Original Effective Date: 06/27/2024
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Last P&T Approval/Version: 10/30/2024
Next Review Due By: 10/2025
Policy Number: C27709-A

Zilbrysq (zilucoplan)

PRODUCTS AFFECTED

Zilbrysq (zilucoplan)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Generalized Myasthenia Gravis (gMG)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. GENERALIZED MYASTHENIA GRAVIS (gMG):
1. Documented diagnosis of generalized myasthenia gravis
   AND
2. Documentation member has a Myasthenia Gravis Foundation of America (MGFA) Clinical

Classification of class II, III, or IV confirmed by positive serologic test for binding anti-acetylcholine receptor antibodies (AChR)
AND

3. Documentation of member's Myasthenia Gravis-Specific Activities of Daily Living (MG- ADL) total score (or other means for treatment plan efficacy monitoring)
AND
4. Documentation of an inadequate treatment response (2 week trial), serious side effects, or contraindication to pyridostigmine AND formulary glucocorticoids
AND
5. Prescriber attests zilucoplan will not be used concurrently with Rystiggo (rozanolixizumab), Soliris (eculizumab), Ultomiris (ravulizumab), or Vyvgart/Vyvgart Hytrulo (efgartigimod)
AND
6. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review. [Contraindications to Zilbrysq (zilucoplan) include: Patients with unresolved serious Neisseria meningitidis infection, Patients who are not currently vaccinated against Neisseria meningitidis, unless the risks of delaying treatment outweigh the risks of developing a meningococcal infection.]

CONTINUATION OF THERAPY:

A. GENERALIZED MYASTHENIA GRAVIS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms as evidenced by ONE of the following:
   (a) Improvement (reduction in score) from pre-treatment baseline on the Myasthenia Gravis-Specific Activities of Daily Living (MG-ADL) assessment OR
   (b) Reduction in signs and symptoms of myasthenia gravis OR
   (c) Stabilization, reduction, or discontinuation of dose(s) of baseline immunosuppressive therapy (IST) prior to starting therapy

DURATION OF APPROVAL:

Initial authorization: 6 months; Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by, or in consultation with, a board-certified immunologist, neurologist, or rheumatologist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

Once daily subcutaneous injection based on actual body weight

Body Weight	Once Daily Dosage
Less than 56 kg	16.6 mg
56 kg to less than 77 kg	23 mg
77 kg and above	32.4 mg

PLACE OF ADMINISTRATION:
The recommendation is that the subcutaneous medication in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Complement C5 Inhibitor

FDA-APPROVED USES:
Indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Myasthenia gravis (MG) is a relatively rare acquired autoimmune disorder caused by an antibody- mediated blockade of neuromuscular transmission resulting in skeletal muscle weakness. MG is characterized by a pattern of progressively reduced muscle strength with repeated use and recovery of muscle strength after a period of rest. MG is classified into 2 major clinical types: ocular MG and generalized MG (gMG). gMG is a debilitating, chronic and progressive autoimmune neuromuscular disease that can occur at any age. There is no known cure for MG. The mainstay of therapy for symptomatic treatment of MG involves use of acetylcholinesterase (AChE) inhibitors. If treatment with AChE inhibitors is not effective, or they are not suitable for long-term use, then short-term immunosuppression with oral corticosteroids such as prednisolone is used. Nonsteroidal immunosuppressive agents (azathioprine, cyclosporine, cyclophosphamide, methotrexate, mycophenolate mofetil, rituximab, and tacrolimus) may be used in addition to steroids, with the aim of reducing the steroid dose over time. Approximately 10% to 15% of patients with MG have refractory gMG. These patients do not respond to long-term treatment with corticosteroids or multiple immunosuppressive treatments, or they have intolerable side effects to these therapies or require ongoing treatment with either intravenous immunoglobulin (IVIG) or plasma exchange (PE). Patients with refractory gMG experience difficulties with speech, swallowing, and mobility, impairment of respiratory function, and extreme fatigue, and may have frequent exacerbations, which can be life-threatening and require hospital admission.

Zilbrysq is the first complement C5 inhibitor for generalized myasthenia gravis given subcutaneously once daily that can be self-administered.

