eculizumab (Soliris®) J1300 (10mg)

ravulizumab-cwvz (Ultomiris®) J1303 (10mg)

inebilizumab-cdon (Uplizna®) J1823 (1mg)

Covered with prior authorization

Eculizumab (Soliris®) may be authorized when the following criteria are met:

- Individual has a diagnosis of **paroxysmal nocturnal hemoglobinuria (PNH)** confirmed by flow cytometry analysis with presence of:
  - PNH type III red cell clone or a measurable granulocyte or monocyte clone; **OR**
  - Glycosylphosphatidylinositol-anchored proteins (GPI-AP)-deficient polymorphonuclear cells (PMNs); **AND**
- Individual is 18 years or older; **AND**
- Individual has:
  - Documentation of lactate dehydrogenase greater than 1.5 times the upper limit of normal, and documentation is provided; **AND**
  - Documented PNH-related signs and symptoms such as dyspnea, anemia, abdominal pain, unexplained thrombosis, hemolysis, kidney disease, or history of a major adverse vascular event from thromboembolism; **AND**
- Individual has no evidence of an active meningococcal infection; **AND**
- Individual has been immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose, unless the clinical record documents the risks of delaying treatment outweigh the risk of meningococcal infection; **AND**
- Individual or guardian has attested that individual will adhere to the treatment regimen; **AND**
- Prescribed by or in consultation with hematologist or oncologist; **AND**
- Request includes documentation of failed treatment with ravulizumab-cwvz (Ultomiris®), defined by hemoglobin levels < 10.5 g/dL directly following at least 3 months of stable FDA-approved ravulizumab-cwvz (Ultomiris®) dosing documented in the medical record; **AND**
- Prescribed dosing is scheduled at recommended dosage regimen time points or within two days of the time points:
  - Weeks 1-4: 600 mg dose each week (doses 1-4); **AND**
  - Week 5: 900 mg for one dose 1 week later (dose 5); **AND**
  - Beginning Week 7: 900 mg two weeks later (dose 6) and every 2 weeks thereafter;

OR

- Individual has a diagnosis of **atypical hemolytic uremic syndrome (aHUS)**; **AND**
- Documentation shows individual does not have Shiga toxin E. coli related hemolytic syndrome (STEC-HUS); **AND**
- Thrombotic thrombocytopenic purpura has been ruled out (normal ADAMTS 13 activity and no evidence of an ADAMTS 13 inhibitor), or if thrombotic thrombocytopenic purpura cannot be

ruled out by laboratory and clinical evaluation, a trial of plasma exchange did not result in clinical improvement; **AND**

- Individual is ≥2 months of age or older (Note: pediatric (≥2 months to <18 years) use of eculizumab is restricted to aHUS); **AND**
- Individual has no evidence of an active meningococcal infection; **AND**
- Individual has been immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose, unless the clinical record documents the risks of delaying treatment outweigh the risk of meningococcal infection; **AND**
- Individual or guardian has attested that individual will adhere to the treatment regimen; **AND**
- Prescribed by or in consultation with nephrologist, hematologist, or oncologist; **AND**
- Request includes documentation of failed treatment with ravulizumab-cwvz (Ultomiris®), defined insufficient improvement in disease activity following at least 3 months of stable FDA-approved ravulizumab-cwvz (Ultomiris®) dosing documented in the medical record; **AND**
- Prescribed dosing is scheduled at recommended dosage regimen time points or within two days of the time points:
    - For individuals ≥18 years of age:
        - Weeks 1-4: 900 mg dose each week (doses 1-4); **AND**
        - Week 5: 1200 mg for one dose 1 week later (dose 5); **AND**
        - Beginning Week 7: 1200 mg two weeks later (dose 6) and every 2 weeks thereafter; **AND**
    - For individuals patients < 18 years of age, dosing is based on actual body weight:

