# Medical Policy

**Utilization Management and Clinical Medical Policy**

| Policy Name: | Policy Number: | Scope: | Origination Date: | Effective Date: |
|---|---|---|---|---|
| **Inebilizumab-cdon (Uplizna®)** | **MP-RX-FP-98-23** | ☒ **MMM MA**<br>☒ **MMM MultiHealth** | 11/30/2023 | 03/24/2026 |
| | | | **Last Review Date:** | **Frequently Revision:** |
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## Service Category:

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Other: Part B Drugs

## Service Description:

This document addresses the use of Inebilizumab-cdon (Uplizna®), a drug approved by the Food and Drug Administration (FDA) for the treatment of neuromyelitis optica spectrum disorder (NMSOD), immunoglobulin G4-related disease (IgG4-RD, and generalized myasthenia gravis (gMG).

## Background Information:

This document addresses the use of Uplizna (inebilizumab-cdon), a CD19-directed cytolytic, humanized monoclonal antibody that depletes CD19-positive B cells (including plasmablasts and some antibody-secreting cell populations) through cytolytic mechanisms, thereby reducing pathogenic autoantibody activity across multiple immune-mediated diseases.

*Neuromyelitis optica spectrum disorder (NMOSD)*

Uplizna is indicated for the treatment of NMOSD in adult patients who are anti–aquaporin-4 (AQP4) antibody positive. NMOSD is a severe autoimmune disease of the central nervous system caused by immune-mediated demyelination and axonal damage predominantly targeting optic nerves and spinal cord. This damage is triggered by antibodies against aquaporin-4 (AQP4), which are considered biomarkers for NMOSD. The disease is characterized by clusters of attacks of optic neuritis or transverse myelitis with partial recovery between attacks. Progressive visual impairment and paralysis may be caused by repeated attacks, so long-term prevention therapy should be offered to all patients. Treatment may include off label immunosuppressive therapies including rituximab, azathioprine, and mycophenolate. Three agents are FDA approved for NMOSD: Uplizna, Enspryng and Soliris. Uplizna has a unique mechanism of action by causing antibody-dependent cellular cytolysis of B-cells. It is given via intravenous infusion once every 6 months.

*Immunoglobulin G4-related disease (IgG4-RD)*

Uplizna is indicated for the treatment of IgG4-RD in adult patients. IgG4-RD is a chronic, immune-mediated fibroinflammatory condition that may involve one or multiple organs (e.g., pancreas, biliary tree, salivary/lacrimal glands, retroperitoneum, kidneys, lungs) and can lead to progressive tissue fibrosis and organ dysfunction if inadequately controlled. Initial disease control has historically relied on systemic glucocorticoids; however, relapse during tapering and cumulative steroid toxicity are common, and B-cell depletion has been an established steroid-sparing strategy in relapsing/refractory disease. In a randomized, placebo-controlled phase 3 trial, CD19-targeted B-cell depletion with inebilizumab reduced IgG4-RD flares and increased the likelihood of flare-free complete remission at 1 year, supporting its role as a targeted maintenance approach.

*Generalized myasthenia gravis (gMG)*

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Uplizna is indicated for the treatment of gMG in adult patients who are anti–acetylcholine receptor (AChR) or anti–muscle-specific tyrosine kinase (MuSK) antibody positive. gMG is an autoimmune disorder of the neuromuscular junction characterized by fluctuating, fatigable weakness that may affect ocular, bulbar, limb, and respiratory muscles, commonly driven by pathogenic antibodies (AChR or MuSK). Chronic immunotherapy is typically used to reduce relapse/exacerbations and steroid exposure, including glucocorticoids and steroid-sparing immunosuppressants; more recently, targeted biologic therapies have expanded options for appropriate patients. In a phase 3 randomized controlled trial, inebilizumab demonstrated clinical benefit in antibody-positive gMG with a protocolized steroid taper, supporting FDA approval for this population. As with the other approved indications, Uplizna is administered by intravenous infusion with loading doses followed by maintenance dosing at defined intervals per prescribing information.

Uplizna causes B-cell depletion and can increase the risk of infection, as it is an immunosuppressant. It is contraindicated in those with active hepatitis B (HBV) infection and those with active or untreated latent tuberculosis (TB); patients should be assessed for active infection prior to each infusion, and premedication (corticosteroid, antihistamine, antipyretic) is recommended to reduce infusion-related reactions. Prior to initiation of therapy, all individuals should receive HBV screening, TB screening, and quantitative serum immunoglobulin testing. Individuals should also receive all immunizations according to guidelines prior to initiating therapy.

