DRUG DETERMINATION POLICY

Title: DDP-03 Soliris and Ultomiris

Effective Date: 06/04/2019

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs.

This policy does not guarantee or approve Benefits. Coverage depends on the specific Benefit plan. Pharmacy Benefit Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Soliris and Ultomiris are specialty drugs indicated for different diagnoses and are associated with significant toxicity. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses and mitigation of toxicity, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

A. Paroxysmal Nocturnal Hemoglobinuria (PNH)

   1. Age: ≥18 years.

   2. Prescriber: hematologist or nephrologist.

   3. Diagnosis and severity (all below):

      a. Flow cytometry: greater than two different GPI protein deficiencies within two different cell lines from granulocytes, monocytes, or erythrocytes.

      b. Transfusion dependent (one below):

         i. Hemoglobin (Hgb) ≤7 g/dL.

         ii. Hemoglobin (Hgb) ≤9 g/dL and experiencing symptoms of anemia.

      c. Lactate dehydrogenase (LDH) level: 1.5 times the upper limit of normal range.

4. Dosage Regimen: see Appendix I.
5. Approval.
    a. Initial: six months.
    b. Re-approval: six months;
        i. LDH level shows reduction from baseline (within three months).
        ii. Hgb stabilized: did not require a transfusion and hgb 7-9g/dL (depending on baseline).

B. Atypical Hemolytic Uremic Syndrome (aHUS)
1. Age: ≥2 months.
2. Prescriber: hematologist or nephrologist.
3. Diagnosis and severity (both below):
    a. Signs and symptoms: microangiopathic hemolytic anemia, thrombocytopenia and acute kidney injury.
    b. Rule out: Shiga Toxin *E. coli*-related Hemolytic Uremic Syndrome (STEC-HUS).
4. Dosage regimen: see Appendix I.
5. Approval
    a. Initial: six months.
    b. Re-approval: six months (one below):
        i. Increase in platelet count from baseline.
        ii. Maintenance of normal platelet count and LDH levels for ≥4 weeks.
        iii. 25% reduction in serum creatinine for at least four weeks.
        iv. Lack of decrease platelets greater than 25% from baseline (for at least two weeks), plasma exchange or infusion and new dialysis requirement.

C. Generalized Myasthenia Gravis (MG)
1. Prescriber: neurologist.
2. Diagnosis and severity.
    a. Anti-AChR antibodies: positive serologic test.
    b. Severity (both below): see Appendix II/III.
        i. GFA Clinical Classification of class: II, III, or IV.
        ii. MG-ADL: total score at least 6 at initiation of therapy.
3. Other therapies: failed or had significant adverse effects (both below):
    a. Immunosuppressive therapy (two below):
        i. Azathioprine, methotrexate, cyclosporine, or mycophenolate for four to six weeks each over a 1-year time-period.
    b. Alternative treatment (one below):
        i. IVIG over one year.
        ii. Plasmapheresis or plasma exchange two times over a 1-year period.

4. Dosage regimen: see Appendix I.
5. Approval:
   a. Initial: one month in combination with a stable regimen of immunosuppressive treatment.
   b. Re-approval: two months (usually treat total of 12 weeks).
      i. Baseline immunosuppressive therapy (prior to starting Soliris): maintenance, decrease, or discontinue.
      ii. MG-ADL: 3-point improvement and/or maintenance of score from baseline.
   c. Treatment failure: no improvement in four weeks (e.g. add-on treatment, increased dose of immunosuppressive treatment, or additional MG rescue therapy from baseline).

4.0 Coding:

CODES AFFECTED			
Code	**Brand**	**Generic**	**Billing (1u)**
J1300	Soliris IV	Eculizumab	10mg
J3590	Ultomiris IV	Ravulizumab-cwvz	NA

5.0 Unique Configuration/Prior Approval/Coverage Details:

5.0 None.

6.0 References, Citations & Resources:

5.0 1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Soliris accessed June 2019.
5.0 2. Safety and efficacy of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalized myasthenia gravis (REGAN): a phase 3, randomized, double-blind, placebo-controlled, multicenter study. Lancet Neurol 2017;16: 976-86.
5.0 3. Myasthenia gravis: new developments in research and treatment. Curr Opin Neurol 2017, 30:464-470.
5.0 4. Can eculizumab be discontinued in aHUS? Medicine 2016; 95:31.

