rozanolixizumab-noli (Rystiggo®)

Policy # 00865
Original Effective Date: 02/12/2024
Current Effective Date: 02/12/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider rozanolixizumab-noli (Rystiggo®)‡ for the treatment of myasthenia gravis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for rozanolixizumab-noli (Rystiggo) will be considered when the following criteria are met:

- Initial
    - Patient is greater than or equal to 18 years of age; AND
    - Patient has a diagnosis of generalized myasthenia gravis; AND
    - Patient has anti-acetylcholine receptor autoantibody positive serologic test OR an anti-muscle-specific tyrosine kinase autoantibody positive serologic test; AND
    - Patient has a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV; AND
      *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
    - Patient has a baseline IgG level of at least 5.5 g/L; AND
      *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
    - Patient has received or is currently receiving pyridostigmine or corticosteroids unless there is clinical evidence or patient history that suggests the use of pyridostigmine or corticosteroids will cause an adverse effect or inadequate response to the patient; AND

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Patient has received or is currently receiving at least one nonsteroidal immunosuppressive therapy (NSIST) for at least 1 year unless there is clinical evidence or patient history that suggests NSISTs will be ineffective or cause an adverse reaction to the patient. Examples of NSISTs include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus, and cyclophosphamide; AND

  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has evidence of unresolved symptoms of myasthenia gravis, such as difficulty swallowing, difficulty breathing, or a functional disability resulting in the discontinuation of physical activity (e.g., double vision, talking, impairment of mobility); AND

  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Dose does not exceed 840 mg once weekly.

- Continuation
  - Patient has received an initial authorization for Rystiggo; AND
  - It has been at least 63 days since the start of the previous treatment cycle; AND
  - Patient has experienced improvement on therapy as evidenced by at least ONE of the following:
    - Improvement in the Myasthenia Gravis Activities of Daily Living (MG-ADL) total score; OR
    - Improvement in the Quantitative Myasthenia Gravis (QMG) total score; AND

    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
  - Dose does not exceed 840 mg once weekly.

rozanolixizumab-noli (Rystiggo®)

Policy # 00865
Original Effective Date: 02/12/2024
Current Effective Date: 02/12/2024

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of rozanolixizumab-noli (Rystiggo) for myasthenia gravis that is not MGFA class II to IV, when the patient does not have a baseline IgG level of at least 5.5 g/dL, has not tried and failed pyridostigmine in addition to at least one NSIST, or does not have evidence of unresolved symptoms of generalized myasthenia gravis to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of rozanolixizumab-noli (Rystiggo) when the patient selection criteria are not med (Except those denoted above as **not medically necessary****) to be **investigational.***

Policy Guidelines

Myasthenia Gravis Foundation of America (MGFA) Clinical Classification

Class	***Description***
I	Any ocular muscle weakness; may have weakness of eye closure. All other muscle strength is normal
IIa	Mild weakness affecting muscles other than ocular muscles. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles
IIb	Mild weakness affecting muscles other than ocular muscles. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
IIIa	Moderate weakness affecting muscles other than ocular muscles. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
IIIb	Moderate weakness affecting muscles other than ocular muscles. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
IVa	Severe weakness affecting muscles other than ocular muscles. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.

rozanolixizumab-noli (Rystiggo®)

Policy # 00865
Original Effective Date: 02/12/2024
Current Effective Date: 02/12/2024

IVb	Severe weakness affecting muscles other than ocular muscles. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
V	Intubation with or without mechanical ventilation except when employed during routine postoperative management.

Myasthenia Gravis Activities of Daily Living (MG-ADL) profile

Grade	***0***	***1***	***2***	***3***	***Score***
1. Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal, but can be understood	Difficult to understand speech	
2. Chewing	Normal	Fatigue with solid food	Fatigue with soft food	Gastric tube	
3. Swallowing	Normal	Rare episode of choking	Frequent choking necessitating changes in diet	Gastric tube	
4. Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependence	
5. 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	
6. Impairment of ability to arise from a chair	None	Mild, sometimes uses arms	Moderate, always uses arms	Severe, requires assistance	
7. Double vision	None	Occurs, but not daily	Daily, but not constant	Constant	
8. Eyelid droop	None	Occurs, but not daily	Daily, but not constant	Constant	

rozanolixizumab-noli (Rystiggo®)

