Uplizna® (Inebilizumab-Cdon)

Policy Number: 2023D0091F
Effective Date: September 1, 2023

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Coverage Rationale

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Uplizna (inebilizumab-cdon) is proven and medically necessary for the treatment of neuromyelitis optica spectrum disorder (NMOSD) when all the following criteria are met:

- For **initial therapy**:
  - Diagnosis of neuromyelitis optica spectrum disorder (NMOSD) by a neurologist confirming **all** of the following:[1-4]
    - Past medical history of **one** of the following:
      - 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

      and
    - Positive serologic test for anti-aquaporin-4 immunoglobulin G (AQP4-IgG)/NMO-IgG antibodies; **and**
    - Diagnosis of multiple sclerosis or other diagnoses have been ruled out

    and
  - **One** of the following (for Medicare reviews, refer to the CMS section*):[7-14]
    - History of failure of rituximab therapy; **or**
    - **Both** of the following:
      - History of intolerance or contraindication to rituximab; **and**
      - Physician attests that, in their clinical opinion, the same intolerance or severe adverse event would not be expected to occur with Uplizna

    and
  - **One** of the following:[5]

        - History of one or more relapses that required rescue therapy during the previous 12 months prior to initiating Uplizna
        - History of two or more relapses that required rescue therapy during the previous 24 months, prior to initiating Uplizna

      and
    - Uplizna is initiated according to the U.S. FDA labeled dosing for NMOSD; **and**
    - Prescribed by, or in consultation with, a neurologist; **and**
    - Patient is **not** receiving Uplizna in combination with **any** of the following:
        - Disease modifying therapies for the treatment of multiple sclerosis [e.g., Gilenya (fingolimod), Tecfidera (dimethyl fumarate), Ocrevus (ocrelizumab), etc.]
        - Complement inhibitors [e.g., Soliris (eculizumab), Ultomiris (ravulizumab)]
        - Anti-IL6 therapy [e.g., Actemra (tocilizumab)]
        - Anti-CD20 therapy [e.g., rituximab]

      and
    - Initial authorization will be for no more than 6 months
- For **continuation of therapy**:
    - Documentation of positive clinical response; **and**
    - Uplizna is dosed according to the U.S. FDA labeled dosing for NMOSD; **and**
    - Patient is **not** receiving Uplizna in combination with **any** of the following:
        - Disease modifying therapies for the treatment of multiple sclerosis [e.g., Gilenya (fingolimod), Tecfidera (dimethyl fumarate), Ocrevus (ocrelizumab), etc.]
        - Anti-IL6 therapy [e.g., Actemra (tocilizumab)]
        - Complement inhibitors [e.g., Soliris (eculizumab), Ultomiris (ravulizumab)]
        - Anti-CD20 therapy [e.g., rituximab]

      and
    - Reauthorization will be for no more than 12 months

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

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

Diagnosis Code	Description
G36.0	Neuromyelitis optica [Devic]

Background

Uplizna (inebilizumab-cdon) is a CD19-directed humanized afucosylated IgG1 monoclonal antibody. The exact mechanism of action by which inebilizumab exerts its therapeutic effects in neuromyelitis optica spectrum disorder (NMOSD) is not known, but is presumed to involve binding to CD19, a cell surface antigen on pre-B and mature B lymphocytes. After cell surface binding to B lymphocytes, inebilizumab results in antibody-dependent cellular cytolysis.[5]

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under

some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

Clinical Evidence

Proven

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Inebilizumab-cdon is indicated for the treatment of NMOSD.

Cree et al., evaluated the efficacy and safety of inebilizumab, in 230 patients with NMOSD over 44 months in a multicenter, double-blind, randomized placebo-controlled phase 2/3 study. 174 participants received inebilizumab and 56 participants received placebo. Eligible patients were adults (≥ 18 years old), an expanded disability status score (EDSS) of 8 or less, who required at least one rescue therapy treatment during the year prior to screening, or at least 2 attacks requiring rescue therapy in the 2 years before screening. Patients who were AQP4-IgG-seropositive and AQP4-IgG-seronegative were eligible; however, patients who were seronegative also needed to meet the criteria described by Wingerchuk and colleagues. The mean EDSS score was 4.0. The number of relapses in the two years prior to randomization was 2 or more in 83% of the patients. Participants were randomly allocated (3:1) to receive 300 mg intravenous inebilizumab or placebo on days 1 and 15, with a total dose of inebilizumab in the randomized controlled period of 600 mg. No further doses occurred after day 15 within the study period. All participants received oral corticosteroids to minimize the risk of an attack immediately following the first inebilizumab treatment. Primary endpoint was the time in days to the onset of an NMOSD attack, on or before day 197. Secondary endpoints included worsening of EDSS score from baseline, change from baseline in low-contrast visual acuity binocular score; cumulative total number of active MRI lesions, and number of NMOSD-related inpatient hospitalizations, longer than an overnight stay. The randomized controlled period was stopped prior to completion of enrollment, as there was a clear demonstration of efficacy: 12% of participants receiving inebilizumab had an attack, versus 39% of participants receiving placebo (RR 73%; HR 0.272 [95% CI 0.150-0.496]; $p < 0.0001$). In the anti-AQP4 antibody positive population, there was a 77.3% relative reduction (HR 0.227, $p < 0.0001$), whereas, patients who were anti-AQP4 antibody negative had no evidence of benefit.[5] Adverse events occurred in 72% of participants receiving inebilizumab and 73% of participants receiving placebo. Service adverse events occurred in 5% of participants receiving inebilizumab and 9% of participants receiving placebo. The authors concluded that compared to placebo, inebilizumab reduced the risk of an NMOSD attack.[6]

