Clinical Policy: Zilucoplan (Zilbrysq)

Reference Number: LA.PHAR.616
Effective Date:
Last Review Date: 02.22.24
Line of Business: Medicaid **Revision Log**

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description

Zilucoplan (Zilbrysq®) is a complement inhibitor.

FDA Approved Indication(s)

Zilbrysq is indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections® that Zilbrysq is medically necessary when the following criteria are met:

I. Initial Approval Criteria

A. Generalized Myasthenia Gravis (must meet all):

1. **Diagnosis of gMG;**
2. **Prescribed by or in consultation with a neurologist;**
3. **Age ≥ 18 years;**
4. **Myasthenia Gravis-Activities of Daily Living (MG-ADL) score ≥ 6 at baseline;**
5. **Myasthenia Gravis Foundation of America (MGFA) clinical classification of Class II to IV;**
6. **Member has positive serologic test for anti-AChR antibodies;**
7. **Failure of a corticosteroid (*see Appendix B*), unless contraindicated or clinically significant adverse effects are experienced;**
8. **Failure of a cholinesterase inhibitor (*see Appendix B*), unless contraindicated or clinically significant adverse effects are experienced;**
9. **Failure of at least one immunosuppressive therapy (*see Appendix B*), unless clinically significant adverse effects are experienced or all are contraindicated;**
10. **Zilbrysq is not prescribed concurrently with Soliris®, Ultomiris®, or Vyvgart®;**
11. **Documentation of member's current weight in kg;**
12. **Dose does not exceed the following (a and b):**
    a. **One of the following (i, ii, or iii):**
       i. **Weight < 56 kg: 16.6 mg per day;**

ii. **Weight 56 kg to < 77 kg: 23 mg per day;**
iii. **Weight ≥ 77 kg: 32.4 mg per day;**

b. **1 prefilled syringe per day.**

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2):

1. **If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255;**
2. **If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.**

II. Continued Therapy

A. Generalized Myasthenia Gravis (must meet all):

1. **Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria.**
2. **Member is responding positively to therapy as evidenced by a ≥ 2-point reduction from baseline in the MG-ADL total score;**
3. **Zilbrysq is not prescribed concurrently with Soliris, Ultomiris, or Vyvgart;**
4. **Documentation of member's current weight in kg;**
5. **If request is for a dose increase, new dose does not exceed the following (a and b):**
   a. **One of the following (i, ii, or iii):**
      i. **Weight < 56 kg: 16.6 mg per day;**
      ii. **Weight 56 kg to < 77 kg: 23 mg per day;**
      iii. **Weight ≥ 77 kg: 32.4 mg per day;**
   b. **1 prefilled syringe per day.**

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2):

1. **If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255;**
2. **If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53.**

III. Diagnoses/Indications for which coverage is NOT authorized:

A. **Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies –LAPMN.53 for Medicaid or evidence of coverage documents.**

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AChR: acetylcholine receptor
FDA: Food and Drug Administration
gMG: generalized myasthenia gravis
MG-ADL: Myasthenia Gravis-Activities of Daily Living
MGFA: Myasthenia Gravis Foundation of America

