

Title: eculizumab (Soliris)

Origination: 05/27/09	Revised: 11/16/11	Annual Review: 12/15/11
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Purpose:

To provide guidelines and criteria for the review and decision determination of requests for medications that requires prior authorization.

Background Information:

Definitions

- Hemolytic anemia is the abnormal breakdown of intravascular red blood cells (RBC) and release of hemoglobin into the plasma, causing anemia.
- Paroxysmal Nocturnal Hemoglobinuria (PNH) Members suffer from a genetic mutation which leads to the generation of abnormal RBCs (PNH cells). PNH cells are targeted by the immune system and destroyed. The loss of these PNH cells (also called intravascular hemolysis) results in low RBC counts (anemia), fatigue, hemoglobinuria, plasma free hemoglobin, and indirectly thrombosis, abdominal pain, dysphagia, erectile dysfunction, and pulmonary hypertension.

Medication Summary

- Soliris is a monoclonal antibody that specifically binds to the complement protein C5, thereby inhibiting its cleavage to C5a and C5b and preventing the generation of the terminal complement complex C5b-9. Soliris thus inhibits terminal complement mediated intravascular hemolysis.
- Soliris is the first treatment for paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis. PNH is a rare, life-threatening, and genetically acquired form of hemolytic anemia.
- Soliris is supplied as a 300mg single-use vial containing 30ml of 10mg/ml sterile, preservative-free solution. Soliris is diluted to a final concentration of 5mg/ml.

Reference Statement

- Guidelines are compiled from available US Food and Drug Administration (FDA) approved indications, general practice guidelines, and/or evidence-based uses established through phase III clinical studies without published conflicting data. Only clinical studies published in their entirety in reputable peer-reviewed journals will be evaluated.

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Background Information, continued:

Eligibility Criteria

- Member must be eligible and have applicable benefit coverage.
- Prior authorization requests that do not meet clinical criteria in this Procedure will be forwarded to a Clinical Pharmacist for review.

Exclusions

- Member less than 18 years of age, as safety and efficacy have not been established.
- Unresolved serious *Neisseria meningitidis* infection.
- Members not currently vaccinated against *Neisseria meningitidis* (meningococcal vaccination).
- Members with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

Procedure:

- 1.0 Request for *initial therapy* for paroxysmal nocturnal hemoglobinuria (PNH) requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying **ALL** of the following criteria:
 - 1.1 Member must have definitive diagnosis of paroxysmal nocturnal hemoglobinuria as evidenced by **both** of the following:
 - 1.1.1 Elevation of lactate dehydrogenase (LDH) level (within last 30 days) which indicates degree of intravascular hemolysis (Normal LDH range is 105 - 333 IU/L); **AND**
 - 1.1.2 Confirmed PNH type III erythrocytes detectable by flow cytometry (at least 10%):
 - 1.1.2.1 Cytometry should be performed prior to transfusion or at least one (1) month since last transfusion to avoid dilution of abnormal cell proportion;
 - 1.2 Member hemoglobin level less than 9g/dL in the presence of symptoms, or less than 7g/dL without symptoms (lab should be drawn before transfusion or at least one (1) month since last transfusion); **AND**
 - 1.3 Member must be transfusion-dependent, requiring at least four (4) RBC transfusions in the past 12 months; **AND**

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Procedure, continued:

