

PRIOR AUTHORIZATION POLICY

POLICY: Complement Inhibitors – Zilbrysq Prior Authorization Policy

- Zilbrysq[®] (zilucoplan subcutaneous injection – UCB)

REVIEW DATE: 11/01/2023

OVERVIEW

Zilbrysq, a complement C5 inhibitor, is indicated for the treatment of generalized myasthenia gravis in adults who are anti-acetylcholine receptor 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 The hallmark of myasthenia gravis 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 components of the neuromuscular junction, most commonly the acetylcholine receptor.³

Clinical Efficacy

The efficacy of Zilbrysq was evaluated in 12-week, multicenter, randomized, double-blind placebo-controlled study (n = 174).^{1,4} All of the enrolled patients had anti-acetylcholine receptor antibody-positive generalized myasthenia gravis. In addition, patients had a Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV and a Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score of ≥ 6 . 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, 85% of patients in each group received cholinesterase inhibitors, 63% received steroids, and 51% received non-steroidal immunosuppressive therapies, at stable doses. Patients were randomized to receive either Zilbrysq 0.3 mg/kg or placebo. The primary efficacy endpoint was a comparison of the change from baseline between treatment groups in the MG-ADL total score at Week 12. Statistically significantly greater improvement in the MG-ADL total score was observed in the Zilbrysq group compared with placebo: -4.39 points vs. -2.30 points, respectively (P < 0.001). Statistically significant improvement in the secondary efficacy endpoints were also observed in the Zilbrysq group vs. placebo.

Guidelines

An international consensus guidance for the management of myasthenia gravis was published in 2016.³ 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 used in treatment of myasthenia gravis 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/additional recommendations for methotrexate, rituximab, and Soliris® (eculizumab intravenous infusion).⁵ 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-muscle-specific tyrosine kinase antibody-positive myasthenia gravis who have an unsatisfactory response to initial immunotherapy. Soliris should be considered in the treatment of severe, refractory, anti-acetylcholine receptor antibody-positive MG.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Zilbrysq. 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 Zilbrysq as well as the monitoring required for adverse events and long-term efficacy, approval requires Zilbrysq to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

1. **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 the following (i, ii, iii, iv, v, vi, and vii):
 - i. Patient is ≥ 18 years of age; AND
 - ii. Patient has confirmed anti-acetylcholine receptor antibody-positive generalized myasthenia gravis; AND
 - iii. Patient meets both of the following (a and b):
 - a) Myasthenia Gravis Foundation of America classification of II to IV; AND
 - b) Myasthenia Gravis Activities of Daily Living (MG-ADL) score of ≥ 6 ; 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 meets one of the following (a or b):
 - a) Patient received or is currently receiving two different immunosuppressant therapies for ≥ 1 year; OR
 - b) Patient had inadequate efficacy, a contraindication, or significant intolerance to two different immunosuppressant therapies; AND
Note: Examples of immunosuppressant therapies tried include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus, and cyclophosphamide.
 - vi. Patient has evidence of unresolved symptoms of generalized myasthenia gravis; AND
Note: Evidence of unresolved symptoms of generalized myasthenia gravis includes difficulty swallowing, difficulty breathing, and a functional disability resulting in the discontinuation of physical activity (e.g., double vision, talking, impairment of mobility).

- vii. The medication is being prescribed by or in consultation with a neurologist.
- B) Patient is Currently Receiving Zilbrysq. Approve for 1 year if the patient meets the following (i, ii, and iii):
 - i. Patient is ≥ 18 years of age; AND
 - ii. Patient is continuing to derive benefit from Zilbrysq, according to the prescriber; AND
Note: Examples of derived benefit include reductions in exacerbations of myasthenia gravis; improvements in speech, swallowing, mobility, and respiratory function.
 - iii. The medication is being prescribed by or in consultation with a neurologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Zilbrysq is not recommended in the following situations:

1. **Concomitant Use with Another Complement Inhibitor, a Neonatal Fc Receptor Blocker, or a Rituximab Product.** There is no evidence to support concomitant use of Zilbrysq with another complement inhibitor, a neonatal Fc receptor blocker, or a rituximab product.
Note: Examples of complement inhibitors are Soliris (eculizumab intravenous infusion) and Ultomiris (ravulizumab-cwvz intravenous infusion or subcutaneous injection).
Note: Examples of Neonatal Fc receptor blockers are Rystiggo [rozanolixizumab-noli subcutaneous infusion) Vyvgart (efgartigimod alfa-fcab intravenous infusion), and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc 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. Zilbrysq subcutaneous injection [prescribing information]. Symra, GA: UCB: October 2023.
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 October 18, 2023.
3. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis. *Neurology*. 2016;87:419–425.
4. Howard JF, Bresch S, Genge A, et al on behalf of the RAISE study team. Safety and efficacy of zilucoplan in patients with generalized myasthenia gravis (RAISE): a randomized, double-blind, placebo-controlled, phase 3 study. *Lancet Neurology*. 2023;22:395-406.
5. 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	--	11/01/2023