Clinical Studies
NCT04115293- RAISE- Study to Evaluate the Safety and Efficacy of zilucoplan in Patients with Generalized Myasthenia Gravis *Study Population*- Inclusion: aged 18-74; diagnosis of generalized myasthenia gravis classification II-IV; positive for acetylcholine receptor antibodies; MG-ADL score ≥6; QMG score ≥12; those receiving corticosteroids were on stable doses 30 days before baseline and no change was expected during treatment period. Exclusion: those who had a thymectomy within 12 months before baseline or was scheduled to occur during the treatment period; abnormal thyroid function; known positive serology for muscle specific tyrosine kinase autoantibodies; fixed weakness according to investigator judgement; history

of meningococcal infection; current or recent systemic infection requiring IV antibiotics within 4 weeks before baseline; previous treatment with a complement inhibitor; treatment with rituximab within 12 months' treatment with IV immunoglobulin, subcutaneous immunoglobulin, or plasma exchange within 4 weeks before baseline. *Phase, Study Design, Sample Size- phase 3, r*andomized, multicenter, double-blind, placebo-controlled study evaluating the safety and efficacy of zilucoplan in patients with acetylcholine receptor antibody positive generalized myasthenia gravis.

Outcomes
Primary endpoint was the change from baseline in the myasthenia gravis activities of daily living (MG-ADL) score at week 12. A clinically significant change was defined as a 2-point change. Secondary endpoints were the change from baseline in the quantitative myasthenia gravis (QMG) score, myasthenia gravis composite score (MGC) and myasthenia gravis quality of life (MG-QoL) score. A clinically significant change was defined as a 3-point change in the QMG and MGC scores. There was no established clinical significance for the MG-QoL at the time of the study.

Findings showed a statistically significant change in the MG-ADL score in those treated with Zilbrysq compared to placebo (-4.39 vs –2.3 respectively; p<0.001). Additionally, statistical significance is seen in the QMG score (-6.19 vs –3.25; p<0.001), MGC score (-8.62 vs –5.42; p=0.0023) and the MG-QoL score (-5.65 vs –3.16; p=0.013) in those treated with Zilbrysq vs placebo. Clinical significance was seen in the MG-ADL score, QMG score and the MGC score.

The most common adverse reactions were injection site reaction, upper respiratory tract infection and diarrhea. Treatment emergent adverse events occurred in 77% of patients treated with Zilbrysq and 70% with placebo. The most common were injection site bruising and headache.

Zilbrysq REMS
Because of the risk of serious infections, ZILBRYSQ is available only through a restricted program under a REMS. Under the ZILBRYSQ REMS, prescribers must enroll in the program.
Prescribers must counsel patients about the risk of serious meningococcal infection, provide the patients with the REMS educational materials, and ensure patients are vaccinated against meningococcal infections. Enrollment in the ZILBRYSQ REMS and additional information are available by telephone: 1-877-414-8353 or at www.ZILBRYSQREMS.com

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Zilbrysq (zilucoplan) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Zilbrysq (zilucoplan) include: Patients with unresolved *Neisseria meningitidis* infections.

OTHER SPECIAL CONSIDERATIONS:
Zilbrysq (zilucoplan) has a Black Box Warning for serious meningococcal infections. These infections may occur in patients treated with Zilbrysq and may become rapidly life- threatening or fatal if not recognized and treated early. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccinations at least 2 weeks prior to administering the first dose of Zilbrysq unless the risks of delaying therapy outweigh the risks of developing a serious infection. If urgent Zilbrysq therapy is indicated in a patient who is not up to date with both MenACWY and MenB vaccines, administer meningococcal vaccine(s) as soon as possible and provide antibacterial drug prophylaxis. Vaccination reduces, but does not eliminate, the risk of serious infections. Monitor patients for early signs of serious infections and evaluate immediately if infection is suspected. 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.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:
Zilbrysq SOSY 16.6mg/0.416mL single-dose prefilled syringes
Zilbrysq SOSY 23mg/0.574mL single-dose prefilled syringes
Zilbrysq SOSY 32.4mg/0.81mL single-dose prefilled syringes

REFERENCES

1. Zilbrysq (zilucoplan) [prescribing information]. Smyrna, GA: UCB Inc; April 2024.
2. UCB Inc. Study to evaluate the efficacy and safety of zilucoplan in patients with generalized myasthenia gravis. www.clinicaltrials.gov/study/NCT04115293. NLM identifier: NCT04115293.
3. Narayanaswami P, et al. International consensus guidance for management of myasthenia gravis. Neurology. 2021;96:114-122. doi 10.1212/WNL.0000000000011124.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Coding/Billing Information Template Update	Q4 2024
NEW CRITERIA CREATION	Q2 2024