Clinical Policy: Inebilizumab-cdon (Uplizna)

Reference Number: PA.CP.PHAR.458
Effective Date: 10/2020
Last Review Date: 07/2025

Description
Inebilizumab-cdon (Uplizna™) is an anti-CD19-directed cytolytic antibody.

FDA Approved Indication(s)
Uplizna is 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

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

It is the policy of PA Health & Wellness® that Uplizna is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Neuromyelitis Optica Spectrum Disorder (must meet all)**:**

1. Diagnosis of NMOSD;
2. Prescribed by or in in consultation with a neurologist;
3. Age ≥ 18 years;
4. Member has positive serologic test for anti-AQP4 antibodies;
5. Member has experienced at least one relapse within the previous 12 months;
6. Member meets one of the following (a or b):
   a. History of at least one relapse requiring rescue therapy† during the previous 12 months;
   b. History of two relapses requiring rescue therapy† during the previous 24 months;
   † *Rescue therapies include: IV corticosteroids, IV immunoglobulin, and/or plasma exchange*
7. Baseline expanded disability status scale (EDSS) score of ≤ 8;
8. Failure of rituximab (Ruxience™ and Truxima® are preferred) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for rituximab*
9. At the time of request, member does not have active hepatitis B infection (positive results for hepatitis B surface antigen and anti-hepatitis B virus tests) or active or untreated latent tuberculosis;
10. Uplizna is not prescribed concurrently with rituximab, Bkemv™, Soliris®, Epysqli®, Enspryng® or Ultomiris®;;
11. Dose does not exceed a loading dose of 300 mg on Day 1 and Day 15.

Approval duration: 6 months (loading doses only)

B. Immunoglobulin G4-Related Disease (must meet all)**:**
1. Diagnosis of IgG4-RD;
2. Provider attestation that diagnosis meets the American College of Rheumatology/European Union League Against Rheumatism (ACR/EULAR) IgG4-RD classification criteria (*see Appendix D*);
3. Prescribed by or in consultation with a rheumatologist, gastroenterologist, nephrologist, pulmonologist, or internist;
4. Age ≥ 18 years;
5. Documentation that the member has a history of IgG4-RD affecting at least two organs/sites;
6. Member is currently receiving glucocorticoid treatment for an IgG4-RD flare;
7. At the time of request, member does not have active hepatitis B infection (positive results for hepatitis B surface antigen and anti-hepatitis B virus tests) or active or untreated latent tuberculosis;
8. Uplizna is not prescribed concurrently with rituximab;
9. Dose does not exceed a loading dose of 300 mg on Day 1 and Day 15.

Approval duration: 6 months (loading doses only)

C. Other diagnoses/indications
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Neuromyelitis Optica Spectrum Disorder (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy – including but not limited to improvement or stabilization in any of the following parameters:
   a. Frequency of relapse;
   b. EDSS;
   c. Visual acuity;
3. Uplizna is not prescribed concurrently with rituximab, Bkemv, Soliris, Enspryng, Epysqli, or Ultomiris;
4. If request is for a dose increase, new dose does not exceed 300 mg every 6 months.

Approval duration: 12 months

B. Immunoglobulin G4-Related Disease (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. Uplizna is not prescribed concurrently with rituximab;
4. If request is for a dose increase, new dose does not exceed 300 mg every 6 months.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACR: American College of Rheumatology
AQP-4: aquaporin-4
EDSS: expanded disability status scale
EULAR: European League Against Rheumatism
FDA: Food and Drug Administration
IgG4-RD: immunoglobulin G4-related disease
NMOSD: neuromyelitis optica spectrum disorder

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Rituxan®/Riabni™ Ruxience™/ Truxima® (rituximab)*	**NMOSD** IV: 375 mg/m^2 per week for 4 weeks as induction, followed by 375 mg/m^2 biweekly every 6 to 12 months	See regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): previous life-threatening reaction to infusion of Uplizna, active hepatitis B infection, active or untreated latent tuberculosis
- Boxed warning(s): none reported

Appendix D: General Information

- AQP-4-IgG-seropositive status is confirmed with the use of commercially available cell-binding kit assay (Euroimmun).
- ACR/EULAR IgG4-RD classification criteria (all of the following):
  - Meets entry requirements:

- Characteristic clinical or radiologic involvement of a typical organ (e.g., pancreas, salivary glands, bile ducts, orbits, kidney, lung, aorta, retroperitoneum, pachymeninges, or thyroid gland [Riedel's thyroiditis])
  OR
- Pathologic evidence of an inflammatory process accompanied by a lymphoplasmacytic infiltrate of uncertain etiology in one of these same organs

- Does NOT meet any of the classification criteria exclusions:
  - Fever
  - No objective response to glucocorticoids
  - Leukopenia and thrombocytopenia with no explanation
  - Peripheral eosinophilia
  - Positive antineutrophil cytoplasmic antibody (specifically against proteinase 3 or myeloperoxidase)
  - Positive SSA/Ro or SSB/La antibody
  - Positive double-stranded DNA, RNP, or Sm antibody
  - Other disease-specific autoantibody
  - Cryoglobulinemia
  - Known radiologic findings suspicious for malignancy or infection that have not been sufficiently investigated
  - Rapid radiologic progression
  - Long bone abnormalities consistent with Erdheim-Chester disease
  - Splenomegaly
  - Cellular infiltrates suggesting malignancy that have not been sufficiently evaluated
  - Markers consistent with inflammatory myofibroblastic tumor
  - Prominent neutrophilic inflammation
  - Necrotizing vasculitis
  - Prominent necrosis
  - Primarily granulomatous inflammation
  - Pathologic features of macrophage/histiocytic disorder
  - Multicentric Castleman's disease
  - Crohn's disease or ulcerative colitis (if only pancreatobiliary disease is present)
  - Hashimoto thyroiditis (if only the thyroid is affected)

