



Missouri Care

'Ohana Health Plan, a plan offered by WellCare Health Insurance of Arizona

OneCare (Care1st Health Plan Arizona, Inc.)

Staywell of Florida

Children's Medical Services Health Plan (CMS Health Plan)

WellCare (Arizona, Arkansas, California, Connecticut, Florida, Georgia, Illinois, Kentucky, Louisiana, Mississippi, Nebraska, New Jersey, New York, South Carolina, Tennessee, Texas)

WellCare Prescription Insurance

WellCare Texan Plus (Medicare – Dallas & Houston markets)

Soliris[®] (eculizumab)

Policy Number: HS-327

Original Effective Date: 2/1/2018

Revised Date(s): 2/7/2019; 8/_/2019

APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

DISCLAIMER

The Clinical Coverage Guideline (CCG) is intended to supplement certain standard WellCare benefit plans and aid in administering benefits. Federal and state law, contract language, etc. take precedence over the CCG (e.g., Centers for Medicare and Medicaid Services [CMS] National Coverage Determinations [NCDs], Local Coverage Determinations [LCDs] or other published documents). The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this CCG. Additionally, CCGs relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. Providers are responsible for the treatment and recommendations provided to the member. The application of the CCG is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations, and any state-specific Medicaid mandates. Links are current at time of approval by the Medical Policy Committee (MPC) and are subject to change. Lines of business are also subject to change without notice and are noted on www.wellcare.com. Guidelines are also available on the site by selecting the Provider tab, then "Tools" and "Clinical Guidelines".

BACKGROUND

Soliris[®] (eculizumab) is a complement inhibitor which inhibits the terminal part of the complement cascade, a part of the immune system that, when activated in an uncontrolled manner, plays a role in serious rare disorders like paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS) and anti-acetylcholine receptor (AChR) antibody-positive myasthenia gravis (MG).¹ On June 27, 2019, the FDA approved Soliris[®] for the additional indication of neuromyelitis optica spectrum disorder (NMOSD). This approval makes Soliris[®] the first FDA approved drug for this indication.²

The Soliris[®] (eculizumab) Drug Label includes the following Indications and Usage:

Paroxysmal Nocturnal Hemoglobinuria (PNH) - Soliris[®] is indicated for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.³

Atypical Hemolytic Uremic Syndrome (aHUS) - Soliris[®] is indicated for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.³

Generalized Myasthenia Gravis (gMG) - Soliris[®] is indicated for the treatment of adult patients with generalized Myasthenia Gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive.³

Neuromyelitis Optica Spectrum Disorder (NMOSD) - Soliris[®] is indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.³

Generalized Myasthenia Gravis (gMG)

Myasthenia gravis (MG) is a chronic and progressive autoimmune neuromuscular disease which causes weakness in certain muscles including: muscles of the face, muscles of the arms, legs and trunk, and respiratory muscles. Although MG can occur at any age, it most commonly begins for women before the age of 40 and men after the age of 60.^{1,4}

Common symptoms of MG are droopy eyelids, difficulty with vision, trouble chewing, talking and swallowing, loss of facial expression and difficulty holding up the head.³ More serious symptoms of MG can be severe dysphagia, double or blurred vision, disabling fatigue or immobility and shortness of breath or episodes of respiratory failure. Exacerbations of MG or myasthenic crises can cause a patient to require hospitalization and can be potentially life-threatening.¹

If a patient is suspected of having MG, blood work is done to identify antibodies, electrical tests are performed on the nerves and muscles and imaging is done of the thymus gland to rule out tumor. Some doctors will also do a Tensilon test or an ice pack test.⁴

Alexion Pharmaceuticals explains that in patients with anti-AchR antibody-positive MG, the body's own immune system turns on itself to produce antibodies against AchR, a receptor located on muscle cells at the neuromuscular junction (NMJ) and used by nerve cells to communicate with the muscles controlled by these nerves. The binding of these antibodies to AchR activates the complement cascade, another part of the immune system, which leads to localized inflammation and destruction of the muscle membrane at the NMJ. As a result, the communication between the nerve and muscle is impaired, leading to a loss of normal muscle function. Patients with anti-AchR antibody-positive gMG who continue to suffer from severe disease symptoms and complications despite current therapies for MG represent approximately 5-10% of all patients with MG.¹

