Pharmacy Medical Necessity Guidelines: Complement Inhibitors (Soliris® [eculizumab] and Ultomiris™ [ravulizumab])

Effective: January 1, 2021

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	√
Pharmacy (RX) or Medical (MED) Benefit	MED	Department to Review	MM/ PRECERT

These pharmacy medical necessity guidelines apply to the following:

Commercial Products

☒ Tufts Health Plan Commercial products – large group plans
☒ Tufts Health Plan Commercial products – small group and individual plans
☒ Tufts Health Freedom Plan products – large group plans
☒ Tufts Health Freedom Plan products – small group plans
- CareLink℠ – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization

Tufts Health Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product)
☒ Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans
☒ Tufts Health RITogether – A Rhode Island Medicaid Plan

Fax Numbers:

All plans except Tufts Health Public Plans: PRECERT:617.972.9409

Tufts Health Public Plans: MM: 888.415.9055

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

OVERVIEW

FOOD AND DRUG ADMINISTRATION-APPROVED INDICATIONS

Soliris (eculizumab) is a complement inhibitor indicated for the treatment of:

- **Atypical Hemolytic Uremic Syndrome (aHUS)**
  Patients with aHUS to inhibit complement-mediated thrombotic microangiopathy
- **Generalized Myasthenia Gravis (gMG)**
  Adult patients with gMG who are anti-acetylcholine receptor antibody positive
- **Neuromyelitis Optica Spectrum Disorder (NMOSD)**
  NMOSD in adult patients who are anti-aquaporin-4 antibody positive
- **Paroxysmal Nocturnal Hemoglobinuria (PNH)**
  Patients with PNH to reduce hemolysis

Ultomiris (ravulizumab-cwvz) is a complement inhibitor indicated for the treatment of:

- **Atypical Hemolytic Uremic Syndrome (aHUS)**
  Adults and pediatric patients one month of age and older with aHUS to inhibit complement-mediated thrombotic microangiopathy (TMA)
- **Paroxysmal Nocturnal Hemoglobinuria (PNH)**
  Patients with PNH to reduce hemolysis

Complement Inhibitors are not indicated for the treatment of patients with Shiga toxin *E. coli* related hemolytic uremic syndrome (STEC-HUS).

COVERAGE GUIDELINES

The plan may authorize coverage of Soliris (eculizumab) for Members when all of the following criteria are met:

Generalized Myasthenia Gravis (gMG)

1. Documented diagnosis of generalized myasthenia gravis

AND

2. Documentation of a positive serologic test for anti-acetylcholine antibodies

AND

3. Documentation of Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV generalized myasthenia gravis

AND

4. Documentation of a Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score ≥6

AND

5. The prescribing physician is a neurologist

AND

6. Documentation of at least one of the following:

a. At least a 12 month previous trial of two or more immunosuppressive therapies (either in combination or as monotherapy) (e.g., azathioprine, cyclophosphamide, methotrexate)
b. Previous trial of one immunosuppressive therapy with required chronic plasmapheresis, plasma exchange, or intravenous immunoglobulin

Neuromyelitis Optica Spectrum Disorder (NMOSD)

1. Documented diagnosis of neuromyelitis optica spectrum disorder

AND

2. Documentation of a positive serologic test for anti-aquaporin-4 antibodies

AND

3. The prescribing physician is a neurologist or an ophthalmologist
4. Documentation the Member has demonstrated an inadequate response to Uplizna (inebilizumab-cdon) or the provider has indicated clinical inappropriateness with Uplizna (inebilizumab-cdon)

The plan may authorize coverage of Soliris (eculizumab) or Ultomiris (ravulizumab) for Members when all of the following criteria are met:

Atypical Hemolytic Uremic Syndrome (aHUS)

1. Documented diagnosis of atypical hemolytic uremic syndrome

AND

2. The prescribing physician is a hematologist or nephrologist

Paroxysmal Nocturnal Hemoglobinuria (PNH)

1. Documented diagnosis of paroxysmal nocturnal hemoglobinuria

AND

2. The prescribing physician is a hematologist or nephrologist

LIMITATIONS

- Coverage will not be authorized if the Member is receiving combination complement inhibitor therapy.
- For the treatment of NMOSD, combination therapy with Uplizna (enebilizumab-cdon) will not be authorized.
- Complement inhibitors will not be approved for other types of hemolytic uremic syndrome including STEC-HUS.
- For the diagnosis of generalized myasthenia gravis, initial approval of Soliris (eculizumab) will be authorized for 6 months. Subsequent 12 month authorizations will require documentation from a neurologist of a decrease in the MG-ADL total score from baseline.