**Approved Indications**

A. Neuromyelitis Optica Spectrum Disorder (NMSOD) in adults' patients who are anti-aquaporin-4 (AQP4) antibody positive.
B. Immunoglobulin G4-related disease (IgG4-RD) in adult patients.
C. Generalized myasthenia gravis (gMG) in adult patients who are antiacetylcholine receptor (AChR) or anti-muscle specific tyrosine kinase (MuSK) antibody positive.

**Other Uses**

A. N/A

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## Medical Necessity Guidelines:

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.

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

Inebilizumab-cdon (Uplizna®)

### A. Criteria For Initial Approval

Requests for initiation of therapy with Uplizna (inebilizumab-cdon) for neuromyelitis optica spectrum disorder (NMOSD) may be approved if the following criteria are met:

i. Individual is 18 years of age or older; **AND**
ii. Individual has a diagnosis of neuromyelitis optica spectrum disorder (NMOSD); **AND**
iii. Documentation is provided that NMOSD is seropositive as confirmed by the presence of anti-aquaporin-4 (AQP4) antibodies; **AND**
iv. Documentation is provided that individual has a history of at least 1 acute attack or relapse in the last 12 months prior to initiation of therapy;

**OR**

v. Documentation is provided that individual has a history of at least 2 acute attacks or relapses in the last 24 months prior to initiation of therapy (Cree 2019); **AND**
vi. If initiating therapy, individual has been evaluated and tested for Hepatitis B Virus (HBV) infection and latent tuberculosis infection

Requests for initiation of therapy with Uplizna (inebilizumab-cdon) for Immunoglobulin G4-related disease (IgG4-RD) may be approved if the following criteria are met:

i. Individual is 18 years of age or older; **AND**
ii. Individual has a diagnosis of Immunoglobulin G4-related disease (IgG4-RD); **AND**
iii. Documentation is provided that individual is experiencing or recently experienced IgG4-RD flare requiring initiation or continuation of glucocorticoid treatment; **AND**
iv. Individual has a history of IgG4-RD affecting at least 2 organ systems/sites; **AND**
v. If initiating therapy, individual has been evaluated and tested for Hepatitis B Virus (HBV) infection and latent tuberculosis infection.

Requests for initiation of therapy with Uplizna (inebilizumab-cdon) for generalized myasthenia gravis (gMG); may be approved if the following criteria are met:

i. Individual is 18 years of age or older; **AND**
ii. Individual has a diagnosis of generalized myasthenia gravis (gMG); **AND**

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iii. Documentation is provided that individual is seropositive with autoantibodies against acetylcholine receptor (AChR) or muscle-specific tyrosine kinase (MuSK); **AND**
iv. Documentation is provided that individual is on a stable dose of a corticosteroid and/or a specified non-steroidal immunosuppressive therapy (or combination therapy) prior to initiation; **AND**
v. If initiating therapy, individual has been evaluated and tested for Hepatitis B Virus (HBV) infection, latent tuberculosis (TB) infection, and quantitative serum immunoglobulins

**B. Criteria For Continuation of Therapy**

Requests for continued use of Uplizna (inebilizumab-cdon) in NMOSD may be approved if the following criteria are met:

i. Individual has a diagnosis of neuromyelitis optica spectrum disorder (NMOSD); **AND**
ii. Documentation is provided that NMOSD is seropositive as verified by the presence of anti-aquaporin-4 (AQP4) antibodies prior to initiation; **AND**
iii. Documentation is provided that individual has experienced a clinical response (for example, a reduction in the frequency of relapse).

Requests for continued use of Uplizna (inebilizumab-cdon) for IgG4-RD may be approved if the following criteria are met:

i. Individual has a diagnosis of neuromyelitis optica spectrum disorder (NMOSD); **AND**
ii. Documentation is provided that individual has experienced a clinical response (for example, a reduction in the frequency of disease flares or reduction in need for glucocorticoid treatment).

