OCREVUS- ocrelizumab injection
Genentech, Inc.

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

RECENT MAJOR CHANGES

Indications and Usage (1)	5/2026
Dosage and Administration (2.1)	8/2025
Dosage and Administration (2.2, 2.3, 2.6)	5/2026
Warnings and Precautions (5.1, 5.2)	5/2026
Warnings and Precautions (5.7)	8/2025

INDICATIONS AND USAGE

OCREVUS is a CD20-directed cytolytic antibody indicated for the treatment of:

- Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults (1)
- Primary progressive MS, in adults (1)
- Relapsing-remitting MS, in pediatric patients 10 years of age and older who weigh 25 kg or more (1)

DOSAGE AND ADMINISTRATION

- Before initiating OCREVUS, screen for Hepatitis B virus and obtain serum quantitative immunoglobulins, aminotransferases, alkaline phosphatase, and bilirubin (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 (2.3)
- Adults and pediatric patients (10 years of age and older), who weigh 35 kg or more:
  - 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)
- Pediatric patients (10 years of age and older) who weigh 25 kg to less than 35 kg:
  - Start dose: 150 mg intravenous infusion, followed two weeks later by a second 150 mg intravenous infusion (2.3)
  - Subsequent doses: 300 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: Serious, including life-threatening and fatal infections, have occurred. 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)

- Progressive Multifocal Leukoencephalopathy (PML): Withhold OCREVUS at the first sign or symptom suggestive of PML (5.3)
- Reduction in Immunoglobulins: Monitor the level of immunoglobulins at the beginning of treatment. Monitor during and after discontinuation of treatment with OCREVUS, until B-cell repletion, and especially when recurrent serious infections are suspected. Consider discontinuing OCREVUS in patients with serious opportunistic or recurrent serious infections, and if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins (2.1, 5.4)
- Malignancies: An increased risk of malignancy, including breast cancer, may exist with OCREVUS (5.5)
- Immune-Mediated Colitis: Immune-mediated colitis has been reported in the postmarketing setting. Monitor patients for new or persistent diarrhea or other gastrointestinal symptoms, and evaluate promptly if colitis is suspected (5.6)
- Liver Injury: Clinically significant liver injury has occurred. Obtain serum aminotransferases, alkaline phosphatase, and bilirubin levels before initiating OCREVUS, and during treatment as clinically indicated. Discontinue OCREVUS in patients with evidence of liver injury in the absence of an alternative etiology (5.7).

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)
- RRMS in pediatric patients 10 years of age and older: Adverse reactions were consistent with those observed in adults with RMS (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: 5/2026

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

OCREVUS is indicated for the treatment of:

- Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- Primary progressive MS, in adults
- Relapsing-remitting MS, in pediatric patients 10 years of age and older who weigh 25 kg or more.

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)]*.

Serum Immunoglobulins
Prior to initiating OCREVUS, perform testing for quantitative serum immunoglobulins *[see Warnings and Precautions (5.4)]*. For patients with low serum immunoglobulins, consult immunology experts before initiating treatment with OCREVUS.

Vaccinations

Because vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation until B-cell repletion, administer all age-appropriate immunizations according to immunization guidelines at least 4 weeks prior to initiation of OCREVUS for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of OCREVUS for non-live vaccines *[see Warnings and Precautions (5.2) and Clinical Pharmacology (12.2)]*.

Liver Function Tests

Prior to initiating OCREVUS, obtain serum aminotransferases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]), alkaline phosphatase, and bilirubin levels *[see Warnings and Precautions (5.7)]*.

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

To reduce the frequency and severity of infusion reactions, administer the following premedications *[see Warnings and Precautions (5.1)]*:

- Methylprednisolone (or an equivalent corticosteroid) by intravenous infusion to be completed approximately 30 minutes prior to each OCREVUS infusion, as follows:
  - Adults and pediatric patients who weigh 40 kg or more: 100 mg
  - Pediatric patients who weigh less than 40 kg: 2 mg/kg
- An antihistamine (e.g., diphenhydramine) 30 to 60 minutes prior to each OCREVUS infusion.
- An antipyretic (e.g., acetaminophen) may also be considered. Administer the antipyretic 30 minutes to 60 minutes prior to OCREVUS infusion.

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. Observe the patient for at least one hour after the completion of the infusion *[see Warnings and Precautions (5.1)]*.

OCREVUS is administered as an intravenous infusion. The initial dose is split into two

equal infusions administered two weeks apart. Subsequent doses are administered every 6 months thereafter (see Table 1). Dosing for pediatric patients (10 years of age and older) is according to body weight (see Table 2).

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

		Amount and Volume*	Infusion Rate and Duration†
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) every 6 months)‡	Option 1 Infusion of approximately 3.5 hours duration†	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
	OR		
	Option 2 (If no prior serious infusion reaction with any previous OCREVUS infusion)§ Infusion of approximately 2 hours duration†	600 mg in 500 mL	• Start at 100 mL per hour for the first 15 minutes • Increase to 200 mL per hour for the next 15 minutes • Increase to 250 mL per hour for the next 30 minutes • Increase to 300 mL per hour for the remaining 60 minutes • Duration: 2 hours or longer

* 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.
† Infusion time may take longer if the infusion is interrupted or slowed *[see Dosage and Administration (2.5)]*.
‡ Administer the first Subsequent Dose 6 months after Infusion 1 of the Initial Dose.
§ *[see Adverse Reactions (6.1) and Clinical Studies (14.3)]*.

