Medical Benefit Drug Policy

Uplizna (inebilizumab-cdon) injection, for intravenous use

Policy Number: MC/PC 048
Effective Date: August 1, 2026

Instructions for Use

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Related Policies

- N/A

Coverage Rationale

Generalized Myasthenia Gravis (gMG)

For initial coverage of Uplizna (inebilizumab-cdon) for Generalized Myasthenia Gravis (gMG), the following will be required:

- Diagnosis of generalized myasthenia gravis (gMG) **and**
- One of the following:
  - Both of the following:
    - Patient is anti-acetylcholine receptor (AChR) antibody positive **and**
    - One of the following:
      - Trial and failure, contraindication, or intolerance to two immunosuppressive therapies (e.g., glucocorticoids [e.g., prednisone], azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus) **or**
      - Both of the following:
        - Trial and failure, contraindication, or intolerance to one immunosuppressive therapy (e.g., glucocorticoids [e.g., prednisone], azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus) **and**
        - Trial and failure, contraindication, or intolerance to one of the following:
          - Chronic plasmapheresis or plasma exchange (PE)
          - Intravenous immunoglobulin (IVIG)
          - Rituximab **or**
  - Both of the following:
    - Patient is anti-muscle-specific tyrosine kinase (MuSK) antibody positive **and**
    - One of the following:
      - Trial and failure, contraindication, or intolerance to two immunosuppressive therapies (e.g., glucocorticoids [e.g., prednisone], azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus) **or**

- Both of the following:
    - Trial and failure, contraindication, or intolerance to one immunosuppressive therapy (e.g., glucocorticoids [e.g., prednisone], azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus) **and**
    - Trial and failure, contraindication, or intolerance to one of the following:
        - Chronic plasmapheresis or plasma exchange (PE)
        - Intravenous immunoglobulin (IVIG)
        - Rituximab **and**
- Prescribed by or in consultation with a neurologist **and**
- Requested medication is not being used in combination with any one of the following for the indication of Generalized Myasthenia Gravis (gMG):
    - Neonatal Fc Receptor (FcRn) blocker (e.g., Imaavy, Rystiggo)
    - Complement inhibitor (e.g., Soliris, Ultomiris, Zilbrysq)
    - Immune globulin (e.g., IVIG)

For reauthorization coverage of Uplizna (inebilizumab-cdon) for Generalized Myasthenia Gravis (gMG) the following will be required:

- Patient demonstrates positive clinical response to therapy **and**
- Requested medication is not being used in combination with any one of the following for the indication of Generalized Myasthenia Gravis (gMG):
    - Neonatal Fc Receptor (FcRn) blocker (e.g., Imaavy, Rystiggo)
    - Complement inhibitor (e.g., Soliris, Ultomiris, Zilbrysq)
    - Immune globulin (e.g., IVIG)

Immunoglobulin G4-Related Disease (IgG4-RD)

For initial coverage of Uplizna (inebilizumab-cdon) for Immunoglobulin G4-Related Disease (IgG4-RD), the following will be required:

- Diagnosis of Immunoglobulin G4-Related Disease (IgG4-RD) **and**
- Presence of disease involving two or more organ systems or sites (e.g., Pancreas, Submandibular gland, Lymph node(s), Kidneys, Bile Duct, Lungs or Lacrimal glands) **and**
- One of the following:
    - Patient is currently being treatment with a glucocorticoid (e.g., prednisone, methylprednisolone) **or**
    - Trial and failure, contraindication or intolerance to a glucocorticoid (e.g., prednisone, methylprednisolone).

For reauthorization coverage of Uplizna (inebilizumab-cdon) for Immunoglobulin G4-Related Disease (IgG4-RD), the following will be required:

- Presence of positive clinical response to therapy

Neuromyelitis Optica Spectrum Disorder (NMOSD)

For initial coverage of Uplizna (inebilizumab-cdon) for Neuromyelitis Optica Spectrum Disorder (NMOSD), the following will be required:

- Diagnosis of neuromyelitis optica spectrum disorder (NMOSD) **and**
- Patient is anti-aquaporin-4 (AQP4) antibody positive **and**
- Prescribed by or in consultation with one of the following:
    - Neurologist
    - Ophthalmologist

For reauthorization coverage of Uplizna (inebilizumab-cdon) for Neuromyelitis Optica Spectrum Disorder (NMOSD), the following will be required:

- Presence of positive clinical response to therapy

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1823	Injection, inebilizumab-cdon, 1 mg

