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Coverage Policy Number **IP0575**

Rozanolixizumab

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for rozanolixizumab-noli subcutaneous infusion (**Rystiggo®**).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Rozanolixizumab-noli is considered medically necessary when the following are met:

Generalized Myasthenia Gravis. Individual meets **ALL** of the following criteria:
A. Age 18 years or older
B. Documentation of **ONE** of the following:
   i. Confirmed anti-acetylcholine receptor antibody-positive generalized myasthenia gravis

ii. Confirmed anti-muscle-specific tyrosine kinase antibody-positive generalized myasthenia gravis

C. Has a Myasthenia Gravis Foundation of America (MGFA) clinical classification of II-IV (prior to starting therapy with Rystiggo) [See APPENDIX 1]
D. Has a MG-Activities of Daily Living (MG-ADL) score of 3 or higher for non-ocular symptoms (prior to starting therapy with Rystiggo) [See APPENDIX 2]
E. Has objective evidence of unresolved symptoms of generalized myasthenia gravis, such as difficulty swallowing, difficulty breathing, or a functional disability resulting in the discontinuation of physical activity (for example, double vision, talking, impairment of mobility)
F. Documentation of **ONE** of the following:
    i. Is currently receiving pyridostigmine
    ii. Failure, contraindication or intolerance to pyridostigmine
G. Medication is prescribed by or in consultation with a neurologist

Dosing. **ONE** of the following dosing regimens:
1. Individual is less than 50 kg. The dose is 420mg administered by subcutaneous infusion once weekly for 6 weeks. Additional treatment cycles are initiated no sooner than every 63 days from the start of the previous treatment cycle.
2. Individual is 50 kg to less than 100 kg. The dose is 560mg administered by subcutaneous infusion once weekly for 6 weeks. Additional treatment cycles are initiated no sooner than every 63 days from the start of the previous treatment cycle.
3. Individual is 100 kg or more. The dose is 840mg administered by subcutaneous infusion once weekly for 6 weeks. Additional treatment cycles are initiated no sooner than every 63 days from the start of the previous treatment cycle.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of rozanolixizumab-noli is considered medically necessary for generalized myasthenia gravis when **BOTH** of the following are met:
1. The above medical necessity criteria have been met prior to the start of Rystiggo therapy
2. There is documentation of beneficial response (for example, reductions in exacerbations of myasthenia gravis; improvements in speech, swallowing, mobility, respiratory function, improvement in MG-ADL or QMG scores)

Authorization Duration

Initial approval duration: up to 6 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. **Concomitant Use with Another Neonatal Fc Receptor Blocker, a Complement Inhibitor, or a Rituximab Product.** There is no evidence to support concomitant use of Rystiggo with another neonatal Fc receptor blocker, a complement inhibitor, or a rituximab product. Examples of neonatal Fc receptor blockers are Vyvgart (efgartigimod alfa-fcab intravenous infusion] and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc subcutaneous injection). Examples of complement

inhibitors are Soliris (eculizumab intravenous infusion), Ultomiris (ravulizumab-cwvz intravenous infusion or subcutaneous injection), and Zilbrysq (zilucoplan subcutaneous injection).

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs
J3590	Unclassified biologics

Background

OVERVIEW
Rystiggo, a neonatal Fc receptor blocker, is indicated for the treatment of **generalized myasthenia gravis** in adults who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody-positive.[1]

Disease Overview
Myasthenia gravis is a chronic autoimmune neuromuscular disease that causes weakness in the skeletal muscles, which are responsible for breathing and moving parts of the body, including the arms and legs.[2] Myasthenia gravis is caused by the production of pathogenic immunoglobulin G (IgG) autoantibodies against neuromuscular junction components (AChR, MuSK, and low density lipoprotein receptor-related protein 4 [LRP4]).[3] Approximately 85% of patients with myasthenia gravis are anti-AChR antibody-positive and approximately 5% to 8% of patients are anti-MuSK antibody-positive.[4] The result of the antibodies at the junction is unsuccessful nerve transmission and deficiency or weakness of muscle contractions.[3] The hallmark of myasthenia gravis is muscle weakness that worsens after periods of activity and improves after periods of rest.[2] 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.