Table 2 Recommended Dose, Infusion Rate, and Infusion Duration for Pediatric Patients 10 Years of Age and Older

	Infusion	Amount and Volume*	Infusion Rate and Duration†
Body Weight 25 kg to Less Than 35 kg			
Initial Dose (two infusions)	Infusion 1	150 mg in 250 mL	• Start at 30 mL per hour
	Infusion 2	150 mg in 250 mL	

(two infusions)	(2 weeks later)	150 mg in 250 mL	• Increase by 30 mL per hour every 30 minutes • Maximum: 180 mL per hour • Duration: 2.5 hours or longer
Subsequent Doses (one infusion every 6 months)	Single infusion once every 6 months	300 mg in 250 mL	
Body Weight 35 kg or More			
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 every 6 months)	Single infusion once every 6 months	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

* Solutions of OCREVUS for intravenous infusion are prepared by dilution of the drug product into an infusion bag containing 0.9% Sodium Chloride for Injection *[see Dosage and Administration (2.6)]*.

† 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. If this rate is tolerated, increase the rate as described in Table 1 and Table 2 *[see Dosage and Administration (2.3)]*. 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 and Table 2 *[see Dosage and Administration (2.3)]*. 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. A sterile needle and syringe should be used to prepare the diluted infusion solution.

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 the required dose of OCREVUS and further dilute into an infusion bag containing 0.9% Sodium Chloride Injection, as described in Table 3.

Table 3: Dilution of OCREVUS

Dose of OCREVUS (mg)	Volume of OCREVUS (mL)	Volume of 0.9% Sodium Chloride Injection (mL)	Final Drug Concentration (mg/mL)
150 mg	5 mL	250 mL	0.6 mg/mL
300 mg	10 mL	250 mL	1.2 mg/mL
600 mg	20 mL	500 mL	1.2 mg/mL

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

Discard any unused portion left in the vial.

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 to 8°C (36°F to 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 (2.1) 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, tachycardia, and anaphylaxis. These reactions are more commonly reported with the first infusion. In multiple sclerosis (MS) clinical trials, all adult and pediatric patients who were treated with OCREVUS received premedication with methylprednisolone (or an equivalent steroid), and may have also received an antihistamine (all pediatric patients) and/or an analgesic/antipyretic to reduce the risk of infusion reactions prior to each infusion.

In adults, the incidence of infusion reactions in patients treated with OCREVUS was 34 to 40%. There were no fatal infusion reactions, but 0.3% of patients with MS who were treated with OCREVUS experienced infusion reactions that were serious, some requiring hospitalization.

In pediatric patients, the incidence of infusion reactions in patients treated with OCREVUS was 48%, compared with an incidence of 24% in patients who received placebo infusion (fingolimod-treated patients). There were no fatal infusion reactions, but one pediatric patient (1.1%) treated with OCREVUS experienced an infusion reaction that was serious because it required hospitalization *[see Adverse Reactions (6.1)]*.

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 (2.2)].*

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

Serious, including life-threatening or fatal, bacterial, viral, parasitic and fungal infections have been reported in patients receiving OCREVUS. An increased risk of infections (including serious and fatal bacterial, fungal, and new or reactivated viral infections) has been observed in patients during and following completion of treatment with anti-CD20 B-cell depleting therapies.

A higher proportion of adult patients treated with OCREVUS experienced infections compared to patients taking REBIF or placebo. In RMS trials in adults, 58% of patients treated with OCREVUS experienced one or more infections compared to 52% of patients treated with REBIF. In the PPMS trial, 70% of patients treated with OCREVUS 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)].*

In the pediatric study, infections occurred in 73% of patients treated with OCREVUS (1.5 infections per patient-year) and 59% of patients treated with fingolimod (1.2 infections per patient-year) *[see Adverse Reactions (6.1)]*. Upper respiratory tract infections, nasopharyngitis, and influenza, all of which were mild to moderate, were more frequently reported in patients treated with OCREVUS compared to patients treated with fingolimod.

Delay OCREVUS administration in patients with an active infection until the infection is resolved.

Respiratory Tract Infections

A higher proportion of adult patients treated with OCREVUS experienced respiratory tract infections compared to patients taking REBIF or placebo. In RMS trials in adults, 40% of patients treated with OCREVUS experienced upper respiratory tract infections compared to 33% of patients treated with REBIF, and 8% of patients treated with OCREVUS experienced lower respiratory tract infections compared to 5% of patients treated with REBIF. In the PPMS trial, 49% of patients treated with OCREVUS experienced upper respiratory tract infections compared to 43% of patients on placebo and 10% of patients treated with OCREVUS 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 in adults, herpes infections were reported more frequently in patients treated with OCREVUS than in patients treated with REBIF, 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.

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

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 postmarketing 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.

If serious herpes infections occur, OCREVUS should be discontinued or withheld until the infection has resolved, and appropriate treatment should be administered *[see Patient Counseling Information (17)].*

Hepatitis B Virus (HBV) Reactivation

Hepatitis B reactivation has been reported in MS patients treated with OCREVUS in the postmarketing setting. Fulminant hepatitis, hepatic failure, and death caused by HBV reactivation have occurred in patients treated with 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. 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.

Possible Increased Risk of Immunosuppressant Effects with Other Immunosuppressants

When initiating OCREVUS after an immunosuppressive therapy or initiating an immunosuppressive therapy after OCREVUS, consider the potential for increased immunosuppressive effects *[see Drug Interactions (7.1) and Clinical Pharmacology (12.1, 12.2)].* OCREVUS has not been studied in combination with other MS therapies.