The recommended dosing of Soliris[®] in the treatment of gMG is 900 mg weekly for the first 4 weeks, followed by 1200 mg for the fifth dose 1 week later, and then 1200 mg every 2 weeks thereafter.³ The most frequently reported adverse reaction in clinical trials was musculoskeletal pain.¹

Paroxysmal nocturnal hemoglobinuria (PNH)

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare hematopoietic stem cell disorder of the X chromosome. It is estimated that there are as many as 1 to 10 cases per million, however, it is thought that many cases go undiagnosed. The average age of onset is the thirties and males and females are equally affected.⁵

The most commonly experienced symptoms with PNH are those associated with hemolytic anemia including fatigue, jaundice, and discolored, red, pink or black urine. Some patients present with a thrombosis in an unusual location such as an abdominal or cerebral vein. Patients may also have symptoms related to increased smooth muscle tone such as dysphagia, abdominal pain, or erectile dysfunction. The patient may eventually develop renal

insufficiency or pulmonary hypertension due to hemoglobinemia.⁵

It is recommended that any patients with Coombs negative hemolytic anemia, aplastic anemia, refractory anemia, or unexplained thrombosis with cytopenias or hemolysis be screened for PNH. Autoimmune disorders should be ruled out as well as any other causes of hemolysis. Tests for PNH include a complete blood count, a reticulocyte count, and review of a peripheral blood smear for red blood cell abnormalities. The patient will have haptoglobin, lactate dehydrogenase as well as direct and indirect bilirubin and Coombs testing. The patient will also need to have a urine test of hemoglobin and hemosiderin. If the patient's results are consistent with DAT-negative intravascular, the doctor will do a flow cytometry test to confirm a diagnosis of PNH. Flow cytometry incubates peripheral blood cells with fluorescently-labeled monoclonal antibodies that bind to glycosylphosphatidylinositol (GPI) anchored proteins, which are reduced or absent on blood cells in PNH.⁵

Dosing of Soliris[®] for PNH patients 18 years or older is 600 mg weekly for the first 4 weeks, followed by 900 mg for the fifth dose 1 week later, then 900 mg every 2 weeks thereafter.³ The most frequently reported adverse events in clinical studies were headache, nasopharyngitis, back pain and nausea.¹

Atypical Hemolytic Uremic Syndrome (aHUS)

Atypical hemolytic uremic syndrome (aHUS) is a rare disease characterized by low levels of circulating red blood cells, low platelet count and acute kidney failure. aHUS is almost always genetic. However, the disease can be caused by certain antibodies or manifest for no known reason. Typically, aHUS is triggered by event such as an acute infection, chicken pox, or H1N1 influenza. In children, the disease typically shows up suddenly following an infection, particularly upper respiratory or gastroenteritis. Pregnancy is also a common trigger for women. In childhood, aHUS affects males and females in equally. Due to pregnancy as a trigger, females are affected more often than males in adulthood. The exact prevalence of the disease is unknown.⁶

Atypical Hemolytic Uremic Syndrome is very different from the more commonly known, typical hemolytic uremic syndrome, which is caused by E.coli-producing Shiga toxins and is generally a foodborne illness.⁵

Most patients experience generalized symptoms such as fatigue, irritability, and lethargy. The disease may be difficult to diagnosis in early phases and can potentially lead to hospitalization. The condition is usually progressive. The three main findings of aHUS are hemolytic anemia, thrombocytopenia, and acute kidney failure.⁵

Kidney disease varies in severity and tends to worsen with each episode. It is common for patients to have blood and protein in their urine during acute episodes. As the disease progresses, kidney failure can become more severe and patients may need dialysis or transplant. Hypertension is also common with aHUS patients due to kidney disease or lack of blood flow due from the formation small blood clots. The brain, gastrointestinal tract, liver, lungs, and heart can also be affected by clot formation. Specific symptoms depend on the organ involved.⁵

