DR.003.D OCREVUS® (Ocrelizumab)

Original Implementation Date : 06/01/2019
Version [D] Date: 04/24/2023
Last Reviewed Date: 10/15/2025

PRODUCT VARIATIONS

This policy only applies to Jefferson Health Plans Medicare Advantage and Individual and Family Plans product lines.

POLICY STATEMENT

Jefferson Health Plans Medicare Advantage and Jefferson Health Plans Individual and Family Plans considers Ocrevus® (Ocrelizumab) medically necessary for its FDA approved indications when the prior authorization criteria listed in this policy are met.

FDA APPROVED INDICATIONS

Ocrevus® (Ocrelizumab) is a CD20-directed cytolytic antibody used to treat adult patients with relapsing forms of multiple sclerosis (RMS) or primary progressive forms of multiple sclerosis (PPMS).

OFF-LABEL USE

Authorization for off-labeled use of medication will be evaluated on an individual basis. Review of an off-labeled request by the Medical Staff will be predicated on the appropriateness of treatment and full consideration of medical necessity. For off-label use, Medical Directors will review scientific literature and local practice patterns.

PRIOR AUTHORIZATION CRITERIA

INITIAL CRITERIA

*AUTHORIZATION DURATION: IF **ALL CRITERIA MET**, APPROVE FOR 6 MONTHS*

1. Adults 18 years of age and older; AND

2. Medication is being prescribed by or in consultation with a specialist (who specializes in treatment of multiple sclerosis (MS) or a neurologist); AND
3. Patient is being treated for a diagnosis indicated in the U.S. Food and Drug Administration (FDA)-approved labeling or a medically accepted indication at a dose that is FDA-approved, nationally recognized compendia or in peer-reviewed literature.
4. If patient is female and of childbearing potential, has documentation of recent negative pregnancy test; AND
5. For multiple sclerosis, medical records are attached showing the patient does not have a history of contraindication to Ocrevus®; AND
6. For relapsing forms of multiple sclerosis, medical records showing the patient tried and failed or has a contraindications or intolerance to Tysabri AND at least 1 of preferred therapies including but not limited to (Avonex, Rebif, Betaseron®, Copaxone, Gilenya®, Tecfidera) including dates of use, dosage, directions, and treatment response. Failure of an adequate trial of therapy for multiple sclerosis is defined as follows:
    I. Having increasing relapses (defined as two or more relapses in a year, or one severe relapse associated with either poor recovery or MRI lesion progression); or
    II. Having lesion progression by MRI (increased number or volume of gadolinium-enhancing lesions, T2 hyperintense lesions or T1 hypointense lesions); or
    III. The patient has worsening disability (sustained worsening of Expanded Disability Status Scale (EDSS) score or neurological examination findings); AND
7. Documentation, showing absence of active infections and screening for hepatitis B (HBsAG and anti-HBc measurements); AND
8. Documentation that live-attenuated or live vaccines will not be administered during treatment or after discontinuation of Ocrelizumab until B-cell repletion. (Current recommendations- all necessary immunizations per guidelines should be administered at least 6 weeks prior to treatment initiation).
9. Please note: For members who are new to the plan and are already treated and stable with OCREVUS® or Ocrevus Zunovo (records must be attached), the medication will be approved for continuation of treatment.

RENEWAL CRITERIA

*AUTHORIZATION DURATION**: **IF ALL RENEWAL CRITERIA MET**, APPROVE FOR 6 MONTHS*

1. Patient continues to meet criteria identified for initial approval; AND
2. Patient has not received dose of Ocrelizumab within the past 5 months; AND
3. Medical records are attached showing treatment response (including absence of unacceptable toxicity such as severe infusion reactions or infections, malignancy, etc.); AND

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4. The patient has had an improvement of symptoms or stabilization of MS disease course from baseline. (Must attach documentation); AND
5. If patient is female of childbearing potential, documentation of use of adequate contraception to prevent pregnancy during treatment and for 6 months following last infusion.

DOSAGE AND ADMINISTRATION

DOSING RECOMMENDATIONS:

- Recommendation is to pre-medicate with 100 mg methylprednisolone (or an equivalent corticosteroid) and an antihistamine (e.g., diphenhydramine) given intravenously ~30 minutes prior to each infusion with Ocrelizumab®.
- Initial dose: 300 mg intravenous (IV) infusion, followed two weeks later by a second 300 mg IV infusion.
- Following doses: single 600 mg IV infusion beginning 6 months after the first 300 mg dose.
- Patients should be observed for at least one hour after infusion completion.

This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide. Patient-specific variables should be considered.

RISK FACTORS/SIDE EFFECTS

- **Infusion Reactions:**
  Ocrelizumab® can cause infusion reactions with the highest incidence with the first infusion. No fatal infusion reactions occurred but some required hospitalization. Observe patients treated with Ocrelizumab® for at least one hour after completion of the infusion. Patients should be informed that infusion reactions can occur up to 24 hours after the infusion. Pre-medication should be administered to reduce frequency and severity of infusion reactions.

- **Infections:**
  A higher proportion of patients treated with Ocrelizumab® experienced infections compared to those taking REBIF or placebo in clinical trials. Delay Ocrelizumab® administration in patients until active infection resolves.

- **Progressive Multifocal Leukoencephalopathy (PML):**
  At first sign/symptom of PML, Ocrelizumab® should be discontinued, and patient should be appropriately evaluated. Cases of PML have been reported in patients with MS treated with OCREVUS® in the post-market setting. PML occurred in OCREVUS®-treated patients who were not

previously treated with drugs with known association with PML and were not taking immunosuppressive or immunomodulatory medications.

- **Reduction in Immunoglobulins:**

  Monitor immunoglobulin levels at the beginning of treatment. Monitor during and after discontinuation of treatment, until B-cell repletion, and especially when recurrent serious infections are suspected. Consider discontinuation of OCREVUS® in patients with serious opportunistic or recurrent serious infections, and if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins.

- **Hepatitis B Virus (HBV) Reactivation:**
  Perform HBV screening in all patients before starting treatment with Ocrelizumab. No reports of reactivation in MS patients treated with Ocrelizumab occurred. For patients who are negative for surface antigen (HBsAg) and positive for HB core antibody (HBcAb+) or are carriers of HBV (HBsAg+), a liver disease expert should be consulted before starting or during treatment.

- **Immune-Mediated Colitis:**

  Post-market reporting has shown incidences of immune-mediated colitis. Monitor for new or persistent diarrhea or other gastrointestinal symptoms. Prompt evaluation is needed if colitis is suspected.

- **Herpes:**
  Serious cases of infections caused by herpes simplex virus and varicella zoster virus, including central nervous system infections (encephalitis and meningitis), intraocular infections, and disseminated skin and soft tissue infections, have been reported in the post-marketing setting in multiple sclerosis patients receiving OCREVUS®. Serious herpes virus infections may occur at any time during treatment with OCREVUS®. Some cases were life threatening.

- **Malignancies:**
  An increased risk of malignancy may exist in treatment with Ocrelizumab. In clinical trials, malignancies, (including breast cancer), occurred more frequently in patients treated with Ocrelizumab. Patients should follow standard screening guiltiness.

- **Liver Injury:** Clinically significant liver injuries have occurred. Obtain serum aminotransferases, alkaline phosphatase, bilirubin levels before starting treatment, and during treatment as clinically indicated. Discontinue OCREVUS® in patients with evidence of liver injury in the absence of an alternative etiology.

- **The most common adverse reactions were:**

  - RMS: upper respiratory tract infections and infusion reactions.

  - PPMS: upper respiratory tract infections, infusion reactions, skin infections, and lower respiratory tract infections.

Contraindicated in patients with active hepatitis B virus infection and those with history of life threatening infusion reaction to Ocrevus®.

MONITORING

- During therapy: Infusion reactions, liver function, immunoglobulin levels.
- Prior to therapy and during: Infections, liver function, immunoglobulins levels, and Hepatitis B Virus screening.