- 1.0 Request for *initial therapy* for paroxysmal nocturnal hemoglobinuria (PNH) requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying **ALL** of the following criteria, continued:
 - 1.4 Member must have platelet counts of at least 30,000/mm³; **AND**
 - 1.5 Member must have received meningococcal vaccine at least two (2) weeks prior to initiation of Soliris therapy.
- 2.0 If Member meets all of the above criteria, may approve Soliris initially for two (2) months. The recommended dosage regimen for Soliris consists of induction and maintenance phases as outlined below:
 - 2.1 During the induction phase, Soliris 600mg by IV infusion every week for the first four (4) weeks followed by 900mg infusion on week five (5);
 - 2.2 The maintenance phase consists of a 900mg infusion every 14 days thereafter.
- 3.0 Request for *continuation of therapy* for paroxysmal nocturnal hemoglobinuria (PNH) beyond the initial authorization period requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying **ALL** of the following:
 - 3.1 Member must be showing improvement in disease stability by all of the following:
 - 3.1.1 Reduction of intravascular hemolysis as measured by serum LDH levels (should be a reduction from baseline); **AND**
 - 3.1.2 No further PRBC transfusions required secondary to the disease; **AND**
 - 3.1.3 Hemoglobin levels should be above baseline;

AND

 - 3.2 Member is tolerating therapy without any adverse effects;
 - 3.3 If the Member meets all of the above criteria, may approve Soliris for an additional six (6) months at the maintenance infusion dose of 900mg every 14 days.

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Procedure, continued:

- 4.0 Request for *initial therapy* for **atypical hemolytic uremic syndrome (aHUS)** requires documentation from the Member’s medical records maintained by the requesting independent practitioner verifying **ALL** of the following criteria:
 - 4.1 Member is at least two (2) months of age;
 - 4.2 Member weighs at least five (5) kilograms;
 - 4.3 Member has meningococcal vaccine at least two (2) weeks prior to initiation of Soliris therapy.

- 5.0 If Member meets all of the above criteria, may approve Soliris initially for two (2) months. The recommended dosage regimen for Soliris consists of induction and maintenance phases as outlined below:
 - 5.1 For Members \geq 40 kg: During the induction phase, Soliris 900mg by IV infusion every week for the first four (4) weeks followed by 1200mg infusion on week five (5). The maintenance phase consists of a 1200mg infusion every 14 days thereafter;
 - 5.2 For Members <40 kg, see dosage chart below:

Weight-Based Dosing of Soliris for Members <40 kg		
Weight (kg)	Induction	Maintenance dose
30-39	600 mg weekly x 2 weeks	900 mg at week 3 then 900mg every 14 days
20-29	600 mg weekly x 3 weeks	600 mg every 14 days
10-19	600 mg weekly x 1 week	300 mg at week 2 & every 14 days thereafter
5-9	300 mg weekly x 2 weeks	300 mg every 21 days thereafter

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Procedure, continued:

- 6.0 Request for *continuation of therapy* for **atypical hemolytic uremic syndrome (aHUS)** beyond the initial authorization period requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying **ALL** of the following:
- 6.1 Response to treatment, as defined by **one (1)** or more of the following:
- 6.1.1 Platelet count improvement from baseline; **OR**
- 6.1.1 Member shows $\geq 25\%$ reduction in SrCr; **OR**
- 6.1.1 Reduction in the number of plasma infusion interventions or dialysis sessions;
- 6.2 If Member weighs <40 kg, updated weight for weight-based dosing;
- 6.3 If the Member meets all of the above criteria, may approve Soliris for an additional six (6) months at the maintenance infusion dose of 1200mg every 14 days **OR if Member is <40 kg**, see weight-based dosing chart above for **maintenance dose**.

References:

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Disclaimer Information:

Prior Authorization criteria are developed to determine coverage for AvMed Health Plans' benefits, and are published to provide a better understanding of the basis upon which coverage decisions are made. AvMed Health Plans makes coverage decisions based on the Member's benefit plan contract and these criteria. This guideline sets forth concise clinical coverage criteria which have been developed from a review of current literature, policies of the FDA and other government agencies, and other appropriate references, in consultation and with approval from practicing physicians who are members of AvMed's Pharmacy and Therapeutic committee. Treating providers are solely responsible for the medical advice and treatment of Members. This guideline may be updated and therefore is subject to change. The use of these criteria is neither a guarantee of payment nor a final prediction of how specific claim(s) will be adjudicated.