Vaccinations

Administer all age-appropriate immunizations according to immunization guidelines at least 4 weeks prior to initiation of OCREVUS for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of OCREVUS for non-live vaccines.

OCREVUS may interfere with the effectiveness of non-live vaccines *[see Drug Interactions (7.2)].*

The safety of immunization with live or live-attenuated vaccines following OCREVUS therapy has not been studied, and vaccination with live-attenuated or live vaccines is not recommended during treatment and until B-cell repletion *[see Clinical Pharmacology (12.2)]*.

Vaccination of Infants Born to Mothers Treated with OCREVUS During Pregnancy

In infants of mothers exposed to OCREVUS during pregnancy, do not administer live or live-attenuated vaccines before confirming the recovery of B-cell counts as measured by $CD19^+$ B-cells. Depletion of B-cells in these infants may increase the risks from live or live-attenuated vaccines.

If indicated, non-live vaccines may be administered prior to recovery from B-cell depletion, but assessment of vaccine immune responses, including consultation with a qualified specialist, should be considered to assess whether a protective immune response was mounted *[see Use in Specific Populations (8.1)].*

5.3 Progressive Multifocal Leukoencephalopathy

Cases of progressive multifocal leukoencephalopathy (PML) have been reported in patients with MS treated with OCREVUS in the postmarketing setting. PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. PML has occurred in OCREVUS-treated patients who had not been treated previously with natalizumab (which has a known association with PML), were not taking any immunosuppressive or immunomodulatory medications associated with the risk of PML prior to or concomitantly with OCREVUS, and did not have any known ongoing systemic medical conditions resulting in compromised immune system function.

JCV infection resulting in PML has also been observed in patients treated with other anti-CD20 antibodies and other MS therapies.

At the first sign or symptom suggestive of PML, withhold OCREVUS and perform an appropriate diagnostic evaluation. 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.

MRI findings may be apparent before clinical signs or symptoms. Cases of PML, diagnosed based on MRI findings and the detection of JCV DNA in the cerebrospinal fluid in the absence of clinical signs or symptoms specific to PML, have been reported in patients treated with other MS medications associated with PML. Many of these patients subsequently became symptomatic with PML. Therefore, monitoring with MRI for signs that may be consistent with PML may be useful, and any suspicious findings should lead to further investigation to allow for an early diagnosis of PML, if present. Following discontinuation of another MS medication associated with PML, lower PML-related mortality and morbidity have been reported in patients who were initially asymptomatic at diagnosis compared to patients who had characteristic clinical signs and symptoms at diagnosis.

It is not known whether these differences are due to early detection and discontinuation of MS treatment or due to differences in disease in these patients.

If PML is confirmed, treatment with OCREVUS should be discontinued.

5.4 Reduction in Immunoglobulins

As expected with any B-cell depleting therapy, decreased immunoglobulin levels are observed with OCREVUS treatment. The pooled data of OCREVUS clinical studies (RMS and PPMS) in adults and their open-label extensions (up to approximately 7 years of exposure) have shown an association between decreased levels of immunoglobulin G

(IgG<LLN) and increased rates of serious infections. Monitor the levels of quantitative serum immunoglobulins during OCREVUS treatment and after discontinuation of treatment, until B-cell repletion, and especially in the setting of recurrent serious infections. Consider discontinuing OCREVUS therapy in patients with serious opportunistic or recurrent serious infections, and if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins *[see Adverse Reactions (6.1)]*.

5.5 Malignancies

An increased risk of malignancy with OCREVUS may exist. In controlled trials, malignancies, including breast cancer, occurred more frequently in patients treated with OCREVUS. Breast cancer in adults occurred in 6 of 781 females treated with OCREVUS and none of 668 females treated with REBIF or placebo. Patients should follow standard breast cancer screening guidelines.

5.6 Immune-Mediated Colitis

Immune-mediated colitis, which can present as a severe and acute-onset form of colitis, has been reported in patients receiving OCREVUS in the postmarketing setting. Some cases of colitis were serious, requiring hospitalization, with a few patients requiring surgical intervention. Systemic corticosteroids were required in many of these patients. The time from treatment initiation to onset of symptoms in these cases ranged from a few weeks to years. Monitor patients for immune-mediated colitis during OCREVUS treatment, and evaluate promptly if signs and symptoms that may indicate immune-mediated colitis, such as new or persistent diarrhea or other gastrointestinal signs and symptoms, occur.

5.7 Liver Injury

Clinically significant liver injury, without findings of viral hepatitis, has been reported in the postmarketing setting in patients treated with anti-CD20 B-cell depleting therapies approved for the treatment of MS, including OCREVUS. Signs of liver injury, including markedly elevated serum hepatic enzymes with elevated total bilirubin, have occurred from weeks to months after administration.

Patients treated with OCREVUS found to have an alanine aminotransferase (ALT) or aspartate aminotransferase (AST) greater than 3× the upper limit of normal (ULN) with serum total bilirubin greater than 2× ULN are potentially at risk for severe drug-induced liver injury.

