09-J1000-17

Original Effective Date: 03/15/10

Reviewed: 04/10/24

Revised: 09/15/24

Subject: Eculizumab (Soliris®) Injection

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DESCRIPTION:

Eculizumab (Soliris®) is a humanized monoclonal antibody against C5, a protein in the complement cascade that is essential for the formation of the membrane attack complex responsible for cell lysis. Eculizumab is indicated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), generalized myasthenia gravis in persons who are anti-acetylcholine receptor (AchR) antibody positive, and neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

PNH is an uncommon, life-threatening hemolytic anemia; the prevalence of PNH ranges from 1 to 5 cases per million people. In the U.S., there are fewer than 500 cases. PNH results from an acquired genetic deficiency in the cytolytic complement cascade that renders red blood cells (RBCs) susceptible to lysis. Chronic destruction of PNH RBCs by complement leads to serious morbidities. Increased hemolysis at night, hypothesized to result from decreased blood pH and activation of the complement system, leads to characteristic bloody morning urination. Excessive or persistent intravascular hemolysis in persons with PNH results in anemia, hemoglobinuria, and complications related to the presence of plasma-free hemoglobin (e.g., thrombosis, abdominal pain, dysphagia, erectile dysfunction, and pulmonary hypertension). In persons with PNH, eculizumab's inhibition of C5 reduces hemolysis and transfusion requirements.

Evidence for the efficacy and safety of eculizumab in PNH was obtained from the results of the phase 3 study, Transfusion Reduction Efficacy and Safety Clinical Investigation, a Randomized, Multicenter, Double-Blind, Placebo-Controlled, Using Eculizumab in Paroxysmal Nocturnal Hemoglobinuria (TRIUMPH). TRIUMPH included 87 transfusion-dependent PNH subjects who were not thrombocytopenic. Subjects were randomized to receive an intravenous (IV) infusion of eculizumab or placebo. Eculizumab was dosed at 600 mg weekly for 4 weeks, then 900 mg in week 5, and 900 mg every

other week to complete 26 weeks of treatment. Outcome measures included the proportion of subjects with hemoglobin levels maintained above an individualized set point, number of blood transfusions, serum levels of lactate dehydrogenase (LDH; an indication of hemolysis), and quality of life (QOL) outcomes.

- Twenty-one of 43 eculizumab-treated subjects (49%) achieved hemoglobin stabilization compared with none of the 44 placebo-treated subjects ($p<0.001$)
- The median (interquartile range) number of transfusions for 6 months before treatment was 8.5 (7-12.5) units in the placebo group and 9 (6-12) units in the eculizumab group. During six months of treatment, these values were 10 (6-16) and 0 (0-6) in the placebo and eculizumab groups, respectively ($p<0.001$)
- Mean serum LDH levels [± standard error] after treatment were lower in the eculizumab group compared with the placebo group (327.3 [±67.6] U/L vs. 2,418 [±140.3] U/L, $p<0.001$).
- QOL measures worsened in the placebo group and improved in the eculizumab group.

Hemolytic uremic syndrome (HUS) describes the clinical condition of persons who present with simultaneous occurrence of microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure. Typical HUS constitutes 90-95% of HUS and is secondary to infection by Shiga toxin-producing Escherichia coli (STEC). Atypical HUS (aHUS) is the result of uncontrolled activation of the complement system. Persons with aHUS present with nonimmune hemolytic anemia, thrombocytopenia, and severe renal impairment. Microvascular lesions (thrombotic microangiopathy) result from uncontrolled complement action on endothelial walls of capillary beds primarily in the kidney. In aHUS, eculizumab binds to C5, preventing the formation of C5a (inflammatory peptide) and the membrane-attack complex C5b-9 (cytotoxic), inhibiting terminal complement-mediated thrombotic microangiopathy.

