Ocrevus (ocrelizumab) and Ocrevus Zunovo (ocrelizumab and hyaluronidase-ocsq)
(Intravenous/Subcutaneous)

Effective Date: 1/1/2020
Dates Reviewed: 05/20/2019, 09/18/2019, 12/20/2019, 01/22/2020, 06/10/2021, 3/17/2022, 7/13/2023, 12/07/2023, 01/10/2024, 04/02/2025, 03/24/2026
Scope: Medicaid, Commercial, Medicare

I. Length of Authorization

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

II. Dosing Limits

Ocrevus IV Max Units (per dose and over time) [HCPCS Unit]:

Initial dose:

- 300 billable units (300 mg) on day 1 and day 15

Subsequent doses:

- 600 billable units (600 mg) every 6 months

Ocrevus Zunovo SC Max Units (per dose and over time) [HCPCS Unit]:

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

III. Summary of Evidence

Ocrelizumab is a CD20-directed cytolytic antibody indicated for the treatment of relapsing forms of multiple sclerosis (MS) and primary progressive MS in adults. Clinical trials evaluating the efficacy and safety of ocrelizumab in patients with multiple sclerosis (MS) have demonstrated significant reductions in disease activity, including the frequency of relapses, progression of disability, and accumulation of lesions on magnetic resonance imaging (MRI). Non-inferior pharmacokinetic exposure was demonstrated between subcutaneous ocrelizumab and intravenous ocrelizumab. In patients with relapsing forms of MS (RMS), two large 96-week randomized trials showed that Ocrevus significantly reduced disease activity compared to interferon beta-1a (Rebif). Ocrevus lowered the annualized relapse rate by about 46-47%, reduced the risk of 12-week confirmed disability progression by 40%, and produced large reductions in MRI markers of inflammation (94–95% fewer T1 Gd-enhancing lesions and 77–83% fewer new/enlarging T2 lesions). In primary progressive MS (PPMS), a separate randomized trial demonstrated that Ocrevus slowed disability progression, reducing the risk of 12-week confirmed progression by 24% versus placebo. Patients on Ocrevus also showed less worsening on walking speed and reductions in T2 lesion volume. In a safety substudy

evaluating faster infusions, 2-hour Ocrevus infusions had a similar rate of mostly mild/moderate infusion reactions compared with the standard 3.5-hour schedule, with no life-threatening or fatal reactions reported. Common adverse events include infusion-related reactions and upper and lower respiratory tract infections, skin infections, and infusion reactions. Serious adverse events, including infections, progressive multifocal leukoencephalopathy (PML), reduction in immunoglobulins, malignancies, immune-mediated colitis, and liver injury have been reported with Ocrevus treatment.

IV. Initial Approval Criteria [1,7,11]

Coverage is provided in the following conditions:

- Member is at least 18 years of age; **AND**
- Ocrevus or Ocrevus Zunovo is prescribed by, or in consultation with, a neurologist; AND
- Member 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**
- Member has had baseline serum immunoglobulins, serum aminotransferases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]), alkaline phosphatase, and bilirubin level assessed; **AND**
- Member does not have a history of life-threatening administration reactions to ocrelizumab; **AND**
- Member will not receive live or live-attenuated vaccines while on therapy or within 4 weeks prior to initiation of treatment; **AND**
- Member does not have an active infection; **AND**
- Must be used as single agent therapy; **AND**
- Member has not received a dose of ocrelizumab or ublituximab within the past 5 months; **AND**
- Member must have a confirmed diagnosis of multiple sclerosis (MS) as documented by laboratory report (i.e., MRI); **AND**
    - Member 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)*******]; **OR**
    - Member has a diagnosis of primary progressive MS (PPMS)********; **AND**
- Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

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

***Definitive diagnosis of MS with a relapsing-remitting course is based upon:**

- Dissemination in space *(see below)* AND one or more of the following:
    - Positive cerebrospinal fluid (CSF) (e.g., presence of oligoclonal bands or kappa free light chain index)

- Positive central vein sign (CVS) (e.g., presence of six or more lesions with CVS; if fewer than 6 white matter lesions are seen on MRI, the number of CVS positive lesions should outnumber the CVS negative lesions)
- Dissemination in time (DIT) *(see below)*
- Presence of lesions in at least four of five CNS anatomical locations; **OR**

- Lesions present in one CNS site (including members with 12 months or longer progression from onset) AND one or more of the following:
  - CSF positivity and CVS positivity
  - CSF positivity and paramagnetic rim lesion (PRL) positivity (e.g., presence of one or more PRL)
  - DIT *(see below)* and CVS positivity
  - DIT *(see below)* and PRL positivity

Unless contraindicated, MRI should be obtained (even if criteria are met).

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** • Simultaneous presence of gadolinium enhancing and non-enhancing lesions at any time; **OR** • A new T2-hyperintense or gadolinium enhancing lesion on follow-up MRI	• ≥ 2 lesions; **OR** • MRI indicating typical lesions in ≥ 2 of 5 areas of the CNS (optic nerve, intracortical or juxtacortical, periventricular, infratentorial, or spinal cord); **OR** • In members with progressive disease (members with 12 months or longer progression from onset), two spinal cord lesions

****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

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

Coverage can be renewed based on the following criteria:

- Member continues to meet the universal and other indication-specific relevant criteria identified in section IV; **AND**
- Member has not received a dose of ocrelizumab or ublituximab within the past 5 months; **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**
- Member has experienced a beneficial response* to therapy [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

VI. Dosage/Administration [1]

Drug	Dose
Ocrevus IV	Initial dose: 300 mg intravenous infusion, followed two weeks later by a second 300 mg IV infusion Subsequent doses: 600 mg IV infusion every 6 months • Administer first subsequent dose 6 months after infusion of the initial dose
Ocrevus Zunovo SC	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

Drug	Dose
	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.*

VII. Billing Code/Availability Information

HCPCS:

- J2350 – Injection, ocrelizumab, 1 mg; 1 mg = 1 billable unit
- J2351 - Injection, ocrelizumab, 1 mg and hyaluronidase-ocsq; 1 mg = 1 billable unit

NDC:

- Ocrevus 300 mg/10 mL single-dose vial: 50242-0150-xx
- Ocrevus Zunovo 920 mg and 23,000 units/23 mL (40 mg and 1,000 units/mL) single-dose vial: 50242-0554-xx

VIII. References

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16. 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

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
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

Policy Rationale:

Ocrevus and Ocrevus Zunovo were reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Ocrevus or Ocrevus Zunovo according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.