Requests for continued use of Uplizna (inebilizumab-cdon) for generalized myasthenia gravis (gMG) may be approved if the following criteria are met:

i. Individual has a diagnosis of generalized myasthenia gravis (gMG); **AND**
ii. Documentation is provided that individual is seropositive with autoantibodies against acetylcholine receptor (AChR) or muscle-specific tyrosine kinase (MuSK) prior to initiation; **AND**
iii. Documentation is provided that individual has experienced a clinical response (for example, improvement in myasthenia gravis symptom severity or functional status as measured by MG-ADL and/or QMG, reduction in frequency of exacerbations, and/or reduction in need for corticosteroids or rescue therapy).

**C. Conditions not Covered**

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Individual is using in combination with rituximab, eculizumab, satralizumab, or ravulizumab;

**OR**

ii. Individual has active hepatitis B (HBV) infection [repeat testing not required for continuation of therapy];

**OR**

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iii. Individual has active or untreated latent tuberculosis [repeat testing not required for continuation of therapy];

**OR**

iv. When the above criteria are not met and for all other indications.

**D. Authorization Duration**

i. Initial Approval Duration: 1 year

ii. Reauthorization Approval Duration: 1 year

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## Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

*Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.*

| Drug | Recommended Dosage | Limit |
|---|---|---|
| Uplizna (inebilizumab-cdon) 100 mg/10 mL vial | • Initial dose: 300 mg intravenous infusion followed two weeks later by a second 300 mg intravenous infusion<br>• Subsequent doses (starting 6 months from the first infusion): single 300 mg intravenous infusion every 6 months | • 3 vials (300 mg) every 6 months |
| **Exceptions** | | |
| • May approve 3 (three) additional vials in the first two weeks of treatment. The total allowed quantity for initiation of therapy is 300 mg once followed by 300 mg two weeks later.<br>• Hepatitis B virus, quantitative serum immunoglobulins, and tuberculosis screening is required before the first dose.<br>• Prior to every infusion: o<br>o Determine if there is an active infection<br>o Premedicate with a corticosteroid, an antihistamine, and an antipyretic. | | |

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## Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. 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.

**ICD-10 Diagnostic Codes:**

| Codes | Description |
|---|---|
| D89.84 | IgG4-related disease [Immunoglobulin G4-related disease] |
| G36.0 | Neuromyelitis optica [Devic] |
| G70.00-G70.01 | Myasthenia gravis |

**HCPCS Codes:**

| Codes | Description |
|---|---|
| J1823 | Injection, inebilizumab-cdon, 1 mg [Uplizna] |

## Reference Information:


1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2022. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: September 30, 2022.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
5. Cree BAC, Bennett JL, Kim HJ, et al. Inebilizumab for the treatment of neuromyelitis optica spectrum disorder (N-MOmentum): a double-blind, randomised placebo-controlled phase 2/3 trial. Lancet. 2019 Oct 12;394(10206):1352-1363. doi: 10.1016/S0140- 6736(19)31817-3. Epub 2019 Sep 5.
6. Amgen Inc. Uplizna (inebilizumab-cdon) injection, for intravenous use: Full Prescribing Information. Accessed February 9, 2026. https://www.pi.amgen.com/united_states/uplizna/uplizna_fpi_english.pdf?utm_source=chatgpt.com
7. UpToDate. Chronic immunotherapy for myasthenia gravis. Accessed February 9, 2026. (uptodate.com)
8. UpToDate. Treatment and prognosis of IgG4-related disease. Accessed February 9, 2026. (uptodate.com)


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.


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## Policy History:

| Type of Review | Summary of Changes | P&T Approval Date | UM/CMPC Approval Date |
|---|---|---|---|
| **Focus Review** | Updated Background Information and Approved indications to include new indications for Immunoglobulin G4-related disease and myasthenia gravis. Added Initial and Continuation criteria for myasthenia gravis. Updated Continuation Criteria. Added recommended dosing to the table and screening/ premedication requirements. Coding Reviewed: Added ICD-10-CM G70.00-G70.01and removed G36.1-G36.9. Updated references. Administrative update to incorporate new template. | 3/17/2026 | 3/24/2026 |
| **Annual Review** | Update clinical criteria with new indication in Immunoglobulin G4-related disease. Coding Reviewed: Added ICD-10-CM D89.84 and removed G36.1-G36.9. | 10/31/2025 | 11/10/2025 |
| **Annual Review** | Update infectious disease testing requirements per label, wording and formatting updates. Coding Reviewed: No changes. | 3/14/2025 | 4/2/2025 |
| **Policy Inception** | Elevance Health's Medical Policy adoption. | N/A | 11/30/2023 |