Policy Number	**RX501.127**
Policy Effective Date	**5/7/26**

Inebilizumab-cdon

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Related Policies (if applicable)
None

Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of care developed by: nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of American Medical Association, New England Journal of Medicine, and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated, and coverage is not required for non-formulary drugs.

Coverage

Neuromyelitis Optica Spectrum Disorder
Inebilizumab-cdon (Uplizna®) **may be considered medically necessary** when **ALL** the following criteria are met:

- Individual is 18 years of age or older; AND
- Has a diagnosis of neuromyelitis optica spectrum disorder; AND
- Is anti-aquaporin-4 antibody seropositive; AND
- Has a history of at least one relapse requiring rescue therapy during the previous 12 months **OR** at least two relapses requiring rescue therapy during the previous 24 months.

Immunoglobulin G4-Related Disease
Inebilizumab-cdon (Uplizna) **may be considered medically necessary** when **ALL** the following criteria are met:

- Individual is 18 years of age or older; AND
- Has a diagnosis of newly diagnosed or recurrent IgG4-RD that required glucocorticoid treatment at screening; AND
- Has a confirmed history of organ involvement at any time in the course of disease.

Generalized Myasthenia Gravis
Inebilizumab-cdon (Uplizna) **may be considered medically necessary** when **ALL** the following criteria are met:

- Individual is 18 years of age or older; AND
- Has a diagnosis of generalized myasthenia gravis; AND
- Is anti-acetylcholine receptor or anti-muscle specific tyrosine kinase antibody positive; AND
- Myasthenia Gravis Foundation of America Clinical Classification Class II to IV; AND
- Myasthenia Gravis-Activities of Daily Living (MG-ADL) score between 6 and 10 with > 50% of this score attributed to non-ocular items **or** an MG-ADL score ≥ 11; AND
- On a stable dose of a corticosteroid or a specified non-steroidal immunosuppressive therapy, or a combination of both.

Inebilizumab-cdon (Uplizna) **is considered experimental, investigational and/or unproven** for all other non-Food and Drug Administration indications.

Policy Guidelines

Myasthenia Gravis Foundation of America Clinical Classification
In 1997, the Medical Scientific Advisory Board of the MGFA formed a task force to address the need for universally accepted classifications, grading systems, and analytic methods for the management of individuals undergoing therapy and for use in therapeutic research trials. As a result, the MGFA Clinical Classification was created. This classification divides myasthenia gravis into 5 main classes and several subclasses, as follows (8):

- Class I: Any ocular muscle weakness; may have weakness of eye closure. All other muscle strength is normal.
- Class II: Mild weakness affecting muscles 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 muscles 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 muscles other than ocular muscles; may also have ocular muscle weakness of any severity.
  - IVa. Predominantly affecting limb, axial muscles, or both. 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 as intubation, with or without mechanical ventilation, except when employed during routine postoperative management. The use of a feeding tube without intubation places the individual in class IVb.

Myasthenia Gravis-Activities of Daily Living Scale

The MG-ADL Scale was developed in the late 1990s to assess the status of symptoms and activities in MG. (13) It is an 8-item, patient reported questionnaire that can be completed in 2–3 minutes with no need for specialized equipment or training. See Table 1.

Table 1. MG Activities of Daily Living Profile

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 choking necessitating changes in diet	Gastric tube
Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependent
Impairment of ability to brush teeth or comb hair	None	Extra effort, but no rest periods needed	Rest periods needed	Cannot do one of these functions
Impairment of ability to arise from a chair	None	Mild, sometimes uses arms	Moderate, always uses arms	Severe, requires assistance
Double vision	None	Occurs, but not daily	Daily, but not constant	Constant
Eyelid droop	None	Occurs, but not daily	Daily, but not constant	Constant

Each activity is scored 0-3; and all scores are totaled to represent the overall MG-ADL score.