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Uplizna is a CD19-directed cytolytic antibody indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.[5]

Centers for Medicare and Medicaid Services (CMS)

Medicare does not have a National Coverage Determination (NCD) for Uplizna® (inebilizumab-cdon). Local Coverage Determinations (LCDs)/Local Coverage Articles (LCAs) do not exist.

In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals. (Accessed June 13, 2023)

*Preferred therapy criteria is not applicable for Medicare Advantage members.

References

1. Trebst C, Jarius S, Berthele A, et al. Update on the diagnosis and treatment of neuromyelitis optica: Recommendations of the Neuromyelitis Optica Study Group (NEMOS). J Neurol. 2014 Jan;261(1):1-16. doi: 10.1007/s00415-013-7169-7. Epub 2013 Nov 23.
2. Scott TF, Frohman EM, DeSeze J, et al. Evidence-based guideline: Clinical evaluation and treatment of transverse myelitis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2011 Dec 13;77(24):2128-34.
3. Sellner J1, Boggild M, Clanet M, et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. Eur J Neurol. 2010 Aug;17(8):1019-32.
4. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015 Jul 14;85(2):177-89.
5. Uplizna [prescribing information]. Gaithersburg, MD: Viela Bio, Inc.; July 2021.
6. Cree B, Bennett J, et al. Inebilizumab for the treatment of neuromyelitis optica spectrum disorder (N-MOmentum): a double-blind, randomised placebo-controlled phase 2/3 trial. The Lancet. 2019 Oct;394(10206): 1352-1363.
7. Pittock SJ, Berthele A, Fujihara K, et al. Eculizumab in Aquaporin-4-Positive Neuromyelitis Optica Spectrum Disorder. N Engl J Med. 2019 May 3.
8. Kim SH, Huh SY, Lee SJ, et al. A 5-year follow-up of rituximab treatment in patients with neuromyelitis optica spectrum disorder. JAMA Neurol. 2013 Sep 1;70(9):1110-7.
9. Mealy MA, Wingerchuk DM, Palace J, et al. Comparison of Relapse and Treatment Failure Rates Among Patients With Neuromyelitis Optica: Multicenter Study of Treatment Efficacy. JAMA Neurol. 2014 Mar;71(3):324-30.
10. Sato D, Callegaro D, Lana-Peixoto MA, Fujihara K. Treatment of neuromyelitis optica: an evidence based review. Arq Neuropsiquiatr 2012;70(1);59-66.
11. Ciron J, Audoin B, Bourre B, et al. Recommendations for the use of Rituximab in neuromyelitis optica spectrum disorders. Rev Neurol (Paris). 2018 Apr;174(4):255-264.
12. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015 Jul 14;85(2):177-89.
13. Nikoo Z, Badihian S, Shaygannejad V, et al. Comparison of the efficacy of azathioprine and rituximab in neuromyelitis optica spectrum disorder: a randomized clinical trial. J Neurol. 2017 Sep;264(9):2003-2009.
14. Gao F, Chai B, Gu C, et al. Effectiveness of rituximab in neuromyelitis optica: a meta-analysis. BMC Neurol. 2019 Mar 6;19(1):36.

Policy History/Revision Information

Date	Summary of Changes
09/01/2023	**Coverage Rationale** • Revised coverage criteria: ***Initial Therapy*** ○ Replaced criterion requiring "*submission of medical records (e.g., chart notes, laboratory values, etc.) to support the* diagnosis of neuromyelitis optica spectrum disorder (NMOSD) by a neurologist confirming all of the [criteria listed in the policy]" with "diagnosis of neuromyelitis optica spectrum disorder (NMOSD) by a neurologist confirming all of the [criteria listed in the policy]" ○ Updated list of examples of complement inhibitors the patient cannot receive in combination with Uplizna; added Ultomiris (ravulizumab) ***Continuation of Therapy*** ○ Removed criterion requiring:

Date	Summary of Changes
	▪ Submission of medical records (e.g., chart notes, laboratory tests) to demonstrate a positive clinical response from baseline as demonstrated by at least both of the following: – Reduction in the number and/or severity of relapses or signs and symptoms of NMOSD – Maintenance, reduction, or discontinuation of dose(s) of any baseline immunosuppressive therapy (IST) prior to starting Uplizna; add on, dose escalation of IST, or additional rescue therapy from baseline to treat NMOSD or exacerbation of symptoms while on Uplizna therapy will be considered as treatment failure ▪ Prescribed by, or in consultation with, a neurologist ○ Updated list of examples of complement inhibitors the patient cannot receive in combination with Uplizna; added Ultomiris (ravulizumab) **Supporting Information** ● Archived previous policy version 2022D0091E

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.