BLACK BOX WARNING

N/A.

CLINICAL EVIDENCE

Relapsing Forms of MS

The efficacy of OCREVUS® was demonstrated in two randomized, double-blind, double-dummy, active comparator-controlled clinical trials of identical design, in patients with RMS treated for 96 weeks. The dose of OCREVUS® was 600 mg every 24 weeks (initial treatment was given as two 300 mg IV infusions administered 2 weeks apart, and subsequent doses were administered as a single 600 mg IV infusion) and placebo subcutaneous injections were given 3 times per week. The dose of REBIF (interferon beta-1a), the active comparator, was 44 mcg given as subcutaneous injections 3 times per week and placebo IV infusions were given every 24 weeks. The primary outcome of both Study 1 and Study 2 was the annualized relapse rate (ARR). Results for this outcome were as follows: 0.156 ARR for the Ocrevus® group compared to 0.292 ARR for the REBIF group in Study 1, and 0.155 ARR for the Ocrevus® group compared to 0.290 ARR for the REBIF group in Study 2 (both with a p-value under 0.0001). Of note, the MRI secondary endpoint for these two studies included the amount of new and/or enlarging T2 hyperintense lesions shown on MRI with 0.323 lesions in the Ocrevus® group and 1.413 lesions in the REBIF group.

Primary Progressive MS

Study 3 was a randomized, double-blind, placebo-controlled clinical trial in patients with PPMS. Patients were randomized 2:1 to receive either OCREVUS® 600 mg or placebo as two 300 mg intravenous infusions 2 weeks apart every 24 weeks for at least 120 weeks. In Study 3, the primary outcome was the time to onset of disability progression attributable to MS confirmed to be present at the next neurological assessment at least 12 weeks later. Disability progression occurred when the EDSS score increased by 1 point or more from the baseline EDSS if the baseline EDSS was 5.5 points or less, or by 0.5 points or more if the baseline EDSS was more than 5.5 points. Discontinuation of the study was also considered disability progression. The time to onset of

disability progression confirmed at 12 weeks after onset was significantly longer for OCREVUS®-treated patients than for placebo-treated patients. With a risk reduction (RR) of 24% using a p-value of 0.0321. MRI results showed a mean decrease in T2 lesion volume for Ocrevus® of 0.39 and an increase of 0.79 for the placebo group (p-value under 0.0001). There is a limitation in this study where it is being compared to placebo and not to the standard of treatment for primary progressive MS.

BACKGROUND

N/A

CODING

Note*:* The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that *may* be listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service is covered and is not a guarantee of payment. Other policies and coverage guidelines may apply. When reporting services, providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.

CPT Code	Description
N/A	N/A

HCPCS Code	Description
J2350	Injection, Ocrelizumab, 1 mg.

ICD-10 Codes	Description
G35	Multiple sclerosis.

DISCLAIMER

Approval or denial of payment does not constitute medical advice and is neither intended to guide nor influence medical decision making. Policy Bulletins are developed to assist in administering plan benefits and constitute neither offers of coverage nor medical advice. This Policy Bulletin may be updated and therefore is subject to change.

POLICY HISTORY

This section provides a high-level summary of changes to the policy since the previous version.

Summary	Version	Version Date
2025 Annual review. Additions to risk factor, monitoring, clinical evidence and background sections.	D	04/24/2023
2024 Annual review. Minor revision to prior authorization criteria.	D	04/24/2023
2023 Annual review. Risk factors and reference sections were updated. (Minor revisions).	D	04/24/2023
2022 Annual review. No changes. Reissue as written.	C	04/01/2021
2021 Annual review. Prior authorization criteria made more specific to ask for trial of 3 agents including Tysabri.	C	04/01/2020
2020 Annual review. Prior Authorization criteria updated to be in alignment with FDA approved prescribing information/package labeling. Policy changed to “Medicare Only” line of business. References were updated accordingly.	B	05/01/2019
New policy.	A	06/01/2019

REFERENCES

1. Ocrevus®. Prescribing information. Genentech, INC. March 2023.