Diagnostic criteria for aHUS include hemolytic anemia, low platelet count and kidney dysfunction. Without family history, aHUS can be difficult to diagnose. In order for aHUS to be considered genetic, two or more family members must be affected at least six months apart and exposure to a common trigger must be excluded or a disease causing mutation must be identified on one of the genes associated with an aHUS family history.⁵

Atypical hemolytic uremic syndrome patients do not typically present with the same bloody diarrhea that is common with typical hemolytic uremic syndrome, although some children may have diarrhea. Stool is cultured for Shiga toxin producing-E. coli and patients are monitored for the progressive course indicative of aHUS and indications of nephrotic syndrome such as edema, blood or protein in the urine, reduced serum albumin and elevated blood pressure.⁵

Although typical HUS is usually treatable and patients fully recover, aHUS is more likely to become a chronic disease with a potential for serious complications such as severe hypertension and renal failure. Soliris[®] is used to block excessive complement activation in individuals with aHUS and has led to improvement with the blood abnormalities and reversed acute kidney injury.⁵

The recommended Dosage Regimen for aHUS patients 18 years of age and older is 900 mg weekly for the first 4 weeks, followed by 1200 mg for the fifth dose 1 week later, and then 1200 mg every 2 weeks thereafter. For patients less than 18 Years of age induction maintenance for those with a weight of 40 kg and over is 900 mg weekly x 4 doses 1200 mg at week 5; then 1200 mg every 2 weeks. For patients 30 kg to less than 40 kg, 600 mg weekly x 2 doses 900 mg at week 3; and then 900 mg every 2 weeks is recommended. For those 20 kg to less than 30 kg 600 mg weekly x 2 doses 600 mg at week 3; and then 600 mg every 2 weeks is the dosing. Patients weighing 10 kg to less than 20 kg are dosed at 600 mg weekly x 1 dose 300 mg at week 2; and then 300 mg every 2 weeks. Finally, those who weigh 5 kg to less than 10 kg are given 300 mg weekly x 1 dose 300 mg at week 2; and then 300 mg every 3 weeks.³ The most frequently reported adverse events observed with Soliris in clinical studies for the treatment of aHUS were headache, diarrhea, hypertension, upper respiratory infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections and pyrexia.¹

Neuromyelitis Optica Spectrum Disorder (NMOSD)

General Discussion

Neuromyelitis optica spectrum disorder (NMOSD), also known as Devic disease, is a chronic disorder of the brain and spinal cord dominated by optic neuritis and myelitis. NMOSD may easily be confused with multiple sclerosis. The disease occurs in individuals of all races with a prevalence of approximately 1-10 per 100,000. It occurs more frequently in individuals of Asian and African descent. NMOSD can occur at any age and in both genders, but women are four to five times more likely than men to be affected by the recurring form. NMOSD is regarded as an autoimmune disease though the exact cause for the autoimmunity is unknown.⁷

The most common signs and symptoms of NMOSD are optic neuritis and transverse myelitis. Optic neuritis causes pain inside the eye and loss of vision. Typically only one eye will be affected although both eyes may be affected. Individuals with transverse myelitis may experience pain in the spine or limbs, mild to severe paralysis of the lower limbs and loss of bowel or bladder control. They may also experience stiff neck, back or limb pain, or headaches.⁷

In order to diagnose NMOSD, a patient will need to give a detailed health history, have thorough clinical evaluation, and a variety of specialized tests such as blood tests, examination of cerebrospinal fluid, spinal taps, or x-ray procedures such as MRIs or CAT scans. A blood test, AQP4-IgG, is highly specific and moderately sensitive for NMOSD. Early in the course of the disease, it may be difficult to distinguish between NMOSD and multiple sclerosis because both may cause optic neuritis and myelitis. However, the optic neuritis and myelitis tend to be more severe in NMOSD; the brain MRI is more commonly normal, and the spinal fluid analysis does not usually show oligoclonal bands in NMOSD, which are features that help distinguish it from MS.⁷

