BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

ZILBRYSQ® (zilucoplan) subcutaneous injection Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Zilbrysq (zilucoplan) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

  2. Individual is 18 years of age or older

  3. Individual has a confirmed diagnosis of generalized myasthenia gravis (gMG) in an individual who is anti-acetylcholine receptor (AChR) antibody positive

  4. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:

a. Complete or update meningococcal vaccination prior to administering the first dose, unless the risk of delaying therapy outweighs the risk of developing a meningococcal infection
b. Amylase and lipase
c. Individual has positive serology for AChR binding autoantibodies
d. Individual's Myasthenia Gravis Foundation of America (MGFA) clinical classification is class II- IV
e. Individual's MG-Activities of Daily Living (MG-ADL) total score of 6 or more
f. Quantitative Myasthenia Gravis (QMG) total score of 12 or more

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **ALL** the following:
   a. Pyridostigmine with or without a glucocorticoid
   b. Azathioprine or mycophenolate mofetil

7. Individual **does not have** the FDA-label contraindications of unresolve *Neisseria meningitidis* infection

8. Individual is not receiving Zilbrysq in combination with another complement inhibitor (e.g., Soliris (eculizumab), Ultomiris (ravulizumab)) or a neonatal Fc receptor blocker (e.g., Rystiggo (rozanolixizumab), Vyvgart (efgartigimod), Vyvgart Hytrulo (efgartigimod + hyaluronidase))

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Zilbrysq (zilucoplan) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

2. Individual's condition has responded while on therapy with response defined as **BOTH** of the following:
   a. Improvement in MG-ADL of 2-points or more
   b. Improvement in QMG of 3-points or more

3. Individual has been adherent with the medication

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed contraindications or other significant adverse drug effects that may exclude continued use such as:
   a. Pancreatitis and pancreatic cysts
   b. Other infections, especially encapsulated bacteria, such as by non-groupable strains of Neisseria meningitidis, Streptococcus influenzae, and Neisseria gonorrhoeae

6. Individual is not receiving Zilbrysq in combination with another complement inhibitor (e.g., Soliris (eculizumab), Ultomiris (ravulizumab)) or a neonatal Fc receptor blocker (e.g., Rystiggo (rozanolixizumab), Vyvgart (efgartigimod), Vyvgart Hytrulo (efgartigimod + hyaluronidase))

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Zilbrysq (zilucoplan) is a complement inhibitor indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive. Zilucoplan is a 15 amino acid synthetic macrocyclic peptide. Zilucoplan binds to the complement protein C5 and inhibits its cleavage to C5a and C5b, preventing the generation of the terminal complement complex, C5b-9. The precise mechanism by which zilucoplan exerts its therapeutic effect in gMG is unknown but is presumed to involve reduction of C5b-9 deposition at the neuromuscular junction.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Myasthenia Gravis Foundation of America clinical classification	
Class I	Any ocular muscle weakness May have weakness of eye closure All other muscle strength is normal
Class II	Mild weakness affecting other than 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
Class III	Moderate weakness affecting other than 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

Class IV	Severe weakness affecting other than ocular muscles May also have ocular muscle weakness of any severity
IVa	Predominantly affecting limb and/or axial muscles 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
Class V	Defined by intubation, with or without mechanical ventilation, except when employed during routine postoperative management. The use of a feeding tube without intubation places the patient in class IVb.
Weakness class is assessed according to the most severely affected muscle or muscle group at the patient's maximum severity	

MG Activities of Daily Living (MG-ADL):

Grade	0	1	2	3
Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal 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 chocking 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	Normal	Extra effort but no rest periods needed	Rest periods needed	Cannot do one of these functions
Impairment of ability to arise from a chair	Normal	Mild, sometimes uses arms	Moderate always uses arms	Severe requires assistance
Double vision	Normal	Occurs but not daily	Daily but not constant	Constant
Eyelid droop	Normal	Occurs but not daily	Daily but not constant	Constant
The total score was the sum of all individual item scores and range from 0 to 24. Higher scores indicate more severe disability due to MG. A decrease from baseline score indicate improvement. A 2-point change in MG-ADL Score is considered clinically meaningful.				

