# Zilbrysq (zilucoplan) Prior Authorization with Quantity Limit Program Summary

Your health benefit plan may not cover certain prescription drug products or drug categories included in this document. Please consult your benefit plan materials for details about your particular benefit. This document may include drugs that are not included on your plan's formulary. For drug coverage status, please consult your plan's formulary.

## POLICY REVIEW CYCLE

| Effective Date | Date of Origin |
|---|---|
| 01-01-2026 | 11-09-2023 |

## FDA LABELED INDICATIONS AND DOSAGE

| Agent(s) | FDA Indication(s) | Notes | Ref# |
|---|---|---|---|
| Zilbrysq®<br><br>(zilucoplan)<br><br>Subcutaneous injection | Treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive | | 1 |

*See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm*

## CLINICAL RATIONALE

| | |
|---|---|
| Generalized Myasthenia Gravis (gMG) | Myasthenia gravis (MG) is a neuromuscular disorder primarily characterized by muscle weakness and muscle fatigue. Although the disorder usually becomes apparent during adulthood, symptom onset may occur at any age. The condition may be restricted to certain muscle groups, particularly those of the eyes (ocular myasthenia), or may become more generalized (generalized myasthenia gravis [gMG]), involving multiple muscle groups. Most individuals with myasthenia gravis develop weakness and drooping of the eyelids (ptosis); weakness of eye muscles, resulting in double vision (diplopia); and excessive muscle fatigue following activity. Additional features commonly include weakness of facial muscles; impaired speech (dysarthria); difficulties chewing and swallowing (dysphagia); and weakness of the upper arms and legs (proximal limb weakness). In addition, about 10% of affected patients may develop potentially life-threatening complications due to severe involvement of muscles used during breathing (myasthenic crisis). Myasthenia gravis results from an abnormal immune reaction in which antibodies inappropriately attack and gradually injure certain receptors in muscles that receive nerve impulses (antibody-mediated autoimmune response).(2)<br><br>The course of myasthenia gravis is highly variable. For example, the degree of muscle weakness may vary over hours, from day to day, or over weeks and months, tending to increase with repeated muscle use and to improve with rest. In addition, particularly during the first years after disease onset, some affected individuals may experience alternating periods in which symptoms temporarily subside or worsen. A short-term aggravation of symptoms may be triggered by a variety of factors, including infection, excessive physical activity, menstruation, and after delivery of a child.(2)<br><br>Corticosteroids are a standard treatment for MG but may cause transient worsening within the first 2 weeks and patients should be monitored closely for this possibility. As a result, a MG consensus panel lists corticosteroids as one of many agents to avoid or use with caution in MG. A nonsteroidal immunosuppressive agent should be used initially in treating MG. Nonsteroidal immunosuppressive agents that can be used in MG include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and |


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|---|---|
| | tacrolimus. For nonsteroidal immunosuppressive agents, once treatment goals have been achieved and maintained for 6 months to 2 years, the immunosuppressive dose should be tapered slowly to the minimal effective amount. Patients must be monitored for potential adverse effects and complications from immunosuppressive drugs. Changing to an alternative immunosuppressive agent should be considered if adverse effects and complications are medically significant or create undue hardship for the patient.(3)<br><br>Plasma exchange and intravenous immunoglobulin (IVIG) are appropriately used as short-term treatments in patients with MG with life-threatening signs such as respiratory insufficiency or dysphagia; in preparation for surgery in patients with significant bulbar dysfunction; when a rapid response to treatment is needed; when other treatments are insufficiently effective; and prior to beginning corticosteroids if deemed necessary to prevent or minimize exacerbations. The use of IVIG as maintenance therapy can be considered for patients with refractory MG or for those in whom immunosuppressive agents are contraindicated. Refractory MG is defined as post-intervention status is unchanged or worse after corticosteroids and at least 2 other immunosuppressive agents, used in adequate doses for an adequate duration, with persistent symptoms or side effects that limit functioning, as defined by the patient and physician.(3)<br><br>The time of onset and maximal effect varies between products. Azathioprine, mycophenolate mofetil, cyclosporine, and tacrolimus can take between 6 to 12 months to onset and up to 1 to 2 years to see maximal effect in MG. Rapid therapies such as plasmapheresis or IVIG therapy take approximately 1 week to onset and between 1 to 3 weeks to see maximal effect.(7)<br><br>Certain medications have established pharmacologic adverse effects on neuromuscular transmission. Use of these medications in a patient with MG can further reduce the effectiveness of neuromuscular transmission and cause increased clinical weakness. However, reported associations do not necessarily mean these medications should never be prescribed in MG. Clinical judgment and the risk-to-benefit ratio of the drug should be considered when it is deemed important for a patient's treatment. Medications that can cause a significant increase in weakness in patients with MG include fluoroquinolones, botulinum toxin, ketolides (particularly telithromycin) and aminoglycoside antibiotics, beta blockers, macrolide antibiotics, procainamide, quinidine, quinine, and magnesium. A number of other medications may unmask or exacerbate MG, particularly the neuromuscular blocking agents used during anesthesia, which can lead to prolonged postoperative weakness and ventilator dependence.(3) |
| Efficacy | The efficacy of Zilbrysq for the treatment of gMG in adult patients who are anti-acetylcholine receptor (AChR) positive was established in a 12-week, multicenter, randomized, double-blind placebo-controlled study (NCT04115293). Patients who met the following criteria at screening were enrolled in this study:(1)<br><br>• Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV<br>• Positive serology for AChR binding autoantibodies<br>• AG-Activities of Daily Living (MG-ADL) total score of greater than or equal to 6<br>• Those on MG therapy prior to screening (including acetylcholinesterase [AChE] inhibitors, steroids, or non-steroidal immunosuppressive therapies either in combination or alone), needed to maintain a stable dose<br><br>The primary efficacy endpoint was a comparison of the change from baseline between treatment groups in the MG-ADL total score after 12 weeks of treatment. The efficacy of Zilbrysq was also measured using the Quantitative MG (QMG) total score. Other secondary endpoints included the proportion of patients with improvements of at least 3 in the MG-ADL total score and at least 5 points in the QMG total score at week 12 without rescue therapy. At week 12, treatment with Zilbrysq demonstrated a |


