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Rozanolixixumab-noli

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of and developed by nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated and coverage is not required for non-formulary drugs.

Coverage

Rozanolixizumab-noli (Rystiggo®) - Initial Treatment

Rozanolixizumab-noli **may be considered medically necessary** for individuals with generalized myasthenia gravis (gMG) if they meet criteria 1 through 6:

1. 18 years of age or older.
2. Diagnosis of gMG with class II to IVa disease per the Myasthenia Gravis Foundation of America (MGFA) classification system (see Policy Guidelines).
3. Anti-acetylcholine receptor antibody (Anti-AChR) antibody positive or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.
4. Impaired activities of daily living defined as a myasthenia gravis activities of daily living (MG-ADL) total score of ≥3 and at least 3 points from non-ocular symptom(s).
5. Meets any one of the following:
    a. If anti-AChR antibody positive: inadequate treatment response, intolerance, or contraindication to an acetylcholinesterase inhibitor (e.g., pyridostigmine, neostigmine) and at least one immunosuppressive therapy (e.g., azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, methotrexate, cyclophosphamide) either in combination or as monotherapy.
    b. If anti-MuSK antibody positive: inadequate treatment response, intolerance, or contraindication to at least one immunosuppressive therapy (e.g., azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, methotrexate, cyclophosphamide).
6. IgG levels ≥5.5 g/L.

Rozanolixizumab-noli (Rystiggo®) - Continuation of Treatment

Reauthorization of rozanolixizumab-noli **may be considered medically necessary** for individuals with gMG if they meet criteria 1 through 2:

1. Individual continues to meet the initial treatment criteria cited above.
2. Decrease of 2 points in MG-ADL total score from pre-treatment baseline value.

Rozanolixizumab-noli (Rystiggo®) **is considered experimental, investigational and/or unproven** for all other non-FDA indications, and when the above criteria are not met.

Policy Guidelines

Rozanolixizumab-noli is supplied single-dose glass vial containing 280 mg/2 mL. The recommended dosage regimen of rozanolixizumab-noli is weight-based as follows:

- <50 kg: 420 mg (3 mL) subcutaneous infusion once weekly for 6 weeks;
- 50 to <100 kg: 560 mg (4 mL) subcutaneous infusion once weekly for 6 weeks;

- ≥100 kg: 840 mg (6 mL) subcutaneous infusion once weekly for 6 weeks.

Administer subsequent treatment cycles based on clinical evaluation. The safety of initiating subsequent cycles sooner than 63 days from the start of the previous treatment cycle has not been established. If a scheduled infusion is missed, the drug may be given up to 4 days after the scheduled time point. Thereafter, resume the original dosing schedule until the treatment cycle is completed.

It is recommended that individuals be monitored during administration and for 15 minutes thereafter for clinical signs and symptoms of hypersensitivity reactions, including angioedema and rash. If such a reaction occurs, discontinue therapy and institute appropriate supportive measures. In clinical trials, hypersensitivity reactions occurred up to 2 weeks post-administration.

It is recommended that individuals are monitored for symptoms consistent with aseptic meningitis. In clinical trials, a total of 3 individuals developed drug-induced aseptic meningitis, which lead to hospitalization and discontinuation of rozanolixizumab-noli.

Rozanolixizumab-noli (Rystiggo®) is for subcutaneous infusion only using an infusion pump and should be administered by a healthcare provider.

Myasthenia Gravis Foundation of America Clinical Classification (1)
In 1997, the Myasthenia Gravis Foundation of America (MGFA) formed a task force to address the need for universally accepted classifications, grading systems, and analytic methods for management of individuals undergoing therapy and for use in therapeutic research trials. As a result, the MGFA Clinical Classification was created. This classification divides myasthenia gravis (MG) into 5 main classes and several subclasses, as follows:

- 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.