Description

Neuromyelitis Optica Spectrum Disorder (2)
Neuromyelitis optica spectrum disorder (NMOSD, previously known as Devic disease or neuromyelitis optica) is an inflammatory disorder of the central nervous system characterized by severe, immune-mediated demyelination and axonal damage predominately targeting the optic nerves and spinal cord. NMOSD can be distinguished from multiple sclerosis and other central nervous system inflammatory disorders by the presence of the disease-specific serum NMO-immunoglobulin G antibody that selectively binds to the aquaporin-4 antibody, which plays a direct role in the pathogenesis of NMOSD. AQP4, the target antigen of NMO-IgG, is a water channel protein abundant in spinal cord gray matter, periaqueductal and periventricular regions, and astrocytic foot processes at the blood-brain barrier.

The incidence of NMOSD in women is up to 10 times higher than in men. The median age of onset is 32 to 41 years, but cases are described in children and older adults. Comparatively, the medical age of onset for multiple sclerosis is 24 years.

Hallmark features of NMOSD include acute attacks of bilateral or rapidly sequential optic neuritis (leading to severe visual loss) or transverse myelitis (often causing limb weakness, sensory loss, and bladder dysfunction) with a typically relapsing course. Other suggestive symptoms include episodes of intractable nausea, vomiting, hiccups, excessive daytime somnolence or narcolepsy, reversible posterior leukoencephalopathy syndrome, neuroendocrine disorders, and (in children) seizures. While no clinical features are disease-specific, some are highly characteristic.

NMOSD has a relapsing course in 90 percent or more of cases. In some patients, optic neuritis and transverse myelitis occur concurrently; in others, clinical episodes are separated by a variable time delay. Relapse occurs within the first year following an initial event in 60 percent of patients and within three years in 90 percent. As a rule, severe residual deficits follow initial and subsequent attacks, leading to rapid development of disability due to blindness and paraplegia within five years. Unlike multiple sclerosis, a secondary progressive phase of the disease is rare, and disability is associated with specific attacks. Patients with cerebral presentations may have continued brain attacks without involvement of the optic nerves or spinal cord.

Immunoglobulin G4-Related Disease (3)
Immunoglobulin G4-related disease is an immune-mediated fibroinflammatory condition that is capable of affecting multiple organs. Organs affected by IgG4-RD share pathologic, serologic, and clinical features.

In a 2023 study, the overall incidence of IgG4-RD was estimated to be 0.78 to 1.39 per 100,000 person-years.

Immunoglobulin G4-related disease can involve one or multiple organs, and manifestations of this disease have been demonstrated in nearly every organ system. Patients often feel well at the time of diagnosis and often present with subacute development of a mass in the affected organ or diffuse enlargement of an organ. Lymphadenopathy is common, but patients are generally afebrile. However, symptoms of asthma or allergy are present in approximately 40 percent of patients. Additionally, patients with multiorgan disease often lose substantial amounts of weight (e.g., 20 to 30 pounds), which may be due to IgG4-related autoimmune pancreatitis (AIP).

IgG4-RD is often recognized incidentally based on a radiologic finding or histopathologic examination of a tissue specimen. Imaging studies (e.g., computed tomography, magnetic resonance imaging [MRI], positron emission tomography may demonstrate diffuse or focal organ lesions (usually a mass or swelling). Clinicians should be alert to the possibility that IgG4-RD can mimic some autoimmune rheumatic diseases such as Sjögren's disease, systemic lupus erythematosus, and granulomatosis with polyangiitis, as well as a number of other conditions.

Myasthenia Gravis

Myasthenia gravis is an acquired, autoimmune disorder that affects the neuromuscular junction of the skeletal muscles. Eighty to 90 percent of individuals with myasthenia gravis have autoantibodies against the acetylcholine receptor detectable in serum, and these antibodies are believed to play a central role in disease pathomechanism. The AChR antibodies in myasthenia gravis are primarily immunoglobulin G1 and G3. In addition to blocking ACh binding to the AChR and cross-linking and internalizing the AChRs, these antibodies act through complement activation. (4) Some individuals with myasthenia gravis who are seronegative for AChR antibodies have antibodies directed against another target on the surface of the muscle membrane, muscle-specific receptor tyrosine kinase. (5) In contrast with AChR antibody-positive myasthenia gravis, in which complement-fixing immunoglobulin G1 and G3 subclasses predominate (6), muscle-specific kinase antibodies are mainly IgG4, (7) the IgG subtype that does not activate complement.