Patient Body Weight	Induction	Maintenance
5 kg to <10 kg	300 mg weekly for 1 dose	300 mg at week 2, then 300 mg **every 3 weeks**
10 kg to <20 kg	600 mg weekly for 1 dose	300 mg at week 2, then 300 mg every 2 weeks
20 kg to <30 kg	600 mg weekly for 2 doses	600 mg at week 3, then 600 mg every 2 weeks
30 kg to <40 kg	600 mg weekly for 2 doses	900 mg at week 3 then 900 mg every 2 weeks
≥40 kg	900 mg weekly for 4 doses	1,200 mg at week 5, then 1,200 mg every 2 weeks

OR

- Individual has a diagnosis of **anti-acetylcholine receptor (AchR) antibody positive generalized myasthenia gravis (gMG)** with MFGA (Myasthenia Gravis Foundation of American) clinical classification of Class II, III or IV prior to complement inhibitor therapy; **AND**
- Individual has a Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 6 or higher upon initiation of therapy; **AND**
- Individual is 18 years or older; **AND**
- Individual has no evidence of an active meningococcal infection; **AND**
- Individual has been immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose, unless the clinical record documents the risks of delaying treatment outweigh the risk of meningococcal infection; **AND**
- Individual or guardian has attested that individual will adhere to the treatment regimen; **AND**

- Prescribed by or in consultation with neurologist; **AND**
- Documentation is provided that individual has had an inadequate response to, is intolerant of, or has a contraindication to
    - two or more immunosuppressive drug agents (such as azathioprine, cyclosporine, or methotrexate) as monotherapy or in combination therapy for greater than or equal to 12 months; **OR**
    - one or more immunosuppressive drug agents as monotherapy or in combination therapy and requires chronic plasma exchange or plasmapheresis or intravenous immunoglobulin therapy; **AND**
- Documentation of failed treatment with ravulizumab-cwvz (Ultomiris®), defined as insufficient improvement in disease activity following at least 3 months of stable FDA-approved ravulizumab-cwvz (Ultomiris®) dosing documented in the medical record; **AND**
- Prescribed dosing is scheduled at recommended dosage regimen time points or within two days of the time points:
    - Weeks 1-4: 900 mg dose each week (doses 1-4); **AND**
    - Week 5: 1200 mg for one dose 1 week later (dose 5); **AND**
    - Beginning Week 7: 1200 mg two weeks later (dose 6) and every 2 weeks thereafter;

OR

- Individual has a diagnosis of **neuromyelitis optica spectrum disorder (NMOSD)**; **AND**
- NMOSD is seropositive as confirmed by the presence of anti- aquaporin-4 (AQP4) antibodies; **AND**
- Individual has documented history of
    - at least 2 acute attacks or relapses in the most recent 12 months prior to therapy; **OR**
    - at least 3 acute attacks or relapses in the last 24 months AND at least 1 of those occurring in the most recent 12 months prior to therapy; **AND**
- Individual has documented failure, intolerance, or contraindication to at least **ALL** of the following therapies:
    - oral steroids; **AND**
    - rituximab (Rituxan®); **AND**
    - satralizumab (Enspryng®); **AND**
    - inebilizumab (Uplizna®); **AND**
- Individual is 18 years or older; **AND**
- Individual has no evidence of an active meningococcal infection; **AND**
- Individual has been immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose, unless the clinical record documents the risks of delaying treatment outweigh the risk of meningococcal infection; **AND**
- Individual or guardian has attested that individual will adhere to the treatment regimen; **AND**
- Prescribed by or in consultation with neurologist; **AND**
- Prescribed dosing is scheduled at recommended dosage regimen time points or within two days of the time points:
    - Weeks 1-4: 900 mg dose each week (doses 1-4); **AND**
    - Week 5: 1200 mg for one dose 1 week later (dose 5); **AND**
    - Beginning Week 7: 1200 mg two weeks later (dose 6) and every 2 weeks thereafter.

ravulizumab-cwvz (Ultomiris®) may be authorized when the following criteria are met:

