FDA Approved Indications
Eculizumab (Soliris®)

**Paroxysmal Nocturnal Hemoglobinuria (PNH)**

Soliris® is indicated for the treatment of patients with PNH to reduce hemolysis.

The recommended dosing regimen for eculizumab for PNH consists of:
- 600 mg every seven days for the first four weeks followed by
- 900 mg for the fifth dose seven days later, then
- 900 mg every 14 days thereafter.

Eculizumab should be administered at the recommended dosage regimen time points, or within two days of these time points.

**Atypical Hemolytic Uremic Syndrome (aHUS)**

Soliris® is indicated for the treatment of patients with aHUS to inhibit complement-mediated thrombotic microangiopathy.

There is no history or evidence of injection drug abuse that might be associated with atypical HUS or TTP (specifically Opana).

The recommended dosing regimen for eculizumab in aHUS for patients 18 years of age and older consists of:
- 900 mg every seven days for the first four weeks, followed by
- 1200 mg for the fifth dose seven days later, then
- 1200 mg every 14 days thereafter.

The recommended dosing regimen for eculizumab in aHUS for patients less than 18 years of age is weight based.

The FDA issued a Black Box Warning for Soliris® regarding serious meningococcal infection risk. Therefore, patients should receive a meningococcal vaccination at least 2 weeks prior to receiving the first eculizumab treatment and have revaccination according to current medical guidelines. Patients must be monitored and evaluated immediately for early signs of meningococcal infections and treated with antibiotics as indicated.

Eculizumab (Soliris®) is being studied in a variety of conditions, including myasthenia gravis and neuromyelitis optica spectrum disorders. There is insufficient evidence regarding safety and efficacy, therefore treatment of conditions other than aHUS or PNH are considered investigational.

Eculizumab is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS). While the few studies available demonstrate possible efficacy of eculizumab in treating Shiga toxin E. coli-related hemolytic uremic syndrome, further studies are needed to demonstrate that it is both safe and effective for this indication. Plasma therapy should be initiated quickly in any patient in whom noninfectious HUS is suspected while awaiting the results of complement testing and genotyping. If not initiated, irreversible renal lesions may develop within a few days. Plasma therapy may need to continue until complement genotyping is completed.

**Administration of eculizumab (Soliris) - Site of Care Eligibility**
Eculizumab (Soliris®)

1. Administration of eculizumab (Soliris) may be given in an inpatient setting if the inpatient setting is medically necessary. An inpatient admission for the sole purpose of eculizumab (Soliris) infusion is not medically necessary, OR
2. Administration of eculizumab (Soliris) in a hospital outpatient setting is considered medically necessary if the following criteria are met:
   a. History of mild adverse events that have not been successfully managed through mild pre-medication (diphenhydramine, acetaminophen, steroids, fluids, etc.), OR
   b. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity, OR
   c. First infusion, OR
   d. Less than 3 months since first eculizumab (Soliris) infusion, OR
   e. First infusion after six months of no eculizumab (Soliris) infusions, OR
   f. Requirement of a change in eculizumab (Soliris) product.
3. Members who do not meet the criteria above are appropriate for eculizumab (Soliris) administration in a home-based infusion or physician office setting with or without supervision by a certified healthcare professional. Inpatient and hospital outpatient infusion, in the absence of the criteria in #1 or #2 above is considered not medically necessary.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: J1300

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

http://www.solirisrems.com/docs/SOL1135_Soliris_Dosing_and_Admin_Brochure.pdf


Eculizumab (Soliris®)


Specialty Matched Consultant Advisory Panel review 4/2017

Medical Director review 4/2017


Specialty Matched Consultant Advisory Panel review 4/2018

Policy Implementation/Update Information

8/26/14 New policy developed. BCBSNC will provide coverage for Eculizumab (Soliris®) when it is determined to be medically necessary because the medical criteria and guidelines are met. Medical Director review 8/2014. Policy noticed 8/26/14 for effective date 10/28/14. (mco)


12/29/17 Policy Guidelines updated to include guidelines for “Site of Care Eligibility related to infusion of eculizumab (Soliris). Policy notification given 1/1/18, effective 4/1/18. Medical Director review. (jd)

Eculizumab (Soliris®)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.