The clinical manifestations can vary from mild and focal weakness in some individuals to severe tetraparesis with respiratory failure in others. Symptom severity may also vary substantially in an individual patient throughout the day and over the course of the condition. Classification systems stratify individuals by symptoms or diagnostic findings to specify the severity of impairment and to aid with management. There are 2 clinical forms - ocular and generalized. In ocular from, weakness is limited to the eyelids and extraocular muscles while in generalized form, weakness involves a variable combination of ocular, bulbar, limb, and respiratory muscles. Myasthenia gravis may be categorized by symptom severity to guide treatment decisions, determine eligibility for clinical trials, and help with

prognostication. A widely used classification system from a task force of the Myasthenia Gravis Foundation of America stratifies individuals by the extent and severity of muscle weakness (8) and is summarized in the section of "Policy Guidelines". Myasthenia gravis is a relatively uncommon disorder. Both incidence and prevalence have significant geographical variations. Reported prevalence rates range from 150 to 200 cases per million, and they have steadily increased over the past 50 years, at least partly due to improvements in recognition, diagnosis, treatment, and an overall increase in life expectancy. (9) More recent studies addressing incidence rates have been conducted in Europe and show a wide range from 4.1 to 30 cases per million person-years. (10, 11) The annual rate is lower in studies coming from North America and Japan, with the incidence ranging from 3 to 9.1 cases per million. (12)

The diagnosis is primarily based on clinical testing. Laboratory investigations and procedures can aid the clinician in confirming clinical findings. These may include serologic tests, electrophysiologic exams (e.g., repetitive nerve stimulation test and single-fiber electromyography), an edrophonium test, an ice-pack test, imaging, and laboratory testing for other coexisting autoimmune disorders (e.g., anti-nuclear antibodies, rheumatoid factor, and thyroid function). For most individuals with clinical features of myasthenia gravis, the diagnosis is confirmed by the presence of autoantibodies against the AChRs or against other muscle receptor-associated proteins. A positive anti-AChR antibody is present in 80% of individuals with gMG and confirms the diagnosis in an individual with classical clinical findings. About 5 to 10% of individuals will demonstrate anti-muscle specific kinase antibodies. Individuals who are seronegative for either of these antibodies will have anti-LRP4 antibodies.

Regulatory Status (1)
Inebilizumab-cdon (Uplizna) was approved by the U.S. Food and Drug Administration in June 2020 for the treatment of adult patients with neuromyelitis optica spectrum disorder who are anti-aquaporin-4 antibody positive.

In April 2025, inebilizumab-cdon (Uplizna) was approved by the FDA for the treatment of adults with newly diagnosed or recurrent IgG4-RD.

In December 2025, inebilizumab-cdon (Uplizna) was approved by the FDA for generalized myasthenia gravis, making it the first and only CD19-targeted therapy for adults with anti-acetylcholine receptor or anti-muscle specific tyrosine kinase antibody positive gMG.

Rationale

This medical policy is based on the U.S. Food and Drug Administration labeled indications for inebilizumab-cdon (Uplizna).

Inebilizumab-cdon (Uplizna) (1)

Neuromyelitis Optica Spectrum Disorder

The efficacy of Uplizna for the treatment of neuromyelitis optica spectrum disorder was established in Study 1 (NCT02200770), a randomized (3:1), double-blind, placebo-controlled trial that enrolled 213 patients with NMOSD who were anti-AQP4 antibody positive and 17 who were anti-AQP4 antibody negative.

