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Policy Number: C4867-A

Soliris_Ultomiris (eculizumab_ravulizumab)

PRODUCTS AFFECTED

Soliris (eculizumab), Ultomiris (ravulizumab)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Paroxysmal nocturnal hemoglobinuria (PNH), Generalized Myasthenia Gravis (gMG), Atypical Hemolytic Uremic Syndrome (aHUS), Soliris (eculizumab) ONLY: Neuromyelitis optica spectrum disorder (NMOSD)

D59.3 Hemolytic-uremic syndrome, D59.5 Paroxysmal nocturnal hemoglobinuria, G70.00 Myasthenia gravis without (acute) exacerbation, G36.0 Neuromyelitis optica

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review.

ALL INDICATIONS:

1. Prescriber attests that member has been vaccinated against meningococcal infection (at least 2 weeks prior to treatment, if not previously vaccinated).

AND

2. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Soliris (eculizumab) and Ultomiris (ravulizumab) include: Patients with unresolved serious Neisseria meningitidis infection, Patients who are not currently vaccinated against Neisseria meningitidis, unless the risks of delaying treatment outweigh the risks of developing a meningococcal infection.]
   AND
3. Documentation of member's current weight (within the last 30 days) EXCEPTION: Requests for Soliris for gMG or PNH or NMOSD

A. PAROXYSMAL NOCTURNAL HEMOGLOBINURIA:

1. Documented diagnosis of PNH
   AND
2. Documentation of baseline labs and status [DOCUMENTATION REQUIRED]:
   a. Hemoglobin level
      AND
   b. Documentation of Lactate dehydrogenase (LDH) level which is 1.5 times the upper limit of the normal range (within the last 30 days). Submit laboratory results with reference range.
      AND
   c. Documentation that member is transfusion-dependent, defined by having a transfusion within the last 12 months and ONE (1) of the following: Transfusion dependent as defined as hemoglobin level less than 9g/dL in the presence of symptoms, or Hemoglobin less than 7g/dL without symptoms (*Lab should be drawn before transfusion or at least one (1) month since last transfusion)

   AND
3. Member meets ONE of the following criteria: Thrombotic event event(s) attributable to PNH (i.e. arterial/venous thrombosis, hepatic vein thrombosis, etc.) or major adverse vascular events from thromboembolism, Symptoms of PNH that inhibit the patient's quality of life (i.e. Anemia, fatigue, difficulty swallowing, thromboses, frequent paroxysms of pain, recurrent abdominal pain, erectile dysfunction, chronic kidney disease, organ damage secondary to chronic hemolysis) OR Pregnant and potential benefit outweighs potential fetal risk
   AND
4. FOR SOLIRIS (ECULIZUMAB) AND ULTOMIRIS (RAVULIZUMAB): Documentation that member has a trial and failure, or FDA labeled contraindication to Empaveli (pegcetacoplan)

B. ATYPICAL HEMOLYTIC UREMIC SYNDROME:

1. Documentation of a definitive diagnosis of atypical Hemolytic Uremic Syndrome (aHUS)
   AND
2. Documentation of baseline Serum LDH, serum creatinine/eGFR, platelet count, and plasma exchange/infusion requirement [DOCUMENTATION REQUIRED]

C. GENERALIZED MYASTHENIA GRAVIS:

1. Documentation of diagnosis of myasthenia gravis with a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of class II, III, or IV confirmed by positive serologic test for binding anti-acetylcholine receptor antibodies (AChR-ab) [DOCUMENTATION REQUIRED]
   AND
2. Myasthenia Gravis-Specific Activities of Daily Living (MG-ADL) total score of greater than or equal to 6 [DOCUMENTATION REQUIRED]
   AND
3. (a) Documentation of inadequate response to, is intolerant of, or has a labeled contraindication to TWO or more immunosuppressive drug agents used alone or in combination

for at least 12 months one year [i.e., azathioprine (Imuran), mycophenolate mofetil (Cellcept), cyclosporine (Sandimmune), cyclophosphamide, methotrexate, tacrolimus, rituximab (Rituxan)]
OR
(b) Documentation of inadequate response to, is intolerant of, or has a labeled contraindication to ONE or more immunosuppressive drug agents as monotherapy or in combination therapy AND requires chronic plasma exchange, plasmapheresis or intravenous immunoglobulin therapy

D. NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOSD) (SOLIRIS ONLY):
1. Documentation of diagnosis of NMOSD confirmed by blood serum test for anti- aquaporin- 4 antibody positive (AQP4-IgG AND at least one core clinical characteristic must be identified from among the following: ON, acute myelitis, acute postrema syndrome (APS, characterized by unexplained hiccups or nausea and vomiting), acute brainstem syndrome, symptomatic narcolepsy, or acute diencephalic clinical syndrome with NMOSD- typical diencephalic MRI lesions, and symptomatic cerebral syndrome with NMOSD-typical brain lesions [DOCUMENTATION REQUIRED]
AND
2. Prescriber attests all other alternative diagnoses have been excluded
AND
3. Documentation of member baseline status [DOCUMENTATION REQUIRED]:
(a) One or more relapses that required rescue therapy within the previous 12 months OR 2 or more relapses that required rescue therapy in 2 years prior to screening
NOTE: Rescue therapies include: IV corticosteroids, and/or plasma exchange
AND
(b) Documentation that member has a baseline Expanded Disability Status Scale (EDSS) score ≤ 8
AND
(c) Documentation of baseline relapse rate

CONTINUATION OF THERAPY:

A. ALL INDICATIONS:
1. Documentation of member's current weight (within the last 30 days) EXCEPTION: Requests for Soliris for gMG or PNH or NMOSD

B. PAROXYSMAL NOCTURNAL HEMOGLOBINURIA:
1. Documentation of disease improvement or stabilization by any of the following: decrease in serum LDH, hemoglobin level above baseline or reduction in the need for blood transfusions

C. ATYPICAL HEMOLYTIC UREMIC SYNDROME:
1. Documentation of disease improvement or stabilization by any of the following: decrease in serum LDH, Increase or improvement in serum creatinine/Egfr, Increase or normalization of platelet counts, Decrease in plasma exchange/infusion requirement

D. GENERALIZED MYASTHENIA GRAVIS:
1. Documentation of disease improvement or stabilization by all of the following: Improvement of at least 3 points (reduction in score) from pre-treatment baseline on the Myasthenia Gravis-Specific Activities of Daily Living (MG-ADL) assessment, reduction in signs and symptoms of myasthenia gravis and Stabilization, reduction, or discontinuation of dose(s) of baseline immunosuppressive therapy (IST) prior to starting therapy. NOTE: Add on, dose escalation of IST, or additional rescue therapy from baseline to treat myasthenia gravis or exacerbation of symptoms while on therapy will be considered as treatment failure.

E. NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOSD) (SOLIRIS ONLY):
1. Documentation therapy has resulted in clinical improvement or stabilization from baseline or from the previous authorization, including but not limited to frequency of relapse; EDSS,

DURATION OF APPROVAL:
Initial authorization: 6 months; Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a board-certified hematologist, oncologist, immunologist, genetic specialist or neurologist. Prescriber must be enrolled in Soliris or Ultomiris REMS program.
[If prescribed in consultation, consultation notes must be submitted within initial request and reauthorization requests]

AGE RESTRICTIONS:
Soliris (eculizumab):
Atypical Hemolytic Uremic Syndrome (aHUS): 2 months of age and older
Paroxysmal Nocturnal Hemoglobinuria (PNH) to reduce hemolysis, Generalized Myasthenia Gravis (gMG), Neuromyelitis Optica Spectrum Disorder (NMOSD): 18 years of age and older

Ultomiris (ravulizumab-cwvz):
Atypical Hemolytic Uremic Syndrome (aHUS), Paroxysmal Nocturnal Hemoglobinuria (PNH): one month of age and older
Generalized Myasthenia Gravis (gMG): 18 years of age and older

QUANTITY:
Maximum of 28-day supply per claim
See Appendix for Vial Optimization chart

Maximum Allowed Quantities by HCPCS units:
Soliris (eculizumab) aHUS (J1300):
Load: 900 mg/90 HCPCS units (10 mg per unit) weekly for the first 4 weeks
1200 mg/120 HCPCS units 1 week after the fourth dose
Maintenance: 1200 mg/120 HCPCS units every 2 weeks

Soliris (eculizumab) MG/NMSOD (J1300):
Load: 900 mg/90 HCPCS units weekly for the first 4 weeks
1200 mg/120 HCPCS units 1 week after the fourth dose
Maintenance: 1200 mg/120 HCPCS units every 2 weeks

Soliris (eculizumab)PNH (J1300):
Load: 600 mg/60 HCPCS units weekly for the first 4 weeks
900 mg/90 HCPCS units 1 week after the fourth dose
Maintenance: 900 mg/90 HCPCS units every 2 weeks

