LOUISIANA BLUE

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

Policy # 00559
Original Effective Date: 05/17/2017
Current Effective Date: 01/13/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider ocrelizumab (Ocrevus™)‡ and ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo™)‡ for the treatment of multiple sclerosis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for ocrelizumab (Ocrevus) and ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo) will be considered when the following criteria are met:

- Patient has a diagnosis of a relapsing form of multiple sclerosis (RMS) (i.e., clinically isolated syndrome, relapsing remitting disease, or active secondary progressive disease); OR
- Patient has a diagnosis of primary progressive multiple sclerosis (PPMS); AND
- If the request is for ocrelizumab (Ocrevus), the requested dose does not exceed 300 mg IV on day 1, followed by 300 mg IV 2 weeks later and 600 mg IV every 6 months for subsequent doses (which begin 6 months after the first 300 mg dose); OR
- If the request is for ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo), the requested dose does not exceed ocrelizumab 920 mg/ hyaluronidase 23,000 units subcutaneously every 6 months.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of ocrelizumab (Ocrevus) or ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo) when the patient selection criteria are not met to be **investigational.***

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

Policy # 00559
Original Effective Date: 05/17/2017
Current Effective Date: 01/13/2025

Background/Overview

Ocrelizumab, the active ingredient in both Ocrevus and Ocrevus Zunovo, is a CD20 directed cytolytic antibody that is indicated for the treatment of patients with relapsing or primary progressive forms of multiple sclerosis. It is unknown exactly how ocrelizumab exerts its therapeutic effects in multiple sclerosis. Ocrevus is administered via an intravenous infusion. The starting dose is 300 mg, followed by another 300 mg 2 weeks later. Subsequent doses are 600 mg every 6 months. Ocrevus is supplied in a 300 mg per 10 mL single-dose vial. Ocrevus Zunovo is formulated with hyaluronidase which allows it to be administered subcutaneously. Ocrevus Zunovo should be administered as a 920 mg subcutaneous infusion once every 6 months. Ocrevus Zunovo is available as a 920 mg ocrelizumab and 23,000 units hyaluronidase per 23 mL solution in a single-dose vial to be infused in the abdomen over approximately 10 minutes. The two formulations are not interchangeable, and both products must be administered by a healthcare professional.

Multiple Sclerosis

Multiple sclerosis is believed to have an immunologic mechanism that is characterized by demyelination in the brain and spinal cord. This is often expressed by symptoms such as visual and oculomotor abnormalities, weakness, urinary dysfunction, and mild cognitive impairment. Often patients will experience remissions and exacerbations. Treatment can include corticosteroids for acute exacerbations and immunomodulatory (disease modifying) drugs to prevent exacerbations. Disease modifying drugs for the treatment of relapsing forms of multiple sclerosis include oral products such as fingolimod (Gilenya®)‡, siponimod (Mayzent®)‡, dimethyl fumarate (Tecfidera®)‡, diroximel fumarate (Vumerity®)‡, teriflunomide (Aubagio®)‡, and cladribine (Mavenclad®)‡; subcutaneous and intramuscular injectable products such as glatiramer acetate (Copaxone®)‡, ofatumumab (Kesimpta®)‡, interferon beta-1a (Avonex®, Rebif®)‡, interferon beta-1b (Extavia®, Betaseron®)‡, and peginterferon beta-1a (Plegridy®)‡; and intravenous infusions such as ocrelizumab (Ocrevus), ublituximab (Briumvi™)‡, natalizumab (Tysabri®)‡, and alemtuzumab (Lemtrada®)‡.

Relapsing forms of multiple sclerosis include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease. Relapsing forms of multiple sclerosis make up about 85-90% of the multiple sclerosis population, while primary progressive multiple sclerosis (PPMS) makes up about 10-15% of the multiple sclerosis population. Relapsing forms of multiple sclerosis typically present as recurrent subacute events of neurological dysfunction followed by a complete or partial recovery and is more common in females than males. PPMS presents as a worsening of neurological dysfunction at disease onset with little or no recovery. PPMS affects an older population (40 years) vs. relapsing forms (30 years) of multiple sclerosis. PPMS is evenly distributed amongst males and females and leads to a rapid progression of disability.