Patients met the following eligibility criteria:

- A history of one or more relapses that required rescue therapy within the year prior to screening, or 2 or more relapses that required rescue therapy in 2 years prior to screening.
- Expanded Disability Status Scale score of 7.5 or less. Patients with an EDSS score of 8.0 were eligible if they were deemed capable of participating.
- Patients were excluded if previously treated with immunosuppressant therapies within an interval specified for each such therapy.

The use of immunosuppressants during the blinded phase of the trial was prohibited.

The use of oral or intravenous corticosteroids during the blinded phase of the trial was prohibited, with the exception of premedication for investigational treatment and treatment for a relapse.

Of the 213 enrolled anti-AQP4 antibody positive patients, a total of 161 were randomized to receive treatment with Uplizna, and 52 were randomized to receive a placebo.

The baseline demographic and disease characteristics were balanced between the treatment groups. Females accounted for 94% of the study population. Fifty-two percent of patients were White, 21% Asian, and 9% Black or African American. The mean age was 43 years (range 18 to 74 years). The mean EDSS score was 4.0. The number of relapses in the two years prior to randomization was 2 or more in 83% of the patients.

Uplizna was administered according to the recommended dosage regimen.

All potential relapses were evaluated by a blinded, independent, adjudication committee, who determined whether the relapse met protocol-defined criteria. Patients who experienced an adjudicated relapse in the randomized-controlled period, or who completed the day 197 visit without a relapse, exited the RCP.

The primary efficacy endpoint was the time to the onset of the first adjudicated relapse on or before Day 197.

The time to the first adjudicated relapse was significantly longer in patients treated with Uplizna compared to patients who received placebo (relative risk reduction 73%; hazard

ratio: 0.272; p < 0.0001). In the anti-AQP4 antibody positive population there was a 77.3% relative reduction (hazard ratio: 0.227, p < 0.0001). There was no evidence of a benefit in patients who were anti-AQP4 antibody negative.

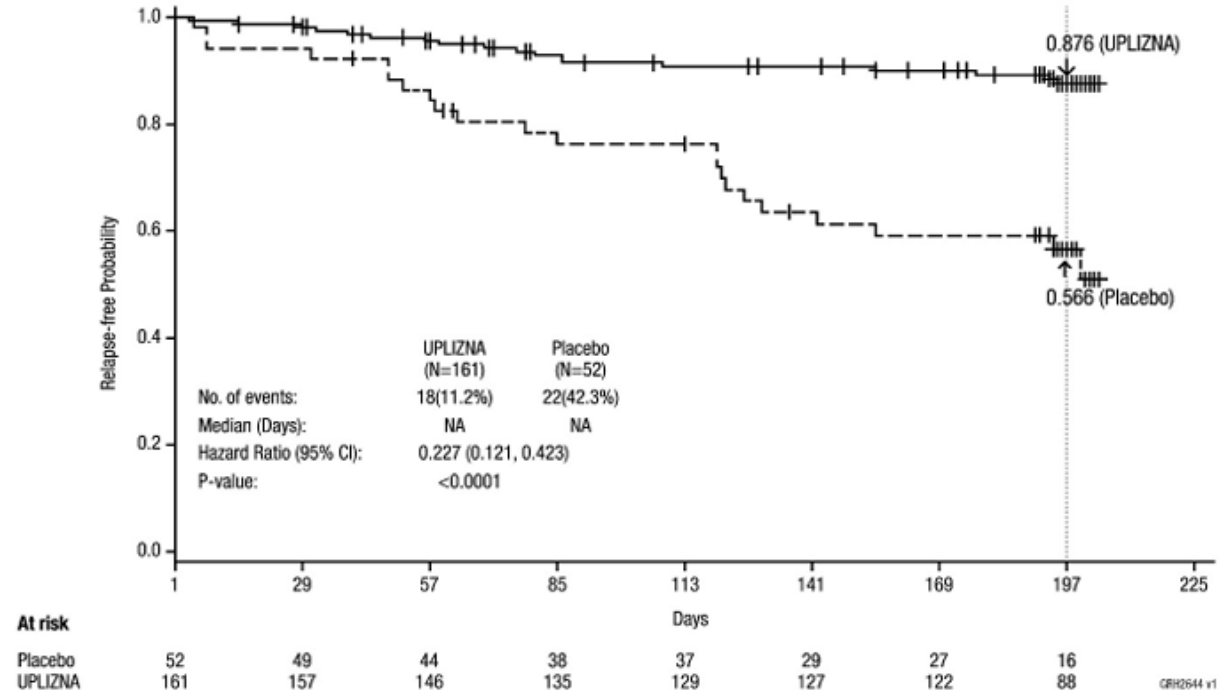
Table 2. Efficacy Results in Study 1 in anti-AQP4 Antibody Positive NMOSD Patients

