Medical Drug Clinical Criteria

Subject:	Zilbrysq (zilucoplan)		
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Overview

This document addresses the use of Zilbrysq, a complement inhibitor approved for the treatment of generalized myasthenia gravis in adult patients who are anti-acetylcholine receptor (AchR) antibody positive. Zilbrysq is the first self-administered complement inhibitor approved for gMG.

Generalized myasthenia gravis (gMG) is an autoimmune neuromuscular disorder characterized by fluctuating motor weakness causing dyspnea, dysphagia, diplopia, dysarthria, and ptosis. Generalized myasthenia gravis is commonly mediated by IgG autoantibodies directed against the neuromuscular junction. Treatment strategies include symptomatic therapy (with anticholinesterase agents such as pyridostigmine), chronic immunotherapy with steroids or other immunosuppressive drugs (such as azathioprine, cyclosporine, or methotrexate), rapid immunotherapy (with plasmapheresis or IV immune globulin), and/or surgical treatment. Complement inhibitors, including Soliris, Ultomiris, and Zilbrysq, are immunotherapies which block complement activation triggered by acetylcholine receptor antibodies at the neuromuscular junction. Rystiggo (rozanolixizumab-noli), Vyvgart (efgartigimod alfa-fcab), and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) reduce autoantibodies by binding to the neonatal Fc receptor (FcRn), but differ in product administration, frequency, and population. Only Rystiggo is additionally approved for MuSK-positive individuals. Myasthenia Gravis Foundation of America (MGFA) international consensus guidelines, published prior to the approval of FcRn inhibitors and Zilbrysq, recommend immunosuppressive drugs and/or corticosteroids for individuals who have not met treatment goals after an adequate trial of pyridostigmine.

Current published evidence for Zilbrysq includes one phase 3, multicenter, randomized, placebo-controlled trial that included individuals with AChR-positive gMG. Trial inclusion criteria required Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV disease and a Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 6 or higher. Individuals with clinically relevant active infection or recent severe infections were excluded. Participants in the trial were treated with Zilucoplan 0.3 mg/kg or placebo administered subcutaneously daily. The primary endpoint was change from baseline to week 12 in MG-ADL score. There was a significantly greater and clinically meaningful change in MG-ADL score in the Zilbrysq group compared to placebo. Additionally, a greater proportion of patients in the Zilbrysq group experienced a minimal clinically important difference in MG-ADL score (defined as ≥2-point change). The incidence of serious infections was low and similar between treatment and placebo groups. No cases of meningococcal infections were reported.

Zilbrysq has a black box warning for serious meningococcal infections. Life-threatening and fatal meningococcal infections have occurred in patients treated with complement inhibitors and meningococcal infection may become rapidly life-threating or fatal if not recognized and treated early. Individuals should complete or update meningococcal vaccination (for serogroups A, C, W, and Y, and serogroup B) at least 2 weeks prior to initiation of therapy unless the risks of delaying therapy outweigh the risk of developing a meningococcal infection. The FDA has required the manufacturers to develop comprehensive risk management programs that include the enrollment of prescribers in the Zilbrysq REMS. Additional information and forms for individuals, prescribers, and pharmacists may be found on the manufacturer's websites: www.ZILBRYSQREMS.com.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Zilbrysq (zilucoplan)

Requests for initiation of therapy with Zilbrysq (zilucoplan) may be approved if the following criteria are met:

I. Individual is 18 years of age or older with gMG; **AND**
II. Documentation is provided that individual has a positive serologic test for binding anti-acetylcholine receptor antibodies (AChR-ab); **AND**
III. Individual has Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV disease; **AND**
IV. Documentation is provided that individual has a Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 6 or higher;

AND
V. Documentation is provided that individual meets both of the following (A and B)
    A. Individual has had a trial and inadequate response or intolerance to an acetylcholinesterase inhibitor (MGFA 2020); **OR**
        1. Individual is on a stable dose of an acetylcholinesterase inhibitor; **OR**
        2. Individual has a contraindication to acetylcholinesterase inhibitors;

    AND
    B. Individual has had a trial and inadequate response or intolerance to one or more immunosuppressive agents (including but not limited to systemic corticosteroids or non-steroidal immunosuppressants) (MGFA 2020); **OR**
        1. Individual is on a stable dose of one or more immunosuppressive agents (including but not limited to systemic corticosteroids or non-steroidal immunosuppressants); **OR**
        2. Individual has a contraindication to systemic corticosteroids and non-steroidal immunosuppressants;

AND
VI. Individual has completed or updated meningococcal vaccination (for serogroups A, C, W, and Y, and serogroup B) at least 2 weeks prior to administration of the first dose of Zilbrysq, unless the risks of delaying Zilbrysq outweigh the risk of meningococcal infection.

Initial Approval Duration: 26 weeks

Requests for continued use of Zilbrysq (zilucoplan) may be approved if the following criteria are met:

I. Individual has completed or updated meningococcal vaccination (for serogroups A, C, W, and Y, and serogroup B); **AND**
II. Individual has experienced a clinical response as evidenced by both of the following:
    A. Reduction in signs or symptoms that impact daily function; **AND**
    B. Documentation is provided to show at least a 2-point reduction in MG-ADL total score from baseline.

Requests for Zilbrysq (zilucoplan) may not be approved for the following:

I. Individual is using in combination with efgartigimod alfa, rozanolixizumab, eculizumab, ravulizumab, or rituximab; **OR**
II. Individual has evidence of an active meningococcal infection; **OR**
III. When the above criteria are not met and for all other indications.

Continuation Approval Duration: 1 year

Quantity Limits

Zilbrysq (zilucoplan) Quantity Limit

Drug	Limit
Zilbrysq (zilucoplan) 16.6 mg/ 0.416 mL prefilled syringe	1 syringe per day
Zilbrysq (zilucoplan) 23 mg/ 0.574 mL prefilled syringe	1 syringe per day

Zilbrysq (zilucoplan) 32.4 mg/ 0.81 mL prefilled syringe	1 syringe per day

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J3490	Unclassified drugs (when specified as [Zilbrysq] (zilucoplan)

ICD-10 Diagnosis

	All diagnoses pend

Document History

New: 11/17/2023
Document History:

- 11/17/2023 – Select Review: Create clinical criteria document for Zilbrysq. Coding Reviewed: Added HCPCS J3490. All diagnoses pend.

References

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: October 25, 2023.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
4. Narayanaswami P, Sanders DB, Wolfe G, et al for the Task Force of the Myasthenia Gravis Foundation of America (MGFA). International consensus guidance for management of myasthenia gravis 2020 update. Neurology 2021; 96:114-122.
5. Howard, J. F. Jr et al. Safety and efficacy of zilucoplan in patients with generalized myasthenia gravis (RAISE): a randomized, double-blind, placebo-controlled phase 3 study. Lancet Neurol. 22, 395–406 (2023)

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.