The efficacy of eculizumab in the treatment of aHUS was evaluated in four prospective single-arm studies, which were published as two abstracts. One abstract describes subjects with plasma therapy-resistant aHUS (n=17 aged 12 years or older) treated with eculizumab for 26 weeks. The comparator was baseline levels at the start of therapy. Outcomes of interest included the reduction in the signs of thrombotic microangiopathy (TMA; e.g., reduction of serum LDH levels, increased platelet count, improvements in creatinine clearance [CrCl]). These subjects experienced a mean platelet count (primary endpoint) increase from 109,000±32,000 at baseline to 210,000±68,000 after 26 weeks of therapy. The second abstract reported subjects with plasma therapy-sensitive aHUS (n=20 aged 12 years or older), also treated with eculizumab for 26 weeks. The comparator in this study was a baseline measure recorded over an 8 week observation period. The outcome of interest was reduction in the signs of TMA, but in subjects already stabilized on plasma therapy and where eculizumab was substituted, outcomes of interest were maintaining the corrected levels of TMA indicators already achieved with plasma therapy (platelet count and serum LDH levels remain stable compared to baseline). The primary endpoint for the cohort with plasma therapy sensitive aHUS was TMA event free status, defined as 12 weeks or more of stable platelet count, no plasma therapy and no new dialysis. The primary endpoint was achieved in 80% (95% CI 0.56-0.94) of the cohort.

Standard treatment options for PNH include corticosteroids, androgens, splenectomy, blood transfusions, and iron and folate supplementation. For persons with an associated bone-marrow failure syndrome or with major complication of PNH (e.g., refractory transfusion-dependent hemolytic anemia or recurrent life-threatening thromboembolic complications), hematopoietic stem-cell transplant is

considered. The American Society of Hematology (ASH) recommends eculizumab for the treatment of PNH.

Any person suspected of having aHUS should be transferred to a specialized center able to provide supportive care for acute renal failure and severe hypertension, and where dialysis and plasma exchange are common practice. Plasma exchange or plasma infusion (PE/PI), which have been used for 30 years, reduce mortality related to acute aHUS episodes from 50% to 25%.

POSITION STATEMENT:

Site of Care: If eculizumab (Soliris) is administered in a hospital-affiliated outpatient setting, additional requirements may apply depending on the member's benefit. Refer to 09-J3000-46: Site of Care Policy for Select Specialty Medications.

Initiation of eculizumab (Soliris) **meets the definition of medical necessity** when used to treat **ONE** of the following indications and the indication-specific criteria are met:

1. **Paroxysmal Nocturnal Hemoglobinuria (PNH)**
    a. Flow cytometry to confirm PNH in both red and white blood cells (with at least 5% granulocyte or monocyte clone size) – lab documentation must be provided
    b. Member's lactate dehydrogenase (LDH) is elevated (i.e., 1.5 times greater than the upper limit of normal [ULN] as determined by the laboratory performing the test) – lab documentation must be provided
    c. **ONE** of the following:
        i. Member has been vaccinated against meningococcal infection at least 2 weeks prior to therapy initiation
        ii. Member has been vaccinated against memingococcal infection less than 2 weeks prior to therapy initiation and will receive prophylactic antibiotics for at least 2 weeks following vaccination
    d. There is no evidence of an active meningococcal infection
    e. **ONE** of the following – documentation must be provided:
        i. Member's disease is transfusion-dependent evidenced by 2 or more transfusions in the 12 months prior to eculizumab initiation
        ii. Member has a history of a major adverse vascular event (MAVE) from thromboembolism (e.g., myocardial infarction, cerebrovascular accident, deep vein thrombosis)
        iii. Member has anemia with a hemoglobin less than the lower limit of normal
    f. The member has an inadequate response or contraindication to ALL of the following – documentation must be provided:
        i. ravulizumab (Ultomiris)
        ii. pegcetacoplan (Empaveli)
        iii. crovalimab (Piasky)

g. The member will not receive treatment in combination with an additional complement inhibitor (crovalimab, iptacopan, pegcetacoplan, ravulizumab, zilucoplan), efgartigimod, efgartigimod-hyaluronidase, inebilizumab, rituximab, rozanolixizumab, satralizumab, tocilizumab or chronic immune globulin therapy

h. The dose does not exceed 600 mg weekly for the first 4 weeks, followed by 900 mg for the fifth dose 1 week later and then 900 mg every 2 weeks

