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Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Hematological Agents	**Original Policy Date:**	November 10, 2023
Subject:	Zilbrysq	**Page:**	1 of 5

Last Review Date: June 13, 2024

Zilbrysq

Description

Zilbrysq (zilucoplan)

Background
Zilbrysq (zilucoplan) binds to complement protein C5 and inhibits cleavage into C5a and C5b. Blocking the formation of C5b inhibits the subsequent formation of terminal complex C5b-9. The precise mechanism by which Zilbrysq exerts its therapeutic effect in generalized myasthenia gravis is unknown but is presumed to involve reduction in C5b-9 deposition at the neuromuscular junction (1).

Regulatory Status
FDA-approved indication: Zilbrysq is a complement inhibitor indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive (1).

The International Consensus Guidance for Management of Myasthenia Gravis recommends the use of chronic IVIG and immunosuppressants. There is a lack of data demonstrating the safety and efficacy of concomitant therapy of IVIG with Zilbrysq (2).

Zilbrysq includes a boxed warning citing the risk of life-threatening and fatal meningococcal infections. Additionally, all patients must be vaccinated with a meningococcal vaccine at least 2 weeks prior to receiving their first dose (1).

Zilbrysq is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Zilbrysq REMS, prescribers must enroll in the program (1).

In addition, Zilbrysq has warnings regarding pancreatitis and pancreatic cysts and using caution when administering Zilbrysq to patients with any other systemic infection (1).

The safety and effectiveness of Zilbrysq in pediatric patients less than 18 years of age have not been established (1).

Related policies
Rystiggo, Soliris, Ultomiris

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Zilbrysq may be considered **medically necessary** if the conditions indicated below are met.

Zilbrysq may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Generalized myasthenia gravis (gMG)

AND ALL of the following:

a. Positive serologic test for anti-AChR antibodies
b. Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV
c. Documented baseline MG-Activities of Daily Living (MG-ADL) total score ≥ 6 (*http://c.peerview.com/inReview/programs/150204324/downloads/PVI_practiceaids_RMU.pdf*)
d. Patient has had an inadequate treatment response, intolerance, or contraindication to an acetylcholinesterase inhibitor and at least **ONE**

immunosuppressive therapy either in combination or as monotherapy, such as:

i. azathioprine
ii. cyclosporine
iii. mycophenolate mofetil
iv. tacrolimus
v. methotrexate
vi. cyclophosphamide

e. **NO** dual therapy with another Prior Authorization (PA) C5 complement inhibitor for gMG (see Appendix 1)
f. Vaccination against Neisseria meningitidis at least 2 weeks prior to initiation [unless Zilbrysq (zilucoplan) treatment cannot be delayed]
g. Prescriber is enrolled in Zilbrysq REMS program

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Generalized myasthenia gravis (gMG)

AND ALL of the following:

a. Decrease of MG-ADL total score from baseline of ≥ 2 points *(http://c.peerview.com/inReview/programs/150204324/downloads/PVI_practiceaids_RMU.pdf)*
b. **NO** dual therapy with another Prior Authorization (PA) C5 complement inhibitor for gMG (see Appendix 1)
c. Absence of unacceptable toxicity from the drug
d. Prescriber is enrolled in Zilbrysq REMS program

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Duration 6 months

Prior – Approval *Renewal* Limits

Duration 12 months

Rationale

Summary

Zilbrysq (zilucoplan) is a complement inhibitor indicated for the treatment of patients with generalized myasthenia gravis (gMG). Zilbrysq includes a boxed warning citing the risk of life-threatening and fatal meningococcal infections. Zilbrysq is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). In addition, Zilbrysq has warnings regarding pancreatitis and pancreatic cysts and using caution when administering Zilbrysq to patients with any other systemic infection. The safety and effectiveness of Zilbrysq in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Zilbrysq while maintaining optimal therapeutic outcomes.

References

1. Zilbrysq [package insert]. Smyrna, GA: UCB, Inc.; October 2023.
2. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: Executive summary. *Neurology*. 2016; 87(4):419. Epub 2016 Jun 29.

Policy History

Date	Action
November 2023	Addition to PA
June 2024	Annual review. Per SME, added statement regarding concomitant use of IV immunoglobulin and Zilbryzq to regulatory status section

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.

Appendix 1 - List of PA C5 complement inhibitors for gMG

Generic Name	Brand Name
eculizumab	Soliris
ravulizumab-cwvz	Ultomiris
zilucoplan	Zilbrysq