Description

Myasthenia gravis is an acquired, autoimmune disorder that affects the neuromuscular junction of the skeletal muscles. Eighty to 90 percent of individuals with myasthenia gravis have autoantibodies against the acetylcholine receptor (AChR) detectable in serum, and these antibodies are believed to play a central role in disease pathomechanism. The AChR antibodies in myasthenia gravis are primarily immunoglobulin G1 (IgG1) and G3 (IgG3). In addition to blocking ACh binding to the AChR and cross-linking and internalizing the AChRs, these antibodies act through complement activation. (2) Some individuals with myasthenia gravis who are seronegative for AChR antibodies have antibodies directed against another target on the surface of the muscle membrane, muscle-specific receptor tyrosine kinase. (3) In contrast with AChR antibody-positive myasthenia gravis, in which complement-fixing immunoglobulin G1 (IgG1) and G3 (IgG3) subclasses predominate (4), muscle-specific kinase antibodies are mainly IgG4 (5), the IgG subtype that does not activate complement.

The clinical manifestations can vary from mild and focal weakness in some individuals to severe tetraparesis with respiratory failure in others. Symptom severity may also vary substantially in an individual patient throughout the day and over the course of the condition. Classification systems stratify individuals by symptoms or diagnostic findings to specify the severity of impairment and to aid with management. There are 2 clinical forms - ocular and generalized. In ocular from, weakness is limited to the eyelids and extraocular muscles while in generalized form, weakness involves a variable combination of ocular, bulbar, limb, and respiratory muscles. Myasthenia gravis may be categorized by symptom severity to guide treatment decisions, determine eligibility for clinical trials, and help with prognostication. A widely used classification system from a task force of the Myasthenia Gravis Foundation of America stratifies individuals by the extent and severity of muscle weakness (6) and is summarized in the section of "Policy Guidelines". Myasthenia gravis is a relatively uncommon disorder. Both incidence and prevalence have significant geographical variations. Reported prevalence rates range from 150 to 200 cases per million, and they have steadily increased over the past 50 years, at least partly due to improvements in recognition, diagnosis, treatment, and an overall increase in life expectancy. (7) More recent studies addressing incidence rates have been conducted in Europe and show a wide range from 4.1 to 30 cases per million person-years. (8, 9) The annual rate is lower in studies coming from North America and Japan, with the incidence ranging from 3 to 9.1 cases per million. (10)

The diagnosis is primarily based on clinical testing. Laboratory investigations and procedures can aid the clinician in confirming clinical findings. These may include serologic tests, electrophysiologic exams (e.g., repetitive nerve stimulation test and single-fiber electromyography), an edrophonium test, an ice-pack test, imaging, and laboratory testing for other coexisting autoimmune disorders (e.g., anti-nuclear antibodies, rheumatoid factor, and thyroid function). For most individuals with clinical features of myasthenia gravis, the diagnosis is confirmed by the presence of autoantibodies against the AChRs or against other muscle receptor-associated proteins. A positive anti-AChR antibody is present in 80% of individuals with gMG and confirms the diagnosis in an individual with classical clinical findings. About 5 to 10% of individuals will demonstrate anti-muscle specific kinase antibodies. Individuals who are seronegative for either of these antibodies will have anti-LRP4 antibodies.

Treatment

The goals of therapy are to render individuals minimally symptomatic or better while minimizing side effects from medications. The 4 basic therapies for myasthenia gravis include: 1) symptomatic therapy with an acetylcholinesterase inhibitor such as pyridostigmine and neostigmine; 2) chronic immunotherapies (such as glucocorticosteroids, eculizumab, rituximab, maintenance intravenous immunoglobulin (IVIG) or plasma exchange, and cyclophosphamide); 3) rapid but transient immunomodulatory therapies (plasma exchange and intravenous immune globulin) and 4) thymectomy. Approximately 10 percent of individuals with gMG have symptoms that are refractory or limited by specific toxicities of conventional immunomodulatory therapies (e.g., high-dose glucocorticoids). Therapeutic options for refractory disease include azathioprine, cyclosporine, eculizumab, efgartigimod, mycophenolate, ravulizumab, and tacrolimus.