Quantitative Myasthenia Gravis (QMG) score:

Item	None	Mild	Moderate	Severe
Grade	0	1	2	3
Double vision (lateral gaze) (seconds) Measured both to the right and to the left (take worst score between both eyes)	61	11-60	1-10	Spontaneous

Ptosis (upward gaze) (seconds)	61	11-60	1-10	Spontaneous
Facial muscle	Normal lid closure	Complete, weak, some resistance	Complete, without resistance	Incomplete
Swallowing (4 oz water, ½ cup)	Normal	Minimal coughing or throat clearing	Severe coughing or nasal regurgitation	Cannot swallow (test not attempted)
Speech following counting aloud from 1 to 50 (onset of dysarthria)	None at 50	Dysarthria at 30-49	Dysarthria at 10-39	Dysarthria at 9
Right arm outstretched (90° sitting) (seconds)	240	90-239	10-89	0-9
Left arm outstretched (90° sitting) (seconds)	240	90-239	10-89	0-9
Forced vital capacity	≥ 80%	65-79%	50-64%	< 50%
Right hand grip (kg)	≥ 45 male ≥ 30 female	15-44 male 10-29 female	5-14 male 5-9 female	0-4 male 0-4 female
Left hand grip (kg)	≥ 35 male ≥ 25 female	15-34 male 10-24 female	5-14 male 5-9 female	0-4 male 0-4 female
Head, lifted (45% supine) (seconds)	120	30-119	1-29	0
Right leg outstretched (45-50% supine) (seconds)	100	31-99	1-30	0
Right leg outstretched (45-50% supine) (seconds)	100	31-99	1-30	0
The higher score for each item indicates severity. The total score ranges from 0-39 with higher score indicative of severe disease activity. A decrease from baseline score shows improvement. A change in the QMG Score of 3-points or more may be considered clinically meaningful.				

Resources:

Zilbrysq (zilucoplan) subcutaneous injection product information, revised by UCB, Inc. 04-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 27, 2024.

Bird SJ. Pathogenesis of myasthenia gravis. In: UpToDate, Shefner JM, Goddeau RP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2024. Topic last updated June 06, 2024. Accessed January 10, 2025.

Bird SJ. Diagnosis of myasthenia gravis. In: UpToDate, Shefner JM, Goddeau RP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2024. Topic last updated October 16, 2024. Accessed January 10, 2025.

Bird SJ. Clinical manifestations of myasthenia gravis. In: UpToDate, Shefner JM, Goddeau RP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2024. Topic last updated November 26, 2024. Accessed January 10, 2025.

ORIGINAL EFFECTIVE DATE: 02/15/2024 | ARCHIVE DATE: | LAST REVIEW DATE: 02/20/2025 | LAST CRITERIA REVISION DATE: 02/20/2025

Bird SJ. Overview of the treatment of myasthenia gravis. In: UpToDate, Shefner JM, Goddeau RP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2024. Topic last updated September 06, 2024. Accessed January 10, 2025.

Bird SJ. Chronic immunotherapy for myasthenia gravis. In: UpToDate, Shefner JM, Goddeau RP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2024. Topic last updated November 18, 2024. Accessed January 10, 2025.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT04115293: 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. Available from: http://clinicaltrials.gov. Last update posted May 03, 2023. Last verified May 2023. Accessed February 09, 2024. Re-valuated January 10, 2025.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT04115293: 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. Statistical Analysis Plan Amendment 5.0 Available from: http://clinicaltrials.gov. Accessed February 09, 2024. Re-valuated January 10, 2025.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT04115293: 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. RAISE Protocol Available from: http://clinicaltrials.gov. Accessed February 09, 2024. Re-valuated January 10, 2025.