2. **Atypical Hemolytic Uremic Syndrome (aHUS)**

   a. Diagnosis is supported by **BOTH** of the following - documentation must be provided:

      i. No evidence of Shiga toxin-producing E. coli infection - all initial and subsequent tests have been negative for the toxin

      ii. ADAMTS-13 level is greater than 5%

   b. **ONE** of the following:

      i. Member has been vaccinated against meningococcal infection at least 2 weeks prior to therapy initiation

      ii. Member has been vaccinated against memingococcal infection less than 2 weeks prior to therapy initiation and will receive prophylactic antibiotics for at least 2 weeks following vaccination

   c. There is no evidence of an active meningococcal infection

   d. The member has an inadequate response or contraindication to ravulizumab (Ultomiris) – documentation must be provided

   e. The member will not receive treatment in combination with an additional complement inhibitor (crovalimab, iptacopan, pegcetacoplan, ravulizumab, zilucoplan), efgartigimod, efgartigimod-hyaluronidase, inebilizumab, rituximab, rozanolixizumab, satralizumab, tocilizumab or chronic immune globulin therapy

   f. The dose does not exceed 900 mg weekly for the first 4 weeks, followed by 1200 mg for the fifth dose 1 week later, then 1200 mg every 2 weeks

3. Refractory Generalized Myasthenia Gravis (MG)

   a. Member meets **ALL** of the following - documentation must be provided:

      i. Anti-acetylcholine receptor (AchR) antibody positive disease - lab documentation must be provided

      ii. Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II – IV

      iii. Myasthenia Gravis Activities of Daily Living (MG-ADL) total score greater than or equal to 6

      iv. **ONE** of the following – documentation must be provided[a]:

         1. Member had an inadequate response to at least one year trial of **TWO** of the following immunosuppressants:

a. azathioprine
b. cyclosporine
c. mycophenolate mofetil
d. tacrolimus
e. methotrexate
f. cyclophosphamide
g. rituximab

2. Member had an inadequate response to at least one year trial of **ONE** immunosuppressant in combination with either chronic immune globulin therapy or plasmapheresis

b. The member will not receive treatment in combination with an additional complement inhibitor (crovalimab, iptacopan, pegcetacoplan, ravulizumab, zilucoplan), efgartigimod, efgartigimod-hyaluronidase, inebilizumab, rituximab, rozanolixizumab, satralizumab, tocilizumab or chronic immune globulin therapy

c. The member has an inadequate response to **ONE** of the following **OR** the member has a contraindication to **ALL** of the following – documentation must be provided:

i. efgartigimod (Vyvgart) OR efgartigimod-hyaluronidase (Vyvgart Hytrulo)

ii. ravulizumab (Ultomiris)

iii. rozanolixizumab (Rystiggo)

d. Treatment is prescribed by or in consultation with a neurologist

e. **ONE** of the following:

i. Member has been vaccinated against meningococcal infection at least 2 weeks prior to therapy initiation

ii.Member has been vaccinated against memingococcal infection less than 2 weeks prior to therapy initiation and will receive prophylactic antibiotics for at least 2 weeks following vaccination

f. There is no evidence of an active meningococcal infection

g. The dose does not exceed 900 mg weekly for the first 4 weeks, followed by 1200 mg for the fifth dose 1 week later, then 1200 mg every 2 weeks

4. Neuromyelitis Optica Spectrum Disorder (NMOSD)

a. Member meets **ALL** of the following - documentation must be provided:

i. Anti-aquaporin-4 (AQP4) antibody positive disease - lab documentation must be provided

ii. Member has **ONE** core clinical characteristic of NMOSD and alternative diagnoses have been excluded:

1. Optic neuritis

2. Acute myelitis
3. Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
4. Acute brainstem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions

iii. **ONE** of the following[b]:

1. Member has a history of at least 2 relapses in the past 12 months
2. Member has a history of at least 3 relapses in the past 24 months with at least 1 relapse in the previous 12 months

iv. Member has an Expanded Disability Status Scale (EDSS) score less than or equal to 7

v. Member had an inadequate response to at least **ONE** of the following or has a contraindication to **ALL** of the following – documentation must be provided:

1. inebilizumab (Uplizna)
2. ravulizumab (Ultomiris)
3. satralizumab (Enspryng)

vi. Member had an inadequate response to a sufficient trial of, or has a contraindication to, rituximab therapy[c]

b. The member will not receive treatment in combination with an additional complement inhibitor (crovalimab, iptacopan, pegcetacoplan, ravulizumab, zilucoplan), efgartigimod, efgartigimod-hyaluronidase, inebilizumab, rituximab, rozanolixizumab, satralizumab, tocilizumab or chronic immune globulin therapy

c. Treatment is prescribed by or in consultation with a neurologist

d. **ONE** of the following:

i. Member has been vaccinated against meningococcal infection at least 2 weeks prior to therapy initiation

ii.Member has been vaccinated against memingococcal infection less than 2 weeks prior to therapy initiation and will receive prophylactic antibiotics for at least 2 weeks following vaccination

e. There is no evidence of an active meningococcal infection

f. The dose does not exceed 900 mg weekly for the first 4 weeks, followed by 1200 mg for the fifth dose 1 week later, then 1200 mg every 2 weeks

Approval duration: 60 days

Continuation of eculizumab **meets the definition of medical necessity** when **ALL** of the following are met

1. Member has a history of beneficial response to eculizumab therapy for the treatment of **ONE** of the following indications:
    a. Paroxysmal nocturnal hemoglobinuria (PNH) - examples of beneficial response include decreased requirement for transfusions, stabilization of hemoglobin, reduction of LDH – documentation must be provided
    b. Atypical hemolytic uremic syndrome (aHUS) – examples of beneficial response include improved platelet count, reduction of LDH, improved renal function – documentation must be provided
    c. Refractory Generalized Myasthenia Gravis – examples of beneficial response include improved MG-ADL total score, Quantitative myasthenia gravis total score – documentation must be provided
    d. Neuromyelitis Optica Spectrum Disorder (NMOSD)– example of beneficial response includes either the absence of relapse or reduction in relapses – documentation must be provided
2. The member has been previously approved for eculizumab in the treatment of PNH, aHUS, refractory generalized myasthenia gravis or NMOSD by Florida Blue or another health plan in the past 2 years, **OR** the member has previously met all indication-specific criteria for coverage
3. For continuation of therapy for Refractory Generalized Myasthenia Gravis, member's diagnosis has been confirmed by the following – lab documentation must be provided:
    a. Anti-acetylcholine receptor (AchR) antibody positive disease
4. For continuation of therapy for Neuromyelitis Optica Spectrum Disorder (NMOSD), the member's diagnosis has been confirmed by the following – lab documentation must be provided:
    a. Anti-aquaporin-4 (AQP4) antibody positive disease
5. Member has been revaccinated against meningococcal infection according to current medical guidelines for vaccination while on eculizumab therapy
6. There is no evidence of an active meningococcal infection
7. The member will not receive treatment in combination with an additional complement inhibitor (crovalimab, iptacopan, pegcetacoplan, ravulizumab, zilucoplan), efgartigimod, efgartigimod-hyaluronidase, inebilizumab, rituximab, rozanolixizumab, satralizumab, tocilizumab or chronic immune globulin therapy
8. The dose does not exceed indication specific limitations:
    a. PNH: 900 mg every 14 days
    b. aHUS: 1200 mg every 14 days
    c. Refractory Generalized Myasthenia Gravis: 1200 mg every 14 days
    d. NMOSD: 1200 mg every 14 days