Ultomiris (ravulizumab) (J1303):
Load: 3000 mg/300 HCPCS units (10 mg per unit)
Maintenance 3600 mg/360 HCPCS units every 8 weeks

Maximum Allowed Quantities by National Drug Code (NDC) Units
Soliris (eculizumab) aHUS 300 mg vials:
Load: 3 vials/90 mL weekly for the first 4 weeks
Maintenance: 4 vials/120 mL every 2 weeks

Soliris (eculizumab) MG/NMSOD 300 mg vials:
Load: 3 vials/90 mL weekly for the first 4 weeks
Maintenance: 4 vials/120 mL every 2 weeks

Soliris (eculizumab) PNH 300 mg vials:
Load: 2 vials/60 mL weekly for the first 4 weeks
Maintenance: 3 vials/90 mL every 2 weeks

Ultomiris (ravulizumab) (300 mg/3 mL or 1100 mg/11 mL):
Load: 30 mL (of 100 mg/mL concentration), 300 mL (of 10 mg/mL concentration)
Maintenance: 36 mL (of 100 mg/mL concentration), 360 mL (of 10 mg/mL concentration) every 8 weeks

Maximum Quantity Limits – << based on FDA label>>

PLACE OF ADMINISTRATION:
The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Soliris (eculizumab) and ULTOMIRIS (ravulizumab-cwvz). For information on site of care, see
Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous

DRUG CLASS:
Complement Inhibitor

FDA-APPROVED USES:
ULTOMIRIS (ravulizumab-cwvz) is indicated for:
- the treatment of adult and pediatric patients one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH)
- the treatment of adults and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA)
- the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti- acetylcholine receptor (AchR) antibody positive

Soliris (eculizumab) is indicated for:
- The treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.
- The treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement- mediated thrombotic microangiopathy.
- The treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AchR) antibody positive.
- The treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti- aquaporin-4 (AQP4) antibody positive

Limitation of Use:
Soliris and Ultomiris are not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:

Vial Optimization

Soliris 300mg/30ml (Single dose)								
Diagnosis	Age	Weight	Loading Dose/# of Vials	Frequency	# of Vials Needed for 3 Month Initial Approval (weeks 1-12)/# of Doses	Maintenance Dose/# of Vials	Frequency	# of Vials Needed for 6 month Continuation Approval (24 weeks)/# of Doses
PNH	≥ 18	N/A	600mg/2 vials	Weekly x 4 weeks	20 vials/8 doses	900mg/3 vials	Every 2 weeks	36 vials/12 doses
gMG/NMOSD	≥ 18	N/A	900mg/3 vials	Weekly x 4 weeks	28 vials/8 doses	1200mg/4 vials	Every 2 weeks	48 vials/12 doses
aHUS	<18	5 kg- <10 kg	300mg/1 vial	Once, Start maintenance Week 2	5 vials/5 doses	300mg/1 vial	Every 3 weeks	8 vials/8 doses
aHUS	<18	10 kg- <20 kg	600mg/2 vials	Once, Start maintenance Week 2	8 vials/7 doses	300mg/1 vial	Every 2 weeks	12 vials/12 doses
aHUS	<18	20 kg- <30 kg	600mg/2 vials	Weekly x 2 weeks	14 vials/7 doses	600mg/2 vials	Every 2 weeks	24 vials/12 doses
aHUS	<18	30 kg- <40 kg	600mg/2 vials	Weekly x 2 weeks	19 vials/7 doses	900mg/3 vials	Every 2 weeks	36 vials/12 doses
aHUS	<18	≥ 40kg	900mg/3 vials	Weekly x 4 weeks	28 vials/8 doses	1200mg/4 vials	Every 2 weeks	48 vials/12 doses
aHUS	≥ 18	N/A	900mg/3 vials	Weekly x 4 weeks	28 vials/8 doses	1200mg/4 vials	Every 2 weeks	48 vials/12 doses

Ultomiris 300mg/3ml (Single dose), 1100mg/11ml (Single dose)					
Loading Dose					
Weight	Initial Dose	# of 100mg/ml Vials (3ml – 300mg)	# of 100mg/ml Vials (11ml – 1100mg)	Frequency	Total # of Doses Needed for 3 Month Initial Approval (Weeks 1-12)
5 kg- <10 kg	600mg	2		1 dose	4
10 kg- <20 kg	600mg	2		1 dose	4
20 kg-<30 kg	900mg	3		1 dose	3
30 kg- <40 kg	1200mg	4		1 dose	3