7.0 Appendices:

5.0 Appendix I: Dosage Regimens per Diagnosis

5.0

Agent	Loading Dose	Maintenance Dose
Soliris IV (eculizumab)		
PNH	600mg weekly x 4	900mg week 5, then 900mg every 2 weeks
aHUS	900mg weekly x 4	1,200mg week 5, then 1,200mg every 2 weeks. PPH: last dose ≥ 600mg - 600mg; 300mg - 300mg @ 1 hr post
Pediatric aHUS 5 - <10Kg 10 - <20Kg 20 - <30Kg 30 - ≤40Kg ≥40Kg	 300mg weekly x1 600mg weekly x1 600mg weekly x 2 600mg weekly x 2 900mg weekly x 4	 300mg @ week 2, then 300mg q 3 weeks. 300mg @ week 2, then 300mg q 2 weeks. 600mg @ week 3, then 600mg q 2 weeks. 900mg @ week 3, then 900mg q 2 weeks. 1200mg @ week 5, then 1200mg q 2 weeks

Agent	Loading Dose	Maintenance Dose
MG	900mg weekly x 4	1,200mg week 5, then 1,200mg every 2 weeks. PPH: Last dose ≥ 600mg - 600mg; 300mg - 300mg @ 1hr post
Ultomiris IV (ravulizunab-cwvz)		
PNH ≥40 to <60Kg ≥60 kg to <100 kg ≥100 kg	 2,400 mg 2,700 mg 3,000 mg	 3,000 mg every 8 weeks, 2 weeks after the load 3,300 mg every 8 weeks, 2 weeks after the load 3,600 mg every 8 weeks, 2 weeks after the load

PNH - Paroxysmal Nocturnal Hemoglobinuria; PPH - plasmapheresis or plasma exchange. aHUS - Atypical Hemolytic Uremic Syndrome; MG - Generalized Myasthenia Gravis

Appendix II: MGFA Clinical Classification & MG-ADL

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.

A. IIa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.

B. 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.

A. IIIa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.

B. 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.

A. IVa. Predominantly affecting limb, axial muscles, or both. May also have lesser Involvement of oropharyngeal muscles.

C. 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.

Appendix III

MG Activities of Daily Living (MG-ADL)

Grade	0	1	2	3	Score
Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal, but can be understood	Difficult to understand speech	
Chewing	Normal	Fatigue with solid food	Fatigue with soft food	Gastric tube	
Swallowing	Normal	Rare episode of choking	Frequent choking necessitating changes in diet	Gastric tube	
Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependence	
Impairment of ability to brush teeth or comb hair	None	Extra effort, but no rest periods needed	Rest periods needed	Cannot do one of these functions	
Impairment of ability to arise from a chair	None	Mild, sometimes uses arms	Moderate, always uses arms	Severe, requires assistance	
Double vision	None	Occurs, but not daily	Daily, but not constant	Constant	
Eyelid droop	None	Occurs, but not daily	Daily, but not constant	Constant	

Total score _____

Appendix IV: Patient Safety and Monitoring

Drug	Adverse Reactions	Monitoring	REMS
Soliris IV Eculizumab IV	• CV: tachycardia (20-40%), Peripheral edema (8-29%), hypotension (12-20%) • CNS: HA (17-50%), insomnia (10-24%), fatigue (7-20%) • Derm: rash (12-20%), pruritis (6-15%) • Endo/met: Hypokalemia (10-18%) • GI: diarrhea (20-47%), vomiting (10-47%), nausea (12-40%), ad. pain (8-33%), gastroenteritis (5-20%) • GU: UTI (15-35%), uropathy (17%), proteinuria (12-24% • Hem/Onc: anemia (17-35%), neoplasm (6-30%), leukopenia (12-24%) • MSCK: weakness (15-20%), back pain (5-19%), arthralgia (6-17%), msck pain, muscle spasm • Opth: eye disease (10-29%) • Renal: renal insufficiency (15-29%) • Respiratory: cough (20-60%), nasopharyngitis (6-17%) nasal congestion	• Labs: CBC w dif., LDH, Sr Cr, AST, urinalysis • S & sx: meningococcal infection, infusion rx • aHUS (after D/C) TMA complications (angina, dyspnea, mental status change, seizure or thrombosis), Sr Cr, LDH, Plts • PNH (after D/C): S & sx of intravascular hemolysis (anemia, fatigue, pain, dark urine,	Meningococcal infection awareness Prescriber enrollment in Soliris REMS program

Drug	Adverse Reactions	Monitoring	REMS
	(20-40%), URI (5-40%), rhinitis (22%), bronchitis (10-18%) • Misc.: infection (24%), catheter infection (17%), fever (7-80%)	dyspnea, thrombosis)	
Ultomiris IV (ravulizunab-cwvz)	• CNS: HA (32%) • Resp: URI (29%)	• S & sx: meningococcal infection, infusion rx • After D/c: monitor for hemolysis & major vascular events	

8.0 Revision History:

Original Effective Date: April 25, 2018

Last Approval Date: 06/04/2019

Next Review Date: 06/04/2020

Revision Date	**Reason for Revision**
2/19	Transitioned to new format
4/19	Revise/ahf