Complement Inhibitors – Eculizumab and Rayulizumab-cwz
Medical Necessity Guideline

Medical Necessity Guideline (MNG) Title: Complement Inhibitors – Eculizumab and Ravulizumab-cwvz		
MNG #: 020	**☒SCO ☒One Care** **☒ MA Medicare Premier** **☒ MA Medicare Value** **☒ RI Medicare Preferred** **☒ RI Medicare Value** **☒ RI Medicare Maximum**	**Prior Authorization Needed?** **☒ Yes (always required)** **☐ Yes (only in certain situations. See this MNG for details)** **☐ No**
Clinical: ☒	**Operational: ☒**	**Informational: ☐**
Medicare Benefit: **☒Yes ☐No**	**Approval Date:** 06/06/2019; 12/14/23	**Effective Date:** 09/15/2019; 12/14/23
Last Revised Date: 3/26/2020, 4/30/2021; 6/3/2022; 12/14/23	**Next Annual Review Date:** 06/06/2020, 3/26/2021; 4/30/2022; 6/3/2023; 12/14/24	**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 this complementary pathway to immunity. The complement cascade is an earlier more 'primitive' immune system which organisms are born with and which does not need antibodies to work. As such it also does not learn to adapt the way antibody immune systems do. Since a complement cascade is not as specific as antibodies, it is imperative to regulate it tightly to prevent its severe damage to our bodies' own tissues and organs.

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. This halting of the complement cascade is very effective in limiting certain autoimmune health problems. At the same time this halting can lead to severe and life-threatening disease or death. For this reason its approval for use must meet all criteria.

DECISION GUIDELINES:

Clinical Coverage Criteria:

Commonwealth Care Alliance (CCA) follows applicable Medicare and Medicaid regulations and uses InterQual Smart Sheets, when available, to review prior authorization requests for medical necessity. This Medical Necessity Guideline (MNG) applies to all CCA Products unless a more expansive and applicable CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), or state-specific medical necessity guideline exists.

Clinical Coverage Criteria:

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

- Hemolytic Uremic Syndrome, Atypical.

- Myasthenia Gravis, Anti-acetylcholine receptor antibody positive.
- Paroxysmal Nocturnal Hemoglobinuria.
- Neuromyelitis Optica Spectrum Disorder, Anti-aquaporin-4 antibody positive

Eculizumab (Soliris) may also be approved for biopsy-proven dense deposit disease.

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

- Hemolytic Uremic Syndrome, Atypical.
- Myasthenia Gravis, Anti-acetylcholine receptor antibody positive.
- Paroxysmal Nocturnal Hemoglobinuria.

FDA Requirements:
Immunization with Meningococcal vaccine at least 2 weeks before beginning treatment.

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:

- If use is identified as not indicated by CMS or the FDA, or if a use is specifically identified as not indicated in the American Hospital Formulary Services (AHFS), Elsevier/Gold Standard Clinical Pharmacology, NCCN Drugs and **BIOLOGIC**s Compendium, Truven Health Analytics Micromedex DrugDex® and/or Wolters Kluwer Lexi-Drugs® compendium, the off-label use is not supported, and the drug will not be covered.

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

REGULATORY NOTES:
Medical Necessity Guidelines are published to provide a better understanding of the basis upon which coverage decisions are made. CCA makes coverage decisions on a case-by-case basis by considering the individual member's health care needs. If at any time an applicable CMS LCD or NCD or state-specific MNG is more expansive than the criteria set forth herein, the

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NCD, LCD, or state-specific MNG criteria shall supersede these criteria. This MNG references the specific regulations, coverage, limitations, service conditions, and/or prior authorization requirements in the following:

1. U.S. Center for Medicare & Medicaid Services. (2019). *Local coverage article: Billing and coding: Eculizumab (A54548).* Retrieved from https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleid=54548&ver=24. Accessed 12/7/2023.
2. U.S. Center for Medicare & Medicaid Services. (2019). *Local coverage determination (LCD): Drugs and biologicals, coverage of, for label and off-label uses (L33394)*. Retrieved from https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=33394&ver=47. Accessed 12/7/2023.
3. U.S. Food and Drug Administration. (2017). *Soliris (eculizumab) injection, for intravenous use*. Retrieved from https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125166s422lbl.pdf
4. U.S. Food and Drug Administration. (2018). *Ultomiris (ravulizumab-cwvz), for intravenous use*. Retrieved from https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761108s000lbl.pdf

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.

RELATED REFERENCES:

1. Brodsky, R. (2019). *Clinical manifestations and diagnosis of paroxysmal nocturnal hemoglobinuria.* Retrieved from https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-paroxysmal-nocturnal-hemoglobinuria?search=paroxysmal%20nocturnal%20hemoglobinuria%20&source=search_result&selectedTitle=1~84&usage_type=default&display_rank=1
2. Callaghan, B., Shaughnessy, A., Rae-Grant, A., Freimer, M. (2018). *DynaMed: Myasthenia gravis.* Retrieved from https://www-dynamed-com.ahs.idm.oclc.org/topics/dmp-AN-T113873
3. DeZern, A., Fedorowicz, Z. & Aird, W. (2018). *DynaMed: Paroxysmal nocturnal hemoglobinuria*. Retrieved from https://www-dynamed-com.ahs.idm.oclc.org/topics/dmp-AN-T115903

REVISION LOG:

REVISION DATE	DESCRIPTION
12/31/23	Utilization Management Committee approval

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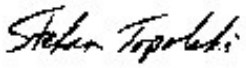
12/14/23	Updated description of complement, risks, and mechanism of action. Added requirement for meningococcal vaccine prior to therapy. Updated references.
6/3/2022	Template update. Added NGS LCD off-label indication.
4/30/2021	Added definitions, limitations/exclusions, authorization (with HCPCS codes), 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:

Stefan Topolski, MD	Medical Director
CCA Senior Clinical Lead [Print]	**Title [Print]**
	12/14/2023
Signature	**Date**
CCA Senior Operational Lead [Print]	**Title [Print]**
Signature	**Date**
	Chief Medical Officer
Nazlim Hagmann, MD	
CCA CMO or Designee [Print]	**Title [Print]**
	12/14/2023
Signature	**Date**