	Treatment Group	
	Uplizna N=161	**Placebo N=52**
Time to Adjudication Committee-Determined Relapse (Primary Efficacy Endpoint)		
Number (%) of patients with relapse	18 (11.2%)	22 (42.3%)
Hazard ratio (95% CI)	0.227 (0.121, 0.423)	
p-value[a]	<0.0001	

NMOSD: neuromyelitis optica spectrum disorder; CI: confidence interval; AQP4: aquaporin-4 antibody.

[a] Cox regression method, with placebo as the reference group.

Figure 1. Kaplan-Meier Plot of Time to First Adjudication Committee-Determined NMOSD Relapse in the Randomized-Controlled Period (ITT Population; anti-AQP4 Antibody Positive Patients)



ITT: intention-to-treat; NMOSD: Neuromyelitis Optica Spectrum Disorder; AQP4: aquaporin-4; NA: not available; CI: confidence interval.

Note: Numbers of patients at risk are shown at each time point.

Compared to placebo-treated patients, patients treated with Uplinza who were anti-AQP4 antibody positive had reduced annualized rates of hospitalizations (0.11 for UP versus 0.50 for placebo).

Immunoglobulin G4-Related Disease

The efficacy of Uplinza for the treatment of IgG4-RD was established in Study 2 (NCT04540497), a randomized, double-blind, multicenter, 52-week placebo-controlled trial that enrolled 135 adult patients who met the following eligibility criteria:

- Newly diagnosed or recurrent IgG4-RD that required glucocorticoid treatment at screening.
- Confirmed history of organ involvement at any time in the course of disease.

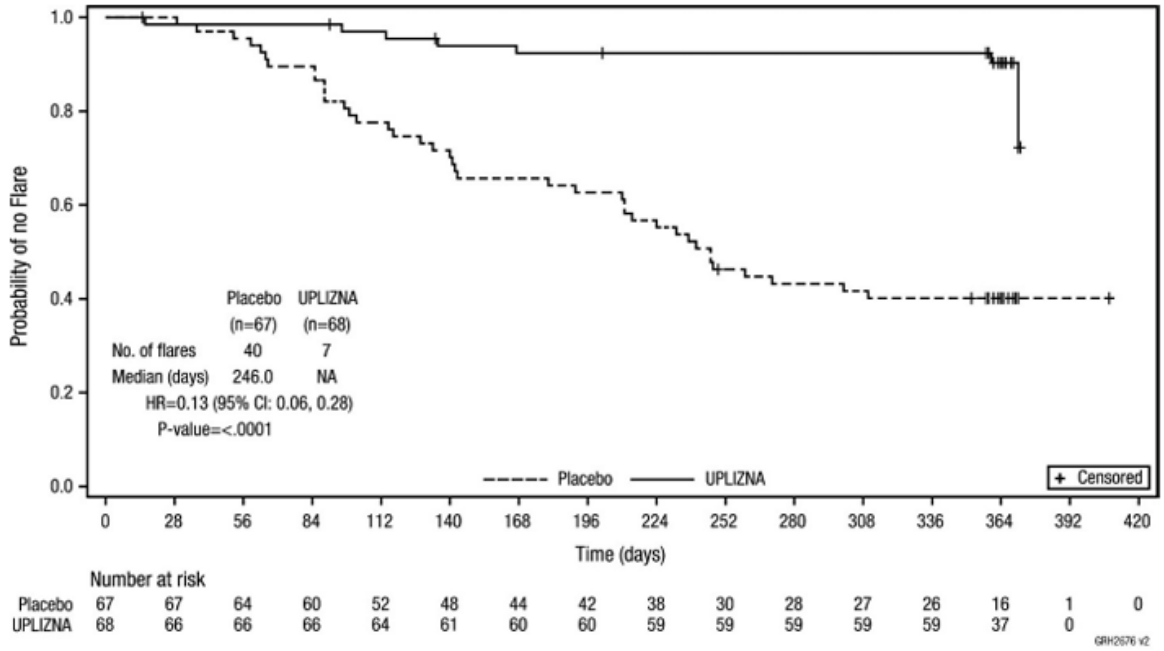
The concomitant use of biologic and non-biologic immunosuppressive agents was prohibited during the blinded phase of the trial. Of the 135 enrolled IgG4-RD patients, 68 patients were randomized to receive Uplinza and 67 were randomized to receive placebo. The baseline demographic and disease characteristics were generally balanced between the treatment groups. Females accounted for 35% of the study population. Thirty-nine percent of patients were White, 47% Asian, and 1% Black or African American. The mean age was 58 years (range 24 to 80 years). The median disease duration was 0.9 years. Forty-six percent of patients were newly diagnosed with IgG4-RD and 54% had recurrent disease.