Clinical Efficacy
The efficacy of Rystiggo was evaluated in an 18-week, multicenter, randomized, double-blind, placebo-controlled trial in adults with anti-AChR or anti-MuSK antibody-positive generalized myasthenia gravis (n = 200).[1,5] Two doses of Rystiggo were studied: 7 mg/kg and 10 mg/kg. Among other criteria, patients in the study had a Myasthenia Gravis Foundation of America classification of II to IVa and a Myasthenia Gravis Activities of Daily Living (MG-ADL) score of ≥ 3, with at least 3 points from non-ocular symptoms. MG-ADL assesses the impact of generalized myasthenia gravis on daily functions of eight signs or symptoms that are typically impacted by this disease. Each sign or symptom is assessed on a 4-point scale; a higher score indicates greater impairment. At baseline, over 83% of patients received acetylcholinesterase inhibitors, over 50% of patients received oral steroids, and approximately 50% received non-steroidal immunosuppressant therapies, at stable doses. The primary endpoint was the change from baseline to Day 43 in the MG-ADL total score. Statistically significantly greater improvement in the MD-ADL score was observed in both Rystiggo 7 mg/kg and Rystiggo 10 mg/kg groups vs. placebo: -3.4 points in the Rystiggo-treated group at either dose vs. -0.8 points in the placebo group ($P < 0.001$). Statistically significant improvements in the secondary efficacy endpoints were also observed in the Rystiggo groups vs. placebo.

Dosing Information

Rystiggo is administered as a subcutaneous (SC) infusion, at a rate of up to 20 mL/h; infusions are given once weekly by a healthcare professional.[1] For patients weighing < 50 kg, the recommended dose is 420 mg; for patients 50 kg to < 100 kg, the recommended dose is 560 mg; and for patients ≥ 100 kg, the recommended dose is 840 mg. Each treatment cycle is 6 injections (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.

Guidelines
An international consensus guidance for the management of myasthenia gravis was published in 2016.[6] The guidelines recommend pyridostigmine for the initial treatment in most patients with myasthenia gravis. The ability to discontinue pyridostigmine can indicate that the patient has met treatment goals and may guide the tapering of other therapies. Corticosteroids or immunosuppressant therapy should be used in all patients with myasthenia gravis who have not met treatment goals after an adequate trial of pyridostigmine. Nonsteroidal immunosuppressant agents include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus. It is usually necessary to maintain some immunosuppression for many years, sometimes for life. Plasma exchange and intravenous immunoglobulin can be used as short-term treatments in certain patients. A 2020 update to these guidelines provides new recommendations for methotrexate, rituximab, and Soliris® (eculizumab intravenous infusion).[7] All recommendations should be considered extensions or additions to recommendations made in the initial international consensus guidance (2016). Oral methotrexate may be considered as a steroid-sparing agent in patients with generalized myasthenia gravis who have not tolerated or responded to steroid-sparing agents. Rituximab should be considered as an early therapeutic option in patients with anti-MuSK antibody-positive myasthenia gravis who have an unsatisfactory response to initial immunotherapy. Soliris should be considered in the treatment of severe, refractory, anti-AChR antibody-positive generalized myasthenia gravis.

APPENDIX 1
[Myasthenia Gravis Foundation of America (MGFA) classification]
The Myasthenia Gravis Foundation of America (MGFA) classification is aimed at separating patients in groups based on disease severity and the localization of the symptoms, and does not have an evaluative purpose. The MGFA classes are pure ocular (class I), mild generalized (class II), moderate generalized (class III), severe generalized (class IV), and intubation/myasthenic crisis (class V). Within the generalized categories II, III, and IV, patients are subclassified as class A if their symptoms are predominantly generalized or class B if their symptoms are predominantly bulbar.[8] The MGFA also has a system to classify patients based on postintervention outcomes and includes remission, defined as 1 year or longer without signs or symptoms and without any symptomatic (pyridostigmine) treatment, and which can be divided in complete (no pharmacologic treatment at all) or pharmacologic remission. Minimal manifestation status is defined as minimal signs or symptoms (no specific time-frame was defined) and pyridostigmine use may be accepted. Additionally, patients can be improved, unchanged, worse, experiencing an MG exacerbation, or have died of MG.[8] Because the original MGFA severity classification does not take into account those patients who are asymptomatic, many MG studies use a hybrid, whereby symptomatic patients are classified based on the I to V class system, and asymptomatic or oligosymptomatic patients are classified as remission or minimal manifestation status.[8]

APPENDIX 2
[Myasthenia Gravis Activities of Daily Living (MG-ADL)]
The Myasthenia Gravis Activities of Daily Living (MG-ADL) is a patient-reported outcome that combines 2 items on daily life activities—ability to brush teeth or comb hair, and limitations in the ability to rise from a chair—with 6 items reflecting other MG symptoms: diplopia, ptosis, chewing, swallowing, voice/speech problems, and respiratory symptoms. Each item is scored between 0 and 3 and total scores range from 0 to 24, where higher scores indicate more disease severity. The main advantages of the MG-ADL are that it is very easy to use, and it is completely patient reported. A drawback is that it does not have a specific recall time frame (eg, 2 or 4 weeks) because it relies on comparing with the last visit, and that it is prone to floor effects.[9]

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Supplemental References

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