- Individual has a diagnosis of **paroxysmal nocturnal hemoglobinuria (PNH)** confirmed by flow cytometry analysis with presence of:
    - PNH type III red cell clone or a measurable granulocyte or monocyte clone; **OR**
    - Glycosylphosphatidylinositol-anchored proteins (GPI-AP)-deficient polymorphonuclear cells (PMNs); **AND**
- Individual is age 1 month or older; **AND**
- Individual has:
    - Documentation of lactate dehydrogenase greater than 1.5 times the upper limit of normal, and documentation is provided; **AND**
    - Documented PNH-related signs and symptoms such as dyspnea, anemia, abdominal pain, unexplained thrombosis, hemolysis, kidney disease, or history of a major adverse vascular event from thromboembolism; **AND**
- Individual has no evidence of an active meningococcal infection; **AND**
- Individual has been immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose, unless the clinical record documents the risks of delaying treatment outweigh the risk of meningococcal infection; **AND**
- Individual or guardian has attested that individual will adhere to the treatment regimen; **AND**
- Prescribed by or in consultation with hematologist or oncologist; **AND**
- Prescribed weight-based dosing is scheduled at recommended dosage regimen time points or within seven days of the time points (adhering to original schedule for subsequent doses):

Patient Body Weight Range	Loading Dose (mg)	Maintenance Dose (mg) and Interval Beginning 2 weeks after Loading Dose
5 kg to <10 kg	600 mg	300 mg every 4 weeks
10 kg to <20 kg	600 mg	600 mg every 4 weeks
20 kg to <30 kg	900 mg	2,100 mg every 8 weeks
30 kg to <40 kg	1,200 mg	2,700 mg every 8 weeks
40 kg to <60 kg	2,400 mg	3,000 mg every 8 weeks
60 kg to <100 kg	2,700 mg	3,300 mg every 8 weeks
≥ 100 kg	3,000 mg	3,600 mg every 8 weeks

OR

- Individual has a diagnosis of **atypical hemolytic uremic syndrome (aHUS)**; **AND**
- Documentation shows individual does not have Shiga toxin E. coli related hemolytic syndrome (STEC-HUS); **AND**
- Thrombotic thrombocytopenic purpura has been ruled out (normal ADAMTS 13 activity and no evidence of an ADAMTS 13 inhibitor), or if thrombotic thrombocytopenic purpura cannot be ruled out by laboratory and clinical evaluation, a trial of plasma exchange did not result in clinical improvement; **AND**
- Individual is ≥1 month of age or older; **AND**
- Individual has no evidence of an active meningococcal infection; **AND**

- Individual has been immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose, unless the clinical record documents the risks of delaying treatment outweigh the risk of meningococcal infection; **AND**
- Individual or guardian has attested that individual will adhere to the treatment regimen; **AND**
- Prescribed by or in consultation with nephrologist, hematologist, or oncologist; **AND**
- Prescribed weight-based dosing is scheduled at recommended dosage regimen time points or within seven days of the time points (adhering to original schedule for subsequent doses):

Patient Body Weight Range	Loading Dose (mg)	Maintenance Dose (mg) and Interval Beginning 2 weeks after Loading Dose
5 kg to <10 kg	600 mg	300 mg every 4 weeks
10 kg to <20 kg	600 mg	600 mg every 4 weeks
20 kg to <30 kg	900 mg	2,100 mg every 8 weeks
30 kg to <40 kg	1,200 mg	2,700 mg every 8 weeks
40 kg to <60 kg	2,400 mg	3,000 mg every 8 weeks
60 kg to <100 kg	2,700 mg	3,300 mg every 8 weeks
≥ 100 kg	3,000 mg	3,600 mg every 8 weeks

