Uplizna (inebilizumab-cdon)
PAM – 035

Iowa Medicaid Program	Prior Authorization	**Effective Date**	07/01/2021
Revision Number	5	**Last Reviewed**	07/18/2025
Reviewed By	Medicaid Medical Director	**Next Review**	07/17/2026
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	07/16/2021

Overview

Medication: [1]	inebilizumab-cdon
Brand Name:	Uplizna®
Pharmacologic Category:	Ophthalmic agents; CD19-directed cytolytic antibody
FDA-Approved Indication(s):	1. Treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive. 2. Treatment of immunoglobulin G4-related disease (IgG4-RD) in adult patients. ▶ **NEW** indication (FDA-approved 4/3/2025)
How Supplied:	One carton containing three 100 mg/10 mL single-dose vials
Dosage and Administration:	• Intravenous (IV) infusion • Initial dose: 300 mg on Days 1 and 15 • Subsequent doses: 300 mg every 6 months (starting 6 months from first infusion)
Benefit Category:	Medical

Descriptive Narrative

Neuromyelitis optica spectrum disorder (NMOSD)

Neuromyelitis optica spectrum disorder (NMOSD), previously known as Devic disease or neuromyelitis optica, is an inflammatory disorder of the central nervous system. 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 (NMOSD has a relapsing course in 90 percent or more of patients). Attacks most often occur over days, with variable degrees of recovery over weeks to months.

It was previously believed that NMOSD and multiple sclerosis (MS) represented one disease entity with variable phenotypes and expression. However, the discovery of a disease-specific serum NMO-immunoglobulin G (IgG) antibody that selectively binds aquaporin-4 (AQP4) has led to increased understanding that NMOSD is distinct from classic relapsing-remitting MS with respect to pathogenesis, imaging features, biomarkers, neuropathology, and treatment.

The prevalence of NMOSD in adults in various studies ranges from 0.37 to 10 per 100,000. The reported incidence of AQP4-antibody seropositive NMOSD in females is up to 10 times higher than in males, whereas the female-to-male incidence with MS is approximately 2:1. Median age of onset for NMOSD is 32 to 41 years of age, but cases are described in children and older adults (comparatively, the median age of onset for MS is 24 years).

Aquaporin-4 (AQP4) is a water channel protein that is abundant in the astrocytic foot processes at the blood-brain barrier and highly concentrated in spinal cord gray matter, periaqueductal, and periventricular regions. APQ4-IgG autoantibodies play a direct role in the pathogenesis of NMOSD (serum AQP4 autoantibody titers at the nadir of clinical attacks have been shown to correlate with the length of longitudinally extensive spinal cord lesions. In addition, serum anti-AQP4 titers have been shown in several studies to correlate with clinical disease activity, drop after immunotherapy, and remain low during remissions).[2]

Immunoglobulin G4-Related Disease (IgG4-RD)

Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated fibroinflammatory condition that can affect multiple organs. Early recognition and treatment are important because of the indolent nature of the condition and the risk of progression from a typically treatment-responsive proliferative and inflammatory stage to poorly responsive fibrotic disease and serious organ damage.

The majority of patients respond to glucocorticoids, particularly in early stages of disease, but the duration of this response treatment is variable. Most patients experience disease flares during or after glucocorticoid tapers. Thus, additional therapy may also be required. Although rituximab (an anti-CD20 monoclonal antibody) is commonly used for the treatment of IgG4-RD refractory to glucocorticoids, this practice has not been well validated in clinical trials. Recently, the US Food and Drug Administration (FDA) granted approval for the use of inebilizumab (Uplizna®), an anti-CD19 monoclonal antibody, for the treatment of IgG4-RD.

The goals of therapy for IgG4-RD are to reduce inflammation and induce disease remission, with the aim of preserving organ function while minimizing the adverse effects of therapy with glucocorticoids and other agents.[3]

Guidelines

Neuromyelitis optica spectrum disorder (NMOSD)

Consensus diagnostic criteria for neuromyelitis optica spectrum disorder (NMOSD) was last published by the International Panel for NMO Diagnosis (IPND) in 2015.[4]

Treatment of NMOSD focuses on acute attacks as well as attack prevention. Treatment of acute attacks is recommended for all patients with suspected NMOSD. High-dose intravenous (IV) methylprednisolone is the treatment of choice, with concomitant therapeutic plasma exchange for patients with severe symptoms or vision loss that is unresponsive to glucocorticoids (exchange every other day up to a total of seven exchanges).