Regulatory Status

On June 26, 2023, rozanolixizumab-noli (Rystiggo®, UCB Inc) was approved by the U.S. FDA for the treatment of gMG in adult patients who are anti-acetylcholine receptor or antimuscle-specific tyrosine kinase antibody positive.

Rationale

Medical policies assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the

intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Generalized Myasthenia Gravis

Clinical Context and Therapy Purpose

The purpose of rozanolixizumab-noli in adults who have gMG who are anti-acetylcholine receptor antibody positive is to provide a treatment option that is an alternative to existing therapeutic management for individuals with refractory disease.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population(s) of interest is adults with gMG who are anti-acetylcholine receptor antibody positive.

Interventions

The therapy being considered is rozanolixizumab.

Rozanolixizumab-noli is a humanized IgG4 monoclonal antibody that binds to the neonatal Fc receptor resulting in the reduction of circulating IgG.

Comparators

The following therapies are currently being used to make decisions about the treatment of gMG: acetylcholinesterase inhibitors, immunosuppressive agents, monoclonal antibodies, intravenous immunoglobulin/plasmapheresis, and thymectomy. Treatment is dependent upon response to therapy, setting (e.g., preoperative), presence of myasthenic crisis, and etiology of myasthenia gravis

Outcomes

The general outcomes of interest are symptoms, quality of life, hospitalizations, and resource utilization. Health outcome measures relevant to gMG in adults are summarized in Table 1.

Follow-up of months to years is of interest to monitor outcomes.

Table 1. Health Outcome Measures Relevant to Generalized Myasthenia Gravis in Adults (11)

Outcome	Description and Administration	Thresholds for Improvement/Decline or

		Clinically Meaningful Difference (if known)
Quantitative Myasthenia Gravis	• Measure of disease severity; includes 13 items that assess muscle strength and fatigability using objective measures of double vision, ptosis, facial muscles, dysphagia, dysarthria, proximal limb, hand muscles, neck muscles, and respiratory function • Assessments are time consuming and require equipment; use in clinical practice is challenging	• Each item is given a score of 0-3, resulting in an unweighted total score of 0-39; a higher score corresponds to more severe disease • A 3-point change is considered clinically meaningful, with a modification in milder cases where a 2-point change is considered sufficient
Myasthenia Gravis-Activity of Daily Living	• Patient-reported outcome; quickly administered set of questions examining frequency and severity of key myasthenia gravis symptoms • Eight questions assessing ocular function, speech, chewing, swallowing, respiratory function, and strength of proximal upper and lower extremities	• Each item is scored from 0-3, which results in an unweighted total score of 0-24 points; a higher score indicates more severe symptoms • A 2-point change is considered clinically meaningful
Myasthenia Gravis Composite	• Uses the top performing items of the Quantitative Myasthenia Gravis, Myasthenia Gravis-Activity of Daily Living, and the Manual Muscle Test; 6 physician-assessed examinations evaluate ocular, neck, and proximal limb muscles with 4 patient-reported items assessing speech, chewing, swallowing, and respiratory function	• Total score spans from 0-50; a higher score indicating more severe disease • A 3-point change is considered clinically meaningful based on physician's impression of change
Myasthenia Gravis Quality of Life 15-items	• Patient reported 15 questions assess ocular symptoms, swallowing, speech, proximal limb function, mobility, personal grooming, work, social	• Each question is scored from 0-4, resulting in a total score in the range of 0-60; a higher score

	life, activities, fluctuations, and psychological items	indicates poorer quality of life • QOL15 was slightly revised to the current QOL15r that retains the original questions and reduces the item score to a range of 0-2

QOL: quality of life.

Study Selection Criteria

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought;
- Studies with duplicative or overlapping populations were excluded.