Approval duration: 1 year

[a] Step not required if the member previously received treatment with efgartigimod (Vyvgart), efgartigimod-hyaluronidase (Vyvgart Hytrulo), ravulizumab (Ultomiris), rozanolixizumab (Rystiggo), or zilucoplan (Zilbrysq)

[b] Step not required if the member previously received treatment with inebilizumab (Uplizna), ravulizumab (Ultomiris), rituximab (Rituxan), or satralizumab (Enspryng)

[c] Step not required if the member previously received treatment with inebilizumab (Uplizna), ravulizumab (Ultomiris), or satralizumab (Enspryng)

NOTE: Quest Diagnostics® can perform the following tests used in the diagnosis of PNH or aHUS

- Flow cytometry assay (PNH with FLAER) used in the diagnosis of PNH
- ADAMTS-13 activity immunoassay used in diagnosis of aHUS
- Shiga Toxin, EIA with reflex to E. coli O157 culture used in the diagnosis of aHUS

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved: eculizumab is indicated for the treatment of persons with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis and treatment of persons with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy. Eculizumab is not indicated for the treatment of persons with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS). Eculizumab is indicated for the treatment of generalized myasthenia gravis in persons who are anti-acetylcholine receptor (AchR) antibody positive. Eculizumab is indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

Eculizumab is administered as an intravenous infusion over 35 minutes in adults and 1 to 4 hours in pediatric patients via gravity feed, a syringe-type pump, or an infusion pump. The recommended dosage regimen is dependent on the disease. Eculizumab should be administered at the recommended dosage regimen time points, or within 2 days of these time points.

1. PNH
    a. 600 mg weekly for weeks 1-4
    b. 900 mg for the fifth dose on week 5
    c. 900 mg every 14 days thereafter
2. aHUS
    a. 18 years of age and older
        - 900 mg weekly for weeks 1-4

- 1200 mg for the fifth dose on week 5
- 1200 mg every 14 days thereafter

b. Less than 18 years of age: eculizumab dose is based on body weight. The recommended doses based on body weight are outline in table 1.

3. Generalized myasthenia gravis and Neuromyelitis optica spectrum disorder
    a. 900 mg weekly for weeks 1-4
    b. 1200 mg for the fifth dose on week 5
    c. 1200 mg every 14 days thereafter

Table 1

Dosing recommendations in members less than 18 years of age		
Member Body Weight	**Induction**	**Maintenance**
40 kg and greater	900 mg weekly x 4 doses	1200 mg at week 5; then 1200 mg every 2 weeks
30 kg to less than 40 kg	600 mg weekly x 2 doses	900 mg at week 3; then 900 mg every 2 weeks
20 kg to less than 30 kg	600 mg weekly x 2 doses	600 mg at week 3; then 600 mg every 2 weeks
10 kg to less than 20 kg	600 mg weekly x 1 dose	300 mg at week 2; then 300 mg ever 2 weeks
5 kg to less than 10 kg	300 mg weekly x 1 dose	300 mg at week 2; then 300 mg every 3 weeks

Dose Adjustments

- Supplemental dosing of eculizumab is required in the setting of concomitant support with plasmapheresis/plasma exchange (PE) or fresh frozen plasma infusion (FFPI). Table 2 outlines recommended supplemental dosing following PE or PI.

