# Clinical Policy: Eculizumab (Soliris)

Reference Number: CP.PHAR.97
Effective Date: 03/12
Last Review Date: 04/17

Coding Implications
Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

**Description**
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for eculizumab (Soliris®).

**Policy/Criteria**
It is the policy of health plans affiliated with Centene Corporation® that Soliris is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Paroxysmal nocturnal hemoglobinuria** (must meet all):

1. Prescribed by or in consultation with a hematologist;
2. Diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) confirmed by flow cytometry showing PNH cells;
3. Severe PNH indicated by one or more of the following (a or b):
   a. Thrombosis;
   b. Flow cytometry showing ≥10% PNH cells and one of the following:
      i. History of ≥4 transfusions in the last 12 months;
      ii. Disabling fatigue;
      iii. Frequent pain paroxysms;
      iv. Worsening or significant renal insufficiency;
      v. Other end-organ complications from the disease;
4. Prescribed dose of Soliris does not exceed 600 mg for the first 4 weeks, followed by j900 mg for the fifth dose 1 week later, then 900 mg every 2 weeks thereafter;
5. Member is currently up to date with the meningococcal vaccination per ACIP recommendations, or will receive meningococcal vaccine at least 2 weeks prior to the first dose of Soliris;
6. At the time of request, member does not have unresolved serious *Neisseria meningitidis* infection.

**Approval duration: 6 months**

**B. Atypical hemolytic uremic syndrome** (must meet all):

1. Prescribed by or in consultation with a hematologist;
2. Diagnosis of atypical hemolytic uremic syndrome (aHUS) (i.e., complement-mediated HUS) as evidenced by the following clinical presentation (a, b, and c):
   a. Microangiopathic hemolytic anemia;
   b. Thrombocytopenia;
   c. Acute kidney injury;
3. Potential infectious causes of aHUS have been ruled out;

4. Prescribed dose of Soliris does not exceed 900 mg for the first 4 weeks, followed by 1200 mg for the fifth dose 1 week later, then 1200 mg every 2 weeks thereafter;
5. Member is currently up to date with the meningococcal vaccination per ACIP recommendations or meningococcal vaccine will be given at least 2 weeks prior to the first dose of Soliris;
6. At the time of request, member does not have unresolved serious *Neisseria meningitidis* infection.

**Approval duration: 6 months**

**C. Other diagnoses/indications:** Refer to CP.PHAR.57 - Global Biopharm Policy.

**II. Continued Approval**

**A. Paroxysmal nocturnal hemoglobinuria** (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Efficacy of Soliris therapy to reduce hemolysis evidenced by one of the following:
   a. Improved measures of intravascular hemolysis (e.g., normalization of lactate dehydrogenase);
   b. Reduced need for red blood cell (RBC) transfusions;
   c. Less fatigue;
   d. Improved health-related quality of life;
   e. Fewer thrombotic events;
3. Prescribed dose of Soliris does not exceed 900 mg every 2 weeks.

**Approval duration: 12 months**

**B. Atypical hemolytic uremic syndrome** (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Efficacy of Soliris therapy to inhibit complement-mediated thrombotic microangiopathy evidenced by one of the following:
   a. Decreased need for plasma therapy (plasmapheresis/fresh frozen plasma infusion);
   b. Decreased need for dialysis;
   c. Increased glomerular filtration rate;
   d. Normalization of platelet counts and/or lactate dehydrogenase levels;
3. Prescribed dose of Soliris does not exceed 1200 mg every 2 weeks;

