ZILBRYSQ®
(zilucoplan) Injection

# Guide to Writing a Letter of Appeal*

When a patient's health plan denies a PA (prior authorization) request for ZILBRYSQ (zilucoplan), you can submit a letter of appeal in response to the official denial letter. In the letter of appeal, you can explain your clinical rationale for prescribing ZILBRYSQ, provide supporting documentation that addresses the reason(s) given for the denial, and request approval.

This resource includes information on the appeal process, a checklist that can be followed when creating a letter of medical appeal, and a sample letter that has information health plans often require.

## INDICATION

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

## IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING

### WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

**Life-threatening and fatal meningococcal infections have occurred in patients treated with complement inhibitors; ZILBRYSQ is a complement inhibitor. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.**

- **Complete or update meningococcal vaccination (for serogroups A, C, W, and Y, and serogroup B) at least 2 weeks prior to administering the first dose of ZILBRYSQ, unless the risk of delaying therapy outweighs the risk of developing a meningococcal infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccinations in patients receiving a complement inhibitor.**
- **Persons receiving ZILBRYSQ are at increased risk for invasive disease caused by *N. meningitidis*, even if they develop antibodies following vaccination. Monitor patients for signs of meningococcal infections and evaluate immediately if infection is suspected.**

**Because of the risk of serious meningococcal infections, ZILBRYSQ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called ZILBRYSQ REMS.**

*Use of the information in this letter does not guarantee that the health plan will provide reimbursement for ZILBRYSQ. **The information in this letter is not intended to be a substitute for, or an influence on, your independent medical judgment.** It is presented for informational purposes only and is not intended to provide reimbursement or legal advice. HCPs are encouraged to contact third-party payers for specific information on their current coverage policies. For other questions, please call ONWARD™ at 1-844-ONWARD-1 (1-844-669-2731).

HCP=healthcare professional.

**Please refer to pages 5 and 6 for additional Important Safety Information.**
**Please refer to the full Prescribing Information, including Boxed Warning for serious meningococcal infections, provided by the UCB representative and visit ZILBRYSQhcp.com.**

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# Guide to Writing Letter of Appeal* (cont'd)

## Preparing an Effective Letter of Appeal

**Refer to the health plan's specific appeals process, as there may be varying processes**

- Some health plans may require you to use their specific appeal form; if not, draft the letter on your letterhead

**Confirm the health plan's time frame for submitting an appeal**

- If appropriate, mark the appeal request "urgent" based on the patient's needs and the health plan's timelines

**Understand the reason for denial and include why you believe the decision should be reconsidered**

- If the denial was for inaccurate or incomplete information, correct or update the discrepancies
- Include specific and relevant medical information that, in your independent clinical judgment, supports the use of ZILBRYSQ for your patient in accordance with the health plan's criteria
- Directly address any specific rationale cited by the health plan for the denial

**Include all required information. Information recommended for a letter of appeal typically includes:**

- Patient's full name, plan identification number, gender, date of birth, and case identification number (if available)
- Patient's medical history, diagnosis (including ICD-10-CM code), prior treatments (including start/stop dates and reason[s] for discontinuation, if applicable), and any other patient characteristics and/or clinical considerations relevant to ZILBRYSQ therapy
- Summary of your treatment recommendations
- Any additional enclosures to be submitted at the same time as the letter of appeal and in the correct order indicated in the health plan's appeal instructions. Additional enclosures typically include:
  - Letter of Medical Necessity
  - A copy of the health plan's denial letter
  - Relevant patient documentation, such as physician notes, lab results, and medical records
  - Clinical support, including trial data or relevant peer-reviewed articles (as applicable)

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HCP=healthcare professional; ICD-10-CM=International Classification of Diseases, 10th Revision, Clinical Modification.

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## Sample Letter of Appeal

This sample letter of appeal may be used as a starting point to address the health plan's specific reasons for denial and help reinforce your reasoning for why ZILBRYSQ is medically necessary for your patient. The content of the letter of appeal should be personalized based on your patient's medical information and the health plan's denial response. Always exercise independent medical judgment and discretion when providing a diagnosis and characterization of the patient's medical condition. It is recommended you use your letterhead for the final draft that you submit to the health plan.