The recommended dosing of Soliris[®] in the treatment of NMOSD is 900 mg weekly for the first 4 weeks, followed by 1200 mg for the fifth dose 1 week later, and then 1200 mg every 2 weeks thereafter.³

POSITION STATEMENT

Applicable To:

- Medicaid – All Markets
- Medicare – All Markets
- Medicaid – Florida (CMS Health Plan - CHIP)

Exclusions^{1,2}

Soliris[®] is **not considered medically necessary** and not a covered benefit when any of the following apply:

- Patients 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

Clinical Coverage Guideline

page 4

- Soliris® is not indicated for the treatment of patients with Shiga-toxin E. coli related hemolytic uremic syndrome (STEC:HUS).

Coverage

Generalized Myasthenia Gravis (gMG)

Soliris® is **considered medically necessary** for members with generalized Myasthenia Gravis and a covered benefit when all of the following criteria apply:

Initial authorization:

- Member is 18 years or older; **AND,**
- Member has Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of Class II to IV disease; **AND,**
- Member has a positive serologic test for anti-acetylcholine receptor (AChR) antibodies; **AND,**
- Member has failed treatment over 1 year or more with 2 or more immunosuppressive therapies (ISTs) either in combination or as monotherapy, or failed at least 1 IST and required chronic plasmapheresis or plasma exchange (PE) or intravenous immunoglobulin (IVIg); **AND,**
- Physician has assessed the baseline Quantitative Myasthenia Gravis (QMG) score; **AND,**
- Member has a MG-Activities of Daily Living (MG-ADL) total score of ≥ 6 .

Continuation of Care:

- Member is 18 years or older; **AND,**
- Member has Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of Class II to IV disease; **AND,**
- Member has a positive serologic test for anti-acetylcholine receptor (AChR) antibodies; **AND,**
- Member has experienced a clinical response defined as one of the following:
 - Improvement of at least 3-points from baseline in the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) total score; **OR,**
 - Improvement of at least 5-points from baseline in the Quantitative Myasthenia Gravis (QMG) total score.

Initial authorization: 6 months **Reauthorization:** 12 months

Paroxysmal Nocturnal Hemoglobinuria (PNH)

Soliris® is **considered medically necessary** for members with Paroxysmal Nocturnal Hemoglobinuria and a covered benefit when all of the following criteria apply:

Initial authorization:

- Member is 18 years of age or older; **AND,**
- Member has a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH); **AND,**
- Member has documented flow cytometry results demonstrating at least 10% PNH cells; **AND,**
- Documentation includes submission of baseline complete blood count (CBC) (must include hemoglobin);

AND,

- Submission of baseline serum LDH; **AND,**
- Documentation includes
- History of RBC transfusion; **OR,**
- History of thrombotic event.

Continuation of Care:

- Member is 18 years of age or older; **AND,**
- Member has a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH); **AND,**
- Member has demonstrated adequate treatment response documented by one or more of the following:
 - Improvement/normalization in hemoglobin levels from pre-treatment baseline; **OR,**
 - Decrease in serum LDH level from pre-treatment baseline; **OR,**
 - Decrease in need for RBC transfusion from pre-treatment baseline

Initial authorization: 6 months **Reauthorization:** 12 months

Atypical Hemolytic Uremic Syndrome (aHUS)

Soliris® is **considered medically necessary** for members with Atypical Hemolytic Uremic Syndrome and a covered benefit when all of the following criteria apply:

Initial authorization:

- Member is 2 years of age or older; **AND,**
- Member has a diagnosis of atypical hemolytic uremic syndrome (aHUS); **AND,**
- Documentation includes submission of baseline complete blood count (CBC) (must include platelet count); **AND,**
- Submission of baseline serum LDH; **AND,**
- Submission of baseline serum creatinine.

