Ocrevus Zunovo™ (ocrelizumab and hyaluronidase-ocsq) (Subcutaneous)

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I. Length of Authorization

Coverage will be provided for 12 months and may be renewed annually thereafter.

II. Dosing Limits

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

- Ocrevus 920 mg ocrelizumab and 23,000 units hyaluronidase per 23 mL solution in a single-dose vial: 1 vial per 6 months

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

- 920 mg ocrelizumab (and 23,000 units hyaluronidase) every 6 months

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**
- Patient has been screened for the presence of Hepatitis B virus (HBV) prior to initiating treatment AND does not have active disease (i.e., positive HBsAg and anti-HBV tests); **AND**
- Patient has had baseline serum immunoglobulins assessed; **AND**
- Patient does not have a history of life-threatening administration reactions to ocrelizumab; **AND**

Universal Criteria [1]

- Patient will not receive live or live-attenuated vaccines while on therapy or within 4 weeks prior to initiation of treatment; **AND**
- Patient does not have an active infection; **AND**
- Must be used as single agent therapy; **AND**
- Patient has not received a dose of ocrelizumab or ublituximab within the past 5 months; **AND**

Multiple Sclerosis † [1,7,11]

- Patient must have a confirmed diagnosis of multiple sclerosis (MS) as documented by laboratory report (i.e., MRI); **AND**

- Patient has a diagnosis of a relapsing form of MS [i.e., relapsing-remitting MS (RRMS)*****, active secondary progressive disease (SPMS)******, or clinically isolated syndrome (CIS)*******]; **AND**

- For relapsing MS: Patient must have had an inadequate response to an adequate trial of one of the following drugs: dimethyl fumarate, fingolimod, teriflunomide, or glatiramer acetate (generic, Glatopa), unless contraindicated or not tolerated; **OR**

- Patient has a diagnosis of primary progressive MS (PPMS)********; **AND**
  - Patient is less than 65 years of age; **AND**
  - Patient has an expanded disability status scale (EDSS) score of ≤ 6.5

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

***Definitive diagnosis of MS with a relapsing-remitting course is based upon BOTH dissemination in time and space. Unless contraindicated, MRI should be obtained (even if criteria are met).** [11]

Dissemination in time (*Development/appearance of new CNS lesions over time*)	**Dissemination in space** (*Development of lesions in distinct anatomical locations within the CNS; multifocal*)

• ≥ 2 clinical attacks; **OR**
• 1 clinical attack AND one of the following:
  ○ MRI indicating simultaneous presence of gadolinium-enhancing and non-enhancing lesions at any time or by a new T2-hyperintense or gadolinium-enhancing lesion on follow-up MRI compared to baseline scan
  ○ CSF-specific oligoclonal bands
	• ≥ 2 lesions; **OR**
	• 1 lesion AND one of the following:
	  ○ Clear-cut historical evidence of a previous attack involving a lesion in a distinct anatomical location
	  ○ MRI indicating ≥ 1 T2-hyperintense lesions characteristic of MS in ≥ 2 of 4 areas of the CNS (periventricular, cortical or juxtacortical, infratentorial, or spinal cord)

****Active secondary progressive MS (SPMS) is defined as the following:** [8,11-13,15]

- Expanded Disability Status Scale (EDSS) score ≥ 3.0; **AND**
- Disease is progressive ≥ 3 months following an initial relapsing-remitting course (i.e., EDSS score increase by 1.0 in patients with EDSS ≤5.5 or increase by 0.5 in patients with EDSS ≥6); **AND**
  - ≥ 1 relapse within the previous 2 years; **OR**
  - Patient has gadolinium-enhancing activity OR new or unequivocally enlarging T2 contrast-enhancing lesions as evidenced by MRI

*****Definitive diagnosis of CIS is based upon ALL of the following:** [11]

- A monophasic clinical episode with patient-reported symptoms and objective findings reflecting a focal or multifocal inflammatory demyelinating event in the CNS
- Neurologic symptom duration of at least 24 hours, with or without recovery
- Absence of fever or infection
- Patient is not known to have multiple sclerosis

****Definitive diagnosis of MS with a primary progressive course is based upon the following: [11]

• 1 year of disability progression independent of clinical relapse; **AND**
• TWO of the following:
  ○ ≥ 1 T2-hyperintense lesion characteristic of MS in one or more of the following regions of the CNS: periventricular, cortical or juxtacortical, or infratentorial
  ○ ≥ 2 T2-hyperintense lesions in the spinal cord
  ○ Presence of CSF-specific oligoclonal bands

IV. Renewal Criteria [1,6,10,14]

Coverage can be renewed based on the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion reactions, severe infections, progressive multifocal leukoencephalopathy malignancy, hypogammaglobulinemia, immune-mediated colitis, etc.; **AND**
- Continuous monitoring of response to therapy indicates a beneficial response***** [manifestations of MS disease activity include, but are not limited to, an increase in annualized relapse rate (ARR), development of new/worsening T2 hyperintensities or enhancing lesions on brain/spinal MRI, and progression of sustained impairment as evidenced by expanded disability status scale (EDSS), timed 25-foot walk (T25-FW), 9-hole peg test (9-HPT)]

*****Note:

– Inadequate response, in those who have been adherent and receiving therapy for sufficient time to realize the full treatment effect, is defined as ≥ 1 relapse, ≥ 2 unequivocally new MRI-detected lesions, or increased disability on examination over a one-year period.

Note: patients with primary progressive MS generally do not have clinical relapses and do not typically develop new lesions on MRI

PPMS

- Patient continues to be ambulatory, defined as an EDSS score of <7.5

V. Dosage/Administration [1]

Indication	Dose
Multiple Sclerosis	The recommended dosage of Ocrevus Zunovo is 920 mg/23,000 units *(920 mg ocrelizumab and 23,000 units of hyaluronidase)* administered as a single 23 mL subcutaneous injection in the abdomen over approximately 10 minutes every 6 months.
Note: *– Ocrevus Zunovo should be administered via subcutaneous injection by a healthcare professional.* *– Ocrevus Zunovo is for subcutaneous use in the abdomen only.* *– Ocrevus Zunovo has different dosage and administration instructions than intravenous ocrelizumab.*	

VI. Billing Code/Availability Information

HCPCS:

- J3590 – Unclassified biologics

NDC:

- Ocrevus Zunovo 920 mg and 23,000 units/23 mL (40 mg and 1,000 units/mL) single-dose vial: 50242-0554-xx

VII. References

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15. Cree BAC, Arnold DL, Chataway J, et al. Secondary Progressive Multiple Sclerosis: New Insights. Neurology. 2021 Aug 24;97(8):378-388. doi: 10.1212/WNL.0000000000012323. Epub 2021 Jun 4.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
G35	Multiple Sclerosis

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

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

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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