**SAMPLE ONLY**
**UPDATE AND PLACE ON YOUR LETTERHEAD**

[Date]

[Contact Name]
[Title]
[Name of Health Insurance Company or Pharmacy Benefit Manager]
[Address]
[City, State Zip Code]
Date(s) of service: [Date(s)]

Re: [First/Second]-Level Appeal for Coverage Denial of ZILBRYSQ® (zilucoplan) Injection For Subcutaneous Use[: Request for Expedited Review Due to Medical Urgency]

Date of Denial Letter: [MM-DD-YEAR]
Denial Reference Number: [Denial Reference Number]
Insured: [Full name of patient]; Date of Birth: [MM-DD-YEAR]; Policy Number: [Number]; Group Number: [Number]

Dear [Name of Contact]:

I am writing on behalf of my patient, [full name of patient], to appeal the coverage denial for treatment with ZILBRYSQ for anti-acetylcholine receptor (AChR) antibody-positive generalized myasthenia gravis (gMG). The aforementioned letter of denial stated [list reasons for denial] as the reason for coverage denial. This appeal letter provides information regarding my patient's medical history and diagnosis, and my treatment rationale for the use of ZILBRYSQ.

**Patient History and Diagnosis**
[Full name of patient] is a[n] [age]-year-old [male/female] born [MM-DD-YEAR] who was diagnosed with anti-AChR antibody-positive gMG on [date of diagnosis MM-DD-YEAR].

[Provide summary of rationale for treatment with ZILBRYSQ for this patient based on your independent clinical assessment and medical opinion. Address the reason for denial directly. Include a description of the patient's relevant gMG clinical signs and symptoms, disease progression, history of prior treatments, as well as specific clinical presentations and relevant patient-specific clinical scenarios demonstrating medical necessity.]

**Summary**
Considering the patient's medical information provided and the supporting documentation enclosed, I believe ZILBRYSQ is indicated and medically necessary for [full name of patient], and, as such, the coverage decision should be reversed. If you have any further questions, please feel free to call me at [prescriber's telephone number] to discuss. Thank you kindly for your prompt attention to this request.

[Physician's Name, Credentials]
[Physician's Identification Number]
[Physician's Practice Name]
[Physician's Phone Number]
[Physician's Fax Number]
[Physician's Email]

Enclosures: [Clinical documentation, Prescribing Information, clinical notes and medical records, FDA approval letter for ZILBRYSQ in gMG, Letter of Medical Necessity, copy of health plan's denial letter, etc.]

Download a copy of the full Prescribing Information.

Directly address the reason for denial and include relevant medical information that, in your clinical judgment, supports your patient's appropriate use in accordance with the health plan's criteria. See next page for specific examples of patient medical history to consider including.

Confirm that the documents are listed and attached in the order specified by the health plan.

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## Examples of Medical History for a Letter of Appeal

- **Documented diagnosis** of gMG[1]
- **Positive serology for AChR binding autoantibodies**,[1] including laboratory results, date, and additional relevant context
- **MGFA Clinical Classification** status based on the Myasthenia Gravis Foundation of America disease scale[2]
  - Class I-V. Note: Only Class II-IV were studied in Phase 3 RAISE clinical trial[1,3]
- **MG-ADL total score**,[2] including related case notes and clinical impressions
  - Only patients with MG-ADL scores of ≥6 were studied in the RAISE clinical trial population[1,3]
- **Previous gMG treatment** including AChE inhibitors, corticosteroids, NSISTs, IVIg, SCIg, PLEX, eculizumab, ravulizumab-cwvz, efgartigimod alfa-fcab, efgartigimod alfa and hyaluronidase-qvfc, and/or rozanolixizumab-noli[4-9]
  - Include treatment name(s), dosage, frequency, duration (with specific start/stop dates, if applicable), and clinical impact, including any inadequate response or intolerance to such treatments
- **Documentation of meningococcal vaccination history**, including initial and additional doses of the following[1,10]:
  - MenACWY
  - MenB-4C or MenB-FHbp
- **History of complications, exacerbations, or myasthenic crises**,[2] which may result in ER visits, hospital admissions, and/or ICU stays
- **Record of signs and symptoms** describing patient's clinical presentation, such as[11,†]
  - Ocular: ptosis, diplopia
  - Bulbar: dysarthria, dysphagia, dysphonia, masticatory weakness
  - Facial: eyelid closure, drooling
  - Limb muscles: commonly proximal, symmetric; arms more affected than legs
  - Axial muscles: neck flexion; neck extension
  - Respiratory muscles: exertional dyspnea, orthopnea, tachypnea, respiratory failure

