

SOLIRIS® (ECULIZUMAB)

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[Instructions for Use](#) ⓘ

Table of Contents	Page
COVERAGE RATIONALE	1
APPLICABLE CODES	1
DESCRIPTION OF SERVICES	2
BENEFIT CONSIDERATIONS	2
CLINICAL EVIDENCE	2
U.S. FOOD AND DRUG ADMINISTRATION	3
REFERENCES	4
GUIDELINE HISTORY/REVISION INFORMATION	5
INSTRUCTIONS FOR USE	5

Related Medical Management Guideline

- [Provider Administered Drugs – Site of Care](#)

COVERAGE RATIONALE

See [Benefit Considerations](#) ⓘ

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

- Atypical hemolytic uremic syndrome (aHUS)¹
- Paroxysmal nocturnal hemoglobinuria (PNH)¹
- Generalized myasthenia gravis^{1,9,11}

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

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 guideline 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 and Guidelines may apply.

HCPCS Code	Description
J1300	Injection, eculizumab, 10 mg

ICD-10 Procedure Code	Description
D59.3	Hemolytic-uremic syndrome
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]
G70.00	Myasthenia gravis without (acute) exacerbation

Maximum Dosage Requirements

Maximum Allowed Quantities by HCPCS Units

This section provides information about the maximum dosage per administration for omalizumab administered by a medical professional.

Medication Name		Diagnosis	Maximum Dosage per Administration	HCPCS Code	Maximum Allowed
Brand	Generic				
Soliris	Eculizumab	aHUS	1200 mg	J1300	120 HCPCS units (10 mg per unit)

Medication Name		Diagnosis	Maximum Dosage per Administration	HCPCS Code	Maximum Allowed
Brand	Generic				
Soliris	Eculizumab	Myasthenia Gravis	1200 mg	J1300	120 HCPCS units (10 mg per unit)
Soliris	Eculizumab	PNH	900 mg	J1300	90 HCPCS units (10 mg per unit)

HCPCS Code Based Maximum Dosage Information

Maximum Allowed Quantities by National Drug Code (NDC) Units

The allowed quantities in this section are calculated based upon both the maximum dosage information supplied within this policy as well as the process by which NDC claims are billed. This list may not be inclusive of all available NDC's for each drug product and is subject to change.

Medication Name		Diagnosis	How Supplied	National Drug Code	Maximum Allowed
Brand	Generic				
Soliris	Eculizumab	aHUS	300 mg vials	25682-0001-01	4 vials/120 ml
Soliris	Eculizumab	Myasthenia Gravis	300 mg vials	25682-0001-01	4 vials/120ml
Soliris	Eculizumab	PNH	300 mg vials	25682-0001-01	3 vials/90ml

DESCRIPTION OF SERVICES

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. The precise mechanism by which eculizumab exerts its therapeutic effect in gMG patients is unknown, but is presumed to involve reduction of terminal complement complex C5b-9 deposition at the neuromuscular junction. ¹⁻³

BENEFIT CONSIDERATIONS

Some Certificates of Coverage allow coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. 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 benefit 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.

****Additional Information:** Clinical coverage in this policy addresses the drug only. It does not address coverage for drug administration in a hospital outpatient department. Please refer to the member specific benefit plan document and the Medical Management Guideline titled [Provider Administered Drugs - Site of Care](#) for more information. The member specific benefit plan document determines coverage.

CLINICAL EVIDENCE

Proven/Medically Necessary

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.⁴ 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). 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.

Generalized Myasthenia Gravis

Eculizumab is indicated for the treatment of generalized myasthenia gravis.¹

Howard et al completed a phase 3 randomized, double-blind, placebo-controlled, multi-center study (REGAIN) that assessed the efficacy and safety of eculizumab in patients 18 years of age and older, with a confirmed diagnosis of generalized myasthenia gravis.^{9,11} Patients were required to be classified by the Myasthenia Gravis Foundation of America as Class II to IV at screening, and a Myasthenia Gravis-Activities of Daily Living (MG-ADL) scale ≥ 6 at screening and randomization, and vaccination against *Neisseria meningitidis*. Patients were also to have failed at least two immunosuppressive agents, or failed at least one agent, and require chronic plasma exchange or IVIG for 12 months without symptom control. One hundred twenty-five patients were randomized to receive either placebo (n=63), or eculizumab (n=62): 900 mg IV weekly for 4 doses, followed by 1,200 mg IV every 2 weeks during weeks 4 through 26. Primary outcome measures included the change in total MG-ADL score and the change in MG-ADL total score from baseline at week 26 as compared to placebo. A clinical response in MG-ADL was defined as at least a 3-point improvement. The primary analysis showed no significant difference between eculizumab and placebo. In evaluating clinically meaningful response, a higher proportion of patients achieved a clinically meaningful response with eculizumab than with placebo ($p < 0.05$). No deaths or cases of meningococcal infection occurred during the study. The most common adverse events in both groups were headache and upper respiratory tract infection. Myasthenia gravis exacerbations were reported by six (10%) patients in the eculizumab group and 15 (24%) in the placebo group. Six (10%) patients in the eculizumab group and 12 (19%) in the placebo group required rescue therapy. The change in the MG-ADL score was not statistically significant between eculizumab and placebo, as measured by the worst-rank analysis. Eculizumab was well tolerated. The authors disclosed that the use of a worst-rank analytical approach proved to be an important limitation of this study since the secondary and sensitivity analyses results were inconsistent with the primary endpoint result. The authors state that further research into the role of complement is needed.

Unproven/Not Medically Necessary

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, further studies are warranted to demonstrate that it is both safe and effective for this indication.

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
- Treatment of adult patients with generalized Myasthenia Gravis (gMG) who are antiacetylcholine receptor (AChR) antibody positive

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:

- Vaccinate for meningococcal disease according to the most current Advisory Committee on Immunization Practices (ACIP) recommendations for patients with complement deficiencies
- Revaccinate patients in accordance with ACIP recommendations, considering the duration of Soliris therapy
- Immunize patients without a history of meningococcal vaccination at least 2 weeks prior to receiving the first dose of Soliris.
 - If urgent Soliris therapy is indicated in an unvaccinated patient, administer meningococcal vaccine(s) as soon as possible.
- Closely monitor patients for early signs and symptoms of meningococcal infection and evaluate patients immediately if an infection is suspected.

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 at <http://www.solirisrems.com/>.^{1,3}

REFERENCES

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GUIDELINE HISTORY/REVISION INFORMATION

Date	Action/Description
09/01/2019	<p>Related Policies</p> <ul style="list-style-type: none"> Updated reference link to reflect title change for <i>Provider Administered Drugs – Site of Care</i> (previously titled <i>Provider Administered Drugs – Site of Care Review Guidelines</i>) <p>Supporting Information</p> <ul style="list-style-type: none"> Updated <i>References</i> section to reflect the most current information; no change to coverage rationale or list of applicable codes Archived previous policy version MMG142.J

INSTRUCTIONS FOR USE

This Medical Management Guideline provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard benefit plan. In the event of a conflict, the member specific benefit plan document governs. Before using this guideline, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Management Guideline 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. UnitedHealthcare West Medical Management 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.

Member benefit coverage and limitations may vary based on the member’s benefit plan Health Plan coverage provided by or through UnitedHealthcare of California, UnitedHealthcare Benefits Plan of California, UnitedHealthcare of Oklahoma, Inc., UnitedHealthcare of Oregon, Inc., UnitedHealthcare Benefits of Texas, Inc., or UnitedHealthcare of Washington, Inc.