Obtain liver function tests prior to initiating treatment with OCREVUS *[see Dosage and Administration (2.1)]* and monitor for signs and symptoms of any hepatic injury during treatment. Measure serum aminotransferases, alkaline phosphatase, and bilirubin levels promptly in patients who report symptoms that may indicate liver injury, including new or worsening fatigue, anorexia, nausea, vomiting, right upper abdominal discomfort, dark urine, or jaundice. If liver injury is present and an alternative etiology is not identified, discontinue OCREVUS.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in the labeling:

- Infusion Reactions *[see Warnings and Precautions (5.1)]*

- Infections *[see Warnings and Precautions (5.2)]*
- Progressive Multifocal Leukoencephalopathy *[see Warnings and Precautions (5.3)]*
- Reduction in Immunoglobulins *[see Warnings and Precautions (5.4)]*
- Malignancies *[see Warnings and Precautions (5.5)]*
- Immune-Mediated Colitis *[see Warnings and Precautions (5.6)]*
- Liver Injury *[see Warnings and Precautions (5.7)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reactions rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Adults

The safety of OCREVUS has been evaluated in 1311 adult patients across MS clinical studies, which included 825 patients in active-controlled clinical trials in patients with relapsing forms of MS (RMS) and 486 patients in a placebo-controlled study in patients with primary progressive MS (PPMS).

Adverse Reactions in Adult Patients with Relapsing Forms of MS

In active-controlled clinical trials (Study 1 and Study 2), 825 patients with RMS received OCREVUS 600 mg intravenously every 24 weeks (initial treatment was given as two separate 300 mg infusions at Weeks 0 and 2) *[see Clinical Studies (14.1)].* The overall exposure in the 96-week controlled treatment periods was 1448 patient-years.

The most common adverse reactions in RMS trials (incidence ≥ 10%) were upper respiratory tract infections and infusion reactions. Table 4 summarizes the adverse reactions that occurred in RMS trials (Study 1 and Study 2).

Table 4 Adverse Reactions in Adult Patients with RMS with an Incidence of at least 5% for OCREVUS and Higher than REBIF

Adverse Reactions	**Studies 1 and 2**	
	OCREVUS 600 mg IV Every 24 Weeks* (n=825) %	**REBIF 44 mcg SQ 3 Times per Week (n=826) %**
Upper respiratory tract infections	40	33
Infusion reactions	34	10
Depression	8	7
Lower respiratory tract infections	8	5
Back pain	6	5
Herpes virus- associated infections	6	4
Pain in extremity	5	4

* The first dose was given as two separate 300 mg infusions at Weeks 0 and 2.

Adverse Reactions in Adult Patients with Primary Progressive MS

In a placebo-controlled clinical trial (Study 3), a total of 486 patients with PPMS received one course of OCREVUS (600 mg of OCREVUS administered as two 300 mg infusions two weeks apart) given intravenously every 24 weeks and 239 patients received placebo intravenously *[see Clinical Studies (14.2)].* The overall exposure in the controlled treatment period was 1416 patient-years, with median treatment duration of 3 years.

The most common adverse reactions in the PPMS trial (incidence ≥ 10%) were upper respiratory tract infections, infusion reactions, skin infections, and lower respiratory tract infections. Table 5 summarizes the adverse reactions that occurred in the PPMS trial (Study 3).

Table 5 Adverse Reactions in Adult Patients with PPMS with an Incidence of at least 5% for OCREVUS and Higher than Placebo

Adverse Reactions	Study 3	
	OCREVUS 600 mg IV Every 24 Weeks* (n=486) %	**Placebo (n=239) %**
Upper respiratory tract infections	49	43
Infusion reactions	40	26
Skin infections	14	11
Lower respiratory tract infections	10	9
Cough	7	3
Diarrhea	6	5
Edema peripheral	6	5
Herpes virus associated infections	5	4

* One dose of OCREVUS (600 mg administered as two 300 mg infusions two weeks apart)

Adverse Reactions in Adult Patients who Received 2-hour Infusions

Study 4 was designed to characterize the safety profile of OCREVUS infusions administered over 2 hours in patients with Relapsing-Remitting Multiple Sclerosis who did not experience a serious infusion reaction with any previous OCREVUS infusion. In this study, the incidence, intensity, and types of symptoms of infusion reactions were consistent with those of infusions administered over 3.5 hours *[see Clinical Studies (14.3)]*.

Laboratory Abnormalities in Adults

Decreased Immunoglobulins

OCREVUS decreased total immunoglobulins with the greatest decline seen in IgM levels; however, a decrease in IgG levels was associated with an increased rate of serious infections.

In the active-controlled (RMS) trials (Study 1 and Study 2), the proportion of patients at baseline reporting IgG, IgA, and IgM below the lower limit of normal (LLN) in OCREVUS-

treated patients was 0.5%, 1.5%, and 0.1%, respectively. Following treatment, the proportion of OCREVUS-treated patients reporting IgG, IgA, and IgM below the LLN at 96 weeks was 1.5%, 2.4%, and 16.5%, respectively.

In the placebo-controlled (PPMS) trial (Study 3), the proportion of patients at baseline reporting IgG, IgA, and IgM below the LLN in OCREVUS-treated patients was 0.0%, 0.2%, and 0.2%, respectively. Following treatment, the proportion of OCREVUS-treated patients reporting IgG, IgA, and IgM below the LLN at 120 weeks was 1.1%, 0.5%, and 15.5%, respectively.

The pooled data of OCREVUS clinical studies (RMS and PPMS) and their open-label extensions (up to approximately 7 years of exposure) have shown an association between decreased levels of IgG and increased rates of serious infections. The type, severity, latency, duration, and outcome of serious infections observed during episodes of immunoglobulins below LLN were consistent with the overall serious infections observed in patients treated with OCREVUS.