**Note:** This is not an all-inclusive list of potential gMG clinical signs and symptoms. Please always use your independent clinical judgment when deciding what to include for review.

## Frequent Reasons for Denial

Listed below are some of the most common reasons why a health plan may initially deny coverage of ZILBRYSQ that can be addressed in a letter of appeal, using the patient's medical history and your clinical judgment.

- Unclear understanding of ZILBRYSQ indication
- Lack of information regarding previous treatments, including those required for initiation of ZILBRYSQ
- Missing clinical information to support initiation of ZILBRYSQ, including MG-ADL score, QMG score, antibody testing results, and the patients' vaccination records

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†This list is not inclusive of all gMG clinical signs and symptoms.

AChE=acetylcholinesterase; AChR=acetylcholine receptor; ER=emergency room; gMG=generalized myasthenia gravis; HCP=healthcare professional; ICU=intensive care unit; IVIg=intravenous immunoglobulin; MenACWY=meningococcal serogroups ACWY; MenB-4C=4-component meningococcal group B; MenB-FHbp=meningococcal serogroup B factor H binding protein; MG-ADL=Myasthenia Gravis Activities of Daily Living; MGFA=Myasthenia Gravis Foundation of America; NSIST=non-steroidal immunosuppressive therapy; PLEX=plasma exchange; QMG=Quantitative Myasthenia Gravis; SCIg=subcutaneous immunoglobulin.

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## Patient Support

If you have questions about getting your ZILBRYSQ patients started in the ONWARD™ Patient Support Program, please visit ucbONWARD.com to access resources for healthcare professionals or contact your Rare Reimbursement Executive for assistance.

ONWARD
SUPPORT FOR RARE DISEASE MADE SIMPLE

ONWARD is provided as a service of UCB and is intended to support the appropriate use of UCB medicines. ONWARD may be amended or canceled at any time without notice. Some program and eligibility restrictions may apply.

## IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING

### WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

**Life-threatening and fatal meningococcal infections have occurred in patients treated with complement inhibitors; ZILBRYSQ is a complement inhibitor. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.**

- **Complete or update meningococcal vaccination (for serogroups A, C, W, and Y, and serogroup B) at least 2 weeks prior to administering the first dose of ZILBRYSQ, unless the risk of delaying therapy outweighs the risk of developing a meningococcal infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccinations in patients receiving a complement inhibitor.**
- **Persons receiving ZILBRYSQ are at increased risk for invasive disease caused by *N. meningitidis*, even if they develop antibodies following vaccination. Monitor patients for signs of meningococcal infections and evaluate immediately if infection is suspected.**

**Because of the risk of serious meningococcal infections, ZILBRYSQ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called ZILBRYSQ REMS.**

### CONTRAINDICATIONS

ZILBRYSQ is contraindicated in patients with unresolved *Neisseria meningitidis* infection.

### WARNINGS AND PRECAUTIONS

**Serious Meningococcal Infections**

Life-threatening and fatal meningococcal infections have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors; ZILBRYSQ is a complement inhibitor. The use of ZILBRYSQ increases a patient's susceptibility to serious and life-threatening meningococcal infections (septicemia and/or meningitis) caused by any serogroup, including non-groupable strains.

Complete or update meningococcal vaccination (for both serogroups A, C, W, and Y [MenACWY] and serogroup B [MenB]) at least 2 weeks prior to administering the first dose of ZILBRYSQ, according to current ACIP recommendations for meningococcal vaccinations in patients receiving a complement inhibitor.

