HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use OCREVUS safely and effectively. See full prescribing information for OCREVUS.

OCREVUS™ (ocrelizumab) injection, for intravenous use
Initial U.S. Approval: 2017

---------- INDICATIONS AND USAGE----------
OCREVUS is a CD20-directed cytolytic antibody indicated for the treatment of patients with relapsing or primary progressive forms of multiple sclerosis (1)

----------DOSAGE AND ADMINISTRATION----------
- Hepatitis B virus screening is required before the first dose (2.1)
- Pre-medicate with methylprednisolone (or an equivalent corticosteroid) and an antihistamine (e.g., diphenhydramine) prior to each infusion (2.2)
- Administer OCREVUS by intravenous infusion
  - Start dose: 300 mg intravenous infusion, followed two weeks later by a second 300 mg intravenous infusion (2.3)
  - Subsequent doses: 600 mg intravenous infusion every 6 months (2.3)
- Must be diluted prior to administration (2.3, 2.6)
- Monitor patients closely during and for at least one hour after infusion (2.3, 2.5)

---------- DOSAGE FORMS AND STRENGTHS----------
- Injection: 300 mg/10 mL (30 mg/mL) in a single-dose vial. (3)

---------- CONTRAINDICATIONS ----------
- Active hepatitis B virus infection (4)
- History of life-threatening infusion reaction to OCREVUS (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Infusion reactions: Management recommendations for infusion reactions depend on the type and severity of the reaction. Permanently discontinue OCREVUS if a life-threatening or disabling infusion reaction occurs (2.3, 5.1)
- Infections: Delay OCREVUS administration in patients with an active infection until the infection is resolved. Vaccination with live-attenuated or live vaccines is not recommended during treatment with OCREVUS and after discontinuation, until B-cell repletion (5.2)
- Malignancies: An increased risk of malignancy, including breast cancer, may exist with OCREVUS (5.3)

---------- ADVERSE REACTIONS ----------
The most common adverse reactions were:
- RMS (incidence ≥10% and > REBIF): upper respiratory tract infections and infusion reactions (6.1)
- PPMS (incidence ≥10% and > placebo): upper respiratory tract infections, infusion reactions, skin infections, and lower respiratory tract infections (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- USE IN SPECIFIC POPULATIONS ----------
- Pregnancy: Based on animal data, may cause fetal harm. (8.1)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 3/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

---

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

OCREVUS is indicated for the treatment of adult patients with relapsing or primary progressive forms of multiple sclerosis.

2 DOSAGE AND ADMINISTRATION

2.1 Assessments Prior to First Dose of OCREVUS

Hepatitis B Virus Screening

Prior to initiating OCREVUS, perform Hepatitis B virus (HBV) screening. OCREVUS is contraindicated in patients with active HBV confirmed by positive results for HBsAg and anti-HBV tests. For patients who are negative for surface antigen [HBsAg] and positive for HB core antibody [HBcAb+] or are carriers of HBV [HBsAg+], consult liver disease experts before starting and during treatment *[see Warnings and Precautions (5.2)]*.

Vaccinations

Because vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation until B-cell repletion, administer all necessary immunizations according to immunization guidelines at least 6 weeks prior to initiation of OCREVUS *[see Warnings and Precautions (5.2) and Clinical Pharmacology (12.2)]*.

2.2 Preparation Before Every Infusion

Infection Assessment

Prior to every infusion of OCREVUS, determine whether there is an active infection. In case of active infection, delay infusion of OCREVUS until the infection resolves *[see Warnings and Precautions (5.2)]*.

Recommended Premedication

Pre-medicate with 100 mg of methylprednisolone (or an equivalent corticosteroid) administered intravenously approximately 30 minutes prior to each OCREVUS infusion to reduce the frequency and severity of infusion reactions *[see Warnings and Precautions (5.1)]*. Pre-medicate with an antihistamine (e.g., diphenhydramine) approximately 30-60 minutes prior to each OCREVUS infusion to further reduce the frequency and severity of infusion reactions.

The addition of an antipyretic (e.g., acetaminophen) may also be considered.

2.3 Recommended Dosage and Dose Administration

Administer OCREVUS under the close supervision of an experienced healthcare professional with access to appropriate medical support to manage severe reactions such as serious infusion reactions.

- Initial dose: 300 mg intravenous infusion, followed two weeks later by a second 300 mg intravenous infusion.
- Subsequent doses: single 600 mg intravenous infusion every 6 months.
- Observe the patient for at least one hour after the completion of the infusion *[see Warnings and Precautions (5.1)]*.

Table 1 Recommended Dose, Infusion Rate, and Infusion Duration for RMS and PPMS

		Amount and Volume[1]	Infusion Rate and Duration[3]
Initial Dose (two infusions)	Infusion 1	300 mg in 250 mL	• Start at 30 mL per hour • Increase by 30 mL per hour every 30 minutes • Maximum: 180 mL per hour • Duration: 2.5 hours or longer
	Infusion 2 (2 weeks later)	300 mg in 250 mL	
Subsequent Doses (one infusion)	One infusion every 6 months[2]	600 mg in 500 mL	• Start at 40 mL per hour • Increase by 40 mL per hour every 30 minutes • Maximum: 200 mL per hour • Duration: 3.5 hours or longer

[1] Solutions of OCREVUS for intravenous infusion are prepared by dilution of the drug product into an infusion bag containing 0.9% Sodium Chloride Injection, to a final drug concentration of approximately 1.2 mg/mL.
[2] Administer the first Subsequent Dose 6 months after Infusion 1 of the Initial Dose.
[3] Infusion time may take longer if the infusion is interrupted or slowed *[see Dosage and Administration (2.5)]*.

2.4 Delayed or Missed Doses

If a planned infusion of OCREVUS is missed, administer OCREVUS as soon as possible; do not wait until the next scheduled dose. Reset the dose schedule to administer the next sequential dose 6 months after the missed dose is administered. Doses of OCREVUS must be separated by at least 5 months *[see Dosage and Administration (2.3)]*.

2.5 Dose Modifications Because of Infusion Reactions

Dose modifications in response to infusion reactions depends on the severity.

Life-threatening Infusion Reactions

Immediately stop and permanently discontinue OCREVUS if there are signs of a life-threatening or disabling infusion reaction *[see Warnings and Precautions (5.1)]*. Provide appropriate supportive treatment.

Severe Infusion Reactions

Immediately interrupt the infusion and administer appropriate supportive treatment, as necessary *[see Warnings and Precautions (5.1)]*. Restart the infusion only after all symptoms have resolved. When restarting, begin at half of the infusion rate at the time of onset of the infusion reaction *[see Dosage and Administration (2.2)]*. If this rate is tolerated, increase the rate as described in Table 1. This change in rate will increase the total duration of the infusion but not the total dose.

Mild to Moderate Infusion Reactions

Reduce the infusion rate to half the rate at the onset of the infusion reaction and maintain the reduced rate for at least 30 minutes *[see Warnings and Precautions (5.1)]*. If this rate is tolerated, increase the rate as described in Table 1. This change in rate will increase the total duration of the infusion but not the total dose.

2.6 Preparation and Storage of the Dilute Solution for Infusion

Preparation

OCREVUS must be prepared by a healthcare professional using aseptic technique.

Visually inspect for particulate matter and discoloration prior to administration. Do not use the solution if discolored or if the solution contains discrete foreign particulate matter. Do not shake.

Withdraw intended dose and further dilute into an infusion bag containing 0.9% Sodium Chloride Injection, to a

- Withdraw 10 mL (300 mg) of OCREVUS and inject into 250 mL
- Withdraw 20 mL (600 mg) of OCREVUS and inject into 500 mL

Do not use other diluents to dilute OCREVUS since their use has not been tested. The product contains no preservative and is intended for single use only.

Storage of Infusion Solution

Prior to the start of the intravenous infusion, the content of the infusion bag should be at room temperature.

Use the prepared infusion solution immediately. If not used immediately, store up to 24 hours in the refrigerator at 2°C–8°C (36°F–46°F) and 8 hours at room temperature up to 25°C (77°F), which includes infusion time. In the event an intravenous infusion cannot be completed the same day, discard the remaining solution.

No incompatibilities between OCREVUS and polyvinyl chloride (PVC) or polyolefin (PO) bags and intravenous (IV) administration sets have been observed.

Administration

Administer the diluted infusion solution through a dedicated line using an infusion set with a 0.2 or 0.22 micron in-line filter.

3 DOSAGE FORMS AND STRENGTHS

Injection: 300 mg/10 mL (30 mg/mL) clear or slightly opalescent, and colorless to pale brown solution in a single-dose vial.

4 CONTRAINDICATIONS

OCREVUS is contraindicated in patients with:

- Active HBV infection *[see Dosage and Administration (2.6) and Warnings and Precautions (5.2)]*
- A history of life-threatening infusion reaction to OCREVUS *[see Warnings and Precautions (5.1)]*

5 WARNINGS AND PRECAUTIONS

5.1 Infusion Reactions

OCREVUS can cause infusion reactions, which can include pruritus, rash, urticaria, erythema, bronchospasm, throat irritation, oropharyngeal pain, dyspnea, pharyngeal or laryngeal edema, flushing, hypotension, pyrexia, fatigue, headache, dizziness, nausea, and tachycardia. In multiple sclerosis (MS) clinical trials, the incidence of infusion reactions in OCREVUS-treated patients [who received methylprednisolone (or an equivalent steroid) and possibly other pre-medication to reduce the risk of infusion reactions prior to each infusion] was 34 to 40%, with the highest incidence with the first infusion. There were no fatal infusion reactions, but 0.3% of OCREVUS-treated MS patients experienced infusion reactions that were serious, some requiring hospitalization.

Observe patients treated with OCREVUS for infusion reactions during the infusion and for at least one hour after completion of the infusion. Inform patients that infusion reactions can occur up to 24 hours after the infusion.

Reducing the Risk of Infusion Reactions and Managing Infusion Reactions

Administer pre-medication (e.g., methylprednisolone or an equivalent corticosteroid, and an antihistamine) to reduce the frequency and severity of infusion reactions. The addition of an antipyretic (e.g., acetaminophen) may also be considered *[see Dosage and Administration (2.3)]*.

Management recommendations for infusion reactions depend on the type and severity of the reaction *[see Dosage and Administration (2.5)]*. For life-threatening infusion reactions, immediately and permanently stop OCREVUS and administer appropriate supportive treatment. For less severe infusion reactions, management may involve temporarily stopping the infusion, reducing the infusion rate, and/or administering symptomatic treatment.

5.2 Infections

A higher proportion of OCREVUS-treated patients experienced infections compared to patients taking REBIF or placebo. In RMS trials, 58% of OCREVUS-treated patients experienced one or more infections compared to 52% of REBIF-treated patients. In the PPMS trial, 70% of OCREVUS-treated patients experienced one or more infections compared to 68% of patients on placebo. OCREVUS increased the risk for upper respiratory tract infections, lower respiratory tract infections, skin infections, and herpes-related infections *[see Adverse Reactions (6.1)]*. OCREVUS was not associated with an increased risk of serious infections in MS patients. Delay OCREVUS administration in patients with an active infection until the infection is resolved.

Respiratory Tract Infections

A higher proportion of OCREVUS-treated patients experienced respiratory tract infections compared to patients taking REBIF or placebo. In RMS trials, 40% of OCREVUS-treated patients experienced upper respiratory tract infections compared to 33% of REBIF-treated patients, and 8% of OCREVUS-treated patients experienced lower respiratory tract infections compared to 5% of REBIF-treated patients. In the PPMS trial, 49% of OCREVUS-treated patients experienced upper respiratory tract infections compared to 43% of patients on placebo and 10% of OCREVUS-treated patients experienced lower respiratory tract infections compared to 9% of patients on placebo. The infections were predominantly mild to moderate and consisted mostly of upper respiratory tract infections and bronchitis.

Herpes

In active-controlled (RMS) clinical trials, herpes infections were reported more frequently in OCREVUS-treated patients than in REBIF-treated patients, including herpes zoster (2.1% vs. 1.0%), herpes simplex (0.7% vs. 0.1%), oral herpes (3.0% vs. 2.2%), genital herpes (0.1% vs. 0%), and herpes virus infection (0.1% vs. 0%). Infections were predominantly mild to moderate in severity. There were no reports of disseminated herpes.

In the placebo-controlled (PPMS) clinical trial, oral herpes was reported more frequently in the OCREVUS-treated patients than in the patients on placebo (2.7% vs 0.8%).

Progressive Multifocal Leukoencephalopathy (PML)

PML is an opportunistic viral infection of the brain caused by the John Cunningham (JC) virus that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. Although no cases of PML were identified in OCREVUS clinical trials, JC virus infection resulting in PML has been observed in patients treated with other anti-CD20 antibodies and other MS therapies and has been associated with some risk factors (e.g., immunocompromised patients, polytherapy with immunosuppressants). At the first sign or symptom suggestive of PML, withhold OCREVUS and perform an appropriate diagnostic evaluation. MRI findings may be apparent before clinical signs or symptoms. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.

Hepatitis B Virus (HBV) Reactivation

There were no reports of hepatitis B reactivation in MS patients treated with OCREVUS. Fulminant hepatitis, hepatic failure, and death caused by HBV reactivation have occurred in patients treated with other anti-CD20 antibodies. Perform HBV screening in all patients before initiation of treatment with OCREVUS. Do not administer OCREVUS to patients with active HBV confirmed by positive results for HBsAg and anti-HB tests.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.