Reference number(s)
4722-A

Standard Medicare Part B Management Uplizna

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Uplizna	inebilizumab-cdon

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[1]

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 will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

Documentation

The following documentation must be available, upon request, for all submissions:

- Neuromyelitis optica spectrum disorder (NMOSD)

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    - For initial requests: Immunoassay used to confirm anti-aquaporin-4 (AQP4) antibody is present.
    - For continuation requests: Chart notes or medical record documentation supporting benefit from therapy.
- 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 benefit from therapy.

Coverage Criteria

Neuromyelitis Optica Spectrum Disorder (NMOSD)[1,2]

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

- The member is anti-aquaporin-4 (AQP4) antibody positive.
- The 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)[1,3-5]

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

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- 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

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The member is receiving benefit from 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 for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The member is receiving benefit from 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[4,5]

- Clinical or radiological features:

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    - 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[4,5]

- 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)

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Uplizna.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex

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    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- International consensus diagnostic criteria for neuromyelitis optica spectrum disorders.
- The 2020 Revised Comprehensive Diagnostic (RCD) Criteria for IgG4-RD.
- The 2019 American College of Rheumatology/European League Against Rheumatism Classification Criteria for IgG4-Related Disease

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Uplizna are covered.

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for the list of core clinical characteristics of NMOSD can be found in the International Consensus Diagnostic Criteria for Neuromyelitis Optica Spectrum Disorder (Wingerchuk et al). There are six clinical characteristics cited in the diagnostic criteria:

- 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 MRI lesions
- Symptomatic cerebral syndrome with NMOSD-typical brain lesions

Currently there are no treatment guidelines or literature supporting the concomitant use with other biologics for the treatment of NMOSD.

Support for clinical, radiologic, and pathologic evaluations to confirm the diagnosis as well as common mimicker's of IgG4-RD can be found The 2020 Revised Comprehensive Diagnostic (RCD) Criteria for IgG4-RD and The 2019 American College of Rheumatology/European League Against Rheumatism Classification Criteria for IgG4-Related Disease.

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.

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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.

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