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

Policy # 00559
Original Effective Date: 05/17/2017
Current Effective Date: 01/13/2025

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Ocrevus is a CD20 directed cytolytic antibody that is indicated for the treatment of patients with relapsing or primary progressive forms of multiple sclerosis. A label change in July 2019 clarified that relapsing forms of multiple sclerosis include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease. Ocrevus Zunovo was approved in September 2024 for the same indication as Ocrevus.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The safety and efficacy of Ocrevus in patients with relapsing multiple sclerosis was established in two identical randomized, double-blind, active controlled parallel group trials that used Rebif as the active comparator. The trial length was 96 weeks. The annualized relapse rates at 96 weeks were lower with Ocrevus in both studies as compared with Rebif (0.16 vs. 0.29, $P < 0.0001$). This equates to a 46% and 47% lower rate with Ocrevus vs. Rebif. MRI parameters were also more favorable with Ocrevus vs. Rebif.

The safety and efficacy of Ocrevus in patients with PPMS was established in one randomized, parallel group, double blind, placebo controlled trial. Treatment was for 120 weeks. The proportion of patients with PPMS with 12 week confirmed disability progression was 32.9% with Ocrevus vs. 39.3% with placebo (p=0.03). This represents a 24% risk reduction. The proportion of patients with 20% worsening on the timed 25 foot walk confirmed at 12 weeks was 49% in those that received Ocrevus compared with 59% among those patients that received placebo. More favorable magnetic resonance imaging (MRI) results were also observed with Ocrevus.

The efficacy and safety of Ocrevus Zunovo was based on a study demonstrating comparable bioavailability, pharmacokinetics, pharmacodynamics, safety, and immunogenicity of Ocrevus Zunovo compared with intravenous ocrelizumab in patients with either RMS or PPMS.

References

1. Ocrevus [package insert]. Genentech, Inc. South San Francisco, California. Updated December 2019.
2. Ocrevus Drug Evaluation. Express Scripts. Updated March 2017.
3. Ocrevus Zunovo [package insert]. Genentech, Inc. South San Francisco, California. Updated September 2024.

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

Policy # 00559
Original Effective Date: 05/17/2017
Current Effective Date: 01/13/2025

Policy History

Original Effective Date: 05/17/2017
Current Effective Date: 01/13/2025

05/04/2017	Medical Policy Committee review
05/17/2017	Medical Policy Implementation Committee approval. New policy.
10/01/2017	Coding update
01/01/2018	Coding update
05/03/2018	Medical Policy Committee review
05/16/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/02/2019	Medical Policy Committee review
05/15/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/07/2020	Medical Policy Committee review
05/13/2020	Medical Policy Implementation Committee approval. Updated background information with new treatments for multiple sclerosis, and updated indication and criteria to include the FDA clarification of the definition of relapsing disease.
05/06/2021	Medical Policy Committee review
05/12/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/05/2022	Medical Policy Committee review
05/11/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/04/2023	Medical Policy Committee review
05/10/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/02/2024	Medical Policy Committee review
05/08/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/05/2024	Medical Policy Committee review
12/11/2024	Medical Policy Implementation Committee approval. Title changed from "ocrelizumab (Ocrevus™)" to "ocrelizumab (Ocrevus™), ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo™)." Added new product, Ocrevus Zunovo, to the policy with relevant criteria and background information. Updated criteria to include FDA approved dosing for each product to ensure intent of policy is met.
03/25/2025	Coding update

Next Scheduled Review Date: 12/2025

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

Policy # 00559
Original Effective Date: 05/17/2017
Current Effective Date: 01/13/2025

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Louisiana Blue Medical Policy Coverage Guidelines is with Louisiana Blue and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Louisiana Blue Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Louisiana Blue Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	C9399, J2350, J3590 Add codes effective 04/01/2025: J2351
ICD-10 Diagnosis	G35

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.