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statistically significant improvement from baseline compared to placebo for MG-ADL total score and QMG total score.(1)

| **Efficacy Endpoints: Least Square (LS) Mean (95% CI)** | **Zilbrysq** | **Placebo** | **Zilbrysq change LS mean difference vs placebo (95% CI)** | **p-value** |
|---|---|---|---|---|
| MG-ADL Total Score | -4.39 (-5.28, -3.50) | -2.30 (-3.17, -1.43) | -2.09 (-3.24, -0.95) | < 0.001 |
| QMG Total Score | -6.19 (-7.29, -5.08) | -3.25 (-4.32,-2.17) | -2.94 (-4.39, -1.49) | < 0.001 |

MG-ADL:(4)

| Grade | 0 | 1 | 2 | 3 | Score |
|---|---|---|---|---|---|
| Talking | Normal | Intermittent slurring or nasal speech | Constant slurring or nasal speech, but can be understood | Difficult to understand speech | |
| Chewing | Normal | Fatigue with solid food | Fatigue with soft food | Gastric tube | |
| Swallowing | Normal | Rare episode of choking | Frequent choking necessitating changes in diet | Gastric tube | |
| Breathing | Normal | Shortness of breath with exertion | shortness of breath at rest | Ventilator dependence | |
| Impairment of ability to brush teeth or comb hair | None | Extra effort, but no rest periods | Rest periods needed | Cannot do one of these functions | |
| Impairment of ability to arise from a chair | None | Mild, sometimes uses arms | Moderate, always uses arms | Severe, requires assistance | |
| Double vision | None | Occurs but not daily | Daily, but not constant | Constant | |
| Eyelid droop | None | Occurs, but not daily | Daily, but not constant | Constant | |
| | | | | Total Score _____ | |

The MGFA clinical classification divides MG into 5 main classes and several subclasses. It is designed to identify subgroups of patients with MG who share distinct clinical features or severity of disease that may indicate different prognoses or responses to therapy:(6)

| Class | Features |
|---|---|
| I | Any ocular muscle weakness: may have weakness of eye closure; All other muscles are normal |


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| | |
|---|---|
| II | Mild weakness affecting muscles other than the ocular muscles: may also have ocular muscle weakness of any severity |
| IIa | Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles |
| IIb | Predominantly affecting oropharyngeal, respiratory muscles or both. May also have lesser or equal involvement of limb, axial muscles, or both. |
| III | Moderate weakness affecting muscles other than the ocular muscles; may also have ocular muscle weakness of any severity |
| IIIa | Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles. |
| IIIb | Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both. |
| IV | Severe weakness affecting muscles other than the ocular muscles; may also have ocular muscle weakness of any severity. |
| IVa | Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles |
| IVb | Predominantly affecting oropharyngeal, respiratory muscles or both. May also have lesser or equal involvement of limb, axial muscles, or both. |
| V | Intubation with or without mechanical ventilation (exception: intubation for routine perioperative management). The use of a feeding tube without intubation places a patient in class IVb. |

