Medical Necessity Guideline

Medical Necessity Guideline (MNG) Title: Eculizumab		
MNG #: 020	**☒SCO ☒One Care**	**Prior Authorization Needed? ☒Yes ☐No**
Clinical: ☒	**Operational: ☒**	**Informational: ☐**
Medicare Benefit: ☒Yes ☐No	**Approval Date: 06/06/2019**	**Effective Date: 09/15/2019**
Last Revised Date: 3/26/2020, 4/30/2021	**Next Annual Review Date:** 06/06/2020, 3/26/2021; 4/30/2022	**Retire Date:**

OVERVIEW:

Complement inhibitors are therapeutic agents (such as Eculizumab and Ravulizumab-cwvz) that target different levels and/or steps of the complement cascade to prevent the triggering and progression of the pathway. Eculizumab (Soliris) and Ravulizumab-cwvz (Ultomiris) are monoclonal antibodies that bind with high affinity to complement protein C5. This inhibits the cleavage of C5a (the proinflammatory anaphylatoxin) and C5b (initiating subunit of the terminal complement complex C5b9) to prevent the generation of the terminal complement complex C5b9.

Eculizumab (Soliris) is a U.S. Food and Drug Administration (FDA) -approved complement inhibitor indicated for the treatment of:

- *Atypical Hemolytic Uremic Syndrome* (aHUS) by inhibiting complement-mediated thrombotic microangiopathy,
- *Generalized Myasthenia Gravis* (gMG) who are anti-acetylcholine receptor antibody positive by (presumptively) reducing the terminal complement complex C5b-9 deposition at the neuromuscular junction,
- *Paroxysmal Nocturnal Hemoglobinuria* (PNH) by inhibiting terminal complement-mediated intravascular hemolysis, and
- *Neuromyelitis Optica Spectrum Disorder (NMOSD)* who are anti-aquaporin-4 (AQP4) antibody positive by (presumptively) inhibiting the aquaporin-4-antibody induced terminal complement C5b-9 deposition

Ravulizumab-cwvz (Ultomiris) is an FDA-approved alternative anticomplement therapy that has been engineered from eculizumab. This long-acting complement protein C5 inhibitor is indicated for the treatment of:

- *Atypical Hemolytic Uremic Syndrome* (aHUS) by inhibiting complement-mediated thrombotic microangiopathy, and
- *Paroxysmal Nocturnal Hemoglobinuria* (PNH) by inhibiting terminal complement-mediated intravascular hemolysis

DEFINITIONS:

Atypical Hemolytic Uremic Syndrome (aHUS): Condition that is a type of thrombotic microangiopathy in patients without a coexisting infection or underlying disease. It is caused by the uncontrolled activation of the complement system and results in nonimmune hemolytic anemia, thrombocytopenia, and organ damage (predominantly renal failure).

Generalized Myasthenia Gravis (gMG): Autoimmune disorder that affects the neuromuscular junction and is characterized by generalized weakness of the skeletal and extraocular muscles.

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Paroxysmal Nocturnal Hemoglobinuria (PNH): Rare acquired clonal disorder of the hematopoietic stem cell that is associated with hemolytic anemia, bone marrow failure, and thrombosis.

Neuromyelitis Optica Spectrum Disorder (NMOSD): Rare inflammatory disorders of the central nervous system that is characterized by severe and necrotizing immune-mediated demyelination that result in axonal damage that predominantly target the optic nerves and spinal cord.

DECISION GUIDELINES:

Clinical Coverage Criteria:

Commonwealth Care Alliance may cover the use of Eculizumab (Soliris) or Ravulizumab-cvwz (Ultomiris) for the treatment of **Atypical Hemolytic Uremic Syndrome (aHUS)**, when all the following criteria are met:

- Documented diagnosis of atypical hemolytic uremic syndrome, AND
- The prescribing physician is a hematologist or nephrologist, AND
- The prescribing physician is enrolled in the Soliris and/or Ultomiris REMS program, AND
- The member has been vaccinated against meningococcal infection (at least 2 weeks prior to initiating treatment if not previously vaccinated), AND
- The member does not have Shiga Toxin E. coli related hemolytic uremic syndrome (STEC-HUS)

Commonwealth Care Alliance may cover the use of Eculizumab (Soliris) for the treatment of **Generalized Myasthenia Gravis (gMG)**, when all the following criteria are met:

- Documented diagnosis of generalized myasthenia gravis (gMG), AND
- Documentation of a positive serologic test for anti-acetylcholine antibodies, AND
- Documentation of Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV gMG, AND
- Documentation of Myasthenia Gravis – Activities of Daily Living (MG-ADL) total score ≥6, AND
- The prescribing physician is a neurologist, AND
- The prescribing physician is enrolled in the Soliris REMS program, AND
- Documentation of at least one of the following, AND:
    - Previous trial at least 12 months ago of one or more immunosuppressive therapies as a monotherapy or in combination, OR
        - Immunosuppressive therapies: Azathioprine, Cyclophosphamide, Methotrexate
    - Previous trial of one immunosuppressive therapy for at least 12 months
        - Immunosuppressive therapies: Chronic plasmapheresis, Plasma exchange, Intravenous immunoglobulin without symptom control
- The member has been vaccinated against meningococcal infection (at least 2 weeks prior to initiating treatment if not previously vaccinated)

