Uplizna® (inebilizumab-cdon)
(Intravenous)

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I. Length of Authorization

Initial coverage will be provided for 6 months and may be renewed annually thereafter.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

Uplizna 100 mg/10 mL single-dose vial for injection:

- Loading Doses: 3 vials on days 1, 15
- Maintenance Dose: 3 vials every 6 months

B. Max Units (per dose and over time) [HCPCS Unit]:

- 300 billable units (300 mg) on days 1, 15 and then 300 billable units (300 mg) every 6 months thereafter

III. Initial Approval Criteria [1,2]

> Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e. genetic and mutational testing) supporting initiation when applicable. Medical records may be submitted via direct upload through the PA web portal or by fax.

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**
- Patient has been evaluated and screened for the presence of hepatitis B virus (HBV) prior to initiating treatment and confirmed to be negative for active HBV; **AND**
- Patient has had baseline serum immunoglobulin measured prior to the start of therapy; **AND**

- Patient has not received intravenous immunoglobulin (IVIG) within 1 month prior to the start of therapy; **AND**
- Patient does not have an underlying immunodeficiency disorder (i.e., acquired/congenital primary immunodeficiency, HIV, etc.); **AND**

Universal Criteria [1,2]

- Patient has been evaluated and screened for the presence of latent tuberculosis (TB) infection prior to initiating treatment and will receive ongoing monitoring for the presence of TB during treatment; **AND**
- Patient does not have an active infection, including clinically important localized infections; **AND**
- Live or live-attenuated vaccinations will not be administered within the 4-weeks prior to the start of therapy and will not be administered concurrently while on therapy; **AND**
- Patient has not previously received, and will not concomitantly receive, therapy with any of the following:
    - Other drugs which can result in prolonged additive immunosuppression [i.e., alemtuzumab, natalizumab, cyclosporin, methotrexate, mitoxantrone, cyclophosphamide, tocilizumab, maintenance corticosteroids *(not including pre-medications or rescue therapy),* etc.]; **AND**
    - Other immunosuppressant procedures (e.g., total lymphoid irradiation, bone marrow transplant, T-cell vaccination therapy, etc.); **AND**
- Patient will not concomitantly receive therapy with any of the following:
    - Complement-inhibitors (e.g., eculizumab, ravulizumab, etc.); **AND**
    - Anti-CD20-directed antibody (e.g., rituximab); **AND**
    - IL-6 inhibitor (e.g., satralizumab, tocilizumab, sarilumab, etc.) therapies; **AND**

Neuromyelitis Optica Spectrum Disorder (NMOSD) † Φ [1,2,4,5]

- Patient has a confirmed diagnosis based on the following:
    - Patient was found to be seropositive for aquaporin-4 (AQP4) IgG antibodies; **AND**
    - Patient has at least one core clinical characteristic § *(Note: some core clinical characteristics require both clinical and typical MRI findings)*; **AND**
    - Alternative diagnoses have been excluded [e.g., myelin oligodendrocyte glycoprotein (MOG) antibody disease (MOGAD), multiple sclerosis, sarcoidosis, cancer, chronic infection, etc.]; **AND**
- Patient has a history of one or more relapses that required rescue therapy within the prior year OR two or more relapses that required rescue therapy within the prior 2 years; **AND**
- Patient has an Expanded Disability Status Score (EDSS) of ≤ 7.5 (i.e., inability to take more than a few steps; restricted to wheelchair and may need aid in transferring; can wheel self

but cannot carry on in standard wheelchair for a full day and may require a motorized wheelchair)

§ Core Clinical Characteristics of NMOSD [5]
▪ Acute optic neuritis ▪ Acute myelitis ▪ Area postrema syndrome (APS): episode of otherwise unexplained hiccups and/or nausea and vomiting (lasting for at least 48 hours or with MRI evidence of a dorsal brainstem lesion) ▪ Acute brainstem syndrome other than APS ▪ Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic lesion on MRI ¥ ▪ Acute cerebral syndrome with NMOSD-typical brain lesion on MRI ψ
¥ Diencephalic syndrome: Periependymal lesion (3rd ventricle) OR hypothalamic/thalamic lesion ψ Cerebral syndrome: Extensive periependymal lesion (lateral ventricle; often with Gd) OR long (> 1⁄2 length), diffuse, heterogeneous or edematous corpus callosum lesion OR long corticospinal tract lesion (unilateral or bilateral, contiguously involving internal capsule and cerebral peduncle) OR large, confluent (unilateral or bilateral) subcortical or deep white matter lesion

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,2]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: serious infusion related reactions (e.g., headache, nausea, somnolence, dyspnea, fever, myalgia, rash, etc.), serious infections including progressive multifocal leukoencephalopathy (PML), hypogammaglobulinemia necessitating IVIG treatment or leading to recurrent infections, etc.; **AND**
- Disease response as indicated by stabilization/improvement in one or more of the following:
    - Neurologic symptoms as evidenced by a decrease in acute relapses, improvement in stability, or improvement in EDSS
    - Reduced hospitalizations
    - Reduction/discontinuation in plasma exchange treatments

V. Dosage/Administration [1]

Indication	Dose
Neuromyelitis Optica Spectrum Disorder (NMOSD)	Uplizna is administered as an intravenous infusion, as follows: • Initial dose: 300 mg IV infusion followed 2 weeks later by a second 300 mg IV infusion.

	• Subsequent doses *(starting 6 months from the first infusion)*: single 300 mg IV infusion every 6 months.

– *Uplizna must be diluted prior to administration. Prior to the start of the intravenous infusion, the prepared infusion solution should be at room temperature.*
– *Administer Uplizna under the close supervision of an experienced healthcare professional with access to appropriate medical support to manage potential severe reactions such as serious infusion reactions.*
– *Administer the prepared solution intravenously via an infusion pump at an increasing rate to completion, approximately 90 minutes, according to the schedule in the PI.*
– *Administer through an intravenous line containing a sterile, low-protein binding 0.2 or 0.22 micron in-line filter.*

VI. Billing Code/Availability Information

HCPCS Code:

- J1823 – Injection, inebilizumab-cdon, 1 mg; 1 billable unit = 1 mg

NDC:

- Uplizna 100 mg/10 mL single-dose vials for injection: 75987-0150-xx

VII. References

1. Uplizna [package insert]. Dublin, Ireland; Horizon Therapeutics Ireland DAC; July 2021. Accessed September 2023.
2. Cree BAC, Bennett JL, Kim HJ, et al; N-MOmentum study investigators. Inebilizumab for the treatment of neuromyelitis optica spectrum disorder (N-MOmentum): a double-blind, randomised placebo-controlled phase 2/3 trial. Lancet. 2019 Oct 12;394(10206):1352-1363. doi: 10.1016/S0140-6736(19)31817-3. Epub 2019 Sep 5.
3. 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; 261:1.
4. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015 Jul;85(2):177-89. Epub 2015 Jun 19.
5. Jarius, S., Aktas, O., Ayzenberg, I. et al. Update on the diagnosis and treatment of neuromyelits optica spectrum disorders (NMOSD) – revised recommendations of the Neuromyelitis Optica Study Group (NEMOS). Part I: Diagnosis and differential diagnosis. J Neurol 270, 3341–3368 (2023). https://doi.org/10.1007/s00415-023-11634-0.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
G36.0	Neuromyelitis optica [Devic]

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Article (LCAs) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC