09-J4000-55

Original Effective Date: 10/15/23

Reviewed: 05/14/25

Revised: 09/15/25

Subject: Rozanolixizumab-noli (Rystiggo) Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Generalized myasthenia gravis is an autoimmune neuromuscular disorder characterized by muscle weakness and fatigue. IgG antibodies occur in up to 85% of patients which are most frequently directed at the acetylcholine receptor (85% of patients) or the anti-muscle-specific tyrosine kinase (MuSK) antibody (6% of patients). Treatment includes the use of cholinesterase inhibitors to prevent the breakdown of acetylcholine at the neuromuscular junction, immunosuppressive therapies, and thymectomy. Myasthenic crisis may occur which is a medical emergency due to respiratory failure and treatment includes plasmapheresis, IVIG, and corticosteroids.

Rozanolixizumab (Rystiggo) is FDA-approved for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive or anti-muscle-specific tyrosine kinase (MuSK) antibody positive. It is a recombinant, humanized immunoglobulin G4 (IgG4) monoclonal antibody that binds to the neonatal Fc receptor (FcRn) and reduces circulating IgG.

Rozanolixizumab was compared to placebo in 200 patients with AChR antibody positive or anti-MuSK antibody positive generalized myasthenia gravis in a 18-week study. The study consisted of a 4-week initial screening period, a 6 week dosing period and an 8 week observation period. The patients were randomized to receive either a weight-based dose of rozanolixizumab as 7 mg/kg or 10 mg/kg or placebo. The patients were included if they had a Myasthenia Gravis Foundation of America (MGFA) clinical classification of class II – IVa and a Myasthenia Gravis Activities of Daily Living (MG-ADL) total score of at least 3 (with at least 3 points from non-ocular symptoms). The patients also had to be on a stable dose of medication that included acetylcholinesterase (AChE) inhibitors, steroids, or non-steroidal immunosuppressive therapies alone or in combination. There were over 83% of patients who received AChE inhibitors, over 56% receiving steroids, and approximately 50% received non-steroidal immunosuppressive therapies. Patients had IgG levels of at least 5.5 g/L, a median time since diagnosis

of MG of 6 years, a median MG-ADL total score of 8, and the median Quantitative Myasthenia Gravis (QMG) total score of 15. The MG-ADL was used to evaluate the efficacy of treatment. The MG-ADL quantifies the impact of gMG on 8 signs or symptoms with a score ranging from 0 to 24, with a higher score indicating less ability to perform a function. The primary endpoint was the change in baseline MG-ADL between groups at day 43. A statistically significant improvement in the percentage of MG-ADL responders was demonstrated with the use of rozanolixizumab as compared to placebo (-3.4 points for each weight based dosing groups vs 0.8 points for placebo, $p<0.001$). The QMG was used to assess secondary endpoint of change in baseline to day 43 (range 0-39 with higher score indicating severe weakness). The percentage of QMG responders was significantly higher in the patients treated with rozanolixizumab vs the placebo group (-5.4 points for 7 mg/kg group and -6.7 points for 10 mg/kg group vs -1.9 points for placebo, $p<0.001$). The most common adverse reactions in patients with treated with rozanolixizumab included headache, respiratory tract infections, diarrhea, and pyrexia.

POSITION STATEMENT:

Site of Care: If rozanolixizumab (Rystiggo) 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 rozanolixizumab (Rystiggo) **meets the definition of medical necessity** when **ALL** of the indication- specific criteria are met:

1. Generalized Myasthenia Gravis (MG)
    a. Member meets **ALL** of the following - documentation must be provided:
        i. **ONE** of the following – lab documentation must be provided:
            1. Anti-acetylcholine receptor (AchR) antibody positive disease
            2. Anti-muscle-specific tyrosine kinase (MuSK) antibody positive disease
        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 3 (with at least 3 points from non-ocular symptoms)
        iv. **ONE** of the following[a]:
            1. Member had an inadequate response to at least **ONE** of the following immunosuppressants:
                a. azathioprine
                b. cyclosporine
                c. mycophenolate mofetil
                d. tacrolimus
                e. methotrexate
                f. cyclophosphamide

g. rituximab

2. Member required chronic immune globulin therapy or chronic plasmapheresis/plasma exchange

b. Rozanolixizumab is not used concurrently with rituximab, eculizumab and biosimilars, efgartigimod, efgartigimod-hyaluronidase, nipocalimab, ravulizumab, zilucoplan, or immune globulin therapy