OR

- Individual has a diagnosis of **anti-acetylcholine receptor (AchR) antibody positive generalized myasthenia gravis (gMG)** with MFGA (Myasthenia Gravis Foundation of American) clinical classification of Class II, III or IV prior to complement inhibitor therapy; **AND**
- Individual has a Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 6 or higher upon initiation of therapy; **AND**
- Individual is 18 years or older; **AND**
- Individual has no evidence of an active meningococcal infection; **AND**
- Individual has been immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose, unless the clinical record documents the risks of delaying treatment outweigh the risk of meningococcal infection; **AND**
- Individual or guardian has attested that individual will adhere to the treatment regimen; **AND**
- Prescribed by or in consultation with neurologist; **AND**
- Documentation is provided that individual has had an inadequate response to, is intolerant of, or has a contraindication to:
    - two or more immunosuppressive drug agents (such as azathioprine, cyclosporine, or methotrexate) as monotherapy or in combination therapy for greater than or equal to 12 months; **OR**
    - one or more immunosuppressive drug agents as monotherapy or in combination therapy and requires chronic plasma exchange or plasmapheresis or intravenous immunoglobulin therapy; **AND**
- Prescribed weight-based dosing is scheduled at recommended dosage regimen time points or within seven days of the time points (adhering to original schedule for subsequent doses):

Patient Body Weight Range	Loading Dose (mg)	Maintenance Dose (mg) and Interval Beginning 2 weeks after Loading Dose
40 kg to <60 kg	2,400 mg	3,000 mg every 8 weeks
60 kg to <100 kg	2,700 mg	3,300 mg every 8 weeks
≥ 100 kg	3,000 mg	3,600 mg every 8 weeks

inebilizumab-cdon (Uplizna®) may be authorized when the following criteria are met:

- **Diagnosis of Neuromyelitis Optica Spectrum Disorder (NMOSD)**; **AND**
- Patient is ≥ 18 years of age **AND;**
- Individual is anti-aquaporin-4 (AQP4) antibody positive; **AND**
  - documented history of one or more neuromyelitis optica spectrum disorder acute relapses that required rescue therapy during the previous 12 months; **OR**
  - two or more neuromyelitis optica spectrum disorder acute relapses that required rescue therapy during the previous 24 months;
- FDA approved initial dose is 300 mg intravenous infusion followed 2 weeks later by a second 300 mg intravenous infusion. Subsequent doses (starting 6 months from the first infusion): Single 300 mg intravenous infusion every 6 months

Exclusion criteria:

Requests may not be approved for the following:

- Treatment of individuals with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS) (Soliris® and Ultomiris® are not indicated);
- Individuals with unresolved serious Neisseria meningitidis infection;
- Patients who are not currently vaccinated against Neisseria meningitidis, unless the risks of delaying Soliris® treatment outweigh the risks of developing a meningococcal infection;
- Co-therapy with other complement inhibitors. Individuals cannot use the requested medication concurrently with another complement inhibitor (Empaveli™, Ultomiris®, Soliris®) [Exception: treatment for PNH with Ultomiris® or Soliris® combination with Empaveli™for 4 weeks or less for PNH];
- Co-therapy with other agents including rituximab (Rituxan®), satralizumab (Enspryng®), or inebilizumab (Uplizna®);
- Product use for non-FDA approved indications or indications not supported by industry-accepted guidelines;
- Doses, durations, or dosing intervals that exceed FDA maximum limits for any FDA-approved indication or are not supported by industry-accepted practice guidelines or peer-reviewed literature for the relevant off-label use;
- Individuals with significant known risk factors unless the record provides an assessment of clinical benefit that outweighs the risk;

Step/Alternative Therapies:

- Eculizumab (Soliris®) J1300 and ravulizumab-cwvz (Ultomiris®) J1303 are Complement C5 Inhibitors requiring PA
- Eculizumab (Soliris®) approval (for three indications: paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), and generalized myasthenia gravis (gMG)) requires a **trial/failure with ravulizumab-cwvz (Ultomiris®) with least 3 months of stable FDA-approved ravulizumab-cwvz (Ultomiris®) dosing documented in the medical record**