ICD-10 Code	Description
G36.0	Neuromyelitis optica [Devic]
D89.84	Immunoglobulin G4-Related Disease (IgG4-RD)
G70	Myasthenia gravis and other myoneural disorders
G70.0	Myasthenia gravis
G70.00	Myasthenia Gravis without (acute exacerbation)
G70.01	Myasthenia Gravis with (acute exacerbation)

Background

Inebilizumab-cdon is a CD19-directed humanized afucosylated IgG1 monoclonal antibody. The precise mechanism by which inebilizumab-cdon exerts its therapeutic effects in NMOSD, IgG4-RD and generalized myasthenia gravis (gMG) is unknown but is presumed to involve binding to CD19, a cell surface antigen presents on pre-B and mature B lymphocytes. Following cell surface binding to B lymphocytes, inebilizumab-cdon results in antibody-dependent cellular cytolysis (Clinical Pharmacology 2026).

Clinical Evidence

Generalized Myasthenia Gravis (gMG)

- In a randomized, double-blind, multicenter, placebo-controlled trial, inebilizumab demonstrated efficacy in gMG in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle specific tyrosine kinase (MuSK) antibody positive. The treatment period was 52 weeks for the anti-AChR antibody positive population and 26 weeks for the anti-MuSK antibody positive population and involved a total of 238 patients randomized in a 1:1 ratio to receive inebilizumab or placebo. 190 individuals (80%) were anti-AChR antibody positive and 48 individuals (20%) were anti-MuSK antibody positive. The primary efficacy endpoint was the change from baseline in the Myasthenia Gravis-Activities of Daily Living (MG-ADL) with a baseline score between 6 and 10 (with > 50% of this score attributed to non-ocular items) or an MG-ADL score ≥ 11. Subjects also had Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV and a quantitative Myasthenia Gravis (QMG) score of ≥ 11. The QMG score is a 13-item categorical grading system that assesses muscle weakness. Each item is assessed on a 4-point scale where a score of 0 represents no weakness and a

score of 3 represents severe weakness. A total possible score ranges from 0 to 39, where higher scores indicate more severe impairment.

- The secondary endpoint was the change from baseline in the QMG score at week 26 in the overall population.
- A statistically significant difference favoring inebilizumab was observed in the mean change from baseline in MG-ADL total score -4.2 points in the UPLIZNA-treated group compared to (-2.2 points for placebo, difference of -1.9, 95% CI: -2.9, -1.0; p-value < 0.0001). In the secondary endpoint, a statistically significant difference favoring inebilizumab was observed in the mean change from baseline in QMG total score in the overall population (-4.8 points in the inebilizumab-treated group compared to -2.3 for placebo, difference -2.5, 95% CI: -3.8, -1.2; p-value = 0.0002). The primary endpoint was significant in the individual subpopulations for those who were anti-AChR antibody positive and anti-MuSK antibody positive. The secondary endpoint of QMG score was significantly different in the individual subpopulation for those who were anti-AChR antibody positive but did not meet statistical significance in the anti-MuSK antibody positive subpopulation. (Uplizna Prescribing Information)

IgG4-RD

Inebilizumab was approved for the treatment of IgG4-RD based on a randomized trial of 135 patients with IgG4-RD that randomly assigned patients to receive inebilizumab (300 mg intravenous infusions on days 1 and 15 and week 26) or placebo (Stone et al 2025).

- At the end of 52 weeks of observation, patients treated with inebilizumab had fewer flares than patients treated with placebo (10 versus 60 percent). Patients assigned to inebilizumab were also more likely to have a flare-free, glucocorticoid-free, complete remission than patients treated with placebo (odds ratio 5.0).

NMOSD

The N-MOmentum trial was a 28-week, Phase 2/3, double-blind, placebo controlled, multi-center, randomized controlled trial that evaluated the efficacy and safety of inebilizumab in patients with NMOSD (Cree et al 2019).