Policy # 00865
Original Effective Date: 02/12/2024
Current Effective Date: 02/12/2024

	MG-ADL score total (items 1-8)=	

Quantitative Myasthenia Gravis (QMG) Score

Test Item	***None***	***Mild***	***Moderate***	***Severe***	***Score***
Grade	***0***	***1***	***2***	***3***	
Double vision on lateral gaze (secs)	61	11-60	1-10	Spontaneous	
Ptosis (upward gaze)	61	11-60	1-10	Spontaneous	
Facial muscles	Normal lid closure	Complete, weak, some resistance	Complete without resistance	Incomplete	
Swallowing 4 oz water	Normal	Minimal coughing or throat clearing	Severe coughing/choking or nasal congestion	Cannot swallow (test not attempted)	
Speech after counting aloud from 1 to 50 (onset of dysarthria)	None at 50	Dysarthria at 30-49	Dysarthria at 10-29	Dysarthria at 9	
Right arm outstretched (90 degrees sitting), seconds	240	90-239	10-89	0-9	
Left arm outstretched (90 degrees sitting), seconds	240	90-239	10-89	0-9	
Forced Vital Capacity	≥80	65-79	50-64	≤50	
Rt-hand grip, kg					

Men Women	≥45 ≥30	15-44 10-29	5-14 5-9	0-4 0-4	
Lt-hand grip, kg Men Women	 ≥35 ≥25	 15-34 10-24	 5-14 5-9	 0-4 0-4	
Head lifted (45 degrees supine), seconds	120	30-119	1-29	0	
Right leg outstretched (45 degrees supine), seconds	100	31-99	1-30	0	
Left leg outstretched (45 degrees supine), seconds	100	31-99	1-30	0	
				Total QMG Score:	

Background/Overview

Rystiggo is a humanized IgG4 monoclonal antibody indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive. It works by binding to the neonatal Fc receptor, resulting in the reduction of circulating IgG. Because it causes this reduction in IgG levels, immunization with live-attenuated or live vaccines is not recommended during treatment with Rystiggo. If indicated, these vaccines should be administered before initiation of a new treatment cycle with Rystiggo. The recommended dosage of Rystiggo is either 420 mg, 560 mg, or 840 mg depending on the patient's weight. It should be administered as a subcutaneous infusion using an infusion pump once weekly for 6 weeks and should only be prepared and infused by a healthcare provider. If subsequent treatment cycles are needed (determined based on clinical evaluation), they should be initiated no sooner than 63 days from the start of the previous treatment cycle.

rozanolixizumab-noli (Rystiggo®)

Policy # 00865
Original Effective Date: 02/12/2024
Current Effective Date: 02/12/2024

Myasthenia gravis is a chronic autoimmune neuromuscular disease that causes weakness in the skeletal muscles. The hallmark of the condition is muscle weakness that worsens after periods of activity and improves after periods of rest. Certain muscles such as those that control eye and eyelid movement, facial expression, chewing, talking, and swallowing are often involved in the disorder, however the muscles that control breathing and neck and limb movements may also be affected. Acquired myasthenia gravis results from the binding of autoantibodies to the components of the neuromuscular junction, most commonly the acetylcholine receptor (AChR). However, antibodies to other proteins, such as the muscle-specific tyrosine kinase (MuSK) protein, can also lead to impaired transmission at the neuromuscular junction. Myasthenia gravis most commonly occurs in young adult women (<40 years of age) and older men (>60 years of age), but it can occur at any age, including childhood. The incidence ranges from 0.3 to 2.8 per 100,000 and it is estimated to affect more than 700,000 people worldwide. Various clinical scoring systems are available to assess the severity of disease and include the Myasthenia Gravis Foundation of America (MGFA) clinical classification system, Myasthenia Gravis Activities of Daily Living (MG-ADL), and Quantitative Myasthenia Gravis (QMG) test.

