PRIOR AUTHORIZATION POLICY

POLICY: Complement Inhibitors – Zilbrysq Prior Authorization Policy
- Zilbrysq® (zilucoplan subcutaneous injection – UCB)

REVIEW DATE: 12/17/2025; selected revision 02/18/2026

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Zilbrysq, a complement C5 inhibitor, is indicated for the treatment of **generalized myasthenia gravis (gMG)** in adults who are anti-acetylcholine receptor antibody-positive.[1]

Disease Overview

Myasthenia gravis (MG) 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 MG 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 MG 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 gMG. 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 consensus guidance recommend pyridostigmine for the initial treatment in most patients with MG. 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 MG who have not met treatment goals after an adequate trial of pyridostigmine. Nonsteroidal immunosuppressant agents used in treatment of MG 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 this consensus guidance provides new/additional recommendations for methotrexate, rituximab, and eculizumab intravenous infusion (Soliris®, biosimilars).[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 gMG 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 MG who have an unsatisfactory response to initial immunotherapy. Eculizumab should be considered in the treatment of severe, refractory, anti-acetylcholine receptor antibody-positive MG.

Safety

Zilbrysq has a Boxed Warning about serious meningococcal infections.[1] Zilbrysq is only available through a restricted access program, Zilbrysq Risk Evaluation and Mitigation Strategy (REMS).

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.

- **Zilbrysq® (zilucoplan subcutaneous injection – UCB)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

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 ALL of 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; OR

B) Patient is Currently Receiving Zilbrysq. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** According to the prescriber, patient is continuing to derive benefit from Zilbrysq; 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 COVERED

- **Zilbrysq® (zilucoplan subcutaneous injection – UCB)**

is(are) considered not medically necessary for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concomitant Use with Another Complement Inhibitor, a Neonatal Fc Receptor Blocker, a Rituximab Product, or Uplizna® (inebilizumab-cdon intravenous infusion).** There is no evidence to support concomitant use of Zilbrysq with another complement inhibitor, a neonatal Fc receptor blocker, a rituximab product, or Uplizna.
   Note: Examples of complement inhibitors are eculizumab intravenous infusion (Soliris, biosimilars) and Ultomiris (ravulizumab-cwvz intravenous infusion).
   Note: Examples of neonatal Fc receptor blockers are Imaavy (nipocalimab-aahu intravenous infusion), Rystiggo [rozanolixizumab-noli subcutaneous infusion), Vyvgart (efgartigimod alfa-fcab intravenous infusion), and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc subcutaneous injection).

REFERENCES

1. Zilbrysq subcutaneous injection [prescribing information]. Symra, GA: UCB: February 2025.
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 December 2, 2025.
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
Annual Revision	No criteria changes.	12/04/2024

Selected Revision	**Conditions Not Covered, Concomitant Use with Another Complement Inhibitor, a Neonatal Fc Receptor Blocker, or a Rituximab Product:** Imaavy was added to the Note of examples of neonatal Fc receptor blockers.	07/16/2025
Annual Revision	**Conditions Not Covered, Concomitant Use with Another Complement Inhibitor, a Neonatal Fc Receptor Blocker, or a Rituximab Product:** Removed Ultomiris subcutaneous injection from the Note of examples of neonatal Fc receptor blockers (Ultomiris subcutaneous injection will not be marketed by the manufacturer).	12/17/2025
Selected Revision	**Conditions Not Recommended for Approval**, the condition "Concomitant Use with Another Complement Inhibitor, a Neonatal Fc Receptor Blocker, or a Rituximab Product" was revised to "Concomitant Use with Another Complement Inhibitor, a Neonatal Fc Receptor Blocker, a Rituximab Product, or Uplizna® (inebilizumab-cdon intravenous infusion)".	02/18/2026