Randomized Controlled Trials

Trial characteristics and results of the pivotal double-blind, placebo-controlled, phase 3 MycarinG trial are summarized in Tables 2 and 3, respectively. The study met the primary efficacy endpoint. A statistically significant difference favoring rozanolixizumab was observed in the mean change from baseline to day 43 in MG-ADL total scores [-3.4 points in the rozanolixizumab-treated group either doses compared with -0.8 points in the placebo-treated group (p<.001)]. A key secondary endpoint of change from baseline in the QMG total score at week 43 also favored rozanolixizumab [-5.4 points and -6.7 points in the rozanolixizumab-treated group at 7 mg/kg and 10 mg/kg dose level, respectively, compared with -1.9 points in the placebo-treated group (p<.001)]. Results of the open-label extension study (NCT04124965) with a mean follow-up 23.3 weeks reported that rozanolixizumab was generally well tolerated, and clinically relevant improvements across MG-specific outcomes were maintained. (12) The most common adverse reactions (≥10%) were headache, infections, diarrhea, pyrexia, hypersensitivity reactions, and nausea. Serious events of aseptic meningitis were reported. As per the label, symptoms for meningitis should be monitored and diagnostic workup and treatment should be initiated according to the standard of care. (13)

Table 2. Summary of Pivotal RCT Characteristics

Study		MycarinG (13, 14) NCT03971422
Countries		Global
Sites		112
Dates		June 2019- June 2021

Participants		Inclusion • Presence of autoantibodies against AChR or MuSK • MGFA clinical classification class II to IVa • MG-ADL total score ≥3 (with ≥3 points from non-ocular symptoms) • On stable dose of myasthenia gravis therapy prior to screening that included acetylcholinesterase inhibitors, steroids, or non-steroidal immunosuppressive therapies, either in combination or alone • Serum IgG levels of ≥5.5 g/L Primary Endpoint • Change from baseline in the MG-ADL total score from baseline to day 43
Interventions	*Active*	Rozanolixizumab subcutaneously once a week for 6 weeks (n=133); 7 mg/kg (n=66), or 10 mg/kg (n=67)
	Comparator	Placebo given on the same schedule (n=67)

AChR: acetylcholine receptor; IV: intravenous; MG-ADL: Myasthenia Gravis-Activity of Daily Living; MGFA: Myasthenia Gravis Foundation of America; MuSK: antimuscle-specific tyrosine kinase; RCT: randomized controlled trial.

Table 3. Summary of Pivotal RCT Results

Study	**Rozanolixizumab 7 mg/kg**	**Rozanolixizumab 10 mg/kg**	**Placebo**
MycarinG (13, 14) NCT03971422			
N	66	67	67
Primary endpoint (MG-ADL Total Score)			
LS mean change from baseline to day 41 (SE)	-3.4 (0.5)	-3.4 (0.5)	-0.8 (0.5)
Difference from placebo (95% CI)	-2.6 (-4.1 to -1.2)	-2.6 (-4.0 to -1.2)	--
p-value	.001	.001	--
Secondary endpoint (QMG Total Score)			
LS mean change from baseline to day 41 (SE)	-5.4 (0.7)	-6.7 (0.7)	-1.9 (0.7)
Difference from placebo (95% CI)	-3.5 (-5.6 to -1.6)	-4.8 (-6.8 to -2.9)	--
p-value	.001	.001	--

CI: confidence interval; LSM: least squares mean; MG-ADL: Myasthenia Gravis-Activity of Daily Living; QMG: Quantitative Myasthenia Gravis; RCT: randomized controlled trial; SE: standard error.

The purpose of the study limitations table (Table 4) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following the table and provides the conclusions on the sufficiency of evidence supporting the position statement. The limited representations of African Americans, Asians, and Hispanics and anti-MuSK antibody positive individuals makes it challenging to reach conclusions about the efficacy of rozanolixizumab in these groups. No major limitations in the study design and conduct were identified.

