Rystiggo (rozanolixizumab-noli)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Generalized myasthenia gravis (gMG) is a chronic autoimmune neuromuscular disorder characterized by muscle weakness and fatigue. It is caused by the production of autoantibodies that target components of the neuromuscular junction, such as the acetylcholine receptor (AChR) or muscle-specific tyrosine

kinase (MuSK). The condition leads to a breakdown in communication between nerves and muscles, resulting in weakness and fatigue of voluntary muscles.

Symptoms of gMG can vary but commonly include weakness of the eye muscles (ocular myasthenia), drooping eyelids (ptosis), blurred or double vision (diplopia), changes in facial expressions, difficulty swallowing, and shortness of breath. The severity of gMG is often classified using the Myasthenia Gravis Foundation of America (MGFA) Clinical Classification, which categorizes the disease into five main classes (I-V) based on signs, symptoms, and degree of impairment. This classification helps guide treatment decisions and assess disease progression.

Rystiggo (rozanolixizumab-noli), a neonatal Fc receptor blocker, is a prescription medicine indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-AChR or anti-MuSK antibody positive. It is administered through weekly subcutaneous infusions and is designed to target the underlying autoimmune mechanisms of gMG. Management of gMG includes but is not limited to: surgical approaches, cholinesterase inhibitors (e.g., pyridostigmine), immunotherapy (e.g., corticosteroids, azathioprine, mycophenolate mofetil), and intravenous immune globulin. Those with anti-MuSK have been shown to be less responsive to cholinesterase inhibitors, and once started on corticosteroids, often find themselves steroid-dependent despite addition of other therapies. Rystiggo (rozanolixizumab-noli) is the first and only FDA-approved agent for anti-MuSK gMG.

Definitions

"Generalized myasthenia gravis (gMG)" is a chronic autoimmune neuromuscular disorder characterized by fluctuating weakness of voluntary muscles.

"Anti-acetylcholine receptor (anti-AChR) antibodies" are autoantibodies directed against the nicotinic acetylcholine receptor found at the neuromuscular junction.

"Anti-muscle specific tyrosine kinase (anti-MuSK) antibodies" are autoantibodies directed against the muscle-specific tyrosine kinase protein.

"Cholinesterase inhibitors" refer to a class of drugs that prevent the breakdown of acetylcholine, a neurotransmitter which plays a major role in memory and muscle movement and contraction.

"Myasthenia Gravis Foundation of America (MGFA) Clinical Classification" is a system that categorizes disease severity into five main classes (I-V) with subclasses based on signs, symptoms, and degree of impairment.

"Myasthenia Gravis Activities of Daily Living (MG-ADL)" is an 8-item patient-reported questionnaire that assesses daily functions often impacted by myasthenia gravis. Total score ranges from 0 to 24, with a

higher score indicating more disability. A positive change in the score indicates worsening and a negative change indicates improvement.

"Quantitative Myasthenia Gravis (QMG)" is a comprehensive 13-item scale specifically designed to accurately assess the severity of myasthenia gravis. It evaluates various aspects such as endurance, fatigability, and fluctuations in symptoms. The scale assigns scores ranging from 0 to 39, with higher scores indicating a more severe manifestation of the disease. A positive change in the score indicates worsening and a negative change indicates improvement.

Clinical Indications

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Generalized Myasthenia Gravis (gMG)

The Plan considers Rystiggo (rozanolixizumab-noli) medically necessary when ALL of the following criteria are met:

1. Prescribed by or in consultation with a neurologist or neuromuscular disease specialist; *AND*
2. The member is 18 years of age or older; *AND*
3. The member has a confirmed diagnosis of generalized myasthenia gravis (gMG) AND documentation of ALL of the following:
    a. Positive serologic test for anti-acetylcholine receptor (anti-AChR) OR anti-muscle specific tyrosine kinase (anti-MuSK) antibodies; *and*
    b. Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IVa (*see* Appendix A, Table 1); *and*
    c. Baseline Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score of at least 3 (with at least 3 points from non-ocular symptoms); *AND*
4. IF anti-AChR antibody positive, the member is unable to use, limited by toxicity, or has adequately tried and failed or experienced insufficient response to at least TWO (2) standard therapies for gMG, such as[s]:
    a. Cholinesterase inhibitors (eg, pyridostigmine); *and/or*
    b. Corticosteroids (e.g., prednisone) or inability to taper steroids below a reasonably acceptable level without return of symptoms; *and/or*
    c. Immunosuppressive therapies (e.g., azathioprine, cyclosporine, mycophenolate mofetil, cyclophosphamide, tacrolimus); *AND*
5. Will not be used concomitantly with other immunomodulatory biologic therapies for generalized myasthenia gravis (e.g., efgartigimod alfa, inebiluzumab, nipocalimab, rituximab, ravulizumab, zilucoplan, etc.); *AND*

6. Rystiggo (rozanolixizumab-noli) is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication.

If the above prior authorization criteria are met, the requested product will be authorized for up to 16-weeks.[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Generalized Myasthenia Gravis (gMG)

The Plan considers Rystiggo (rozanolixizumab-noli) medically necessary when ALL of the following criteria are met:

