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

Reference Number: CP.PHAR.335
Effective Date: 05.01.17
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
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 antibodies.

## 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®/Extavia®†, Rebif®, or Plegridy®), **glatiramer** (Copaxone®, Glatopa®);^
   *^For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
   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):^*
   *^For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395*
      i. **Dimethyl fumarate** (generic Tecfidera®);
      ii. **Teriflunomide** (generic Aubagio®);
      iii. **Fingolimod** (Gilenya®);
      iv. An **interferon-beta agent** (Avonex, Betaseron/Extavia†, Rebif, or Plegridy) or **glatiramer** (Copaxone, Glatopa);

**Prior authorization may be required for all disease modifying therapies for MS*
*†Betaseron is the preferred interferon beta-1b product for the Commercial and HIM lines of business*

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 one of 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:**
**Medicaid/HIM –** 6 months
**Commercial –** 6 months or to the member's renewal date, whichever is longer

**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 on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and 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.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
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 one of the following (a or b):
   a. For Ocrevus: 600 mg every 6 months;
   b. For Ocrevus Zunovo: 920 mg every 6 months.

**Approval duration:**
**Medicaid/HIM –** 12 months
**Commercial –** 6 months or to the member's renewal date, whichever is longer

**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 on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and 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.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and 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.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and 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 |
|---|---|---|
| teriflunomide (Aubagio®) | 7 mg or 14 mg PO QD | 14 mg/day |
| Avonex®, Rebif® (interferon beta-1a) | *Avonex*: 30 mcg IM Q week<br>*Rebif*: 22 mcg or 44 mcg SC TIW | *Avonex*: 30 mcg/week<br>*Rebif*: 44 mcg TIW |
| Plegridy® (peginterferon beta-1a) | 125 mcg SC Q2 weeks | 125 mcg/2 weeks |
| Betaseron®, Extavia® (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 |
| fingolimod (Gilenya®) | 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®, Tascenso ODT™), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®, and biosimilar Tyruko®), ocrelizumab (Ocrevus®), ocrelizumab/hyaluronidase-ocsq (Ocrevus Zunovo™), cladribine (Mavenclad®), siponimod (Mayzent®), ozanimod (Zeposia®), ponesimod (Ponvory™), ublituximab-xiiy (Briumvi™), and ofatumumab (Kesimpta®).
- Of the disease-modifying therapies for MS that are FDA-labeled for clinically isolated syndrome, only the interferon products, glatiramer, and teriflunomide have demonstrated any efficacy in decreasing the risk of conversion to MS compared to placebo. This is supported by the American Academy of Neurology 2018 MS guidelines.
- In May 2010, the manufacturers of Ocrevus discontinued the Ocrevus clinical developmental program in rheumatoid arthritis due to unfavorable overall benefit to risk profile. The program was initially suspended in March following recommendation from an independent data and safety monitoring board, which concluded that the safety risk outweighed the benefits observed in patients with rheumatoid arthritis based on an infection related safety signal which included serious infections, some of which were fatal, and opportunistic infections.
- The BELONG phase 3 study (Mysler EF et al., 2013) evaluating use of Ocrevus in patients with lupus nephritis due to systemic lupus erythematosus was also terminated

early due to an imbalance of serious and opportunistic infections in the Ocrevus treated patients versus the placebo arm. From an analysis of an incomplete data set, there was no statistically significant differentiation between the Ocrevus and placebo response rates.

## 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 January 23, 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/898. Reaffirmed on October 19, 2024.
4. Biogen. Roche and Biogen Idec announce their decision to discontinue the ocrelizumab clinical development programme in patients with rheumatoid arthritis. Press release published May 19, 2010. Available at: https://investors.biogen.com/news-releases/news-release-details/roche-and-biogen-idec-announce-their-decision-discontinue. Accessed February 12, 2025.
5. 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 |
|---|---|---|
| 2Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated. | 02.08.21 | 05.21 |
| 2Q 2022 annual review: 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; added legacy WellCare line of business (WCG.CP.PHAR.335 to be retired); added Coding Implications section; references reviewed and updated. | 01.28.22 | 05.22 |
| Template changes applied to other diagnoses/indications and continued therapy section. | 09.21.22 | |
| 2Q 2023 annual review: no significant changes; to be inclusive of members continuing therapy from a different benefit, revised Medicaid/HIM continued approval duration to reference the duration of total treatment received rather than the number of re-authorizations; references reviewed and updated. | 01.31.23 | 05.23 |
| Per August SDC, added generic references to Aubagio and Gilenya redirections. | 08.22.23 | 11.23 |
| 2Q 2024 annual review: no significant changes; references reviewed and updated. | 01.30.24 | 05.24 |
| RT4 update: added new dosage form for Ocrevus Zunovo | 10.02.24 | |
| 2Q 2025 annual review: per competitor analysis, removed requirements for documentation of baseline relapses/expanded disability status score and specific measures of positive response; per SDC, removed notation that Extavia is the preferred interferon beta-1b product for the Medicaid line of business as it is no longer available on market; 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. | 02.12.25 | 05.25 |
| Added step therapy bypass for IL HIM per IL HB 5395. | 06.25.25 | |

**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.