BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.60.028

Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	April 7, 2017
Subject:	Ocrevus	**Page:**	1 of 6

Last Review Date: March 7, 2025

Ocrevus

Description

Ocrevus (ocrelizumab)
Ocrevus Zunovo* (ocrelizumab and hyaluronidase-ocsq)
*This medication is currently pending tier determination and may not be available at this time

Background
Ocrevus/Ocrevus Zunovo are multiple sclerosis (MS) disease-modifying agents. Ocrevus/Ocrevus Zunovo can potentially alter the course of disease by lessening the frequency of relapses and disease progression. Ocrevus/Ocrevus Zunovo is a recombinant humanized monoclonal antibody that targets CD20 proteins on premature and mature B cells. Ocrevus/Ocrevus Zunovo binds to CD20 on B cells which results in antibody-dependent cellular cytolysis and complement-mediated lysis. Ocrevus/Ocrevus Zunovo depletes circulating B cells after each treatment (1-2).

Regulatory Status
FDA-approved indication: Ocrevus/Ocrevus Zunovo are CD20-directed cytolytic antibodies indicated for the treatment of: (1-2)

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

Ocrevus/Orevus Zunovo are contraindicated in patients with active hepatitis B virus (HBV) infection. Complete HBV screening prior to the initiation of Ocrevus/Ocrevus Zunovo. HBV reactivation has been reported in the postmarketing setting with Ocrevus/Ocrevus Zunovo and other anti-CD20 antibodies which resulted in fulminant hepatitis, hepatic failure, and death (1-2).

The administration of Ocrevus/Orecuvs Zunovo should be delayed in patients with active infections until the infection has resolved. Ocrevus/Orevus Zunovo increases the risk for upper/lower respiratory tract, skin, and herpes-related infections (1-2).

Administer all immunizations according to immunization guidelines at least 4 weeks prior to initiation of Ocrevus/Orevus Zunovo for live or live-attenuated vaccines and at least 2 weeks prior to initation of Ocrevus/Ocrevus Zunovo for non-live vaccines, and after the repletion of B cells following drug discontinuation. Live, attenuated vaccines are generally not recommended (1-2).

Cases of progressive multifocal leukoencephalopathy (PML), a potentially lethal opportunistic brain infection, have been reported in patients with MS treated with Ocrevus/Orevus Zunovo in the postmarketing setting. PML has occurred in patients who had not been treated previously wth natalizumab, were not taking any immunosuppressive or immunomodulatory medications associated with the risk of PML, and did not have any known ongoing systemic medical conditions resulting in compromised immune system function. Ocrevus/Ocrevus Zunovo should be withheld at the first sign or symptom of PML, and appropriate diagnostic evaluation performed. If PML is confirmed, treatment with Ocrevus/Ocrevus Zunovo should be discontinued (1-2).

As expected with any B-cell depleting therapy, decreased immunoglobulin levels were observed. Monitor the levels of immunoglobulins at the beginning, during, and after discontinuation of treatment with Ocrevus/Ocrevus Zunovo until B-cell repletion (1-2).

According to the algorithm defined by Pharmacotherapy: A Pathophysiologic Approach for the management of clinically definite multiple sclerosis, it may be reasonable for patients with severe disease to use a monoclonal antibody without having tried other MS therapies (3).

Safety and effectiveness of Ocrevus/Ocrevus Zunovo in pediatric patients have not been established (1-2).

Related policies

Acthar Gel, Ampyra, Aubagio, Briumvi, Gilenya, Kesimpta, Lemtrada, Mavenclad, Mayzent, MS Injectables, Ponvory, Tecfidera, Tysabri, Zeposia

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Ocrevus/Ocrevus Zunovo may be considered **medically necessary** if the conditions indicated below are met.