Decreased Neutrophil Levels

In the PPMS clinical trial (Study 3), decreased neutrophil counts occurred in 13% of OCREVUS-treated patients compared to 10% in placebo patients. The majority of the decreased neutrophil counts were only observed once for a given patient treated with OCREVUS and were between LLN - 1.5×10^9/L and 1.0×10^9/L. Overall, 1% of the patients in the OCREVUS group had neutrophil counts less than 1.0×10^9/L and these were not associated with an infection.

Pediatric Patients

Adverse Reactions in Patients 10 to Less Than 18 Years of Age with Relapsing-Remitting MS

The safety of OCREVUS in pediatric patients with relapsing-remitting MS was evaluated in one randomized, double-blind clinical study in 185 patients, 93 of whom received OCREVUS and 92 of whom received fingolimod *[see Clinical Studies (14.4)]*. In the controlled pediatric trial (Study 5), the safety profile in pediatric patients was consistent with that observed in adult patients.

Infusion Reactions

Infusion reactions were the most common adverse reactions in patients treated with OCREVUS with an incidence of 48%, compared to an incidence of 24% in fingolimod-treated patients (placebo infusion). The incidence of infusion reactions was highest at 31% with infusion 1 of the initial dose (on day 1), and decreased to 9% with infusion 2 of the initial dose (on day 15). At the first subsequent dose (at 6 months), 16% of patients had an infusion reaction. The incidence and severity of infusion reactions decreased with additional subsequent infusions. The majority of infusion reactions were mild to moderate. One infusion reaction with infusion 1 of the initial dose was reported as serious because it required hospitalization.

Infections

Infections were observed in 73% of patients treated with OCREVUS (1.5 infections per patient-year) and 59% of patients treated with fingolimod (1.2 infections per patient-year). Serious infections occurred in 3% of patients treated with OCREVUS (0.03 serious infections per patient-year) compared to 3% of fingolimod-treated patients (0.03 serious

infections per patient-year).

Laboratory Abnormalities

Decreased Immunoglobulins

OCREVUS decreased total immunoglobulins over the controlled period of Study 5, with the greatest decline seen in IgM levels. Similar to the pattern observed in the adult population, reduction in IgM occurred earlier and in a higher proportion of patients compared to IgG and IgA.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of OCREVUS. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Gastrointestinal Disorders: Immune-mediated colitis *[see Warnings and Precautions (5.6)]*

Hepatobiliary Disorders: Liver injury *[see Warnings and Precautions (5.7)]*

Infections and Infestations: Serious herpes infections *[see Warnings and Precautions (5.2)]*, progressive multifocal leukoencephalopathy *[see Warnings and Precautions (5.3)]*, and babesiosis

Skin: Pyoderma gangrenosum

7 DRUG INTERACTIONS

7.1 Immunosuppressive or Immune-Modulating Therapies

The concomitant use of OCREVUS and other immune-modulating or immunosuppressive therapies, including immunosuppressant doses of corticosteroids, is expected to increase the risk of immunosuppression. Consider the risk of additive immune system effects when coadministering immunosuppressive therapies with OCREVUS. When switching from drugs with prolonged immune effects, such as daclizumab, fingolimod, natalizumab, teriflunomide, or mitoxantrone, consider the duration and mode of action of these drugs because of additive immunosuppressive effects when initiating OCREVUS *[see Warnings and Precautions (5.2)].*

7.2 Vaccinations

A Phase 3b randomized, open-label study examined the concomitant use of OCREVUS and several non-live vaccines in adults 18-55 years of age with relapsing forms of MS (68 subjects undergoing treatment with OCREVUS at the time of vaccination and 34 subjects not undergoing treatment with OCREVUS at the time of vaccination). Concomitant exposure to OCREVUS attenuated antibody responses to tetanus toxoid-containing vaccine, pneumococcal polysaccharide, pneumococcal conjugate vaccines, and seasonal inactivated influenza vaccines. The impact of the observed attenuation on vaccine effectiveness in this patient population is unknown. The safety and effectiveness of live or live-attenuated vaccines administered concomitantly with OCREVUS have not been assessed *[see Warnings and Precautions (5.2)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

OCREVUS is a humanized monoclonal antibody of an immunoglobulin G1 subtype and immunoglobulins are known to cross the placental barrier. There are no adequate data on the developmental risk associated with use of OCREVUS in pregnant women. However, transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other anti-CD20 antibodies during pregnancy. B-cell levels in infants following maternal exposure to OCREVUS have not been studied in clinical trials. The potential duration of B-cell depletion in such infants, and the impact of B-cell depletion on vaccine safety and effectiveness, is unknown *[see Warnings and Precautions (5.2)]*.

Following administration of ocrelizumab to pregnant monkeys at doses similar to or greater than those used clinically, increased perinatal mortality, depletion of B-cell populations, renal, bone marrow, and testicular toxicity were observed in the offspring in the absence of maternal toxicity *[see Data]*.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is unknown.

Data

Animal Data

Following intravenous administration of OCREVUS to monkeys during organogenesis (loading doses of 15 or 75 mg/kg on gestation days 20, 21, and 22, followed by weekly doses of 20 or 100 mg/kg), depletion of B-lymphocytes in lymphoid tissue (spleen and lymph nodes) was observed in fetuses at both doses.

Intravenous administration of OCREVUS (three daily loading doses of 15 or 75 mg/kg, followed by weekly doses of 20 or 100 mg/kg) to pregnant monkeys throughout the period of organogenesis and continuing through the neonatal period resulted in perinatal deaths (some associated with bacterial infections), renal toxicity (glomerulopathy and inflammation), lymphoid follicle formation in the bone marrow, and severe decreases in circulating B-lymphocytes in neonates. The cause of the neonatal deaths is uncertain; however, both affected neonates were found to have bacterial infections. Reduced testicular weight was observed in neonates at the high dose.