Medications to treat myasthenia gravis include anticholinesterase agents (e.g., pyridostigmine), which slow the breakdown of acetylcholine at the neuromuscular junction and thereby improve neuromuscular transmission and increase muscle strength. Immunosuppressive drugs improve muscle strength by suppressing the production of abnormal antibodies and may include prednisone, azathioprine, mycophenolate mofetil, tacrolimus, and rituximab. Plasmapheresis and intravenous immunoglobulin (IVIG) may be options in severe cases to remove the destructive antibodies; however, their effectiveness frequently only lasts a few weeks to months. Additionally, the Food and Drug Administration (FDA) has approved eculizumab (Soliris®)‡ and ravulizumab (Ultomiris™)‡, both complement inhibitors, as well as efgartigimod alfa products (Vyvgart, Vyvgart Hytrulo) which contain an IgG1 monoclonal antibody that binds to the neonatal Fc receptor for the treatment of generalized myasthenia gravis. Although Soliris, Ultomiris, Vyvgart, Vyvgart Hytrulo, and Rystiggo are the only agents with FDA approval for the condition, the other agents have been used off-label and are still recommended as first-line therapy in clinical practice guidelines. Available guidelines have not been updated to address these newer treatments.

rozanolixizumab-noli (Rystiggo®)

Policy # 00865
Original Effective Date: 02/12/2024
Current Effective Date: 02/12/2024

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Rystiggo was approved in June 2023 for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Rystiggo for the treatment of generalized myasthenia gravis (gMG) in adults who are anti-AChR antibody positive or anti-MuSK antibody positive was established in a multicenter, randomized, double-blind, placebo-controlled study. The study included a 4-week screening period and a 6-week treatment period followed by 8 weeks of observation. During the treatment period, Rystiggo or placebo were administered subcutaneously once a week for six weeks.

Included patients met the following criteria:

- Presence of autoantibodies against AChR or MuSK
- Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to Iva
- Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score of at least 3 (with at least 3 points from non-ocular symptoms)
- On stable dose of MG therapy prior to screening that included acetylcholinesterase (AChE) inhibitors, steroids, or non-steroidal immunosuppressive therapies (NSISTs), either in combination or alone
- Serum IgG levels of at least 5.5 g/L.

In the study, a total of 200 patients were randomized 1:1:1 to receive weight-tiered doses of Rystiggo (n=133), equivalent to 7 mg/kg (n=66) or 10 mg/g (N=67, or placebo (n=67). Baseline characteristics were similar between treatment groups. The majority of patients, 89.5% (n=179) were positive for AChR antibodies and 10.5% (n=21) were positive for MuSK antibodies. At baseline in each group,

over 83% of patients received AChE inhibitors, over 56% of patients received steroids, and approximately 50% received NSISTs, at stable doses. Patients were treated with Rystiggo via subcutaneous infusion once per week for a period of 6 weeks, followed by an observation period of up to 8 weeks.

The efficacy of Rystiggo was measured using the MG-ADL scale, which assesses the impact of gMG on daily functions of 8 signs or symptoms that are typically affected in gMG. Each item is assessed on a 4-point scale where a score of 0 represents normal function and a score of 3 represents loss of ability to perform that function. A total score ranges from 0 to 24, with the higher scores indicating more impairment.

The primary efficacy endpoint was the comparison of the change from baseline between treatment groups in the MG-ADL total score at day 43. A statistically significant difference favoring Rystiggo was observed in the MG-ADL total score change from baseline [-3.4 points in Rystiggo-treated group at either dose vs. -0.8 points in the placebo-treated group ($p<0.001$)].

References

1. Rystiggo [package insert]. UCB, Inc. Smyrna, GA. Updated June 2023.

Policy History

Original Effective Date: 02/12/2024
Current Effective Date: 02/12/2024
01/04/2024 Medical Policy Committee review
01/10/2024 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 01/2025

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

rozanolixizumab-noli (Rystiggo®)

Policy # 00865
Original Effective Date: 02/12/2024
Current Effective Date: 02/12/2024

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J9333
ICD-10 Diagnosis	G70.00-G70.9

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety,

effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

rozanolixizumab-noli (Rystiggo®)

Policy # 00865
Original Effective Date: 02/12/2024
Current Effective Date: 02/12/2024

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.