Preferred Product(s)	Non-Preferred Product(s)
ravulizumab-cwvz (Ultomiris®) (PA Required) J1303	Eculizumab (Soliris®) (PA Required) J1300
inebilizumab-cdon (Uplizna®) (PA Required) J1823	
satralizumab (Enspryng®) (covered under pharmacy benefit with Cigna, PA required)	

SmartHealth ineligible products include Pegcetacoplan (Empaveli™):

- Complement C3 inhibitor
- Indicated (only) for Paroxysmal Nocturnal Hemoglobinuria
- Administered subcutaneously
- Non-formulary due to NOC code and pending future TAG review

Initial authorization
Eculizumab (Soliris®):

- **6 months** for paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), generalized myasthenia gravis (gMG)
- **12 months** for neuromyelitis optica spectrum disorder (NMOSD) indications

Ravulizumab-cwvz (Ultomiris®):

- **6 months** for paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), generalized myasthenia gravis (gMG)

Inebilizumab-cdon (Uplizna®)

- **12 months** for neuromyelitis optica spectrum disorder (NMOSD)

Reauthorizations require medical chart documentation that the patient has been seen within the past 6 months and that markers of disease are improved by therapy. Reauthorization (for either continued use or resumption of use) requires additional indicators for specific indications as listed:

- For paroxysmal nocturnal hemoglobinuria (PNH):
  - stabilization of hemoglobin levels; **OR**
  - reduction in number of transfusions required; **OR**
  - improvement in hemolysis (for example, normalization or decrease of LDH levels);
- For neuromyelitis optica spectrum disorder (NMOSD):
  - a clinical response such as a reduction in the frequency of relapse; **AND**
  - Trial and Failure of Ultomiris (FDA approval for NMOSD pending)
- For atypical hemolytic uremic syndrome (aHUS):
  - reduction in transfusions; **OR**
  - improvement in markers of hemolysis; **OR**

    - platelet count; **OR**
    - documented relapse after discontinuation of therapy;
- For generalized myasthenia gravis (gMG)
    - a 3 point reduction in MG-ADL score from baseline; **OR**
    - Improvement in daily function

Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

U.S. Food and Drug Administration:
This section is to be used for informational purposes. FDA approval alone is not a basis for coverage.

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

Ultomiris® is a complement inhibitor indicated for:
- treatment of adult and pediatric individuals one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH)
- treatment of adult and pediatric individuals one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA)
- treatment of adult individuals with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive

Uplizna® is a CD19-directed cytolytic antibody indicated for:
- the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

References:

Astra Zeneca. (2022, May 5). *Ultomiris met primary endpoint in CHAMPION-NMOSD Phase III trial in adults with neuromyelitis optica spectrum disorder*. AstraZeneca. Retrieved July 7, 2022, from https://www.astrazeneca.com/media-centre/press-releases/2022/ultomiris-nmosd-ph-iii-trial-met-primary-endpoint.htm

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ULTOMIRIS® (ravulizumab-cwvz). (2021, June). Accessdata.fda.gov. Retrieved June 20, 2022, from https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761108s012lbl.pdf
ULTOMIRIS® (ravulizumab-cwvz) i. (2022, April). Alexion. Retrieved June 20, 2022, from https://alexion.com/documents/ultomiris_uspi

Criteria History/ Revision Information:

Date	**Summary of Changes**
September 2021	Criteria for use developed by: Ambulatory Care Expert Review Panel[Eculizumab (Soliris®) only]
September 2021	Criteria for use summary approved by Ascension Therapeutic Affinity Group [Eculizumab (Soliris®) only]
June 2022	Criteria for use summary developed by Ascension Medical Specialty Prior Authorization Team Expanded to include ravulizumab-cwvz (Ultomiris®) J1303 and expanded criteria, Expanded to include
July 2022	Criteria for use summary approved by Ascension Surgery/Anesthesia Expert Review Panel
July 2022	Criteria for use summary approved by Ascension Therapeutic Affinity Group

If you have questions, call 833-980-2352 to speak to a member of the Ascension Rx prior authorization team or email your questions to smarthealthspecialty@ascension.org.