Patients were at a uniform 20 mg per day dose of glucocorticoids at the time of randomization and then began a prespecified taper of 5 mg dose every two weeks until discontinuation at the end of 8 weeks. The use of glucocorticoids during the trial was permitted for premedication for investigational treatment, treatment for a relapse and in certain situations other than an IgG4-RD flare. Uplinza was administered according to the recommended dosage regimen.

Disease flare was defined as new/worsening signs or symptoms that were positively adjudicated and warranted treatment by the investigator. All potential flares were assessed by the investigator and subsequently reviewed by a blinded, independent, adjudication committee, who determined whether the flare met one or more of the protocol-defined, organ-specific flare diagnostic criteria.

The primary efficacy endpoint was the time to First Treated and Adjudication Committee-determined IgG4-RD flare within the 52-week RCP. The time to the First Treated and AC determined IgG4-RD flare was significantly longer in the UPLIZNA group, compared with the placebo group (Figure 2). Uplinza reduced the risk of treated and AC-determined IgG4-RD flare by 87%, compared with placebo (hazard ratio: 0.13; $p < 0.0001$) (see Table 3).

Figure 2. Kaplan-Meier Plot of Time to First Treated and Adjudication Committee-Determined IgG4-RD Flare During the Randomized-Controlled Period



CI: confidence interval; HR: hazard ratio; NA: not applicable; No: number; IgG4-RD: Immunoglobulin G4-Related Disease.
Patients who did not complete the RCP and who did not have a treated and AC-determined flare during the RCP were censored at the time of discontinuation.

Table 3. Efficacy Results in Study 2 in IgG4-RD Patients

	Treatment Group	
	Uplizna N=68	**Placebo N=67**
Time to The First Treated and AC-Determined IgG4-RD Flare (Primary Efficacy Endpoint)		
Number of subjects with a IgG4-RD flare	7 (10.3%)	40 (59.7%)
Hazard ratio (95% CI)[a]	0.13 (0.06, 0.28)	
p-value[a]	< 0.0001	
Annualized Flare Rate for Treated and AC-Determined IgG4-RD Flares	0.10	0.71
Rate ratio (95% CI)[b]	0.14 (0.06, 0.31)	
p-value[b]	< 0.0001	
Proportion of Subjects Achieving Treatment-free, Flare-Free Complete Remission at Week 52[c]	39 (57.4%)	15 (22.4%)
Difference (95% CI)[d]	35.0% (19.5%, 50.5%)	
p-value[d]	< 0.0001	

Proportion of Subjects Achieving Corticosteroid-free, Flare-Free and Complete Remission at Week 52[e]	40 (58.8%)	15 (22.4%)
Difference (95% CI)[d]	36.5% (21.0%, 51.9%)	
p-value[d]	< 0.0001	

CI: confidence interval; IgG4-RD: Immunoglobulin G4-Related Disease; AC: Adjudication Committee.