**Approval duration: 12 months**

**C. Other diagnoses/indications** (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy**.**

## Background

*Description/Mechanism of Action:*
Soliris, a complement inhibitor, is a formulation of eculizumab which is a recombinant humanized monoclonal IgG2/4κ antibody produced by murine myeloma cell culture and purified by standard bioprocess technology. Eculizumab specifically binds to the complement protein C5 with high affinity, thereby inhibiting its cleavage to C5a and C5b and preventing the generation of the terminal complement complex C5b-9. Soliris inhibits terminal complement mediated intravascular hemolysis in PNH patients and complement-mediated TMA in patients with aHUS. A genetic mutation in patients with PNH leads to the generation of populations of abnormal RBCs (known as PNH cells) that are deficient in terminal complement inhibitors, rendering PNH RBCs sensitive to persistent terminal complement-mediated destruction. The destruction and loss of these PNH cells (intravascular hemolysis) results in low RBC counts (anemia), and also fatigue, difficulty in functioning, pain, dark urine, shortness of breath, and blood clots. In aHUS, impairment in the regulation of complement activity leads to uncontrolled terminal complement activation, resulting in platelet activation, endothelial cell damage and thrombotic microangiopathy (TMA).

*FDA Approved Indications:*
Soliris is a monoclonal antibody/concentrated solution for intravenous infusion indicated for:

- Treatment of patients with PNH to reduce hemolysis;
- Treatment of patients with atypical hemolytic uremic syndrome aHUS to inhibit complement-mediated TMA.

Limitations of use:

- Soliris is not indicated for treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome.

*Formulation:*
Soliris is supplied as 300 mg single-use vials containing 30 mL of 10 mg/mL sterile, preservative-free solution per vial.

## Appendices

### Appendix A: Abbreviation Key

ACIP: Advisory Committee on Immunization Practices
aHUS: atypical hemolytic uremic syndrome
PNH: paroxysmal nocturnal hemoglobinuria
TMA: thrombotic microangiopathy

## Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|---|---|
| J1300 | Injection, eculizumab, 10 mg |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| No criteria changes | 04/13 | |
| Converted from SGM to Centene policy template | 05/13 | 05/13 |
| Removed pregnancy and dosing questions from Figure 1<br>Added clinical trial information for PNH and updated safety information | 04/14 | 05/14 |
| Corrected Figure 2 to say "Elevated LDH levels ≥ 1.5 x ULN" and not ≤ 1.5 | 03/15 | 04/15 |
| Policy converted to new template.<br>Age, dosing, and monitoring criteria added per PI; diagnostic criteria edited as follows:<br>PNH: "type III red" is removed – does not have to be RBCs; thrombosis edited to be any thrombosis and not limited by PNH clonal size; specific LDH and Hgb levels deleted; App C - "disabling symptom ms" – is incorporated directly into the diagnostic criteria set.<br>aHUS: the required clinical triad is edited to read AND rather than AND/OR.<br>Efficacy criteria on re-auth splits information from App E, which is a combo of efficacy criteria for the two disease states, and places it directly into the appropriate disease state criteria set. | 03/16 | 04/16 |
| Removed requirement of *Streptococcus pneumoniae* and *Haemophilus influenza* type b (Hib) infections. Modified initial and approval duration to 6 months and 12 months respectively. Removed age requirements. Added max dose to continued approval criteria | 03/17 | 04/17 |

**References**

1. Soliris Prescribing Information. New Haven, CT: Alexion Pharmaceuticals, Inc.; January 2017. Available at www.soliris.com. Accessed March 28, 2017.
2. Brodsky RA. Clinical manifestations and diagnosis of paroxysmal nocturnal hemoglobinuria. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed March 28, 2017.
3. Borowitz MJ, Craig FE, DiGiuseppe JA, et al. Guidelines for the diagnosis and monitoring of paroxysmal nocturnal hemoglobinuria and related disorders by flow cytometry. *Cytometry Part B (Clinical Cytometry).* 2010; 78B: 211–230.
4. CDC. Meningococcal ACIP Vaccine Recommendations. Advisory Committee for Immunization Practices (ACIP). MMWR 2015. Available at http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mening.html. Accessed March 17, 2016.
5. Niaudet P. Complement-mediated hemolytic uremic syndrome. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed March 28, 2017.

6. Loirat C, Fakhouri F, Ariceta G, et al. An international consensus approach to the management of atypical hemolytic uremic syndrome in children. *Pediatr Nephrol.* 2016; 31: 15-39.

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

**Note: For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**Note: For Medicare members,** to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.