Clinical Policy: Ocrelizumab (Ocrevus), Ocrelizumab/Hyaluronidase-ocsq (Ocrevus Zunovo)

Reference Number: MDN.CP.PHAR.335
Effective Date: 04.01.22
Last Review Date: 5.6.25
Line of Business: Meridian IL Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Ocrelizumab (Ocrevus®) and ocrelizumab/hyaluronidase-ocsq (Ocrevus Zunovo™) are CD20-directed cytolytic antibody.

FDA Approved Indication(s)

Ocrevus and Ocrevus Zunovo are indicated for the treatment of:

- Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- Primary progressive MS, in adults

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Ocrevus and Ocrevus Zunovo are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Sclerosis (must meet all)**:**

1. Diagnosis of one of the following (a, b, c, or d):
   a. Clinically isolated syndrome, and member is contraindicated to both, or has experienced clinically significant adverse effects to one, of the following at up to maximally indicated doses: an interferon-beta agent (Avonex®, Betaseron®, or Rebif®), glatiramer (Copaxone®, Glatopa®);
   b. Relapsing-remitting MS, and failure of all of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated (i, ii, iii, and iv):*
      i. Dimethyl fumarate (Tecfidera®);
      ii. Gilenya®;
      iii. An interferon-beta agent (Avonex, Betaseron, or Rebif,) or glatiramer (Copaxone® brand is preferred);
      **Prior authorization is required for all disease modifying therapies for MS*
   c. Secondary progressive MS;
   d. Primary progressive MS;

2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Ocrevus/ Ocrevus Zunovo is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);

5. At the time of request, member does not have active hepatitis B infection (positive results for hepatitis B surface antigen and anti-hepatitis B virus tests);
6. Dose does not exceed the following (a or b):
   a. For Ocrevus (i and ii):
      i. Initial dose: 300 mg, followed by a second 300 mg dose 2 weeks later;
      ii. Maintenance dose: 600 mg every 6 months.
   b. For Ocrevus Zunovo: 920 mg every 6 months.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Multiple Sclerosis (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Ocrevus/ Ocrevus Zunovo is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
4. If request is for a dose increase, new dose does not exceed the following (a or b):
   a. For Ocrevus: 600 mg every 6 months;
   b. For Ocrevus Zunovo: 920 mg every 6 months.

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Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs in the PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT in the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PMN.53 for Medicaid or evidence of coverage documents.

B. Rheumatoid arthritis

C. Lupus nephritis/systemic lupus erythematosus.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MS: multiple sclerosis

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Aubagio® (teriflunomide)	7 mg or 14 mg PO QD	14 mg/day
Avonex®, Rebif® (interferon beta-1a)	*Avonex*: 30 mcg IM Q week *Rebif*: 22 mcg or 44 mcg SC TIW	*Avonex*: 30 mcg/week *Rebif*: 44 mcg TIW
Plegridy® (peginterferon beta-1a)	125 mcg SC Q2 weeks	125 mcg/2 weeks
Betaseron®(interferon beta-1b)	250 mcg SC QOD	250 mg QOD
glatiramer acetate (Copaxone®, Glatopa®)	20 mg SC QD or 40 mg SC TIW	20 mg/day or 40 mg TIW
Gilenya® (fingolimod)	0.5 mg PO QD	0.5 mg/day
dimethyl fumarate (Tecfidera®)	120 mg PO BID for 7 days, followed by 240 mg PO BID	480 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): active hepatitis B virus infection; history of life-threatening infusion reaction to Ocrevus, history of hypersensitivity to ocrelizumab, hyaluronidase, or to any component of Ocrevus Zunovo (*Ocrevus Zunovo only*)

- Boxed warning(s): none reported

Appendix D: General Information

- Disease-modifying therapies for MS are: glatiramer acetate (Copaxone®, Glatopa®), interferon beta-1a (Avonex®, Rebif®), interferon beta-1b (Betaseron®, Extavia®), peginterferon beta-1a (Plegridy®), dimethyl fumarate (Tecfidera®), diroximel fumarate (Vumerity®), monomethyl fumarate (Bafiertam™), fingolimod (Gilenya®), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®),

natalizumab (Tysabri® and biosimilar Tyruko), ocrelizumab (Ocrevus®), ocrelizumab/hyaluronidase-ocsq (Ocrevus Zunovo™), cladribine (Mavenclad®), siponimod (Mayzent®), ozanimod (Zeposia®), and ofatumumab (Kesimpta®).

- Of the disease-modifying therapies for MS that are FDA-labeled for clinically isolated syndrome CIS, only the interferon products, glatiramer, and Aubagio have demonstrated any efficacy in decreasing the risk of conversion to MS compared to placebo. This is supported by the AAN 2018 MS guidelines.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ocrelizumab (Ocrevus)	Relapsing and primary progressive MS	Initial 300 mg IV infusion with a second 300 mg IV infusion two weeks later, followed by subsequent doses of 600 mg via IV infusion every 6 months	600 mg/6 months
Ocrelizumab/ hyaluronidase-ocsq (Ocrevus Zunovo)		920 mg/23,000 units SC every 6 months (must be administered by a healthcare professional)	920 mg/ 23,000 units/6 months

VI. Product Availability

Drug Name	Availability
Ocrelizumab (Ocrevus)	Single-dose vial: 300 mg/10 mL
Ocrelizumab/hyaluronidase-ocsq (Ocrevus Zunovo)	Single-dose vial: 920 mg/23,000 units/23 mL

VII. References

1. Ocrevus Prescribing Information. South San Francisco, CA: Genentech, Inc; June 2024. Available at www.ocrevus.com. Accessed May 10, 2025.
2. Ocrevus Zunovo Prescribing Information. South San Francisco, CA: Genentech, Inc; September 2024. Available at https://www.gene.com/download/pdf/ocrevus_zunovo_prescribing.pdf. Accessed January 23, 2025.
3. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2018; 90(17): 777-788. Full guideline available at: https://www.aan.com/Guidelines/home/GetGuidelineContent/904.
4. Mysler EF, Spindler AJ, Guzman R, et al. Efficacy and safety of ocrelizumab in active proliferative lupus nephritis: Results from a randomized, double-blind, phase III study. Arthritis & Rheumatism. 2013; 65(9): 2368-2379.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2350	Injection, ocrelizumab, 1 mg
J2351	Injection, ocrelizumab, 1 mg and hyaluronidase-ocsq

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created, adapted from CP.PHAR.335	04.01.22	04.22
Corrected continuity errors; added rheumatoid arthritis and lupus nephritis/systemic lupus erythematosus as diagnoses not covered due to safety concerns resulting in termination of the respective clinical studies; template changes applied	3.2.23	
2Q 2024 annual review: no significant changes; references reviewed and updated.	6.5.24	
2Q 2025 annual review: per competitor analysis, added coding implications; removed requirements for documentation of baseline relapses/expanded disability status score and specific measures of positive response; updated Appendix C to include Ocrevus Zunovo's hypersensitivity contraindication; added HCPCS code [J2351] for Ocrevus Zunovo and removed codes [J3590, C9399]; for continued therapy, modified HIM and Medicaid approval duration from "if member has received < 1 year of total treatment – up to a total of 12 months of treatment and if member has received ≥ 1 year of total treatment – 12 months" to "12 months"; references reviewed and updated.	5.6.25	

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.