- A total of 230 adults with AQP4-IgG seropositive (n = 213) or seronegative (n = 17) NMOSD were randomized in a 3:1 fashion to inebilizumab 300 mg IV on Days 1 and 15 then 300 mg IV every 6 months or to placebo; no other immunosuppressants were permitted. All patients received oral prednisone or equivalent for the first 14 days followed by a 7-day taper. At baseline, the mean Expanded Disability Status Scale (EDSS) scores were 3.8 for the inebilizumab group and 4.2 for the placebo group.
- For the primary endpoint of time to first adjudicated relapse on or before Day 197, inebilizumab significantly reduced the risk of an NMOSD relapse by 73% compared with placebo in the overall population (HR, 0.272; 95% CI, 0.150 to 0.496; p < 0.0001). Relapses occurred in 12.1% and 39.3% of patients in the inebilizumab and placebo groups, respectively. In the AQP4-IgG seropositive group, inebilizumab significantly reduced the percentage of patients with relapses (11.2% vs 42.3%; HR, 0.227; 95% CI, 0.121 to 0.423; p < 0.0001). No difference in relapses was seen in the AQP4-IgG seronegative group with inebilizumab (23.1% vs 0%); the placebo group had a total of 4 patients and no reported relapses. The secondary endpoint, number of patients with worsening from baseline in EDSS, favored inebilizumab (16% vs 34%; HR, 0.370; 95% CI, 0.185 to 0.739; p = 0.0049); however, the FDA found that the EDSS findings were uninterpretable due to the variable observation periods between patients inherent in the time-to-event trial design (which also resulted in a significant amount of missing data), a consistent lack of relapse confirmation visits at an acceptable interval, and the protocol's inadequate approach to accounting for the impact of an acute relapse on EDSS changes from baseline (Uplizna FDA Summary Review 2020).
- The secondary endpoint, number of patients with worsening from baseline in EDSS, favored inebilizumab (16% vs 34%; HR, 0.370; 95% CI, 0.185 to 0.739; p = 0.0049); however, the FDA found that the EDSS findings were uninterpretable due to the variable observation periods between patients inherent in the time-to-event trial design (which also resulted in a significant amount of missing data), a consistent lack of relapse confirmation visits at an acceptable interval, and the protocol's inadequate approach to accounting for the impact of an acute relapse on EDSS changes from baseline.

Clinical Guidelines

IgG4-RD

The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) have developed comprehensive guidelines published in 2019 for the classification and treatment of IgG4-related disease (IgG4-RD). The treatment guidelines emphasize that for initial therapy, glucocorticoids are used as first-line treatment for inducing remission. The maintenance therapy is to immunosuppressive agents like rituximab may be used for long-term management. These guidelines have not been updated to include inebilizumab (Wallace et al 2019).

MG
International consensus guidance for the management of MG recommends pyridostigmine as initial symptomatic treatment in most patients with MG. Corticosteroids and/or other immunosuppressive therapy (e.g., azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus) may be used in patients who have not met treatment goals after an adequate trial of pyridostigmine. Patients with refractory MG may require chronic IVIG or PE, cyclophosphamide, or rituximab; complement inhibition with eculizumab should be considered in severe refractory MG (Narayanaswami et al 2021).

NMOSD
The Neuromyelitis Optica Study Group (NEMOS) recommends eculizumab, ravulizumab, inebilizumab, rituximab, or satralizumab for first-line treatment and azathioprine, mycophenolate mofetil, or tocilizumab for second-line treatment. Third-line therapy may include a combination of a monoclonal antibody plus a classical immunosuppressive therapy (e.g., azathioprine or mycophenolate mofetil) (Kumpfel et al 2024).

The European Federation of Neurological Societies (EFNS) guideline for the prevention of NMO relapses recommends oral azathioprine plus prednisone or rituximab as first-line therapy (Sellner et al 2010). Other groups recommend mycophenolate mofetil plus prednisone as an additional first-line choice. Other treatment options include oral methotrexate, mitoxantrone, IV cyclophosphamide, IVIG, or PLEX (Kimbrough et al 2012, Sellner et al 2010).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Uplizna is a CD19-directed cytolytic antibody indicated for the treatment of:

- Neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive. Immunoglobulin G4-related disease (IgG4-RD) in adult patients.
- Generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle specific tyrosine kinase (MuSK) antibody positive

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Policy History/Revision Information

Date	Summary of Changes
12/13/2023	Approved by OptumRx P&T Committee
6/19/2024	Annual review. Updated references.
6/18/2025	Annual review. Added Immunoglobulin G4-Related Disease (IgG4-RD) indication for Uplizna, clinical content, and references.
06/17/2026	Annual review. Added Generalized myasthenia gravis (gMG) indication for Uplizna. Updated background, guideline section, and references.

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. The insurance reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

OptumRx may also use tools developed by third parties to assist us in administering health benefits. OptumRx Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

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Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:
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- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If *you* need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If *you* believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, *you* can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

You can file a *grievance* in person or by mail, fax, or email. If *you* need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help *you*.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

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Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1-800-332-6501 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف1-800-332-6501(رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: _यान द_: य_द आप ि हंदी बोलते ह_ तो आपके ि लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_।1-800-332-6501 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

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Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer1-800-332-6501 (TTY: 711).

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Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al1-800-332-6501 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

Traditional Chinese: 注意：如果您使用繁體中文， 您可以免費獲得語言援助服務。請 致電 1-800-332-6501 (TTY: 711)

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).