If urgent ZILBRYSQ therapy is indicated in a patient who is not up to date with both MenACWY and MenB vaccines according to ACIP recommendations, administer meningococcal vaccine(s) as soon as possible and provide the patient with antibacterial drug prophylaxis.

Closely monitor patients for early signs and symptoms of meningococcal infection and evaluate patients immediately if infection is suspected. Withhold administration of ZILBRYSQ in patients who are undergoing treatment for meningococcal infection until the infection is resolved.

### ZILBRYSQ REMS

Due to the risk of meningococcal infections, ZILBRYSQ is available only through a restricted program under a REMS called ZILBRYSQ REMS.

Under the ZILBRYSQ REMS, prescribers must enroll in the program. Prescribers must counsel patients about the risk of meningococcal infection, provide the patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccines. Additional information on the REMS requirements is available at www.ZILBRYSQREMS.com or 1-877-414-8353.

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## IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (cont'd)

## WARNINGS AND PRECAUTIONS (cont'd)

**Other Infections**

ZILBRYSQ blocks terminal complement activation; therefore, patients may have increased susceptibility to infections, especially with encapsulated bacteria, such as infections caused by *Neisseria meningitidis* but also *Streptococcus pneumoniae*, *Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*. Administer vaccinations for the prevention of *Streptococcus pneumoniae* and *Haemophilus influenzae type b* (Hib) infections according to ACIP guidelines. Persons receiving ZILBRYSQ are at increased risk for infections due to these bacteria, even after vaccination.

**Pancreatitis And Other Pancreatic Conditions**

Pancreatitis and pancreatic cysts have been reported in patients treated with ZILBRYSQ. Patients should be informed of this risk before starting ZILBRYSQ. Obtain lipase and amylase levels at baseline before starting treatment with ZILBRYSQ. Discontinue ZILBRYSQ in patients with suspected pancreatitis and initiate appropriate management until pancreatitis is ruled out or has resolved.

## ADVERSE REACTIONS

In a placebo-controlled study, the most common adverse reactions (reported in at least 10% of gMG patients treated with ZILBRYSQ) were injection site reactions, upper respiratory tract infections, and diarrhea.

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**For more information about ZILBRYSQ, visit ZILBRYSQhcp.com.**

**For additional information, contact UCBCares® at 1-844-599-CARE (2273).**

ACIP=Advisory Committee on Immunization Practices; gMG=generalized myasthenia gravis.

**References: 1.** ZILBRYSQ [prescribing information]. Smyrna, GA: UCB, Inc. **2.** Barnett C, Herbelin L, Dimachkie MM, Barohn RJ. Measuring clinical treatment response in myasthenia gravis. *Neurol Clin.* 2018;36(2):339-353. **3.** Howard JF, Bresch S, Genge A, et al. Safety and efficacy of zilucoplan in patients with generalised myasthenia gravis (RAISE): a randomised, double-blind, placebo-controlled, phase 3 study, *Lancet Neurol.* 2023;22(5):395-406. **4.** Farmakidis C, Pasnoor M, Dimachkie MM, Barohn RJ. Treatment of myasthenia gravis. *Neurol Clin.* 2018;36(2):311-337. **5.** Menon D, Bril V. Pharmacotherapy of generalized myasthenia gravis with special emphasis on newer biologicals. *Drugs.* 2022;82(8):865-887. **6.** ULTOMIRIS [prescribing information]. Boston, MA: Alexion Pharmaceuticals, Inc. **7.** VYVGART [prescribing information]. Boston, MA: argenx US, Inc. **8.** VYVGART Hytrulo [prescribing information]. Boston, MA: argenx US, Inc. **9.** RYSTIGGO [prescribing information]. Smyrna, GA: UCB, Inc. **10.** Mbaeyi SA, Bozio CH, Duffy J, et al. Meningococcal vaccination: recommendations of the Advisory Committee on Immunization Practices, United States, 2020. *MMWR Recomm Rep.* 2020;69(9):1-41. doi:10.15585/mmwr.rr6909a1. **11.** Meriggioli MN, Sanders DB. Autoimmune myasthenia gravis: emerging clinical and biological heterogeneity. *Lancet Neurol.* 2009;8(5):475-490.


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