A no-effect dose for adverse developmental effects was not identified; the doses tested in monkey are 2 and 10 times the recommended human dose of 600 mg, on a mg/kg basis.

8.2 Lactation

Risk Summary

There are no data on the presence of ocrelizumab in human milk, the effects on the breastfed infant, or the effects of the drug on milk production. Ocrelizumab was

excreted in the milk of ocrelizumab-treated monkeys. Human IgG is excreted in human milk, and the potential for absorption of ocrelizumab to lead to B-cell depletion in the infant is unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for OCREVUS and any potential adverse effects on the breastfed infant from OCREVUS or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

Contraception

Females of reproductive potential should use effective contraception while receiving OCREVUS and for 6 months after the last infusion of OCREVUS *[see Clinical Pharmacology (12.3)]*.

8.4 Pediatric Use

The safety and effectiveness of OCREVUS for the treatment of relapsing-remitting MS have been established in pediatric patients 10 years of age and older who weigh 25 kg or more. Use of OCREVUS for this indication is supported by evidence from one randomized, double-blind clinical study in 187 pediatric patients (93 of whom received OCREVUS) and additional pharmacokinetic data in pediatric patients *[see Clinical Pharmacology (12.3)* and *Clinical Studies (14.4)]*.

The overall safety profile in pediatric patients 10 years of age and older receiving OCREVUS was generally consistent with that observed in adult patients *[see Adverse Reactions (6.1)]*.

Safety and effectiveness of OCREVUS have not been established in pediatric patients less than 10 years of age or who weigh less than 25 kg.

8.5 Geriatric Use

Clinical studies of OCREVUS did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

11 DESCRIPTION

Ocrelizumab is a recombinant humanized monoclonal antibody directed against CD20-expressing B-cells. Ocrelizumab is a glycosylated immunoglobulin G1 (IgG1) with a molecular mass of approximately 145 kDa.

OCREVUS (ocrelizumab) injection for intravenous infusion is a preservative-free, sterile, clear or slightly opalescent, and colorless to pale brown solution supplied in single-dose vials. Each mL of solution contains 30 mg ocrelizumab, glacial acetic acid (0.25 mg), polysorbate 20 (0.2 mg), sodium acetate trihydrate (2.14 mg), and trehalose dihydrate (40 mg) at pH 5.3.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The precise mechanism by which ocrelizumab exerts its therapeutic effects in multiple

sclerosis is unknown, but is presumed to involve binding to CD20, a cell surface antigen present on pre-B and mature B lymphocytes. Following cell surface binding to B lymphocytes, ocrelizumab results in antibody-dependent cellular cytolysis and complement-mediated lysis.

12.2 Pharmacodynamics

For B-cell counts, assays for $CD19^+$ B-cells are used because the presence of OCREVUS interferes with the CD20 assay. Treatment with OCREVUS reduces $CD19^+$ B-cell counts in blood by 14 days after infusion in adult and pediatric patients. In clinical studies in adults, B-cell counts rose to above the lower limit of normal (LLN) or above baseline counts between infusions of OCREVUS at least one time in 0.3% to 4.1% of patients. In a clinical study of 51 adult patients, the median time for B-cell counts to return to either baseline or LLN was 72 weeks (range 27-175 weeks) after the last OCREVUS infusion. Within 2.5 years after the last infusion, B-cell counts rose to either baseline or LLN in 90% of adult patients.

12.3 Pharmacokinetics

Pharmacokinetics (PK) of OCREVUS in MS clinical studies fit a two compartment model with time-dependent clearance. The overall exposure at the steady-state (AUC over the 24 week dosing intervals) of OCREVUS was 3,510 mcg/mL per day. In clinical studies in adult MS patients, maintenance doses of ocrelizumab were either 600 mg every 6 months (RMS patients) or two 300 mg infusions separated by 14 days every 6 months (PPMS patients). The mean maximum concentration was 212 mcg/mL in patients with RMS (600 mg infusion over 3.5 hours) and 141 mcg/mL in patients with PPMS (two 300 mg infusions over 2.5 hours administered within two weeks). The mean maximum peak concentrations (C_{max}) of ocrelizumab in patients with relapsing-remitting multiple sclerosis (RRMS) observed after the 3.5-hour infusion and 2-hour infusion were 202 ± 42 (mean ± SD) and 200 ± 46 mcg/mL, respectively, compared to the previously reported C_{max} of 212 mcg/mL. The pharmacokinetics of ocrelizumab was essentially linear and dose proportional between 400 mg and 2000 mg.

Distribution

The population PK estimate of the central volume of distribution was 2.78 L. Peripheral volume and inter-compartment clearance were estimated at 2.68 L and 0.29 L/day, respectively.

Elimination

Constant clearance was estimated at 0.17 L/day, and initial time-dependent clearance at 0.05 L/day, which declined with a half-life of 33 weeks. The terminal elimination half-life was 26 days.

Metabolism

The metabolism of OCREVUS has not been directly studied because antibodies are cleared principally by catabolism.

Specific Populations

Pediatric Patients

The median AUC over the first 24-week dosing interval was 3130 mcg/mL per day, and

C_{max} was 147 mcg/mL, in patients 10 years to less than 18 years of age receiving OCREVUS 600 mg (body weight ≥ 35 kg) or 300 mg (body weight < 35 kg).