[a] Based on Cox regression method, with placebo as the reference group.

[b] Estimated from the negative binomial regression, with placebo as the reference group.

[c] Defined as the lack of evident disease activity (IgG4-RD Responder Index = 0 or investigator's decision) at Week 52, no AC-determined flare during the RCP, and no treatment for flare or disease control except the required 8-week GC taper.

[d] Based on logistic regression model, with placebo as the reference group.

[e] Defined as the lack of evident disease activity (IgG4-RD RI = 0 or investigator's decision) at Week 52, no AC-determined flare during the RCP, and no corticosteroid treatment for flare or disease control except the required 8-week GC taper.

For all patients in the trial, the mean total GC use for IgG4-RD control per patient other than the planned GC taper was lower in the Uplinza-treated group compared with the placebo- treated group, with a mean of 118.25 (438.97) mg prednisone equivalent versus 1384.53 (1723.26) mg prednisone equivalent, respectively during the RCP. Forty-two (62.7%) placebo treated patients, and 7 (10.3%) Uplinza-treated patients received GC for IgG4-RD control other than the planned GC taper. The mean total GC use per patient for the 42 placebo treated patients was 2202.76 (1709) mg prednisone equivalent and for the 7 Uplinza-treated patients was 1148.71 (878) mg prednisone equivalent.

Generalized Myasthenia Gravis (1)

The efficacy of Uplinza for the treatment of gMG in adult patients who are anti-acetylcholine receptor or anti-muscle specific tyrosine kinase (MuSK) antibody positive was established in Study 3 (NCT04524273), a randomized, double-blind, multicenter, placebo controlled trial. The randomized, controlled treatment period was 52 weeks for the anti-AChR antibody positive population and 26 weeks for the anti-MuSK antibody positive population. The primary analysis was conducted after week 26 in both populations. Uplizna was administered according to the recommended dosage regimen.

Patients met the following eligibility criteria:

- Presence of autoantibodies against AChR or MuSK
- Myasthenia Gravis Foundation of America Clinical Classification Class II to IV
- Myasthenia Gravis-Activities of Daily Living score between 6 and 10 with > 50% of this score attributed to non-ocular items or an MG-ADL score ≥ 11
- Quantitative Myasthenia Gravis score of ≥ 11
- On a stable dose of a corticosteroid or a specified non-steroidal immunosuppressive therapy, or a combination of both prior to randomization.

In Study 3, a total of 238 patients with gMG were randomized in a 1:1 ratio to receive Uplizna or placebo. The majority of patients, 80% (n=190) were anti-AChR antibody positive and 20% (n=48) were anti-MuSK antibody positive.

In the overall study population, 61% of the patients were female. Fifty-three percent of patients were White, 42% were Asian, and 2% were Black or African American. The mean age was 47.5 years (range 18 to 82 years). Mean MG-ADL score at baseline was 9.1 and mean QMG score at baseline was 17.0. At baseline, approximately 79% of patients received acetylcholinesterase inhibitors, 64% of patients received corticosteroids only, 7% of patients received non-steroidal immunosuppressive therapy only, and 29% of patients received corticosteroids and 1 nonsteroidal immunosuppressive therapy.

The efficacy of Uplizna was measured using MG-ADL scale, which assesses the impact of gMG on daily functions of 8 signs or symptoms that are typically affected in gMG. Each item is assessed on a 4-point scale, where a score of 0 represents normal function and a score of 3 represents loss of ability to perform that function. The total MG-ADL score ranges from 0 to 24, with higher scores indicating more impairment.

The primary efficacy endpoint was the change from baseline in the MG-ADL score at week 26, in the overall population. A statistically significant difference favoring Uplizna 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).

