Pharmacy Benefit Determination Policy

Policy Subject: Soliris & Ultomiris	**Dates:**
Policy Number: SHS PBD 19	**Effective Date:** April 25, 2018
Category: Monoclonal Antibody	**Revision Date:** March 6, 2019
Policy Type: ☒ **Medical** ☐ **Pharmacy**	**Approval Date:** February 27, 2019
Department: Pharmacy	**Next Review Date:** June 2020
Product (check all that apply):	**Clinical Approval By:**
☒ Group HMO/POS	**Medical Directors**
☒ Individual HMO/POS	Peter Graham, MD
☒ PPO	**Pharmacy and Therapeutics Committee**
☒ ASO	Peter Graham, MD

Policy Statement:

Physicians Health Plan, PHP Insurance & Service Company, and Sparrow PHP will cover Soliris through the Medical Benefit based on approval by the Clinical Pharmacist or Medical Director using the following determination guidelines

Drugs and Applicable Coding:

J-code: Soliris J1300 (10mg/unit)

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: > 2 different GPI protein deficiencies within 2 different cell lines from granulocytes, monocytes, or erythrocytes
      b. Transfusion dependent (1 below)
         - Hemoglobin (Hgb) ≤ 7 g/dL
         - Hemoglobin (Hgb) ≤ 9 g/dL and experiencing symptoms of anemia
      c. Lactate dehydrogenase (LDH) level: 1.5x the upper limit of normal range
   4. Dosage Regimen: See Appendix I
   5. Approval
      a. Initial: 6 months
      b. Re-approval: 6 months;
         - LDH level shows reduction from baseline (within 3 months)
         - Hgb stabilized: Did not required 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)
      a. Dosage regimen: See Appendix I
   4. Approval
      a. Initial: 6 months
      b. Re-approval: 6 months (1 below)
         - Increase in platelet count from baseline
         - Maintenance of normal platelet count and LDH levels for ≥ 4 weeks
         - 25% reduction in serum creatinine for ≥ 4 weeks
         - Lack of decrease platelets >25% from baseline (for ≥12 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
         - GFA Clinical Classification of class: II, III, or IV
         - MG-ADL: Total score ≥ 6 at initiation of therapy;
   3. Other therapies: Failed or had significant adverse effects (both below)
      a. Immunosuppressive therapy: 2 below
         - Azathioprine, methotrexate, cyclosporine, mycophenolate for 4-6 weeks each over 1-year time-period
      b. Alternative treatment (1 below)
         - IVIG over 1 year
         - Plasmapheresis or plasma exchange x 2 over 1 year
   4. Dosage regimen: See Appendix 1
   5. Approval:
      a. Initial: 1 month in combination with a stable regimen of immunosuppressive treatment
      b. Re-approval: 2 months (usually treat total of 12 weeks)
         - Baseline immunosuppressive therapy (prior to starting Soliris): Maintenance, decrease, or discontinue
         - MG-ADL: 3-point improvement and/or maintenance of score from baseline
      c. Treatment failure: No improvement in 4 weeks (e.g. add-on treatment, increased dose of immunosuppressive treatment, or additional MG rescue therapy from baseline)

Appendix I: Dosage Regimens per Diagnosis

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
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.

B. 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 Eculizu-mab 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 (20-40%), URI (5-40%), rhinitis (22%), bronchitis (10-18%) • Misc.: Infection (24%), catheter infection (17%), fever (7-80%)	• Labs: CBC w dif., LDH, Sr Cr, AST, urinalysis • S & Sx: meningococcal in-fection, 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, dyspnea, thrombosis	Mening-ococcal infection awareness Prescriber enrollment in Soliris REMS program

References and Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Soliris, Ultomiris accessed March 2019.
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
3. Myasthenia gravis: new developments in research and treatment. Curr Opin Neurol 2017,30:464-470.
4. Can eculizumab be discontinued in aHUS? Medicine 2016;95:31

Approved By:

2/27/19

Peter Graham, MD – PHP Executive Medical Director — Date

2/27/19

Kurt Batteen - Human Resources — Date