Clinical Policy: Inebilizumab-cdon (Uplizna)

Reference Number: CP.PHAR.458
Effective Date: 06.11.20
Last Review Date: 08.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 health plans affiliated with Centene Corporation® 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*
   ^For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395
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®, Enspryng®, Epysqli®, 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;*
   **For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
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 (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):

a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*

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. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

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 for all relevant lines of business 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 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

Domain/Items	Numeric Weight
	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
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

Domain/Items	Numeric Weight
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	P&T Approval Date
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	10.20.20	02.21
1Q 2022 annual review: no significant changes; specified that Truxima is also a preferred rituximab product; updated HCPCS code; references reviewed and updated.	09.15.21	02.22
Per February SDC and prior clinical guidance, added stepwise redirection requirement if member has failed rituximab, then member must use Enspryng.	02.17.22	05.22
Per August SDC and prior clinical guidance, removed redirection to Enspryng. Template changes applied to other diagnoses/indications and continued therapy section.	08.23.22	11.22
1Q 2023 annual review: no significant changes; references reviewed and updated.	11.03.22	02.23
3Q 2023 annual review: no significant changes; references reviewed and updated.	04.18.23	08.23
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.	05.15.24	08.24
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. Added step therapy bypass for IL HIM per IL HB 5395.	06.24.25	08.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and

limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.