UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Neurology – Rystiggo Utilization Management Medical Policy
- Rystiggo® (rozanolixizumab-noli subcutaneous infusion – UCB)

REVIEW DATE: 06/04/2025

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] Pyridostigmine is recommended 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. Systemic 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 eculizumab intravenous infusion (Soliris®, biosimilars).[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. Eculizumab should be considered in the treatment of severe, refractory, anti-AChR antibody-positive generalized myasthenia gravis.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Rystiggo. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Rystiggo as well as the monitoring required for adverse events and long-term efficacy, approval requires Rystiggo to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Rystiggo is recommended in those who meet the following criteria:

FDA-Approved Indication

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i. Generalized Myasthenia Gravis. Approve for the duration noted if the patient meets ONE of the following (A or B):

- **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, v, vi, and vii):
  - **i.** Patient is ≥ 18 years of age; AND
  - **ii.** Patient meets ONE of the following (a or b):
    - **a)** Patient has confirmed anti-acetylcholine receptor antibody-positive generalized myasthenia gravis; OR
    - **b)** Patient has confirmed anti-muscle-specific tyrosine kinase antibody-positive generalized myasthenia gravis; AND
  - **iii.** Patient meets BOTH of the following (a and b):

a) Myasthenia Gravis Foundation of America class of II to IV; AND
b) Myasthenia Gravis Activities of Daily Living (MG-ADL) score of ≥ 3 for non-ocular symptoms; AND

iv. Patient meets ONE of the following (a or b):
a) Patient received or is currently receiving pyridostigmine; OR
b) Patient has had inadequate efficacy, a contraindication, or significant intolerance to pyridostigmine; AND

v. Patient has evidence of unresolved symptoms of generalized myasthenia gravis; AND
Note: Examples of unresolved symptoms include difficulty swallowing, difficulty breathing, or a functional disability resulting in the discontinuation of physical activity (e.g., double vision, talking, impairment of mobility).

vi. Treatment cycles are no more frequent than every 63 days from the start of the previous treatment cycle; AND

vii. The medication is being prescribed by or in consultation with a neurologist; OR

B) Patient is Currently Receiving Rystiggo. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, and iv):
i. Patient is ≥ 18 years of age; AND
ii. According to the prescriber, patient is continuing to derive benefit from Rystiggo; AND
Note: Examples of derived benefit include reductions in exacerbations of myasthenia gravis; improvements in speech, swallowing, mobility, and respiratory function.
iii. Treatment cycles are no more frequent than every 63 days from the start of the previous treatment cycle; AND
iv. The medication is being prescribed by or in consultation with a neurologist.

Dosing. Approve if the patient meets BOTH of the following (A and B):
A) Patient meets ONE of the following (i, ii, or iii):
i. Patient weighs < 50 kg: The dose is 420 mg administered by subcutaneous infusion once weekly for 6 weeks; OR
ii. Patient weighs 50 kg to < 100 kg: The dose is 560 mg administered by subcutaneous infusion once weekly for 6 weeks; OR
iii. Patient weighs ≥ 100 kg: The dose is 840 mg administered by subcutaneous infusion once weekly for 6 weeks; AND
B) Treatment cycles are no more frequent than every 63 days from the start of the previous treatment cycle.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Rystiggo is not recommended in the following situations:

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.
Note: Examples of neonatal Fc receptor blockers are Imaavy (nipocalimab-aahu intravenous infusion), Vyvgart (efgartigimod alfa-fcab intravenous infusion), and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc subcutaneous injection).
Note: Examples of complement inhibitors are eculizumab intravenous infusion (Soliris, biosimilars), Ultomiris (ravulizumab-cwvz intravenous infusion), and Zilbrysq (zilucoplan subcutaneous injection).
2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Rystiggo subcutaneous injection. Symra, GA: UCB; June 2024.
2. National Institute of Neurological Disorders and Stroke (NINDS). Myasthenia Gravis Fact Sheet. National Institutes of Health (NIH) Publication No. 17-768. Publication last updated: March 2020. Available at: https://www.ninds.nih.gov/sites/default/files/migrate-documents/myasthenia_gravis_e_march_2020_508c.pdf. Accessed on May 23, 2025
3. Cleanthous S, Mork AC, Regnault A, et al. Development of the myasthenia gravis (MG) symptoms PRO: a case study of a patient-centred outcome measure in rare disease. *Orphanet J Rare Dis*. 2021;16:457.
4. Rodolico C, Bonanno C, Toscano A, and Vita G. MuSK-associated myasthenia gravis: clinical features and management. *frontiers in Neurology*. 2020;11:660.
5. Bril V, Drużdż A, Grosskreutz J, et al on behalf of the MG0003 study team. Safety and efficacy of rozanolixizumab in patients with generalized myasthenia gravis (MycarinG): a randomized, double-blind, placebo-controlled, adaptive phase 3 study. *Lancet Neurol*. 2023;22:383-394.
6. Sanders DB, Wolfe GI, Benatar M, et al. International Consensus Guidance for Management of Myasthenia Gravis. *Neurology*. 2016;87:419-425.
7. Narayanaswami P, Sanders DB, Wolfe G, et al. International Consensus Guidance for Management of Myasthenia Gravis: 2020 Update. *Neurology*. 2021;96(3):114-122.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	07/05/2023
Selected Revision	**Conditions Not Recommended for Approval:** Added "Concomitant Use with Another Neonatal Fc Receptor Blocker, a Complement Inhibitor, or a Rituximab Product". Examples of Neonatal Fc Receptor Blockers and Complement Inhibitors are listed as Notes.	10/18/2023
Selected Revision	**Generalized Myasthenia Gravis:** "Treatment cycles are no more frequent than every 63 days from the start of the previous treatment cycle" was added to the Dosing section.	02/28/2024
Annual Revision	**Conditions Not Recommended for Approval, Concomitant Use with Another Neonatal Fc Receptor Blocker, a Complement Inhibitor, or a Rituximab Product:** Removed Ultomiris subcutaneous injection from the Note of examples of complement inhibitors.	07/24/2024
Annual Revision	**Conditions Not Recommended for Approval, Concomitant Use with Another Neonatal Fc Receptor Blocker, a Complement Inhibitor, or a Rituximab Product:** Imaavy was added to the Note of examples of neonatal Fc receptor blockers. Biosimilars to Soliris were added to the Note of examples of complement inhibitors, where only Soliris was previously noted.	06/04/2025