CODES

The following HCPCS/CPT code(s) are:

Code	Description
J1300	Injection, eculizumab, 10 mg
J1303	Injection, ravulizumab-cwvz, 10 mg

REFERENCES

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3. Genetics Home Reference. Atypical hemolytic-uremic syndrome. URL: ghr.nlm.nih.gov/condition/atypical-hemolytic-uremic-syndrome Available from Internet. Accessed 2011 October 12.
4. Hill A, Hillmen P, Richards SJ et al. Sustained response and long-term safety of eculizumab in paroxysmal nocturnal hemoglobinuria. *Blood*. 2005 Oct 1; 106(7):2559-65.
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7. Kanakura Y, Ohyashiki K, Shichishima T et al. Safety and efficacy of the terminal complement inhibitor eculizumab in Japanese patients with paroxysmal nocturnal hemoglobinuria: the AEGIS clinical trial. *Int J Hematol*. 2011 Jan; 93(1):36-46.
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11. Legendre CM, Licht C, Muus P, et al. Terminal complement inhibitor eculizumab in atypical hemolytic-uremic syndrome. *N Engl J Med*. 2013 Jun 6; 368(23):2169-81.
12. Loirat C, Fremeaux-Bacchi V. Atypical hemolytic uremic syndrome. *Orphanet J Rare Dis*. 2011 Sep 8; 6(1):60.
13. Noris M, Remuzzi G. Atypical Hemolytic–Uremic Syndrome. *N Engl J Med*. 2009 Oct 22; 361(17):1676-87.
14. Soliris (eculizumab) [package insert]. Cheshire, CT: Alexion Pharmaceuticals, Inc.; October 2017.
15. The Medical Letter® On Drugs and Therapeutics, *Eculizumab (Soliris) for Paroxysmal Nocturnal Hemoglobinuria.* medicalletter.org, Vol. 49 (Issue 1270), September 24, 2007.
16. Ultomiris (ravulizumab-cwvz) [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc. October 2019.

APPROVAL HISTORY

November 13, 2007: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

1. November 11, 2008: No changes
2. November 10, 2009: No changes
3. January 1, 2010: Removal of Tufts Health Plan Medicare Preferred language (separate criteria have been created specifically for Tufts Health Plan Medicare Preferred)
4. September 14, 2010: No changes
5. September 13, 2011: No changes
6. November 15, 2011: Added coverage guidelines for atypical Hemolytic Uremic Syndrome
7. February 14, 2012: Added nephrologist to prescribing specialists
8. January 15, 2013: No changes
9. November 5, 2013: No changes
10. November 4, 2014: No changes
11. November 10, 2015: No changes
12. January 1, 2016: Administrative change to rebranded template
13. April 12, 2016: Effective 10/1/2016, MNG applies to Tufts Health Together.
14. April 11, 2017: Administrative update. Effective 6/1/2017, Medical Necessity Guideline applies to Tufts Health RITogether.
15. December 12, 2017: Updated Medical Necessity Guidelines to include coverage criteria for the new indication myasthenia gravis.
16. August 7, 2018: No changes
17. April 9, 2019: Updated name of Medical Necessity Guideline to Complement Inhibitors. Added Ultomiris to the Medical Necessity Guideline.
18. July 1, 2019: Administrative update: Added new C code C9052 to Medical Necessity Guideline.
19. August 13, 2019: Added criteria for Soliris for the expanded indication of treatment of NMOSD in adult patients who are anti-aquaporin-4 antibody positive.
20. November 12, 2019: Added Ultomiris to the coverage criteria for aHUS based on updated package labeling. Updated the Limitations section to clarify that all Complement Inhibitors will not be approved for other types of hemolytic uremic syndrome including STEC-HUS based on package labeling.
21. September 15, 2020: Effective January 1, 2021, added the following Limitation: "For the treatment of NMOSD, combination therapy with Uplizna (enebilizumab-cdon) will not be authorized." Removed the following requirement "The Member has been vaccinated against meningococcal infection (at least 2 weeks prior to treatment, if not previously vaccinated)." For Soliris for the indication of Neuromyelitis Optica Spectrum Disorder, added the following requirement "Documentation the Member has demonstrated an inadequate response to Uplizna (inebilizumab-cdon) or the provider has indicated clinical inappropriateness with Uplizna (inebilizumab-cdon."

22. November 10, 2020: Effective January 1, 2021, updated the Limitation "For the treatment of NMOSD, combination therapy with Uplizna (enebilizumab-cdon) will not be authorized." to "For the treatment of NMOSD, combination therapy with other NMOSD disease modifying treatments will not be authorized."

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.