Continuation of Care:

- Member is 2 years of age or older; **AND,**
- Member has a diagnosis of atypical hemolytic uremic syndrome (aHUS); **AND,**
- Member has demonstrated an adequate treatment response documented by one or more of the following:
 - Increase in platelet count from pre-treatment baseline; **OR,**
 - Decrease in serum LDH level from pre-treatment baseline; **OR,**
 - Improvement/normalization in serum creatinine from pre-treatment baseline

Initial authorization: 6 months **Reauthorization:** 12 months

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Soliris® is considered medically necessary for members with Neuromyelitis Optica Spectrum Disorder (NMOSD) and a covered benefit when all of the following criteria apply:

Initial authorization:

- Member is 18 years of age or older; **AND**,
- Documentation of an anti-AQP4 antibody positive test; **AND**,
- History of at least 2 relapses in last 12 months or 3 relapses in the last 24 months, with at least 1 relapse in the 12 months prior to screening; **AND**,

- Documentation that alternative diagnoses have been ruled out.

Continuation of Care:

- Member has demonstrated an adequate treatment response documented by the following:
 - o Documented decreased frequency of symptom relapse

CODING

Covered CPT Codes *Listing is not all-inclusive.*

- 96413** Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
- 96415** Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in

Covered HCPCS Code

- J1300** Injection, eculizumab, 10 mg

Covered ICD-10 Codes

- D59.3** Hemolytic-uremic syndrome
- D59.5** Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]
- G70.00** Myasthenia gravis without (acute) exacerbation
- G70.01** Myasthenia gravis with (acute) exacerbation

Coding information is provided for informational purposes only. The inclusion or omission of a CPT, HCPCS, or ICD-10 code does not imply member coverage or provider reimbursement. Consult the member's benefits that are in place at time of service to determine coverage (or non-coverage) as well as applicable federal/ state law s.

REFERENCES

1. FDA approves Soliris® (eculizumab) for the treatment of patients with generalized myasthenia gravis (gMG). Alexion Web site <http://new.s.alexionpharma.com/press-release/product-news/fda-approves-soliris-eculizumab-treatment-patients-generalized-myasthenia>. Published Monday, October 23, 2017. Accessed January 30, 2019.
2. FDA approves first drug for neuromyelitis optica. Medscape Web Site https://www.medscape.com/viewarticle/914978?nlid=130402_3901&src=wnl_newsalrt_190627_MSCPEDIT&uac=213422HK&impID=2010317&faf=1#vp_2. Published June 27, 2019. Accessed June 28, 2019.
3. Soliris [package insert]. Alexion Pharmaceuticals Inc; revised 1/2017. http://www.alexion.com/Documents/Soliris_USPI.aspx
4. Patient education: Myasthenia gravis (The Basics). UpToDate Web site https://www.uptodate.com/contents/myasthenia-gravis-the-basics?source=search_result&search=myesthenia%20gravis%20basics&selectedTitle=1~150. Accessed January 30, 2019.
5. Brodsky, R.A. Clinical manifestations and diagnosis of paroxysmal nocturnal hemoglobinuria. UpToDate Web site https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-paroxysmal-nocturnal-hemoglobinuria?source=see_link. Published November 13, 2017. Accessed January 30, 2019.
6. Atypical hemolytic uremic syndrome. National Organization for Rare Disorders Web site <https://rarediseases.org/rare-diseases/atypical-hemolytic-uremic-syndrome/>. Published 2016. Accessed January 30, 2019.
7. Neuromyelitis optica spectrum disorder. National Organization for Rare Disorders Web site <https://rarediseases.org/rare-diseases/neuromyelitis-optica/>. Published 2018. Accessed June 28, 2019.
8. Local coverage determination Drugs and Biologics (Non-chemotherapy) (L34741). Centers for Medicare and Medicaid Services Web site. <http://www.cms.hhs.gov/mcd/search.asp>. Accessed January 30, 2019.

-
9. Local Coverage Article: Eculizumab (Soliris[®]) - Related to LCD L33394 (A54548). Centers for Medicare and Medicaid Services Web site. <http://www.cms.hhs.gov/mcd/search.asp>. Accessed January 30, 2019.

MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

Date	Action
8/_/2019	<ul style="list-style-type: none">• Approved by MPC. Added new FDA indication.
2/7/2019	<ul style="list-style-type: none">• Approved by MPC. No changes.
2/1/2018	<ul style="list-style-type: none">• Approved by MPC. New .