40 kg-<60kg	2400mg	8		1 dose	3
60 kg- <100 kg	2700mg	9		1 dose	3
≥ 100kg	3000mg	10		1 dose	3
Maintenance Dose					
Weight	Maintenance Dose	# of 100mg/ml Vials (3ml – 300mg)	# of 100mg/ml Vials (11ml – 1100mg)	Frequency (Starting 2 weeks after initial dose)	Total # of Doses Needed for 6 month Continuation Approval (24 weeks)
5 kg- <10 kg	300mg	1		Every 4 weeks	6
10 kg- <20 kg	600mg	2		Every 4 weeks	6
20 kg-<30 kg	2100mg	7		Every 8 weeks	3
30 kg- <40 kg	2700mg	9		Every 8 weeks	3
40 kg-<60kg	3000mg	10		Every 8 weeks	3
60 kg- <100 kg	3300mg	0	3	Every 8 weeks	3
≥ 100kg	3600mg	1	3	Every 8 weeks	3

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

PNH is a rare acquired clonal disorder caused by a somatic mutation of the phosphatidylinositol glycan-complementation class A (PIG-A) gene in hematopoietic stem cells. The disorder results in a deficiency of glycosylphosphatidylinositol (GPI), which serves as an anchor for several cell surface proteins including the terminal complement regulator, CD59. The absence of CD59 from the surface of the affected PNH red blood cells (RBCs) renders them susceptible to terminal complement- mediated lysis. The subsequent chronic hemolysis is the primary clinical manifestation of the disease and leads to disabling morbidities that include anemia, fatigue, thrombosis, pain, and impaired quality of life. Lactate dehydrogenase (LDH) is released during RBC destruction and grossly elevated serum LDH is a common finding in patients with PNH.

Atypical hemolytic uremic syndrome (aHUS) is a genetic, chronic, and progressive inflammatory disease that affects patients of all ages. This syndrome is caused by defects in regulation of the complement system. These defects are inherited, acquired, or both, and they result in chronic, uncontrolled activation of the complement system which leads to platelet, leukocyte, and endothelial- cell activation and systemic thrombotic microangiopathy. Affected patients have a lifelong risk of systemic clinical complications of thrombotic microangiopathy, including damage to multiple organ systems (e.g., the central nervous system, kidneys, heart, and gastrointestinal tract). Eculizumab, which blocks complement C5 activation, has been demonstrated as an effective agent. Most cases of aHUS are genetic, although some may be acquired due to autoantibodies or idiopathic. The diagnosis of complement-mediated aHUS is made by excluding other forms of TMA. Therefore, aHUS is suspected in patients with TMA without a secondary cause and ADAMTS13 activity >10%, without evidence of STEC-HUS. Plasma exchange or infusion may transiently maintain normal levels of hematologic measures but does not treat the underlying systemic disease aHUS is often misdiagnosed as thrombotic thrombocytopenic purpura (TTP) or STEC-HUS because aHUS shares many of the presenting characteristics of the other thrombotic microangiopathies, and confirmatory genetic results are not available at the time of presentation, the diagnosis relies heavily on the recognition of a clinical syndrome consistent with the diagnosis in the absence of signs of an alternate cause of thrombotic microangiopathy. It is a distinctly different illness from the more common disorder known as typical hemolytic uremic syndrome, which is caused by E.coli-producing Shiga toxins (Stx HUS) and is generally foodborne.

Myasthenia gravis (MG) is relatively rare acquired autoimmune disorder caused by an antibody- mediated blockade of neuromuscular transmission resulting in skeletal muscle weakness. MG is characterized by a pattern of progressively reduced muscle strength with repeated use and recovery of muscle strength after a period of rest. MG is classified into 2 major clinical types: ocular MG and generalized MG (gMG). gMG is

a debilitating, chronic and progressive autoimmune neuromuscular disease that can occur at any age. There is no known cure for MG. The mainstay of therapy for symptomatic treatment of MG involves use of acetylcholinesterase (AChE) inhibitors. If treatment with AChE inhibitors is not effective, or they are not suitable for long-term use, then short-term immunosuppression with oral corticosteroids such as prednisolone is used. Nonsteroidal immunosuppressive agents (azathioprine, cyclosporine, cyclophosphamide, methotrexate, mycophenolate mofetil, rituximab, and tacrolimus) may be used in addition to steroids, with the aim of reducing the steroid dose over time. Approximately 10% to 15% of patients with MG have refractory gMG. These patients do not respond to long-term treatment with corticosteroids or multiple immunosuppressive treatments, or they have intolerable side effects to these therapies or require ongoing treatment with either intravenous immunoglobulin (IVIG) or plasma exchange (PE) (Howard et al., 2017). Patients with refractory gMG experience difficulties with speech, swallowing, and mobility, impairment of respiratory function, and extreme fatigue, and may have frequent exacerbations, which can be life-threatening and require hospital admission.