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Corticosteroids		
betamethasone	Oral: 0.6 to 7.2 mg PO per day	7.2 mg/day
dexamethasone	Oral: 0.75 to 9 mg/day PO	9 mg/day
methylprednisolone	Oral: 12 to 20 mg PO per day; increase as needed by 4 mg every 2-3 days until there is marked clinical improvement	40 mg/day
prednisone	Oral: 15 mg/day to 20 mg/day; increase by 5 mg every 2-3 days as needed	60 mg/day
Cholinesterase Inhibitors		
pyridostigmine (Mestinon®)	Oral immediate-release: 600 mg daily in divided doses (range, 60-1,500 mg daily in divided doses) Oral sustained release: 180-540 mg QD or BID	Immediate-release: 1,500 mg/day Sustained-release:1,080 mg/day
neostigmine (Bloxiverz®)	Oral: 15 mg TID. The daily dosage should be gradually increased at intervals of 1 or more days. The usual maintenance dosage is 15-375 mg/day (average 150 mg) IM or SC: 0.5 mg based on response to therapy	Oral: 375 mg/day
Immunosuppressants		
azathioprine (Imuran®)	Oral: 50 mg QD for 1 week, then increase gradually to 2 to 3 mg/kg/day	3 mg/kg/day
mycophenolate mofetil (Cellcept®)*	Oral: Dosage not established. 1 gram BID has been used with adjunctive	2 g/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	corticosteroids or other non-steroidal immunosuppressive medications	
cyclosporine (Sandimmune®)*	Oral: initial dose of cyclosporine (non-modified), 5 mg/kg/day in 2 divided doses	5 mg/kg/day
Rituxan® (rituximab), Riabni™ (rituximab-arrx), Ruxience™ (rituximab-pvvr), Truxima® (rituximab-abbs)*†	IV: 375 mg/m^2 once a week for 4 weeks; an additional 375 mg/m^2 dose may be given every 1 to 3 months afterwards	375 mg/m^2

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*
†*Prior authorization is required for rituximab products*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): unresolved *Neisseria meningitidis* infection
- Boxed warning(s): serious meningococcal infections

Appendix D: General Information

- Zilbrysq is only available through a REMS (Risk Evaluation and Mitigation Strategy) program due to the risk of life-threatening and fatal meningococcal infection. Patients should be vaccinated with a meningococcal vaccine at least 2 weeks prior to receiving the first dose of Zilbrysq and revaccinated according to current medical guidelines for vaccine use. Patients should be monitored for early signs of meningococcal infections, evaluated immediately if infection is suspected, and treated with antibiotics if necessary.
- The MG-ADL scale is an 8-item patient-reported scale that measures functional status in 8 domains related to MG – talking, chewing, swallowing, breathing, impairment of ability to brush teeth or comb hair, impairment of ability to arise from a chair, double vision, and eyelid droop. Each domain is given a score of 0-3, with 0 being normal and 3 being most severe impairment. A 2-point decrease in the MG-ADL score is considered a clinically meaningful response.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
gMG	Weight < 56 kg: 16.6 mg SC QD Weight 56 kg to < 77 kg: 23 mg SC QD Weight ≥ 77 kg: 32.4 mg SC QD	See regimen

VI. Product Availability

Single-dose prefilled syringes: 16.6 mg/0.416 mL, 23 mg/0.574 mL, 32.4 mg/0.81 mL

VII. References

1. Zilbrysq Prescribing Information. Smyrna, GA: UCB, Inc., October 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216834s000lbl.pdf. Accessed October 24, 2023.
2. UCB. UCB presents efficacy and safety results for zilucoplan and rozanolixizumab in generalized myasthenia gravis. Published May 10, 2022. Available at: https://www.ucb.com/stories-media/Press-Releases/article/UCB-presents-efficacy-and-safety-results-for-zilucoplan-and-rozanolixizumab-in-generalized-myasthenia-gravis. Accessed November 3, 2023
3. Ra Pharmaceuticals. A phase 3, multicenter, randomized, double blind, placebo-controlled study to confirm the safety, tolerability, and efficacy of zilucoplan in subjects with generalized myasthenia gravis. clinicaltrials.gov. Available at: https://clinicaltrials.gov/ct2/show/study/NCT04115293. Accessed November 3, 2023.
4. Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of Myasthenia Gravis. Neurology. 2020;96(3):114-122.
5. Treatment strategy. Myasthenia Gravis Foundation of America. Available at: https://myasthenia.org/Newly-Diagnosed/Treatment-Strategy. Accessed November 3, 2023.
6. Muppidi S, Silvestri N, Tan R, et al. The evolution of Myasthenia Gravis-Activities of Daily Living (MG-ADL) scale utilization to measure myasthenia gravis symptoms and treatment response (1817). Neurology. 2021;96(15 Suppl):1817.

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted corporate policy to local.	02.22.24	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

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