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Commonwealth Care Alliance may cover the use of Eculizumab (Soliris) or Ravulizumab-cwvz (Ultomiris) for the treatment of **Paroxysmal Nocturnal Hemoglobinuria (PNH)**, when all the following criteria are met:

- Documented diagnosis of paroxysmal nocturnal hemoglobinuria (PNH), AND
- Diagnosis must be confirmed by flow cytometry of peripheral blood to detect the absence or severe deficiency of ≥ 2 glycosylphosphatidylinositol anchored proteins (GPI-APs) on ≥ 2 blood cell lineages, AND
- The prescribing physician is a hematologist or nephrologist, AND
- The prescribing physician is enrolled in the Soliris and/or Ultomiris REMS program, AND
- The member has been vaccinated against meningococcal infection (at least 2 weeks prior to initiating treatment if not previously vaccinated)

Commonwealth Care Alliance may cover the use of Eculizumab (Soliris) for the treatment of **Neuromyelitis Optica Spectrum Disorder (NMOSD)**, when all the following criteria are met:

- Documented diagnosis of neuromyelitis optica spectrum disorder (NMOSD), AND
- Documentation of a positive serological test for anti-aquaporin-4 immunoglobulin G (AQP4-IgG) antibodies, AND
- Documentation that the member exhibits one the following core clinical characteristics of, AND:
    - Conditions: Optic neuritis, acute myelitis, area postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy or acute dicephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions, OR symptomatic cerebral syndrome with NMOSD-typical brain lesions
- The prescribing physician is a neurologist or ophthalmologist, AND
- The prescribing physician is enrolled in the Soliris REMS program, AND
- The member has been vaccinated against meningococcal infection (at least 2 weeks prior to initiating treatment if not previously vaccinated)

Note that the primary care physician may prescribe the corresponding complement inhibitor as long as there is documentation (in the form of office notes or its equivalent) or record of active and regular consultation with the appropriate specialist.

LIMITATIONS/EXCLUSIONS:

Commonwealth Care Alliance will not cover the use of Eculizumab (Soliris) or Ravulizumab-cwvz (Ultomiris), under the following conditions, including but not limited to:

- For the treatment of patients with Shiga Toxin E. coli related hemolytic uremic syndrome (STEC-HUS),
- If the member is receiving combination complement inhibitor therapy,
- If the member has unresolved serious Neisseria meningitidis infection,
- If the member has any other systemic infection, OR
- If the member is not currently vaccinated against Neisseria meningitidis (unless the risks of delaying treatment outweigh the risks of developing a meningococcal infection)

AUTHORIZATION:

The following list(s) of codes is provided for reference purposes only and may not be all inclusive. Listing of a code in

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this guideline does not signify 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. This Medical Necessity Guideline is subject to all applicable Plan Policies and Guidelines, including requirements for prior authorization and other requirements in Provider's agreement with the Plan (including complying with Plan's Provider Manual specifications).

HCPCS Code	Description
J1300	Injection, Eculizumab, 10 mg
J1303	Injection, Ravulizumab-cwvz, 10 mg

Disclaimer:

This Medical Necessity Guideline is not a rigid rule. As with all of CCA's criteria, the fact that a member does not meet these criteria does not, in and of itself, indicate that no coverage can be issued for these services. Providers are advised, however, that if they request services for any member who they know does not meet our criteria, the request should be accompanied by clear and convincing documentation of medical necessity. The preferred type of documentation is the letter of medical necessity, indicating that a request should be covered either because there is supporting science indicating medical necessity (supporting literature (full text preferred) should be attached to the request), or describing the member's unique clinical circumstances, and describing why this service or supply will be more effective and/or less costly than another service which would otherwise be covered. Note that both supporting scientific evidence and a description of the member's unique clinical circumstances will generally be required.

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RELATED REFERENCES:

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ATTACHMENTS:

EXHIBIT A:	
EXHIBIT B	

REVISION LOG:

REVISION DATE	DESCRIPTION
4/30/2021	Added definitions, limitations/exclusions, authorization (with HCPCS codes), and related reference sections; Background information on complement inhibitors and mechanisms of actions; Diagnostic criteria for paroxysmal nocturnal hemoglobinuria for coverage; Neuromyelitis optica spectrum disorder as a condition that eculizumab is indicated and deemed medically necessary for; the wording of prescribing physician need to be enrolled in soliris and/or ultomiris REMS program.
3/26/2020	KH Staff reviewed document and update format,
06/06/19	MNG reviewed and passed by the Medical Policy Committee

APPROVALS:

CCA Senior Clinical Lead [Print]	**Title [Print]**
Signature	**Date**
CCA Senior Operational Lead [Print]	**Title [Print]**
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Lori Tishler, MD	Senior Vice President, Medical Services
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