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| **Policy Title:** | Soliris (eculizumab) and Ultomiris (ravulizumab) (**NON-HEMATOLOGY POLICY**<br>Intravenous | | |
| | | **Department:** | PHA |
| **Effective Date:** | 01/01/2020 | | |
| **Review Date:** | 09/18/2019, 12/20/2019, 1/22/2020, 12/2020, 5/27/2021, 3/3/2022, 8/4/2022, 4/27/2023,12/14/2023, 01/10/2024 | | |

**Purpose:** To support safe, effective, and appropriate use of Soliris (eculizumab) and Ultomiris (ravulizumab).

**Scope:** Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

**Policy Statement:**

Soliris (eculizumab) and Ultomiris (ravulizumab) are covered under the Medical Benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process. **For Hematology indications, please refer to the NHPRI Soliris or Ultomiris Hematology Policy.**

**Procedure:**

Coverage of Soliris (eculizumab) and Ultomiris (ravulizumab) will be reviewed prospectively via the prior authorization process based on criteria below.

***Initial Criteria:***

- MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

**Neuromyelitis optica spectrum disorder (NMOSD) for Soliris ONLY**

- Submission of medical records (e.g., chart notes, laboratory values, etc.) to support the diagnosis of neuromyelitis optica spectrum disorder (NMOSD) by a neurologist confirming all of the following:
  - Past medical history of one of the following:
    - Optic neuritis
    - Acute myelitis
    - Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
    - Acute brainstem syndrome
    - Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
    - Symptomatic cerebral syndrome with NMOSD-typical brain lesions; AND

- Positive serologic test for anti-aquaporin-4 immunoglobulin G (AQP4-IgG)/NMO-IgG antibodies; AND
- Diagnosis of multiple sclerosis or other diagnoses have been ruled out; AND

- Patient has not failed a previous course of Soliris therapy; AND
- One of the following:
  - History of at least two relapses during the previous 12 months prior to initiating Soliris; OR
  - History of at least three relapses during the previous 24 months, at least one relapse occurring within the past 12 months prior to initiating Soliris; AND
- Prescribed by, or in consultation with, a neurologist; AND
- Patient is not receiving Soliris in combination with any of the following:
  - Disease modifying therapies for the treatment of multiple sclerosis [e.g., Gilenya (fingolimod), Tecfidera (dimethyl fumarate), Ocrevus (ocrelizumab), etc.]
  - Anti-IL6 therapy [e.g., Actemra (tocilizumab), Enspryng (satralizumab)]
  - Uplizna (inebilizumab)
  - Rituximab; AND
- Patient has experienced a failure, contraindication or intolerance to Enspryng (satralizumab)* AND Uplizna (inebilizumab)

* This requirement **ONLY** applies to **Medicaid** Members

**Generalized myasthenia gravis (gMG) for Soliris and Ultomiris**

- Submission of medical records (e.g., chart notes, laboratory values, etc.) to support the diagnosis of generalized myasthenia gravis (gMG);AND
- Patient is at least 18 years of age: AND
- Prescribed by, or in consultation with, a neurologist; AND
- Patient has positive serologic test for anti-acetylcholine receptor (AChR) antibodies; AND
- Patient has a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of class II-IV disease§; AND
- Physician has assessed objective signs of neurological weakness and fatigability on a baseline neurological examination (e.g., including, but not limited to, the Quantitative Myasthenia Gravis (QMG) score, etc.); AND
- Patient has a Myasthenia Gravis-specific Activities of Daily Living scale (MG-ADL) total score ≥ 6 at initiation of therapy; AND
- Patient had an inadequate response after a minimum of one year trial with either:
  - History of failure of two or more immunosuppressive agents over the course of at least 12 months [e.g., azathioprine, methotrexate, cyclosporine, mycophenolate, etc.]; OR
  - Patient has required chronic treatment with plasmapheresis or plasma exchange (PE) or intravenous immunoglobulin (IVIG) in addition to immunosuppressant therapy; AND

- If the patient is requesting Soliris, the patient must have an inadequate response or contraindication to both ravulizumab (Ultomiris) AND efgartigimod IV (Vyvgart IV) [medical documentation must be provided]; AND
- If the patient is requesting Ultomiris, the patient must have an inadequate response or contraindication to efgartigimod (VyvgartIV) [medical documentation must be provided];
- Will not be used in combination with other immunomodulatory biologic therapies (i.e., rituximab, efgartigimod, etc.); AND
- Patient will avoid or use with caution medications known to worsen or exacerbate symptoms of MG (e.g., certain antibiotics, beta-blockers, botulinum toxins, hydroxychloroquine, etc.); AND
- Must not be administered with live-attenuated or live vaccines during treatment; AND
- Patient does not have an active infection, including clinically important localized infections

§ Myasthenia Gravis Foundation of America (MGFA) Disease Classifications::

- Class I: Any ocular muscle weakness; may have weakness of eye closure. All other muscle strength is normal.
- Class II: Mild weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.
  - IIa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
  - IIb. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
- Class III: Moderate weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.
  - IIIa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
  - IIIb. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
- Class IV: Severe weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.
  - IVa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
  - IVb. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
- Class V: Defined as intubation, with or without mechanical ventilation, except when employed during routine postoperative management. The use of a feeding tube without intubation places the patient in class IVb.