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

d. There is no evidence of an active infection

e. The dose does not exceed the following (a minimum of 63 days is required between the first dose of each 6 week cycle):

i. Less than 50 kg: 420 mg once weekly for 6 weeks

ii. 50 kg to less than 100 kg: 560 mg once weekly for 6 weeks

iii. 100 kg and above: 840 mg once weekly for 6 weeks

Approval duration: 6 months

Continuation of rozanolixizumab (Rystiggo) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. An authorization or reauthorization for rozanolixizumab has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of myasthenia gravis, OR the member has previously met ALL indication-specific criteria.
2. For continuation of therapy for Generalized Myasthenia Gravis, member's diagnosis has been confirmed by **ONE** of the following –lab documentation must be provided:
    a. Anti-acetylcholine receptor (AchR) antibody positive disease
    b. Anti-muscle-specific tyrosine kinase (MuSK) antibody positive disease
3. Member has a history of beneficial response to therapy– examples of beneficial response include improved MG-ADL total score, Quantitative myasthenia gravis total score – documentation must be provided
4. There is no evidence of an active infection
5. Rozanolixizumab is not used concurrently with rituximab, eculizumab and biosimilars, efgartigimod, efgartigimod-hyaluronidase, nipocalimab, ravulizumab, zilucoplan, or immune globulin therapy
6. The dose does not exceed the following (a minimum of 63 days is required between the first dose of each 6 week cycle):
    a. Less than 50 kg: 420 mg once weekly for 6 weeks
    b. 50 kg to less than 100 kg: 560 mg once weekly for 6 weeks
    c. 100 kg and above: 840 mg once weekly for 6 weeks

Approval duration: 1 year

[a] Not required if the member is switching to rozanolixizumab and member and was previously approved by Florida Blue for the use of efgartigimod, efgartigimod-hyaluronidase, eculizumab or biosimilars, nipocalimab, ravulizumab, or zilucoplan for the treatment of myasthenia gravis.

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

For the treatment of generalized myasthenia gravis in adults who are anti-acetylcholine receptor (AChR) antibody positive or anti-muscle-specific tyrosine kinase (MuSK) antibody positive:

Administer subcutaneous infusion once weekly for 6 weeks according to the following weight based dose (do not administer subsequent cycles sooner than 63 days from the start of the previous treatment cycle). Subsequent cycles are administered based on clinical evaluation.

Body weight of patient	Dose	Volume to be infused subcutaneously
Less than 50 kg	420 mg	3 mL
50 kg to less than 100 kg	560 mg	4 mL
100 kg and above	840 mg	6 mL

Evaluate the need to administer age-appropriate vaccines prior to initiating therapy with rozanolixizumab.

PRECAUTIONS:

Boxed Warning

None

Contraindications

None

Precautions/Warnings

- Infections: Delay administration to patients with an active infection. Monitor for signs and symptoms of infection in patients. If serious infection occurs, administer appropriate treatment and consider withholding until the infection has resolved.
- Aseptic Meningitis: Serious events of aseptic meningitis have been reported. Monitor for symptoms; diagnostic workup and treatment should be initiated according to the standard of care.
- Hypersensitivity Reactions: Angioedema and rash have occurred. If a hypersensitivity reaction occurs, discontinue the infusion and institute appropriate therapy.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J9333	Injection, rozanolixizumab-noli, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

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

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

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

None

RELATED GUIDELINES:

Eculizumab (Soliris), 09-J1000-17

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

Immune Globulin Therapy, 09-J0000-06

Ravulizumab (Ultomiris), 09-J3000-26

Rituximab Products, 09-J0000-59

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	Greater or equal to 80	65-79	50-64	Less than 50	

percent of predicted					
(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:	

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc. Accessed May 1, 2025.
2. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Accessed May 1, 2025.
3. National Organization of Rare Diseases. https://rarediseases.org/rare-diseases.
4. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2023 [cited Jul 26, 2023]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
5. Rystiggo (rozanolixizumab-noli) injection. UCB, Inc. Smyrna, GA. June 2024.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 05/14/25.

GUIDELINE UPDATE INFORMATION:

10/15/23	New Medical Coverage Guideline.
01/01/24	Revision: Added HCPCS code J9333 and deleted code J3590.
05/15/24	Revision to guideline including updating lab documentation requirements and agents not to be used in combination in the position statement.
06/15/25	Review and revision to guideline; consisting of updating agents not to be used in combination.
09/15/25	Revision to guideline including updating continuation requirements in the position statement.