The secondary endpoint was the change from baseline in the QMG score at week 26 in the overall population. 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.

A statistically significant difference favoring Uplizna was observed in the mean change from baseline in QMG total score in the overall population (-4.8 points in the Uplizna-treated group compared to -2.3 for placebo, difference -2.5, 95% CI: -3.8, -1.2; p-value = 0.0002).

Secondary endpoints also included change in MG-ADL and QMG scores in the anti-AChR antibody positive and anti-MuSK antibody positive populations.

The results of the primary and secondary endpoints are presented in Table 4.

Table 4. Change from Baseline in MG-ADL and QMG Total Score at Week 26 in Adult gMG Patients who are Anti-AChR Antibody Positive or Anti-MuSK Antibody Positive (Study 3)

	Overall Population (Primary)		Anti-AChR-Ab+ Population		Anti-MuSK-Ab+ Population	
	Uplizna N = 119	Placebo N = 117	Uplizna N = 95	Placebo N = 93	Uplizna N = 24	Placebo N = 24
MG-ADL Score						
LS Mean	-4.2	-2.2	-4.2	-2.4	-3.9	-1.7
Difference	-1.9		-1.8		-2.2	
95% CI	(-2.9, -1.0)		(-2.9, -0.7)		(-4.2, -0.2)	
p-value	<0.0001		0.0015		0.0297	
QMG Score						
LS Mean	-4.8	-2.3	-4.4	-2.0	-5.2	-3.0
Difference	-2.5		-2.5		-2.3	
95% CI	(-3.8, -1.2)		(-3.9, -1.0)		(-5.3, 0.7)	
p-value	0.0002		0.0011		NS	

MG-ADL: Myasthenia Gravis-Activities of Daily Living; QMG: Quantitative Myasthenia Gravis; gMG: generalized myasthenia gravis; Anti-AChR: anti-acetylcholine receptor; Anti-MuSK: anti-muscle specific tyrosine kinase; LS: least square; CI: confidence interval; Ab+: antibody positive; NS: not significant.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J1823

*Current Procedural Terminology (CPT®) ©2025 American Medical Association: Chicago, IL.

References

Food and Drug Administration Label:

1. Prescribing Label: Uplizna (inebilizumab-cdon) for intravenous use. December 2025. Available at: accessdata.fda.gov (accessed January 15, 2026).

Other:

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Centers for Medicare & Medicaid Services

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare & Medicaid Services (CMS does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at cms.hhs.gov.

Policy History/Revision

Date	Description of Change
5/7/26	New medical document. Inebilizumab-cdon (Uplizna) may be considered medically necessary when ALL the following criteria are met: Individual is 18 years of age or older; and has a diagnosis of neuromyelitis optica spectrum disorder; and is anti-aquaporin-4 antibody seropositive; and has a history of at least one relapse requiring rescue therapy during the previous 12 months OR at least two relapses requiring rescue therapy during the previous 24 months. Inebilizumab-cdon (Uplizna) may be considered medically necessary when ALL the following criteria are met: Individual is 18 years of age or older; and has a diagnosis of newly diagnosed or recurrent IgG4-RD that required glucocorticoid treatment at screening; and has a confirmed history of organ involvement at any time in the course of disease. Inebilizumab-cdon (Uplizna) may be considered medically necessary when ALL the following criteria are met: Individual is 18 years of age or older; and Has a diagnosis of generalized myasthenia gravis; and Is anti-acetylcholine receptor or anti-muscle specific tyrosine kinase antibody positive; and Myasthenia Gravis Foundation of America Clinical Classification Class II to IV; AND Myasthenia Gravis-Activities of Daily Living score between 6 and 10 with > 50% of this score attributed to non-ocular items or an MG-ADL score ≥ 11; AND On a stable dose of a corticosteroid or a specified non-steroidal immunosuppressive therapy, or a combination of both. Inebilizumab-cdon (Uplizna) is considered experimental, investigational and/or unproven for all other non-Food and Drug Administration indications.