# Ocrelizumab (Ocrevus, Ocrevus Zunovo)

Disclaimer

*Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.*

*Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.*

## Summary

Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating disease of the central nervous system. It typically presents in young adults (generally diagnosed before 50 years of age) with symptoms such as vision problems, muscle weakness, numbness, and difficulty with balance and coordination. The most common form is relapsing-remitting MS (occurring in about 85% of patients), characterized by acute attacks followed by periods of remission. Treatment goals include reducing relapses, slowing disability progression, and managing symptoms. Disease-modifying therapies (DMTs) are the primary treatment approach and include injectable medications (e.g., interferons, glatiramer acetate), oral medications (e.g., dimethyl fumarate, fingolimod, teriflunomide, etc.), and infusion therapies (e.g., natalizumab, ocrelizumab).

MS is a progressive disease, meaning that symptoms tend to worsen over time, and it can be classified into several types, including relapsing-remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS).

Currently, there is no cure for MS, but various treatment options are available to manage symptoms, slow the progression of the disease, and improve quality of life.

- Disease-modifying therapies (DMTs) are a class of medications that target the immune system to reduce inflammation and slow down the progression of the disease. The type of DMT prescribed will depend on the type and severity of MS, as well as the individual's medical history and preferences. Some common DMTs include interferon beta, glatiramer acetate, dimethyl fumarate, and fingolimod.
- High dose corticosteroids, such as high dose intravenous methylprednisolone or oral prednisone can be prescribed to reduce inflammation during acute MS relapses.
- Symptomatic treatments are also available to manage specific symptoms of MS, such as muscle spasms, bladder problems, and depression. Physical therapy, occupational therapy, and speech therapy can help individuals with MS maintain mobility, independence, and communication skills.

Ocrevus (ocrelizumab) is a humanized monoclonal antibody that selectively targets CD20-positive B cells. It is approved for:

- Relapsing forms of MS (including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease).
- Primary progressive MS (PPMS). Ocrevus (ocrelizumab) is the only DMT approved for PPMS.

Ocrevus (ocrelizumab) is available in two formulations:

1. Ocrevus (ocrelizumab): Intravenous (IV) formulation.
2. Ocrevus Zunovo (ocrelizumab and hyaluronidase-ocsq): Subcutaneous (SC) formulation containing ocrelizumab and hyaluronidase-ocsq.

## Definitions

"Clinically isolated syndrome" refers to a first episode of neurologic symptoms lasting at least 24 hours caused by inflammation or demyelination in the central nervous system.

"Compendia" are summaries of drug information and medical evidence to support decision-making about the appropriate use of drugs and medical procedures. Examples include, but are not limited to:

1. American Hospital Formulary Service Drug Information
2. Clinical pharmacology
3. National Comprehensive Cancer Network Drugs and Biologics Compendium
4. Thomson Micromedex DrugDex
5. United States Pharmacopeia-National Formulary (USP-NF)

"Disease-modifying therapy" is a medication that modifies the course of MS by reducing relapses and slowing disability progression.

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"EDSS" or "Expanded Disability Status Scale" refers to the most widely utilized MS assessment tool that consists of an ordinal clinical rating scale with half point increments ranging from 0 (normal neurologic examination) to 10 (death due to MS).

"Multiple sclerosis" is a chronic autoimmune disease of the central nervous system characterized by inflammation, demyelination, and neurodegeneration.

"No evidence of" indicates that the reviewer has not identified any records of the specified item or condition within the submitted materials or claims history. In the absence of such evidence, the member is considered eligible. If any evidence of the item or condition is present upon review of the request, the member does not qualify.

"Primary Progressive MS (PPMS)" is a form of MS characterized by worsening neurologic function from the onset of symptoms, without early relapses or remissions.

"Relapse" is defined as the appearance of new symptoms or the worsening of existing symptoms lasting at least 24 hours in the absence of fever or infection.

"Relapsing-remitting MS" refers to a disease course characterized by clearly defined attacks of new or increasing neurologic symptoms followed by periods of partial or complete recovery.

"[s]" indicates state mandates may apply.

"Secondary progressive MS" is a disease course following relapsing-remitting MS that is characterized by a progressive worsening of neurologic function over time with or without relapses.

## Clinical Indications

## Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

The Plan considers Ocrelizumab (Ocrevus, Ocrevus Zunovo) medically necessary when ONE of the following criteria are met:

1. Authorization may be granted for pediatric members less than 18 years of age with multiple sclerosis when there is documentation that the benefits outweigh the risks*; OR*
   *Note: If approved, the requested product will be authorized for up until the member reaches 18 years of age.*
2. The member meets the applicable Medical Necessity Criteria for Initial Clinical Review or Subsequent Clinical Review listed below.

## Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Multiple Sclerosis - Adults

The Plan considers Ocrelizumab (Ocrevus, Ocrevus Zunovo) medically necessary when recent (within the last 3 months) clinical chart documentation provided indicates the member meets ALL of the following:

1. Prescribed by or in consultation with a neurologist or physician who specializes in the treatment of multiple sclerosis; *AND*
2. Is 18 years of age or older; *AND*
3. Patient has ONE (1) of the following diagnoses:
   a. Relapsing form of multiple sclerosis (including relapsing-remitting MS, active secondary progressive MS, or clinically isolated syndrome)*; or*
   b. Primary progressive multiple sclerosis (PPMS); *AND*
4. The member meets ONE (1) of the following criteria:
   a. For relapsing forms of MS the member meets ONE (1) of the following:
      i. Documentation of highly active or aggressive disease, as demonstrated by at least ONE (1) of the following:
         1. Frequent relapses (≥2 in the past year)*; or*
         2. At least 1 relapse with incomplete recovery and MRI activity*; or*
         3. Rapidly advancing disability or cognitive impairment*; or*

4. Disabling relapse with suboptimal response to corticosteroids*; or*
5. MRI findings showing high disease activity (e.g., new/enlarging T2 lesions, enhancing lesions)*; or*

ii. Is unable to use, or has tried and failed ONE (1) of the following:[s]

1. Dimethyl Fumarate (generic Tecfidera)*; or*
2. Fingolimod (generic Gilenya)*; or*
3. Teriflunomide (generic Aubagio); *or*

b. For primary progressive MS the member meets ALL of the following:

i. Evidence of disability progression independent of relapses over the past year*; and*

ii. Expanded Disability Status Scale (EDSS) Score of ≤ 6.5; *AND*

5. Has been screened for hepatitis B virus AND has no evidence of active hepatitis B infection; *AND*
6. Ocrelizumab (Ocrevus, Ocrevus Zunovo) will be used as monotherapy for multiple sclerosis (i.e., member is not using and will not use other disease-modifying MS therapies while on Ocrelizumab); *AND*
7. Ocrelizumab (Ocrevus, Ocrevus Zunovo) is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature.
    - *For Ocrevus (IV):*
        - *Initial doses: 300 mg IV infusion, followed two weeks later by a second 300 mg IV infusion.*
            i. *Initial authorization: Up to 600 mg in the first 28 days.*
        - *Subsequent doses: 600 mg intravenous infusion every 6 months.*
            i. *Up to 600 mg every 6 months.*
    - *For Ocrevus Zunovo (SC): 920 mg ocrelizumab/23,000 units hyaluronidase administered as a single 23 mL subcutaneous injection in the abdomen every 6 months.*

If the above prior authorization criteria are met, the requested medication will be approved for up to 12 months.[s]

*Continued Care*

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Multiple Sclerosis - Adults

The Plan considers Ocrelizumab (Ocrevus, Ocrevus Zunovo) medically necessary when recent (within the last 6 months) clinical chart documentation provided indicates the member meets BOTH of the following:

1. The requested medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis; *AND*
2. The member has experienced at least ONE (1) of the following:
    a. Improvement in at least ONE (1) objective measure, such as:
        i. Reduced disease activity on MRI*; and/or*
        ii. Improved or stable disability scores*; and/or*
        iii. Reduced relapse rate*; and/or*
        iv. Improved fatigue or walking assessments; *AND/OR*
    b. The member has shown stabilization or improvement in at least ONE (1) MS symptom, such as:
        i. Motor function*; and/or*
        ii. Fatigue*; and/or*
        iii. Vision*; and/or*
        iv. Bowel/bladder function*; and/or*
        v. Spasticity*; and/or*
        vi. Walking/gait*; and/or*
        vii. Pain/numbness/tingling.

If the above reauthorization criteria are met, the requested medication will be approved for up to 12 months.[s]

### Experimental or Investigational / Not Medically Necessary[s]

Ocrelizumab (Ocrevus, Ocrevus Zunovo) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Use in combination with other disease-modifying therapies for MS.
- The treatment of other autoimmune conditions not specified in the FDA-approved indications (e.g., lupus nephritis, autoimmune encephalitis).

### Applicable Billing Codes

| Table 1 | |
|---|---|
| CPT/HCPCS Codes for multiple sclerosis considered medically necessary if criteria are met: | |
| *Code* | *Description* |
| 96365 | Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour |

| | |
|---|---|
| 96366 | Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure) |
| 96372 | Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular |
| J2350 | Injection, ocrelizumab, 1 mg |
| J2351 | Injection, ocrelizumab, 1 mg and hyaluronidase-ocsq |

| Table 2 | |
|---|---|
| ICD-10 diagnosis codes considered medically necessary for multiple sclerosis with Table 1 (CPT/HCPCS) codes if criteria are met: | |
| *Code* | *Description* |
| G35 | Multiple sclerosis |
| G35.A | Relapsing-remitting multiple sclerosis |
| G35.B0 | Primary progressive multiple sclerosis, unspecified |
| G35.B2 | Non-active primary progressive multiple sclerosis |
| G35.C1 | Active secondary progressive multiple sclerosis |
| G35.D | Multiple sclerosis, unspecified |

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## Clinical Guideline Revision / History Information

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