1. Prescribed by or in consultation with a neurologist or neuromuscular disease specialist; *AND*
2. Documentation of positive clinical response to therapy, such as ONE (1) of the following:
    a. Improvement in Myasthenia Gravis-Activities of Daily Living (MG-ADL), MG Manual Muscle Test (MMT), MG-Composite, OR Quantitative Myasthenia Gravis (QMG) score from baseline; *or*
    b. Achievement of minimal symptom expression or pharmacological remission; *or*
    c. Lack of relapses or reduced frequency/severity of relapses compared to baseline; *AND*
3. Ongoing therapy is required to maintain disease stability and control; *AND*
4. There is no unacceptable toxicity or adverse reaction to therapy, such as:
    a. Serious infections (e.g. serious respiratory or urinary tract infections); *and/or*
    b. Severe hypersensitivity reactions; *and/or*
    c. Severe immunosuppression; *and/or*
    d. Other intolerable side effects or reactions; *AND*
5. Will not be used concomitantly with other immunomodulatory biologic therapies for generalized myasthenia gravis (e.g., efgartigimod alfa, inebiluzumab, nipocalimab, rituximab, rozanolixizumab, ravulizumab, zilucoplan, etc.); *AND*
6. Rystiggo (rozanolixizumab-noli) is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication.

If the above reauthorization criteria are met, the requested product will be authorized for up to 6-months.[s]

Experimental or Investigational / Not Medically Necessary[s]

Rystiggo (rozanolixizumab-noli) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, unproven, or not medically necessary. Non-covered indications include, but are not limited to, the following:

- Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP). Only one small (n=34) randomized, subject-blinded study evaluated Rystiggo (rozanolixizumab-noli) versus placebo for CIDP, which failed to meet the primary outcome of change from baseline to day 85 inflammatory Rasch-built Overall Disability Scale score.
- Fibromyalgia. Only one small (n=63) proof-of-concept study has been conducted evaluating Rystiggo (rozanolixizumab-noli) versus placebo (NCT05643794) for the management of fibromyalgia. This study failed to meet the primary outcome of improvement of brief pain inventory short form (BPI-SF) at week 12.
- Leucine-Rich Glioma Inactivated 1 Autoimmune Encephalitis. Only one terminated study (NCT04875975) has been identified evaluating Rystiggo (rozanolixizumab-noli) for this indication. No high quality studies have evaluated the safety and efficacy of Rystiggo (rozanolixizumab-noli) for this indication.
- Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease (MOG-AD). No high quality studies have evaluated the safety and efficacy of Rystiggo (rozanolixizumab-noli) for this indication.
- Primary Immune Thrombocytopenia (ITP). Clinical trials studying Rystiggo (rozanolixizumab-noli) have failed to show significant improvement in serum markers of ITP, or have been terminated early.
- Thrombocytopenia. No high quality studies have evaluated the safety and efficacy of Rystiggo (rozanolixizumab-noli) for thrombocytopenia.

Applicable Billing Codes

Table 1	
CPT/HCPCS Codes for myasthenia gravis considered medically necessary if criteria are met:	
Code	*Description*
96369	Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); initial, up to 1 hour, including pump set-up and establishment of subcutaneous infusion site(s)
96371	Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); additional pump set-up with establishment of new subcutaneous infusion site(s) (List separately in addition to code for primary procedure)
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
96401	Chemotherapy administration, subcutaneous or intramuscular; non-hormonal anti-neoplastic
J9333	Injection, rozanolixizumab-noli, 1 mg

Table 2	
ICD-10 codes considered medically necessary for myasthenia gravis with Table 1 (CPT/HCPCS) codes if criteria are met:	
Code	*Description*
G70.0	Myasthenia gravis
G70.00	Myasthenia gravis without (acute) exacerbation
G70.01	Myasthenia gravis with (acute) exacerbation
G70.2	Congenital and developmental myasthenia

Appendix A

Table 3: Summary of Myasthenia Gravis Foundation of America (MGFA) Disease Clinical Classification

Class	*Description*
I	Ocular muscle weakness; All other muscles - normal strength
II	Mild generalized weakness
IIa	Predominantly limb/axial weakness; Lesser oropharyngeal involvement possible
IIb	Predominantly oropharyngeal/respiratory weakness; Lesser limb/axial involvement possible
III	Moderate generalized weakness
IIIa	Predominantly limb/axial weakness; Lesser oropharyngeal involvement possible
IIIb	Predominantly oropharyngeal/respiratory weakness; Lesser limb/axial involvement possible
IV	Severe generalized weakness
IVa	Predominantly limb/axial weakness; Lesser oropharyngeal involvement possible
IVb	Predominantly oropharyngeal/respiratory weakness; Lesser limb/axial involvement possible
V	Intubation, with or without ventilation; Not for routine postoperative care

NOTE: The preceding table summarizes key aspects of the Myasthenia Gravis Foundation of America (MGFA) Disease Classifications. This is provided only for quick reference. For the exact definitions and

details on the MGFA Disease Classifications, please refer to the original MGFA Classification document available at https://myasthenia.org/Portals/0/MGFA%20Classification.pdf.

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