***Continuation of Therapy Criteria:***

- **Neuromyelitis optica spectrum disorder (NMOSD)**
  - Patient continues to meet initial criteria; AND
  - Submission of medical records (e.g., chart notes, laboratory tests) to demonstrate a positive clinical response from baseline as demonstrated by at least both of the following:
    - Reduction in the number and/or severity of relapses or signs and symptoms of NMOSD

    - Maintenance, reduction, or discontinuation of dose(s) of any baseline immunosuppressive therapy (IST) prior to starting Soliris. Note: Add on, dose escalation of IST, or additional rescue therapy from baseline to treat NMOSD or exacerbation of symptoms while on Soliris therapy will be considered as treatment failure.
- Soliris is dosed according to the US FDA labeled dosing for NMOSD: up to a maximum of 1200 mg every 2 weeks; AND
- Prescribed by, or in consultation with, a neurologist; AND
- Patient is not receiving Soliris in combination with any of the following:
    - Disease modifying therapies for the treatment of multiple sclerosis [e.g., Gilenya (fingolimod), Tecfidera (dimethyl fumarate), Ocrevus (ocrelizumab), etc.]
    - Anti-IL6 therapy [e.g., Actemra (tocilizumab), Enspryng (satralizumab)]
    - Uplizna (inebilizumab)
    - Vyvgart(efgartigimod)
    - Rituximab

- **Generalized myasthenia gravis (gMG)**
    - Patient continues to meet initial criteria; and
    - Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: serious meningococcal infections (septicemia and/or meningitis), infusion reactions, serious infections, thrombotic microangiopathy complications (TMA), etc; AND
    - Submission of medical records (e.g., chart notes, laboratory tests) to demonstrate a positive clinical response from baseline as demonstrated by all of the following:
        - Improvement and/or maintenance of at least a 3-point improvement (reduction in score) in the MG-ADL score from pre-treatment baseline.
        - Improvement in muscle strength testing with fatigue maneuvers as evidenced on neurologic examination when compared to baseline

(*May substitute an improvement of at least 5-points from baseline in the Quantitative Myasthenia Gravis (QMG) total score, if available)

**Coverage durations:**

- Initial coverage: 6 months
- Continuation of therapy coverage: 6 months

Per §§ 42 CFR 422.101, this clinical medical policy only applies to INTEGRITY in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

**Dosage/Administration:**

**Soliris:**

| Indication | Dose | Maximum dose (1 billable unit = 10 mg) |
|---|---|---|
| Generalized Myasthenia Gravis (gMG) or Neuromyelitis optica spectrum disorder (NMOSD) | Loading dose:<br>900 mg intravenously every 7 days for the first 4 weeks, followed by 1,200 mg intravenously for the fifth dose 7 days later<br>Maintenance dose:<br>1200 mg intravenously every 14 days | Loading dose:<br>90 billable units Days 1, 8, 15, & 22; then 120 billable units Day 29<br>Maintenance dose:<br>120 billable units every 14 days |

**Ultomiris:**

| Indication | Dose | Maximum dose (1 billable unit = 10 mg) |
|---|---|---|
| Generalized Myasthenia Gravis (gMG) | Administer the loading dose based on weight. Two weeks later, begin maintenance doses at a once every 8-week interval: | Loading doses:<br>300 units on day 0<br>Maintenance Dose:<br>360 units on day 14 and every 8 weeks thereafter |

| Body weight range | Loading dose | Maintenance dose |
|---|---|---|
| ≥40 kg - <60kg | 2400 mg | 3000mg |
| ≥60 kg - <100kg | 2700mg | 3300mg |
| ≥100 kg | 3000mg | 3600mg |

**Investigational use:** All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

**Applicable Codes:**
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all-inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT code is:

| HCPCS/CPT Code | Description |
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| J1300 | Injection, eculizumab, 10 mg |
| J1303 | Injection, ravulizumab-cwvz, 10mg |

**References:**


1. Soliris [package insert]. New Haven, CT: Alexion Pharmaceuticals, Inc.; July 2022.
2. Ultomiris [package insert]. New Haven, CT: Alexion Pharmaceuticals, Inc.; April 2023.
3. Sanders D, Wolfe G, Benatar M et al. International consensus guidance for management of myasthenia gravis. *Neurology*. 2016; 87 (4):419-425.
4. Jaretzki A, Barohn RJ, Ernstoff RM et al. Myasthenia Gravis: Recommendations for Clinical Research Standards. *Ann Thorac Surg*. 2000;70: 327-34.
5. Howard JF, Utsugisawa K, Benatar M. Safety and efficacy of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalized myasthenia gravis (REGAIN); a phase 3, randomized, double-blind, placebo-controlled, multicenter study. *Lancet Neurol*. 2017 Oct 20. http://dx.doi.org/10.1016/S1474-4422(17)30369-1Ingenix HCPCS Level II, Expert 2011