Renal Impairment

Patients with mild renal impairment were included in clinical trials. No significant change in the pharmacokinetics of OCREVUS was observed in those patients.

Hepatic Impairment

Patients with mild hepatic impairment were included in clinical trials. No significant change in the pharmacokinetics of OCREVUS was observed in those patients.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in other studies, including those of OCREVUS or of other ocrelizumab products.

Patients in MS trials (Study 1, Study 2, Study 3, and Study 5) were tested at multiple time points (baseline and every 6 months post-treatment for the duration of the trial) for anti-drug antibodies (ADAs).

In Studies 1, 2, and 3, 12 (~1%) out of 1131 adult patients tested positive for ADAs, of which 2 patients tested positive for neutralizing antibodies.

In Study 5, two out of 90 pediatric patients (2.2%) had treatment emergent ADAs.

These data are not adequate to assess the impact of ADAs on the safety and efficacy of OCREVUS.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity studies have been performed to assess the carcinogenic potential of OCREVUS.

No studies have been performed to assess the mutagenic potential of OCREVUS. As an antibody, OCREVUS is not expected to interact directly with DNA.

No effects on reproductive organs were observed in male monkeys administered ocrelizumab by intravenous injection (three loading doses of 15 or 75 mg/kg, followed by weekly doses of 20 or 100 mg/kg) for 8 weeks. There were also no effects on estrus cycle in female monkeys administered ocrelizumab over three menstrual cycles using the same dosing regimen. The doses tested in monkey are 2 and 10 times the recommended human dose of 600 mg, on a mg/kg basis.

14 CLINICAL STUDIES

14.1 Relapsing Forms of Multiple Sclerosis in Adults

The efficacy of OCREVUS was demonstrated in two randomized, double-blind, double-

dummy, active comparator-controlled clinical trials of identical design, in adult patients with relapsing forms of multiple sclerosis (RMS) treated for 96 weeks (Study 1 and Study 2). 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, the active comparator, was 44 mcg given as subcutaneous injections 3 times per week and placebo IV infusions were given every 24 weeks. Both studies included patients who had experienced at least one relapse within the prior year, or two relapses within the prior two years, and had an Expanded Disability Status Scale (EDSS) score from 0 to 5.5. Patients with primary progressive forms of multiple sclerosis (MS) were excluded. Neurological evaluations were performed every 12 weeks and at the time of a suspected relapse. Brain MRIs were performed at baseline and at Weeks 24, 48, and 96.

The primary outcome of both Study 1 and Study 2 was the annualized relapse rate (ARR). Additional outcome measures included the proportion of patients with confirmed disability progression, the mean number of MRI T1 gadolinium (Gd)-enhancing lesions at Weeks 24, 48, and 96, and new or enlarging MRI T2 hyperintense lesions. Progression of disability was defined as an increase of 1 point or more from the baseline EDSS score attributable to MS when the baseline EDSS score was 5.5 or less, or 0.5 points or more when the baseline EDSS score was above 5.5. Disability progression was considered confirmed when the increase in the EDSS was confirmed at a regularly scheduled visit 12 weeks after the initial documentation of neurological worsening. The primary population for analysis of confirmed disability progression was the pooled population from Studies 1 and 2.

In Study 1, 410 patients were randomized to OCREVUS and 411 to REBIF; 11% of OCREVUS-treated and 17% of REBIF-treated patients did not complete the 96-week double-blind treatment period. The baseline demographic and disease characteristics were balanced between the two treatment groups. At baseline, the mean age of patients was 37 years; 66% were female. The mean time from MS diagnosis to randomization was 3.8 years, the mean number of relapses in the previous year was 1.3, and the mean EDSS score was 2.8; 74% of patients had not been treated with a non-steroid therapy for MS in the 2 years prior to the study. At baseline, 40% of patients had one or more T1 Gd-enhancing lesions (mean 1.8).

In Study 2, 417 patients were randomized to OCREVUS and 418 to REBIF; 14% of OCREVUS-treated and 23% of REBIF-treated patients did not complete the 96-week double-blind treatment period. The baseline demographic and disease characteristics were balanced between the two treatment groups. At baseline, the mean age of patients was 37 years; 66% were female. The mean time from MS diagnosis to randomization was 4.1 years, the mean number of relapses in the previous year was 1.3, and the mean EDSS score was 2.8; 74% of patients had not been treated with a non-steroid therapy for MS in the 2 years prior to the study. At baseline, 40% of OCREVUS-treated patients had one or more T1 Gd-enhancing lesions (mean 1.9).

In Study 1 and Study 2, OCREVUS significantly lowered the annualized relapse rate and the proportion of patients with disability progression confirmed at 12 weeks after onset compared to REBIF. Results for Study 1 and Study 2 are presented in Table 6 and Figure 1.