Table 4. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
MycarinG (13, 14)	3. Study population not representative of intended use (<10% of trial participants were anti-MuSK positive) 4. Enrolled populations do not reflect relevant diversity (68% White, 11% Asian, 7% Hispanic or Latino, 3% Black or African American)				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically

significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Summary: Rozanolixizumab

Results of the pivotal RCT MycarinG reported a statistically significant difference in the primary endpoint favoring rozanolixizumab in MG-ADL total scores compared with the placebo (LS mean difference of -2.6 points for either doses of rozanolixizumab). A key secondary endpoint of change from baseline in the QMG total score at week 43 also favored rozanolixizumab [-5.4 points and -6.7 points in the rozanolixizumab-treated group at 7 mg/kg and 10 mg/kg dose level, respectively compared with -1.9 points in the placebo-treated group (p<.001)]. Results of the open-label trial with long-term follow-up with up to 52 weekly infusions reported that treatment was generally well tolerated, and clinically relevant improvements across MG-specific outcomes were maintained, supporting the long-term use of rozanolixizumab in patients with gMG. The most common adverse reactions (≥10%) were headache, infections, diarrhea, pyrexia, hypersensitivity reactions, and nausea. Serious events of aseptic meningitis were reported. The limited representations of African Americans, Asians, and Hispanics makes it challenging to reach conclusions about the efficacy of rozanolixizumab in these racial groups. No major limitations in the study design and conduct were identified.

Summary of Evidence

For individuals with generalized myasthenia gravis who receive rozanolixizumab, the evidence includes a single pivotal RCT. Relevant outcomes are symptoms, quality of life, hospitalizations, and resource utilization. Results of the pivotal RCT MycarinG reported a statistically significant difference in the primary endpoint favoring rozanolixizumab in MG-ADL total scores compared with the placebo (LS mean difference of -2.6 points for either dose of rozanolixizumab). A key secondary endpoint of change from baseline in the QMG total score at week 43 also favored rozanolixizumab [-5.4 points and -6.7 points in the rozanolixizumab-treated group at 7 mg/kg and 10 mg/kg dose level, respectively, compared with -1.9 points in the placebo-treated group (p<.001)]. Results of the open label trial with long-term followup with up to 52 weekly infusions reported that treatment was generally well tolerated, and clinically relevant improvements across MG-specific outcomes were maintained, supporting the long-term use of rozanolixizumab in patients with gMG. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this policy are listed in Table 5.

Table 5. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
NCT05681715	An Open-label, Crossover Study to Evaluate Rozanolixizumab Self-administration by Study Participants With Generalized Myasthenia Gravis	62	Apr 2024

NCT: national clinical trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J9333

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
12/15/2025	Document updated with literature review. The following changes were made to Coverage: 1) Extensively modified the medical necessity criteria; 2) Added criteria for continuation treatment; and 3) Modified the experimental, investigational and/or unproven statement to include “non-Food and Drug Administration”. References 2-14 added; others removed.
05/15/2024	Reviewed. No changes.
12/01/2023	Rozanolixizumab-noli (Rystiggo®) may be considered medically necessary for the treatment of generalized myasthenia gravis (gMG) in adult patients when the following criteria are met: Positive serologic test for anti-acetylcholine receptor (AChR) OR antimuscle-specific tyrosine kinase (MuSK); AND Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IVa; AND Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score of at least 3 (with at least 3 points from nonocular symptoms); AND On stable dose of myasthenia gravis (MG) therapy prior to screening that included acetylcholinesterase (AChE) inhibitors, steroids, or non-

	steroidal immunosuppressive therapies (NSISTs), either in combination or alone; AND Will NOT use rozanolixizumab-noli concurrently with other biologics used to treat MG (e.g., rituximab, eculizumab, intravenous immunoglobulin [IVIG], efgartigimod alfa-fcab). Rozanolixizumab-noli (Rystiggo®) is considered experimental, investigational and/or unproven for all other indications, and when the above criteria are not met.