Table 2

Supplemental dose of eculizumab following PE/FFPI			
Intervention	**Most recent eculizumab dose**	**Supplemental eculizumab dose with each PE/PI intervention**	**Timing of supplemental dose**
PE	300 mg	300 mg per each PE	Within 60 minutes after each PE
	600 mg or more	600 mg per PE	
FFPI	300 mg or more	300 mg per each unit of fresh frozen plasma	60 minutes prior to each 1 unit of FFPI
PE, plasmapheresis or plasma exchange; FFPI, fresh frozen plasma infusion			

Drug Availability: eculizumab is available as a 300 mg single-use vial containing 30 mL of 10 mg/mL sterile, preservative-free solution. Due to the risk of meningococcal infections, eculizumab is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the eculizumab REMS, prescribers must enroll in the program. Enrollment in the eculizumab REMS program and additional information are available by telephone: 1-888-765-4747.

PRECAUTIONS:

Boxed Warning

Life-threatening and fatal meningococcal infections have occurred in persons treated with eculizumab and may become rapidly life-threatening or fatal if not recognized and treated early.

1. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in persons with complement deficiencies.
2. Immunize members with a meningococcal vaccine at least 2 weeks prior to administering the first dose of eculizumab, unless the risks of delaying eculizumab therapy outweigh the risks of developing a meningococcal infection.
3. Monitor members for early signs of meningococcal infections, and evaluate immediately if infection is suspected.
4. Eculizumab is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).

Contraindications

1. Eculizumab is contraindicated in persons with unresolved serious Neisseria meningitidis infection

Precautions/Warnings

1. Discontinue therapy in persons who are being treated for serious meningococcal infections.
2. Use caution when administered eculizumab to members with any other systemic infection.
3. Monitor patient during infusion; interrupt for reactions and provide supportive measures.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J1300	Injection, eculizumab, 10 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

D59.39	Other hemolytic-uremic syndrome (atypical)
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]
G36.0	Neuromyelitis optica [Devic]
G70.00 – G70.01	Myasthenia gravis

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date. The Site of Care Policy for Select Specialty Medications does not apply to Medicare Advantage members.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

DEFINITIONS:

Atypical hemolytic uremic syndrome (aHUS): a rare condition characterized by hemolytic anemia, thrombocytopenia and kidney failure that has no obvious cause.

Hemolysis: breakdown of red blood cells.

Microangiopathic hemolytic anemia: a disorder in which narrowing or obstruction of small blood vessels results in distortion and fragmentation of red blood cells, hemolysis, and anemia.

Paroxysmal nocturnal hemoglobinuria (PNH): A chronic acquired blood cell dysplasia with proliferation of a clone of stem cells producing erythrocytes, platelets, and granulocytes that are abnormally susceptible to lysis by complement; it is marked by episodes of intravascular hemolysis, causing hemolytic anemia, particularly following infections, and by venous thromboses, especially of the hepatic veins.

Thrombocytopenia: a reduced level of circulating platelets, which are cell fragments that normally assist with blood clotting.

RELATED GUIDELINES:

Efgartigimod (Vyvgart, Vyvgart Hytrulo), 09-J4000-18

Inebilizumab (Uplizna), 09-J3000-73

Iptacopan (Fabhalta), 09-J4000-80

Immune Globulin Therapy, 09-J0000-06

Pegcetacoplan (Empaveli), 09-J4000-04

Ravulizumab (Ultomiris), 09-J3000-26

Rituximab Products, 09-J0000-59

Rozanolixizumab-noli (Rystiggo), 09-J4000-55

Satralizumab (Enspryng), 09-J3000-79

Zilucoplan (Zilbrysq), 09-J4000-78

OTHER:

Table 1: Myasthenia Gravis Foundation of America (MGFA) Clinical Classification System

