| Pharmacy Policy Bulletin: J-1361 Zilbrysq (zilucoplan) – Commercial and Healthcare Reform | |
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| **Number:** J-1361 | **Category:** Prior Authorization |
| **Line(s) of Business:**<br>☒ Commercial<br>☒ Healthcare Reform<br>☐ Medicare | **Benefit(s):**<br>**Commercial:**<br>**Prior Authorization (1.):**<br>**1.** Miscellaneous Specialty Drugs Injectable = Yes w/ Prior Authorization<br><br>**Healthcare Reform:** Not Applicable |
| **Region(s):**<br>☒ All<br>☐ Delaware<br>☐ New York<br>☐ Pennsylvania<br>☐ West Virginia | **Additional Restriction(s):**<br>None |
| **Version:** J-1361-001 | **Original Date:** 12/06/2023 |
| **Effective Date: 02/16/2024** | **Review Date:** 12/06/2023 |

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| **Drugs Product(s):** | • Zilbrysq (zilucoplan) |
| **FDA-Approved Indication(s):** | • Treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive (Ab+). |

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| **Background:** | • Zilbrysq (zilucoplan) is a self-administered, subcutaneous (SC) complement component 5 (C5) inhibitor for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive (Ab+).<br>• Zilbrysq binds to and inhibits the cleavage of C5 into C5a and C5b; this prevents the generation of the terminal complement complex, C5b-9. Although the exact mechanism of action is not known, it is thought that Zilbrysq exerts its therapeutic action by reducing C5b-9 deposition at the neuromuscular junction (NMJ).<br>• Myasthenia gravis (MG) is an autoimmune neuromuscular disease characterized by muscle weakness and muscle fatigue. It is caused by an antibody-mediated blockade of neuromuscular transmission. MG is the most common disorder of neuromuscular transmission. As an autoimmune disease, in as many as 85% of generalized cases, immunoglobulin G (IgG) to AchR is present. AChR antibody positive (AChR-Ab+) MG patients have antibodies which are inappropriately directed against acetylcholine receptors, causing a decrease in acetylcholine receptors, failure of nerve transition at neuromuscular junctions, and deficiency or weakness of muscle contractions. There are two clinical forms of MG: ocular MG and gMG. In ocular MG, weakness is limited to the eyelids and extraocular muscles, and in gMG, weakness involves ocular muscles and a variable combination of the arms, legs, and respiratory muscles. The prevalence of MG is approximately 14-40 cases per 100,000 individuals in the United States (U.S.).<br>• Zilbrysq is a new molecular entity and the third C5 inhibitor for the treatment of gMG in patients who are anti-AChR-Ab+. It is however, the first once-daily gMG-target therapy for self-administration. The dose of Zilbrysq is determined by |

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| | actual body weight (ABW). Soliris and Ultomiris are other C5 inhibitors FDA approved for the treatment of gMG. Vyvgart, Vyvgart Hytrulo, and Rystiggo are neonatal Fc receptor blockers also approved for the treatment of gMG.<br>• The 2016 and 2020 Myasthenia Gravis Foundation of America (MGFA) International Consensus Guidance for management of MG recommends pyridostigmine as part of the initial treatment in most patients with MG. Corticosteroids or immunosuppressant (IS) therapy should be used in all patients with MG who have not met treatment goals after an adequate trial of pyridostigmine, A nonsteroidal IS agent should be used alone when corticosteroids are contraindicated or refused. A non-steroidal IS should be used initially in conjunction with corticosteroids when the risk of steroid side effects is high based on medical comorbidities. Non-steroidal IS agents used in MG include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus. Eculizumab should be considered in the treatment of severe, refractory, AChR-Ab+ gMG. The guidelines have not been updated to include Rystiggo, Vyvgart/Vyvgart Hytrulo, Ultomiris, or Zilbrysq.<br>• The MGFA clinical classification divides MG presentations into different classes by clinical features with increasing severity of diseases.<br>• Prescribing Considerations:<br>o Zilbrysq is dosed once daily as a subcutaneous injection; the dose is dependent on the actual body weight.<br>o Patients may self-inject Zilbrysq after training in subcutaneous injection technique. |

## Approval Criteria

**I. Initial Authorization**

When a benefit, coverage of Zilbrysq (zilucoplan) may be approved when all of the following criteria are met **(A. and B.)**:

**A.** The member is 18 years of age or older.

**B.** The member has a diagnosis of generalized myasthenia gravis (gMG) (ICD-10: G70.00, G70.01)

**C.** The member has a positive serologic test for anti-acetylcholine receptor antibodies (AChR Ab+).

**D.** The member has a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class of II to IV at the start of therapy.

**E.** The member has experienced therapeutic failure, contraindication or intolerance to pyridostigmine.

**F.** The member has had a trial and inadequate response or intolerance to one (1) or more immunosuppressive agents (systemic corticosteroids or non-steroidal immunosuppressants).

**II. Reauthorization**

When a benefit, reauthorization of Zilbrysq may be approved when one of the following criteria is met **(A. or B.)**:

**A.** The prescriber attests that the member has experienced improvement in signs and symptoms of gMG (e.g., speech, swallowing, mobility, and/or respiratory function).

**B.** The prescriber attest that the member has experienced a decrease in the number of exacerbations of gMG.

**III.** An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

## Limitations of Coverage

**I.** Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

**II.** For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

## Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

## Automatic Approval Criteria

None

**References:**


1. Zilbrysq [package insert]. Smyrna, GA: UCB, Inc.; October 2023.
2. National Organization for Rare Disorders. Myasthenia Gravis. Available at: https://www.rarediseases.org/rare-diseases/myasthenia-gravis. Accessed October 20, 2023.
3. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis. *Neurology.* 2016;87(4):419-425.
4. Narayanaswami P, Sanders D, Wolfe G, et al. International Consensus Guidance for Management of Myasthenia Gravis. *Neurology*. 2021;96:114-122