The QMG is a 13-item scale used to quantify disease severity in myasthenia gravis (MG). The scale measures ocular, bulbar, respiratory, and limb function, grading each finding and ranges from 0 (no myasthenic findings) to 39 (maximal myasthenic deficits). Drawbacks to the QMG are that it requires special instrumentation (dynamometer for grip strength and spirometer for vital capacity) and is time consuming, requiring 25-30 minutes to perform. The QMG has also been criticized as not being fully representative of MG disease activity due to the lack of weighting of different domains.(8)

There is no evidence to support concomitant use of Zilbrysq with another complement inhibitor (e.g., eculizumab [Soliris, biosimilars], Ultomiris) or neonatal Fc receptor blocker (e.g., Rystiggo, Vyvgart, Vyvgart Hytrulo, Imaavy).

**Safety**

Zilbrysq contains a boxed warning for an increased risk of meningococcal infections. All patients without a history of meningococcal vaccination should receive the vaccine at least two weeks prior to receiving the first dose of Zilbrysq.(1)

Zilbrysq is contraindicated for initiation in patients with unresolved serious *Neisseria meningitidis* infection.(1)

Zilbrysq is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).(1)


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## REFERENCES


| Number | Reference |
|---|---|
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| 2 | National Institute of Neurological Disorders and Stroke. Myasthenia Gravis Fact Sheet. NIH Publication No. 17-768. July 2018. |
| 3 | Narayanaswami P, Sanders DB, Wolfe G, et al. International Consensus Guidance for Management of Myasthenia Gravis. Neurology. 2021;96(3):114-122. doi:10.1212/wnl.0000000000011124. |
| 4 | Wincentsen J. MG Activities of Daily Living (MG-ADL) scale. Conquer Myasthenia Gravis. Published September 29, 2022. https://myastheniagravis.org/mg-activities-of-daily-living-mg-adl-scale/. |
| 5 | Reference no longer used. |
| 6 | Jayam Trouth A, Dabi A, Solieman N, Kurukumbi M, Kalyanam J. Myasthenia gravis: a review. Autoimmune Dis. 2012;2012:874680. doi:10.1155/2012/874680. |
| 7 | Alhaidar MK, Abumurad S, Soliven B, Rezania K. Current treatment of myasthenia gravis. Journal of Clinical Medicine. 2022;11(6):1597. doi:10.3390/jcm11061597. |
| 8 | Barnett C, Katzberg H, Nabavi M, Bril V. The quantitative Myasthenia gravis score. Journal of Clinical Neuromuscular Disease. 2012;13(4):201-205. doi:10.1097/cnd.0b013e31824619d5. |


## POLICY AGENT SUMMARY PRIOR AUTHORIZATION

| Target Brand Agent(s) | Target Generic Agent(s) | Strength | Targeted MSC | Available MSC | Final Age Limit | Preferred Status |
|---|---|---|---|---|---|---|
| | | | | | | |
| Zilbrysq | zilucoplan sodium subcutaneous soln pref syr | 16.6 MG/0.416ML ; 23 MG/0.574ML ; 32.4 MG/0.81ML | M ; N ; O ; Y | N | | |

## POLICY AGENT SUMMARY QUANTITY LIMIT

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | QL Amount | Dose Form | Day Supply | Duration | Addtl QL Info | Allowed Exceptions | Targeted NDCs When Exclusions Exist |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | |
| Zilbrysq 16.6 mg/0.416 mL | zilucoplan | 16.6 MG/0.416ML | 28 | Syringes | 28 | DAYS | | | |
| Zilbrysq 23 mg/0.574 mL | zilucoplan | 23 MG/0.574ML | 28 | Syringes | 28 | DAYS | | | |
| Zilbrysq 32.4 mg/0.81 mL | zilucoplan | 32.4 MG/0.81ML | 28 | Syringes | 28 | DAYS | | | |


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## CLIENT SUMMARY – PRIOR AUTHORIZATION

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | Client Formulary |
|---|---|---|---|
| Zilbrysq | zilucoplan sodium subcutaneous soln pref syr | 16.6 MG/0.416ML ; 23 MG/0.574ML ; 32.4 MG/0.81ML | Accord Enhanced ; Accord Standard |

## CLIENT SUMMARY – QUANTITY LIMITS

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | Client Formulary |
|---|---|---|---|
| Zilbrysq 16.6 mg/0.416 mL | zilucoplan | 16.6 MG/0.416ML | Accord Enhanced ; Accord Standard |
| Zilbrysq 23 mg/0.574 mL | zilucoplan | 23 MG/0.574ML | Accord Enhanced ; Accord Standard |
| Zilbrysq 32.4 mg/0.81 mL | zilucoplan | 32.4 MG/0.81ML | Accord Enhanced ; Accord Standard |

## PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

| Module | Clinical Criteria for Approval |
|---|---|

| Preferred Target Agent(s) | Non-Preferred Target Agent(s) |
|---|---|
| Ultomiris (ravulizumab-cwvz)<br>Rystiggo (rozanolixizumab-noli)<br>Vyvgart (efgartigimod)<br>Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc)<br>Epysqli (eculizumab-aagh) | Zilbrysq (zilucoplan) |

*Preferred Agents may be targeted in another Utilization Management program and require Prior Authorization

**Initial Evaluation**

**Target Agent(s)** will be approved when ALL of the following are met:

1. ONE of the following:
   A. The patient has a diagnosis of generalized Myasthenia Gravis (gMG) AND ALL of the following:
      1. The patient has a positive serological test for anti-AChR antibodies (medical records required) **AND**
      2. The patient has a Myasthenia Gravis Foundation of America (MGFA) clinical classification class of II-IVb **AND**
      3. The patient has a MG-Activities of Daily Living total score of greater than or equal to 6 **AND**
      4. ONE of the following:
         A. The patient's current medications have been assessed and any medications known to exacerbate myasthenia gravis (e.g., beta blockers, procainamide, quinidine, magnesium, anti-programmed death receptor-1 monoclonal antibodies, hydroxychloroquine, aminoglycosides) have been discontinued **OR**
         B. Discontinuation of the offending agent is NOT clinically appropriate **AND**
      5. ONE of the following:
         A. The patient has tried and had an inadequate response to at least ONE conventional agent used for the treatment of myasthenia gravis (i.e., corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, methotrexate, cyclophosphamide) **OR**


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| Module | Clinical Criteria for Approval |
|---|---|
| | B. The patient has an intolerance or hypersensitivity to ONE conventional agent used for the treatment of myasthenia gravis (i.e., corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, methotrexate, cyclophosphamide) **OR**<br>C. The patient has an FDA labeled contraindication to ALL conventional agents used for the treatment of myasthenia gravis (i.e., corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, methotrexate, cyclophosphamide) **OR**<br>D. The patient required chronic intravenous immunoglobulin (IVIG) **OR**<br>E. The patient required chronic plasmapheresis/plasma exchange **AND**<br>6. If the client has preferred agent(s), then the patient has ONE of the following:<br>A. Tried and had an inadequate response to ONE preferred agent **OR**<br>B. An intolerance or hypersensitivity to ONE preferred agent **OR**<br>C. An FDA labeled contraindication to ALL preferred agents(s) **OR**<br>B. The patient has another FDA labeled indication for the requested agent and route of administration **AND**<br>2. If the patient has an FDA approved indication, then ONE of the following:<br>A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**<br>B. There is support for using the requested agent for the patient's age for the requested indication **AND**<br>3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**<br>4. The patient will NOT be using the requested agent in combination with Rystiggo (rozanolixizumab-noli), Soliris (eculizumab), Bkemv (eculizumab-aeeb), Epysqli (eculizumab-aagh), Ultomiris (ravulizumab-cwvz), Vyvgart (efgartigimod), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc), or Imaavy (nipocalimab-aahu) **AND**<br>5. The patient does NOT have any FDA labeled contraindications to the requested agent<br><br>**Length of Approval:** 3 months<br><br>NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.<br><br>**Renewal Evaluation**<br><br>**Target Agent(s)** will be approved when ALL of the following are met:<br><br>1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process (Note: patients not previously approved for the requested agent will require initial evaluation review) **AND**<br>2. The patient has had clinical benefit with the requested agent **AND**<br>3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**<br>4. The patient will NOT be using the requested agent in combination with Rystiggo (rozanolixizumab-noli), Soliris (eculizumab), Bkemv (eculizumab-aeeb), Epysqli (eculizumab-aagh), Ultomiris (ravulizumab-cwvz), Vyvgart (efgartigimod), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc), or Imaavy (nipocalimab-aahu) **AND**<br>5. The patient does NOT have any FDA labeled contraindications to the requested agent<br><br>**Length of Approval:** 12 months<br><br>NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. |

## QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL


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| Module | Clinical Criteria for Approval |
|---|---|
| Universal QL | **Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met:<br><br>1. The requested quantity (dose) does NOT exceed the program quantity limit **OR**<br>2. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following:<br>A. BOTH of the following:<br>1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication **AND**<br>2. There is support for therapy with a higher dose for the requested indication **OR**<br>B. BOTH of the following:<br>1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND**<br>2. There is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR**<br>C. BOTH of the following:<br>1. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND**<br>2. There is support for therapy with a higher dose for the requested indication<br><br>**Length of Approval:** up to 12 months |


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