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

Table 2: Myasthenia Gravis 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					

Table 3: Quantitative Myasthenia Gravis Score for Disease Severity

Test item	None	Mild	Moderate	Severe	Score
Grade	0	1	2	3	
(1) Double vision on lateral gaze, seconds	61	11-60	1-10	Spontaneous	
(2) Ptosis on upward gaze, seconds	61	11-60	1-10	Spontaneous	
(3) Weakness of facial muscles	Normal lid closure	Complete, weak, some resistance	Complete, without resistance	Incomplete	
(4)Swallowing water	Normal	Minimal coughing or throat clearing	Severe coughing/choking or nasal regurgitation	Cannot swallow (test not attempted)	
(5) Speech after counting aloud from 1-50	None at 50	Dysarthria at 30-49	Dysarthria at 10-29	Dysarthria at 9	
(6) Ability to keep right arm outstretched, seconds	240	90-239	10-89	0-9	
(7) Ability to keep left arm outstretched, seconds	240	90-239	10-89	0-9	
(8) Vital capacity as percent of predicted	Greater or equal to 80	65-79	50-64	Less than 50	

(9) Right hand grip strength, kgW	Men – 45 or greater Women – 30 or greater	Men – 15-44 Women – 10-29	Men – 5-14 Women – 5-9	Men –0-4 Women – 0-4	
(10) Left hand grip strength, kgW	Men – 45 or greater Women – 30 or greater	Men – 15-44 Women – 10-29	Men – 5-14 Women – 5-9	Men –0-4 Women – 0-4	
(11) Ability to keep head lifted when lying supine, seconds	120	30-119	1-29	0	
(12) Ability to keep the right leg outstretched, seconds	100	31-99	1-30	0	
(13) Ability to keep the left leg outstretched, seconds	100	31-99	1-30	0	
				Total QMG Score:	

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 04/10/24.

GUIDELINE UPDATE INFORMATION:

03/15/10	New Medical Coverage Guideline.
01/15/11	Revision to guideline; consisting of adding ICD-10 codes.
05/15/11	Review and revision to guideline; consisting of updating references.
11/15/11	Revision to guideline; consisting of adding new FDA-approved indication, updated dosing and coding.
05/15/12	Review and revision to guideline; consisting of updating position statement, precautions and references.
05/15/13	Review and revision to guideline; consisting of revising position statement to include duration of approval and orphan drug designations; revised and reformatted description, dosage/administration, and precautions sections; updated references; added pertinent definitions.
10/15/13	Revision to guideline; consisting of updating diagnosis criteria in the position statement.
05/15/14	Review and revision to guideline; consisting of reformatting position statement and updating references.
05/15/15	Revision to guideline; consisting of updating references.
11/01/15	Revision: ICD-9 Codes deleted.
05/15/16	Review and revision to guideline; consisting of updating position statement, coding and references.
05/15/17	Review and revision to guideline; consisting of updating references.

12/15/17	Revision to guideline; consisting of updating position statement, coding, dosing and references.
05/15/18	Review and revision to guideline; consisting of updating references.
04/15/19	Review and revision to guideline; consisting of updating position statement and references.
09/15/19	Review and revision to guideline; consisting of updating position statement, description, coding, dosing, and references.
10/15/19	Revision to guideline consisting of updating the position statement.
11/11/19	Revision to guideline consisting of adding a reference to the Site of Care Policy for Select Specialty Medications and updating the Program Exceptions.
05/15/20	Revision to guideline consisting of updating position statement and references.
11/15/20	Revision to guideline consisting of updating position statement and references.
10/15/21	Review and revision to guideline; consisting of updating the position statement, warnings and references.
07/15/22	Review and revision to guideline; consisting of updating the position statement and references.
10/01/22	Update to ICD-10 coding.
09/15/23	Review and revision to guideline; consisting of updating the list of agents not to be used in combination and update to references.
10/15/23	Review and revision to guideline; consisting of updating the position statement for Myasthenia Gravis.
05/15/24	Review and revision to guideline; consisting of updating the the position statement to revise neuromyelitis optica spectrum disorder and updating agents not to be used in combination.
09/15/24	Review and revision to guideline; consisting of updating the the position statement to revise the step for paroxysmal nocturnal hemoglobinuria and updating agents not to be used in combination.