- Achieves ≥ 20 classification criteria inclusion points:

Domain/Items	Numeric Weight
Histopathology	
Uninformative biopsy	0
Dense lymphocytic infiltrate	+4
Dense lymphocytic infiltrate and obliterative phlebitis	+6
Dense lymphocytic infiltrate and storiform fibrosis with or without obliterative phlebitis	+13
Immunostaining	0–16, as follows: • 0, if the IgG4+:IgG+ ratio is 0–40% or indeterminate and the

Domain/Items	Numeric Weight
	number of IgG4+ cells/hpf is 0–9 • 7, if 1) the IgG4+:IgG+ ratio is ≥ 41% and the number of IgG4+ cells/hpf is 0–9 or indeterminate; or 2) the IgG4+:IgG+ ratio is 0–40% or indeterminate and the number of IgG4+ cells/hpf is ≥ 10 or indeterminate • 14, if 1) the IgG4+:IgG+ ratio is 41–70% and the number of IgG4+ cells/hpf is ≥ 10; or 2) the IgG4+:IgG+ ratio is ≥ 71% and the number of IgG4+ cells/hpf is 10–50 • 16, if the IgG4+:IgG+ ratio is ≥ 71% and the number of IgG4+ cells/hpf is ≥ 51
Serum IgG4 concentration	
Normal or not checked	0
> Normal but < 2× upper limit of normal	+4
2–5× upper limit of normal	+6
> 5× upper limit of normal	+11
Bilateral lacrimal, parotid, sublingual, and submandibular glands	
No set of glands involved	0
One set of glands involved	+6
Two or more sets of glands involved	+14
Chest	
Not checked or neither of the items listed is present	0
Peribronchovascular and septal thickening	+4
Paravertebral band-like soft tissue in the thorax	+10
Pancreas and biliary tree	
Not checked or none of the items listed is present	0
Diffuse pancreas enlargement (loss of lobulations)	+8
Diffuse pancreas enlargement and capsule-like rim with decreased enhancement	+11

Domain/Items	Numeric Weight
Pancreas (either of above) and biliary tree involvement	+19
Kidney	
Not checked or none of the items listed is present	0
Hypocomplementemia	+6
Renal pelvis thickening/soft tissue	+8
Bilateral renal cortex low-density areas	+10
Retroperitoneum	
Not checked or neither of the items listed is present	0
Diffuse thickening of the abdominal aortic wall	+4
Circumferential or anterolateral soft tissue around the infrarenal aorta or iliac arteries	+8

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NMOSD, IgG4-RD	Loading dose: 300 mg IV, followed by a second 300 mg IV dose 2 weeks later Maintenance dose: 300 mg IV every 6 months, starting 6 months after the first infusion	See regimen

VI. Product Availability

Solution for injection in a single-dose vial: 100 mg/10 mL

VII. References

1. Uplizna Prescribing Information. Gaithersburg, MD: Viela Bio, Inc.; April 2025. Available at: https://www.uplizna.com. Accessed April 21, 2025.
2. Cree BA, Bennet 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; 394(10206): P1352-1363.
3. Sellner J, Boggild M, Clanet M, et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. European Journal of Neurology. 2010; 17: 1019–1032.
4. Kumpfel T, Giglhuber K, Aktas O, et al. Update on the diagnosis and treatment of neuromyelitis optica spectrum disorders (NMOSD) – revised recommendations of the Neuromyelitis Optica Study Group (NEMOS). Part II: Attack therapy and long-term management. Journal of Neurology. 2023; 271: 141-176.
5. Stone JH, Khosroshahi A, Zhang W, et al. Inebilizumab for treatment of IgG4-related disease. N Engl J Med. 2025; 392(12): 1168-1177.
6. Wallace ZS, Naden RP, Chari S, et al. The 2019 American College of Rheumatology/European League Against Rheumatism classification criteria for IgG4-related disease. Arthritis Rheumatol. 2020; 72(1): 7-19.
7. Khosroshahi A, Wallace ZS, Crowe JL, et al. International consensus guidance statement on the management and treatment of IgG4-related disease. Arthritis Rheumatol. 2015; 67(7): 1688-1699.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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

Reviews, Revisions, and Approvals	Date
Policy created	10/2020
1Q 2021 annual review: no significant changes; references reviewed and updated.	01/2021
1Q 2022 annual review: specified that Truxima is also a preferred rituximab product; updated HCPCS code; references reviewed and updated.	01/2022
1Q 2023 annual review: added stepwise redirection requirement if member has failed rituximab; references reviewed and updated.	01/2023
3Q 2023 annual review: no significant changes; references reviewed and updated.	07/2023
3Q 2024 annual review: no significant changes; added Bkemv and Ultomiris to the list of therapies that Uplizna should not be prescribed concurrently with; references reviewed and updated.	07/2024
3Q 2025 annual review: for NMOSD, added Epysqli to the list of therapies that Uplizna should not be prescribed concurrently with, and revised continued approval duration from 6 to 12 months as NMOSD is a chronic condition; RT4: added criteria for the newly approved indication of IgG4-RD; references reviewed and updated.	07/2025