Eculizumab is a recombinant humanized monoclonal antibody that works by binding to complement protein C5, inhibiting its enzymatic cleavage, blocking formation of the terminal complement complex, and thus preventing red cell lysis. In those patients with paroxysmal nocturnal hemoglobinuria (PNH), eculizumab inhibits terminal complement mediated intravascular hemolysis. In patients with atypical hemolytic uremic syndrome (aHUS), impairment in the regulation of complement activity leads to uncontrolled terminal complement activation, resulting in platelet activation, endothelial cell damage and thrombotic microangiopathy. The precise mechanism by which eculizumab exerts its therapeutic effect in gMG patients is unknown but is presumed to involve reduction of terminal complement complex C5b-9 deposition at the neuromuscular junction. Ultomiris is a recombinant humanized monoclonal IgG2/4κ antibody. The antibody binds to the complement component C5 and prevents its cleavage to C5a and C5b, which is required for formation of the membrane attack complex (MAC). RBCs are normally protected from MAC formation by the glycosylphosphatidylinositol (GPI)-linked protein CD59 on their surface; PNH red blood cells (RBCs) lacking CD59 are susceptible to MAC formation. Ultomiris interferes with this step and thus reduces intravascular hemolysis. Approval of Ultomiris was based on two open-label, randomized, active-controlled, non-inferiority phase 3 studies: ALXN1210-PNH-301 (NCT02946463) and ALXN1210- PNH-302 (NCT03056040). Study 301 enrolled 246 patients with PNH who were complement inhibitor naïve and had active hemolysis. Study 302 enrolled 195 patients with PNH who were clinically stable after having been treated with Soliris for at least the past 6 months. In both trials, patients were randomized to receive either Ultomiris or Soliris. Patients randomized to Ultomiris received a loading dose followed by maintenance dosing every 8 weeks. Patients randomized to Soliris received a dose on Days 1, 8, 15, and 22, followed by maintenance treatment on Day 29 and every 2 weeks. The results of Study 301 demonstrated that Ultomiris had similar results to Soliris (non-inferior) – patients did not receive a transfusion and had similar incidence of hemolysis measured by the normalization of LDH levels in patients' blood (lactate dehydrogenase, or LDH, is an enzyme required during the process of turning sugar into energy in the body's cells).

The results of Study 302 demonstrated similar effects to Soliris (non-inferior) based on several clinical measures including hemolysis and avoiding transfusion. In Study 301, efficacy was established based upon transfusion avoidance and reduction of hemolysis as directly measured by normalization of LDH levels. Transfusion avoidance was defined as patients who did not receive a transfusion and did not meet the protocol specified guidelines for transfusion from baseline up to Day 183. Transfusion avoidance was seen in 73.6% and 66.1% of patients who received Ultomiris and Soliris, respectively (rate difference 6.8; 95% CI: -4.66, 18.14) and LDH normalization was seen in 53.6% and 49.4% of patients who received Ultomiris and Soliris, respectively (odds ratio 1.19; 95% CI: 0.80. 1.77). Supportive efficacy data included

LDH percent change, breakthrough hemolysis and proportion of patients with stabilized hemoglobin levels. Non-inferiority of Ultomiris to Soliris was demonstrated across the endpoints. In Study 302, efficacy was established based on hemolysis as measured by LDH percent change from baseline to Day 183. LDH percent change was -0.82% and 8.4% for patients who received Ultomiris and Soliris, respectively (rate difference 9.2; 95% CI: -0.42, 18.8). Supportive efficacy data included transfusion avoidance, proportion of patients with stabilized hemoglobin and proportion of patients with breakthrough hemolysis. Non-inferiority of Ultomiris to Soliris was demonstrated across all endpoint. The efficacy of Soliris for the treatment of NMOSD was established in NMOSD Study 1 (ECU-NMO- 301, NCT01892345), a randomized, double- blind, placebo-controlled, multi-center trial that enrolled 143 patients who were anti-AQP4 antibody positive. The primary endpoint was the time to the first adjudicated on-trial relapse. The time to the first adjudicated on-trial relapse was significantly longer in Soliris-treated patients compared to patients on placebo (relative risk-reduction 94%; hazard ratio 0.058; P<0.0001). DISEASE OVERVIEW Neuromyelitis optica spectrum disorder (NMOSD) is a rare, severe, disabling, and potentially life- threatening autoimmune neuroinflammatory disease characterized by acute optic neuritis (ON) and longitudinal transverse myelitis (TM). The disease can strike men and women of all races, backgrounds, and ages without warning, with a median age of onset of 39 years.

MORBIDITY AND MORTALITY Up to 92.7% of patients with AQP4 antibody-positive NMOSD have had unpredictable relapses, often leading to cumulative disability.3,7,8 In a study of anti-AQP4 antibody-positive NMOSD patients, morbidity was significant, with 18% experiencing permanent visual disability, 34% experiencing permanent motor disability, and 23% experiencing wheelchair dependency after a median disease duration of 75 months.3 Attacks that involve the brainstem can result in respiratory failure.4 The overall mortality rates of patients with NMOSD range from 7% to 9% (7% after a mean disease duration of 6.9 years; 9.4% after a median disease duration of 8.25 years). SIGNS AND SYMPTOMS In addition to vision loss and blindness, NMOSD patients experience immobility involving limb weakness and sensation loss that can give rise to paralysis.

Neuromuscular symptoms, such as cognitive challenges, pain, spasms, loss of bladder or bowel control, hiccups, nausea, vomiting, and seizures, can also arise. Ultimately, respiratory failure and encephalopathy can be among the most injurious consequences of NMOSD. NMOSD ASSOCIATED WITH AQP4 As 73% of patients with NMOSD are anti-AQP4 antibody positive, complement activation by AQP4 antibodies is a major determinant of disease pathogenesis in patients with NMOSD. AQP4 bound to immunoglobulin G (IgG) passes into the central nervous system through the blood-brain barrier and activates the complement system, causing the infiltration of immune leukocyte cells that cause the death of neural cells known as astrocytes and neurons.

Identifying AQP4-IgG in the blood facilitates clinical diagnosis and prognosis, as well as informing appropriate treatment selection. DIAGNOSIS The International Panel for NMO Diagnosis (IPND) established two sets of clinical criteria, both of which involve excluding alternative diagnoses. When patients test positive for blood AQP4-IgG, at least one core clinical characteristic must be identified from among the following: ON, acute myelitis, acute postrema syndrome (APS, characterized by unexplained hiccups or nausea and vomiting), acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions, and symptomatic cerebral syndrome with NMOSD-typical brain lesions. In the absence of a confirmed AQP4-IgG test, at least two of the aforementioned core clinical characteristics must be identified, one of which must be ON, acute myelitis with longitudinally extensive transverse myelitis (LETM), or APS.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Soliris (eculizumab) and Ultomiris (ravulizumab) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy Contraindications to Soliris (eculizumab) and Ultomiris (ravulizumab) include: Patients with unresolved serious Neisseria meningitidis

infection, Patients who are not currently vaccinated against Neisseria meningitidis, unless the risks of delaying treatment outweigh the risks of developing a meningococcal infection.

Eculizumab is not indicated for the treatment of patients with Shigatoxin E. coli related hemolytic uremic syndrome (STEC- HUS). While the few studies available demonstrate possible efficacy of eculizumab in treating Shiga toxin E.

coli-related hemolytic uremic syndrome, further studies are warranted to demonstrate that it is both safe and effective for this indication.

OTHER SPECIAL CONSIDERATIONS:

Black Box Warnings: Serious meningococcal infection Life- threatening and fatal meningococcal infections have occurred in patients treated with eculizumab. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J1300	Injection, eculizumab, 10mg
J1303	Injection ravulizumab-cwvz, 10mg

AVAILABLE DOSAGE FORMS:

Soliris SOLN 300MG/30ML
Ultomiris SOLN 300MG/3ML
Ultomiris SOLN 1100MG/11ML

REFERENCES

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2. ULTOMIRIS (ravulizumab-cwvz) [prescribing information]. Boston, MA: Alexion Pharmaceuticals Inc; April 2022
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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Prescriber Requirements Age Restrictions Quantity FDA-Approved Uses Appendix Contraindications/Exclusions/Discontinuation Coding/Billing Information Available Dosage Forms References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file