Ocrevus/Ocrevus Zunovo may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Diagnoses

Patient must have **ONE** of the following:

1. Relapsing Multiple Sclerosis (RMS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease
2. Primary Progressive Multiple Sclerosis (PPMS)

AND ALL of the following:

1. Patient is not at risk for HBV infection OR patient is at risk for HBV infection and HBV infection has been ruled out or treatment for HBV infection has been initiated
2. Absence of active infection
3. Prescriber agrees to monitor immunoglobulins at the beginning, during, and after discontinuation of therapy
4. **NOT** used in combination with other immune-modulating or immunosuppressive therapies, including immunosuppressant doses of corticosteroids
5. **NOT** used in combination with another MS disease modifying agent
6. **NOT** given concurrently with live vaccines or live attenuated vaccines

Prior – Approval *Renewal* Requirements

Age 18 years of age and older

Diagnoses

Patient must have **ONE** of the following:

1. Relapsing Multiple Sclerosis (RMS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease
2. Primary Progressive Multiple Sclerosis (PPMS)

AND ALL of the following:

1. Absence of active infection
2. Prescriber agrees to monitor immunoglobulins during and after discontinuation of therapy
3. **NOT** used in combination with other immune-modulating or immunosuppressive therapies, including immunosuppressant doses of corticosteroids
4. **NOT** used in combination with another MS disease modifying agent
5. **NOT** given concurrently with live vaccines or live attenuated vaccines

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 2 years

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Ocrevus/Ocrevus Zunovo are indicated for the treatment of patients with relapsing or primary progressive forms of multiple sclerosis. Ocrevus/Ocrevus Zunovo are monoclonal antibodies that targets CD20, a protein prominent on premature and mature B cells, and decreases the amount of circulating B cells through antibody-dependent cellular cytolysis and compliment-mediated lysis. Safety and effectiveness of Ocrevus/Ocrevus Zunovo in pediatric patients have not been established (1-2).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of the Ocrevus/Ocrevus Zunovo while maintaining optimal therapeutic outcomes.

References

1. Ocrevus [package insert]. South San Francisco, CA: Genentech, Inc.; June 2024.
2. Ocrevus Zunovo [package insert]. South San Francisco, CA: Genentech, Inc.; September 2024.
3. Bainbridge, Jacquelyn L., et al. "Multiple Sclerosis." Pharmacotherapy: A Pathophysiologic Approach, 11e, 2020. Available at: https://accesspharmacy.mhmedical.com/content.aspx?bookid=2577&sectionid=231921409.
4. Dorr J, Paul F. The transition from first-line to second-line therapy in multiple sclerosis. Curr Treat Options Neurol. 2015;17:25.
5. Goodin DS, Frohman EM, Garmany GP, et al. Disease modifying therapies in multiple sclerosis. Neurology. 2002;58:169-78.
6. Costello K, Halper J, Kalb R, el al. The use of disease-modifying therapies in multiple sclerosis: principles and current evidence. MS Coalition. 2016. Accessed on April 3, 2017.
7. Disease-modifying therapies for relapsing-remitting and primary-progressive multiple sclerosis: effectiveness and value. Institute for Clinical and Economic Review. Published March 6, 2017.
8. Cahill JF, Izzo A, Garg N. Immunization in patients with multiple sclerosis. Neurological Bulletin. 2010;2(1):17-21.

Policy History

Date	Action
April 2017	Addition to PA
June 2017	Annual review Removed “not used in combination with another MS disease modifying agent” and changed to “not used in combination with other immune-modulating or immunosuppressive therapies, including immunosuppressant doses of corticosteroids” Addition of no live attenuated vaccines requirement to the live vaccines per SME
September 2017	Annual review
November 2018	Annual review and reference update
March 2019	Addition of PA Renewal Requirements and changed PA duration from lifetime to 2 years
June 2019	Annual review and reference update

September 2019	Annual editorial review and reference update. Revised relapsing MS indication to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease
March 2020	Annual review and reference update
September 2020	Annual review and reference update
December 2020	Annual review
June 2021	Annual review and reference update
September 2022	Annual review
December 2022	Annual review and reference update. Per SME, added caveat that t/f of two MS drugs does not apply if the patient has advanced, progressive, or severe disease
January 2023	Added requirement of no dual therapy with another MS disease modifying agent
March 2023	Annual review
June 2023	Annual review and reference update
December 2023	Annual review and reference update
September 2024	Annual editorial review and reference update. Per FEP, removed requirement to t/f 2 MS treatments for relapsing MS and added requirement to monitor immunoglobulins. Also, added PML warning to regulatory section
December 2024	Annual review. Addition of Ocrevus Zunovo to policy
March 2025	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.