Immunoglobulin G4-Related Disease (IgG4-RD)

An international set of classification criteria for immunoglobulin G4-related disease (IgG4-RD) was established in 2019 by the European League Against Rheumatism (EULAR) Executive Committee and the American College of Rheumatology (ACR) Board of Directors.[5]

A 3-step classification process was developed.

1. It must be demonstrated that a potential IgG4-RD case has involvement of at least 1 of 11 possible organs in a manner consistent with IgG4-RD.
2. Exclusion criteria consisting of a total of 32 clinical, serologic, radiologic, and pathologic items must be applied; the presence of any of these criteria eliminates the patient from IgG4-RD classification.
3. Eight (8) weighted inclusion criteria domains, addressing clinical findings, serologic results, radiology assessments, and pathology interpretations, are applied.

Criteria

Prior authorization is required.

Neuromyelitis optica spectrum disorder (NMOSD)

Uplizna® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of neuromyelitis optica spectrum disorder (NMOSD), with a positive test for anti-aquaporin-4 (AQP4) antibody positive (AQP4) antibodies; **AND**
2. Member is 18 years of age or older; **AND**
3. Member has a history of one or more relapses that required rescue therapy within the past 12 months, or of two or more relapses that required rescue therapy within the previous 24 months (prior to initiation of therapy). Rescue therapy involves the administration of intravenous (IV) corticosteroids. For severe attacks, adjunctive plasma exchange is also utilized; **AND**
4. Member does not have active or untreated latent tuberculosis, or an active hepatitis B infection; **AND**
5. Prescribed by, or in consultation with, a neurologist; **AND**
6. Uplizna® is not prescribed concurrently with rituximab, eculizumab (Soliris®), or satralizumab-mwge (Enspryng™); **AND**
7. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 300 mg on Days 1 and 15, followed by 300 mg every 6 months (starting 6 months from first infusion); or
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Uplizna® is considered medically necessary for continuation of therapy when **ALL** of the following are met [Neuromyelitis Optica Spectrum Disorder (NMOSD)]:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy (e.g., a decrease in the frequency of relapses, improvement or stabilization of visual acuity, etc.); **AND**
3. Prescribed by, or in consultation with, a neurologist; **AND**
4. Uplizna® is not prescribed concurrently with rituximab, eculizumab (Soliris®), or satralizumab-mwge (Enspryng™); **AND**
5. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 300 mg every 6 months; or
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Immunoglobulin G4-Related Disease (IgG4-RD)

Uplizna® is considered medically necessary when **ALL** of the following are met:

1. Confirmed diagnosis of Immunoglobulin G4-Related Disease (IgG4-RD) (e.g., physical exam findings, imaging results, laboratory tests, pathological findings in involved organ/sites, etc.); **AND**
2. Other conditions that mimic IgG4-RD have been ruled out (e.g., malignancy, infection, other autoimmune disorders, etc.); **AND**
3. Member is 18 years of age or older; **AND**
4. Member is experiencing (or recently experienced) an IgG4-RD flare that required corticosteroid treatment, and (one of the following):
    a. Member has disease that is refractory to corticosteroids; or,
    b. Member has a clinical contraindication or intolerance to treatment with corticosteroids; **AND**
5. Member is at high risk of recurrent disease flares based on a history of disease in 2 or more organs/sites; **AND**
6. At least one of the following organs are affected:
    a. Pancreas; and/or
    b. Bile ducts/biliary tree; and/or
    c. Orbits; and/or
    d. Lungs; and/or
    e. Kidneys; and/or
    f. Lacrimal glands; and/or
    g. Major salivary glands; and/or
    h. Retroperitoneum; and/or
    i. Aorta; and/or
    j. Pachymeninges; and/or
    k. Thyroid gland; **AND**
7. Prescribed by, or in consultation with, a rheumatologist and/or an appropriate specialist based on the organ(s) affected (e.g., gastro-enterologist, ophthalmologist, neurologist, pulmonologist, etc.); **AND**
8. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 300 mg on Days 1 and 15, followed by 300 mg every 6 months (start 6 months from Day 1); or
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Uplizna® is considered medically necessary for continuation of therapy when **ALL** of the following are met [Immunoglobulin G4-Related Disease (IgG4-RD)]:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by one or more of the following:
    a. Reduction in corticosteroid requirement for IgG4-RD flare treatment from baseline; and/or
    b. Reduction in IgG4-RD flares from baseline; and/or
    c. Stabilization/improvement in symptoms, physical exam findings, imaging results, and/or laboratory tests from baseline; and/or
    d. Stabilization/improvement in pathological findings in IgG4-RD involved organ/sites compared to baseline; **AND**
3. Prescribed by, or in consultation with, a rheumatologist and/or an appropriate specialist based on the organ(s) affected (e.g., gastro-enterologist, ophthalmologist, neurologist, pulmonologist, etc.); **AND**
4. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 300 mg every 6 months; or
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

NMOSD and IgG4-RD	Initial Authorization	Subsequent Authorization(s)
Approval Duration	12 months	12 months
Quantity Limits	Two 300 mg loading doses, then 300 mg every 6 months thereafter	300 mg every 6 months

NMOSD: neuromyelitis optica spectrum disorder **IgG4-RD:** immunoglobulin G4-related disease

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J1823	Injection, inebilizumab-cdon, 1 mg

ICD-10	Description
D89.94	IgG4-related disease
G36.0	Neuromyelitis optica (Devic)

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/ Pkg
75987-0150-03 (100 mg/10 mL per vial; 3 vials per carton)	Horizon Therapeutics USA, Inc. (75987)	1 mg	EA	3	300

Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Uplizna prescribing information (04/2025). Horizon Therapeutics USA, Inc.: Deerfield, IL. Available online: www.upliznahcp.com. Accessed June 9, 2025.

[2] Glisson CC. Neuromyelitis optica spectrum disorders (NMOSD): Clinical features and diagnosis. Dashe JF, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed June 9, 2025.

[3] Moutsopoulos HM, Fragoulis GE, Stone JH. Treatment and prognosis of IgG4-related disease. Seo P, ed. UpToDate. Waltham, MA: UpToDate, Inc. www.uptodate.com. Accessed June 9, 2025.

[4] Wingerchuk DM, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. American Academy of Neurology. Jul 2015, 85 (2) 177-189. PMID 26092914.

[5] Wallace ZS, Naden RP, et al; American College of Rheumatology/European League Against Rheumatism IgG4-Related Disease Classification Criteria

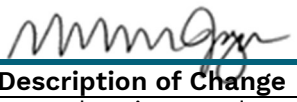
Working Group. The 2019 American College of Rheumatology/European League Against Rheumatism Classification Criteria for IgG4-Related Disease. Arthritis Rheumatol. 2020 Jan;72(1):7-19. Epub 2019 Dec 2. PMID: 31793250.

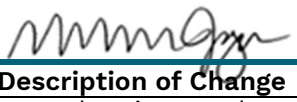
Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

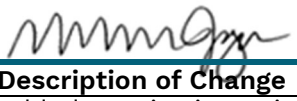
Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
07/18/2025	CAC	Annual review. Updated Overview, Descriptive Narrative, Guidelines, and Criteria to include new indication for treatment of immunoglobulin G4-related disease (IgG4-RD) in adult patients (FDA-approved 4/3/2025).	5
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
07/19/2024	CAC	Annual review. Updated disease information in Descriptive Narrative. Added dosing information to criteria.	4
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
07/21/2023	CAC	Annual review. Updated labeler to Horizon Therapeutics USA, Inc. (from Viela Bio).	3
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
07/15/2022	CAC	Added to criteria: regimen/dosing prescribed must align with FDA-approved dosing.	2
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
07/16/2021	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee