

Uplizna™ (Inebilizumab-Cdon)

Policy Number: PHARMACY 330.1 T2
Effective Date: October 1, 2020

[➔ Instructions for Use](#)

Table of Contents	Page
Coverage Rationale	1
Prior Authorization Requirements	2
Applicable Codes	2
Description of Services	3
Benefit Considerations	3
Clinical Evidence	3
U.S. Food and Drug Administration	4
References	4
Policy History/Revision Information	4
Instructions for Use	4

Related Policies

- [Acquired Rare Disease Drug Therapy Exception Process](#)
- [Review at Launch for New to Market Medications](#)

Coverage Rationale

[➔ See Benefit Considerations](#)

Uplizna has been added to the Review at Launch program. Refer to the Clinical Policy titled [Review at Launch for New to Market Medications](#) for additional details.

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

Initial Therapy

- 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 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: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)]
 - Anti-IL6 therapy [e.g., Actemra (tocilizumab)]
 - Anti-CD20 therapy [e.g., rituximab]
- and
- Initial authorization will be for no more than 6 months

Continuation Therapy

- Documentation of positive clinical response; and
- 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. Note: 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
- and
- Uplizna is dosed 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.]
 - Anti-IL6 therapy [e.g., Actemra (tocilizumab)]
 - Complement inhibitors [e.g., Soliris (eculizumab)]
 - Anti-CD20 therapy [e.g., rituximab]
- and
- Reauthorization will be for no more than 12 months

Prior Authorization Requirements

Prior authorization is not required; however, it is strongly recommended for Uplizna. While no penalty will be imposed for failure to request a pre-service review, if one is not requested, a medical necessity review will be conducted post-service to determine coverage. It is the referring physician's responsibility to provide medical documentation to demonstrate clinical necessity for the medication. Refer to the Clinical Policy titled [Review at Launch for New to Market Medications](#).

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 may apply.

HCPCS Code	Description
C9399	Unclassified drugs or biologicals
J3590	Unclassified biologics

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 cytotoxicity.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. See the Administrative Policy titled [Acquired Rare Disease Drug Therapy Exception Process](#).

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. Serious 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

References

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare national policy that was researched, developed and approved by UnitedHealth Group National Pharmacy & Therapeutics Committee. [2020D0091A]

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Policy History/Revision Information

Date	Summary of Changes
10/01/2020	<ul style="list-style-type: none">• New Clinical Policy

Instructions for Use

This Clinical Policy provides assistance in interpreting UnitedHealthcare Oxford 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 Oxford reserves the right to modify its Policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice.

The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Oxford Clinical 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.