Inebilizumab-cdon (Uplizna™)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
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.

All other indications are considered experimental/investigational and not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- Neuromyelitis optica spectrum disorder (NMOSD)
  - For initial requests: Immunoassay used to confirm anti-aquaporin-4 (AQP4) antibody is present.
  - For continuation requests: Chart notes or medical record documentation supporting positive clinical response.
- Immunoglobulin G4-related disease (IgG4-RD)
  - For initial requests, chart notes or medical records documenting:
    - Member has a clinical diagnosis of IgG4-RD.
    - Member is experiencing an IgG4-RD flare requiring glucocorticoid treatment (within the past 4 weeks).
    - IgG4-RD is affecting at least 1 organ/site.
  - For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

COVERAGE CRITERIA

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Authorization of 12 months may be granted for treatment of neuromyelitis optica spectrum disorder (NMOSD) when all of the following criteria are met:

- Anti-aquaporin-4 (AQP4) antibody positive
- Member exhibits one of the following core clinical characteristics of NMOSD:

  - Optic neuritis
  - Acute myelitis
  - Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
  - Acute brainstem syndrome
  - Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic magnetic resonance imaging (MRI) lesions
  - Symptomatic cerebral syndrome with NMOSD-typical brain lesions
- The member will not receive the requested medication concomitantly with other biologics for the treatment of NMOSD.

Immunoglobulin G4-related Disease (IgG4-RD)

Authorization of 12 months may be granted for treatment of immunoglobulin G4-related disease (IgG4-RD) when all of the following criteria are met:

- Member has a clinical diagnosis of IgG4-RD confirmed by either of the following (please see Appendix A for evaluations and characteristic organs to confirm diagnosis):
  - Clinical or radiologic involvement of a characteristic organ.
  - Pathologic evidence from a characteristic organ.
- Alternative causes of member's clinical signs and symptoms have been evaluated and ruled out (please see Appendix B for common mimickers of IgG4-RD).
- Member is experiencing an IgG4-RD flare that requires initiation or continuation of glucocorticoid treatment (within the past 4 weeks).
- Member has a history of IgG4-RD affecting at least 1 organ/site at any time in the course of IgG4-RD.

CONTINUATION OF THERAPY

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of the following criteria are met:

- There is no evidence of unacceptable toxicity or disease progression while on the current regimen.
- The member demonstrates a positive response to therapy (e.g., reduction in number of relapses).
- The member will not receive the requested medication concomitantly with other biologics for the treatment of NMOSD.

Immunoglobulin G4-related Disease (IgG4-RD)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of the following criteria are met:

- There is no evidence of unacceptable toxicity or disease progression while on the current regimen.
- The member demonstrates a positive response to therapy (e.g., reduction in IgG4-RD flares).

Appendices

Appendix A: Adapted from the 2020 Revised Comprehensive Diagnostic Criteria for IgG4-RD and the 2019 ACR/EULAR Classification Criteria for IgG4-RD

- Clinical or radiological features:
  - One or more organs show diffuse or localized swelling or a mass or nodule characteristic of IgG4-RD. In single organ involvement, lymph node swelling is omitted.

  - Note: Nearly any organ can be affected, but characteristic organs involved include:
    - Pancreas
    - Salivary gland
    - Bile ducts
    - Orbits
    - Kidney
    - Lung
    - Aorta
    - Retroperitoneum
    - Pachymeninges
    - Thyroid gland (Riedel's thyroiditis)
- Pathological diagnosis (positivity for two of the following three criteria):
  - Dense lymphocyte and plasma cell infiltration with fibrosis.
  - Ratio of IgG4-positive plasma cells /IgG-positive cells greater than 40% and the number of IgG4-positive plasma cells greater than 10 per high powered field.
  - Typical tissue fibrosis, particularly storiform fibrosis, or obliterative phlebitis.

Appendix B: Common Mimickers of IgG4-RD

- Malignancy
- Vasculitis
- Sjogren's syndrome
- Primary granulomatous inflammation (including sarcoidosis)
- Infection
- Multicentric Castleman's disease
- Erdheim-Chester disease
- Crohn's disease or ulcerative colitis (if only pancreatobiliary disease is present)
- Hashimoto thyroiditis (if only the thyroid is affected)

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

REFERENCES

1. Uplizna [package insert].Deerfield, IL: Horizon Therapeutics USA, Inc.; April 2025.
2. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015; 85:177-189.

3. Stone JH, Khosroshahi A, Zhang W, et al. Inebilizumab for Treatment of IgG4-Related Disease. N Engl J Med. 2025 Mar 27;392(12):1168-1177.
4. Wallace, Z.S., Naden, R.P., Chari, S., Choi, H., et al. The 2019 American College of Rheumatology/European League Against Rheumatism Classification Criteria for IgG4-Related Disease. Arthritis Rheumatol, 72: 7-19.
5. Umehara H, Okazaki K, Kawa S, et al. The 2020 revised comprehensive diagnostic (RCD) criteria for IgG4-RD. *Mod Rheumatol*. 2021;31(3):529-533.

EFFECTIVE DATE 10/31/2025

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