SmartPA Criteria Proposal

Drug/Drug Class:	C5 Complement Inhibitors Clinical Edit
First Implementation Date:	August 4, 2022
Proposed Date:	July 18, 2023
Prepared for:	MO HealthNet
Prepared by:	MO HealthNet/Conduent
Criteria Status:	☒Existing Criteria ☐Revision of Existing Criteria ☐New Criteria

Executive Summary

Purpose: Ensure appropriate utilization and control of C5 Complement Inhibitors.

Why Issue Selected: The complement system, or cascade, is a major component of the immune system which enhances destruction of pathogens and induces a series of inflammatory responses to fight infection. The system includes many plasma proteins that form three major pathways of complement activation (classical, lectin, and alternative). The major components of the cascade include the C1 complex, C2b and C4b fragments, C3 convertase, C3a and C3b fragments, C5a and C5b fragments, and the membrane attack complex comprised of C5b, C6, C7, C8, and C9. Each component plays a role in clearing foreign microbes or initiating inflammatory responses. Soliris® (eculizumab) and Ultomiris® (ravulizumab) are monoclonal antibodies that bind to and inhibit complement protein C5, preventing its cleavage to C5a and C5b.

Soliris was first approved by the FDA in 2007 for the indication of paroxysmal nocturnal hemoglobinuria (PNH). In 2011, it gained the indication of atypical hemolytic uremic syndrome (aHUS). The FDA then approved Soliris for the indications of generalized myasthenia gravis (gMG) in patients who are anti-acetylcholine receptor (AchR) antibody positive and neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive in 2017 and 2019, respectively. Soliris is administered as an IV infusion and consists of an induction dose followed by maintenance dosing dependent on indication.

Ultomiris was approved by the FDA in 2018 for adult and pediatric patients with PNH, and subsequently approved for aHUS in 2019. In 2022, Ultomiris was also approved for the indication of gMG in patients who are anti-acetylcholine receptor (AchR) antibody positive. Ultomiris is administered as an IV infusion and consists of a weight-based loading dose followed by maintenance dosing.

Due to the high cost and specific approved indications, MO HealthNet will impose clinical criteria to ensure appropriate utilization of C5 Complement Inhibitors.

Program-Specific Information:

Date Range FFS 4-1-22 to 3-31-23				
Drug	**Claims**	**Spend**	**Avg Spend per Month**	**Avg Spend per Claim**
SOLIRIS 300 MG/30 ML	160	$3,075,741.20	$256,311.77	$19,223.38
ULTOMIRIS 300 MG/30 ML	0	-	-	-
ULTOMIRIS 300 MG/3 ML	30	$1,255,980.20	$104,665	$41,866
ULTOMIRIS 1100 MG/11 ML	7	$341,693.49	$28,474.46	$48,813.36

Type of Criteria:
☐ **Increased risk of ADE**
☒ **Appropriate Indications**
☐ **Preferred Drug List**
☒ **Clinical Edit**

Data Sources:
☐ **Only Administrative Databases**
☒ **Databases + Prescriber-Supplied**

Setting & Population

- Drug class for review: C5 Complement Inhibitors
- Age range: All appropriate MO HealthNet participants

Approval Criteria

Initial Therapy:

- Prescribed by or in consultation with an appropriate specialist in the treated disease state **AND**
- Documented diagnosis of aHUS **AND**
  - For Soliris: documented adequate therapeutic trial of Ultomiris (trial defined as 3 claims in the past 12 months) **OR**
- Documented diagnosis of PNH as confirmed by laboratory findings (i.e., flow cytometry, lactate dehydrogenase level of 1.5 times the upper limit of normal, bone marrow aspirate and biopsy) **AND**
  - Participant is transfusion-dependent (Hb ≤ 7 g/dL or Hb ≤ 9 g/dL and experiencing symptoms of anemia) **OR**
  - Documentation of symptomatic thromboembolic complications (e.g., abdominal pain, shortness of breath, chest pain, end-organ damage) **AND**
  - For Soliris:
    - Participant aged ≥ 18 years **AND**
    - Documented adequate therapeutic trial of Ultomiris (trial defined as 3 claims in the past 12 months) **OR**
- Documented diagnosis of gMG **AND**
  - Participant is aged ≥ 18 years **AND**
  - Myasthenia Gravis Foundation of America clinical classification of class II, III, or IV **AND**
  - Documented positive anti-acetylcholine receptor (AchR) antibody test **AND**
  - Documented baseline Myasthenia Gravis-Activities of Daily Living Score (MG-ADL) greater than or equal to 6 **OR**
  - Documented baseline Quantitative Myasthenia Gravis (QMG) score of greater than or equal to 12 **AND**
  - Adequate therapeutic trial of 2 immunosuppressants (e.g., glucocorticoids, azathioprine, mycophenolate, tacrolimus, cyclosporine, methotrexate) (90/120 days) **AND**
  - For Soliris: documented adequate therapeutic trial of Ultomiris (trial defined as 3 claims in the past 12 months) **OR**
- Documented diagnosis of NMOSD **AND**
  - Soliris only **AND**

- Documented adequate therapeutic trial of Enspryng and Uplizna (trial defined as at least 6 months of therapy for each agent), see NMOSD CE for further information regarding criteria for Enspryng and Uplizna **AND**
- Participant is aged ≥ 18 years **AND**
- Participant is seropositive for anti-aquaporin-4 (AQP4) antibodies **AND**
- Documented baseline number and frequency of acute attacks **AND**

Continuation of Therapy:

- Documented compliance to prescribed drug therapy (defined as 3 claims in past 120 days) **AND**
- For PNH: initial approval is for 9 months, renewal of prior authorization for up to 12 months may be given following documentation of one the following:
  - Improvement or less than expected decline in fatigue and quality of life
  - Decrease in transfusion burden
  - Increase in Hb levels from baseline
  - Normalization of LDH levels.
- For gMG: initial approval is for 6 months, renewal of prior authorization for up to 6 months may be given following documentation of clinically significant improvement in MG-ADL score from baseline (defined as at least 2-point improvement in MG-ADL score).
- For NMOSD: initial approval is for 9 months, renewal of prior authorization may be for up to 12 months following documentation of decrease or stabilization in number and frequency of acute attacks from baseline.

Denial Criteria

- Therapy will be denied if all approval criteria are not met
- For Ultomiris: participant is currently pregnant

Required Documentation

Laboratory Results:		Progress Notes:	
MedWatch Form:		Other:	X

Disposition of Edit

Denial: Exception code “0682” (Clinical Edit)
Rule Type: CE

Default Approval Period

9 months

References

- Soliris (eculizumab) [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc.; November 2020.
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