CVS Caremark®

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| Reference number(s) |
| 3968-A |

# Specialty Guideline 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 Indications1

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)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:

* 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)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:

* 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-RD4,5

* 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-RD4,5

* 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)

## 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.