Table 6 Key Clinical and MRI Endpoints in Adult RMS Patients from

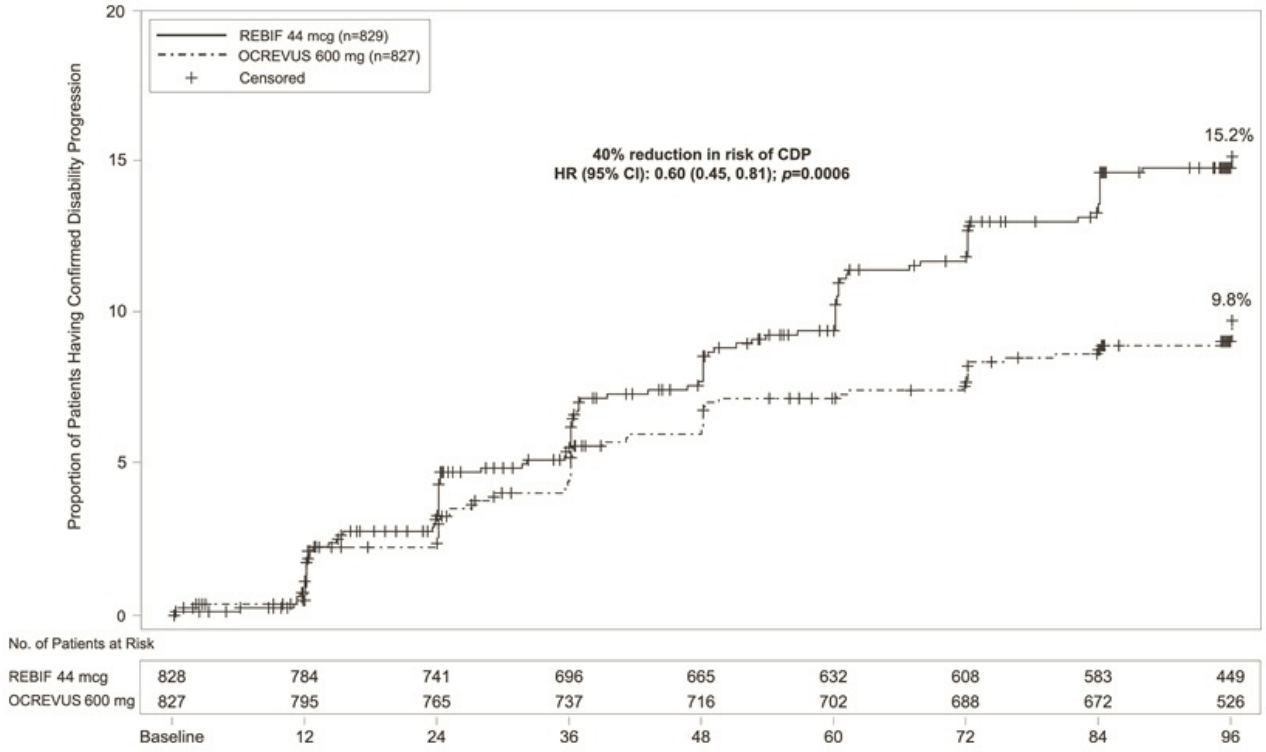
Study 1 and Study 2

Endpoints	Study 1		Study 2	
	OCREVUS 600 mg every 24 weeks N=410	REBIF 44 mcg three times a week N=411	OCREVUS 600 mg every 24 weeks N=417	REBIF 44 mcg three times a week N=418
Clinical Endpoints				
Annualized Relapse Rate (Primary Endpoint)	0.156	0.292	0.155	0.290
Relative Reduction	46% (p<0.0001)		47% (p<0.0001)	
Proportion Relapse-free	83%	71%	82%	72%
Proportion of Patients with 12-week Confirmed Disability Progression*	9.8% OCREVUS vs 15.2% REBIF			
Risk Reduction (Pooled Analysis†)	40%; p=0.0006			
MRI Endpoints				
Mean number of T1 Gd-enhancing lesions per MRI scan	0.016	0.286	0.021	0.416
Relative Reduction	94% (p<0.0001)		95% (p<0.0001)	
Mean number of new and/or enlarging T2 hyperintense lesions per MRI	0.323	1.413	0.325	1.904
Relative Reduction	77% (p<0.0001)		83% (p<0.0001)	

* Defined as an increase of 1.0 point or more from the baseline Expanded Disability Status Scale (EDSS) score for patients with baseline score of 5.5 or less, or 0.5 or more when the baseline score is greater than 5.5, Kaplan-Meier estimates at Week 96.

† Data prospectively pooled from Study 1 and Study 2.

Figure 1 Kaplan-Meier Plot* of Time to Onset of Confirmed Disability Progression Sustained for at Least 12 Weeks with the Initial Event of Neurological Worsening Occurring During the Double-blind Treatment Period in Pooled Studies 1 and 2 in Adult Patients with RMS (Pooled ITT Population)



* Pre-specified pooled analysis of Study 1 and 2

In exploratory subgroup analyses of Study 1 and Study 2, the effect of OCREVUS on annualized relapse rate and disability progression was similar in male and female patients.

14.2 Primary Progressive Multiple Sclerosis in Adults

Study 3 was a randomized, double-blind, placebo-controlled clinical trial in patients with primary progressive multiple sclerosis (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. Selection criteria required a baseline EDSS of 3 to 6.5 and a score of 2 or greater for the EDSS pyramidal functional system due to lower extremity findings. Neurological assessments were conducted every 12 weeks. An MRI scan was obtained at baseline and at Weeks 24, 48, and 120.

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. In Study 3, confirmed disability progression also was deemed to have occurred if patients who had onset of disability progression discontinued participation in the study before the next assessment. Additional outcome measures included timed 25-foot walk, and percentage change in T2 hyperintense lesion volume.

Study 3 randomized 488 patients to OCREVUS and 244 to placebo; 21% of OCREVUS-treated patients and 34% of placebo-treated patients did not complete the trial. The baseline demographic and disease characteristics were balanced between the two treatment groups. At baseline, the mean age of patients was 45; 49% were female. The mean time since symptom onset was 6.7 years, the mean EDSS score was 4.7, and

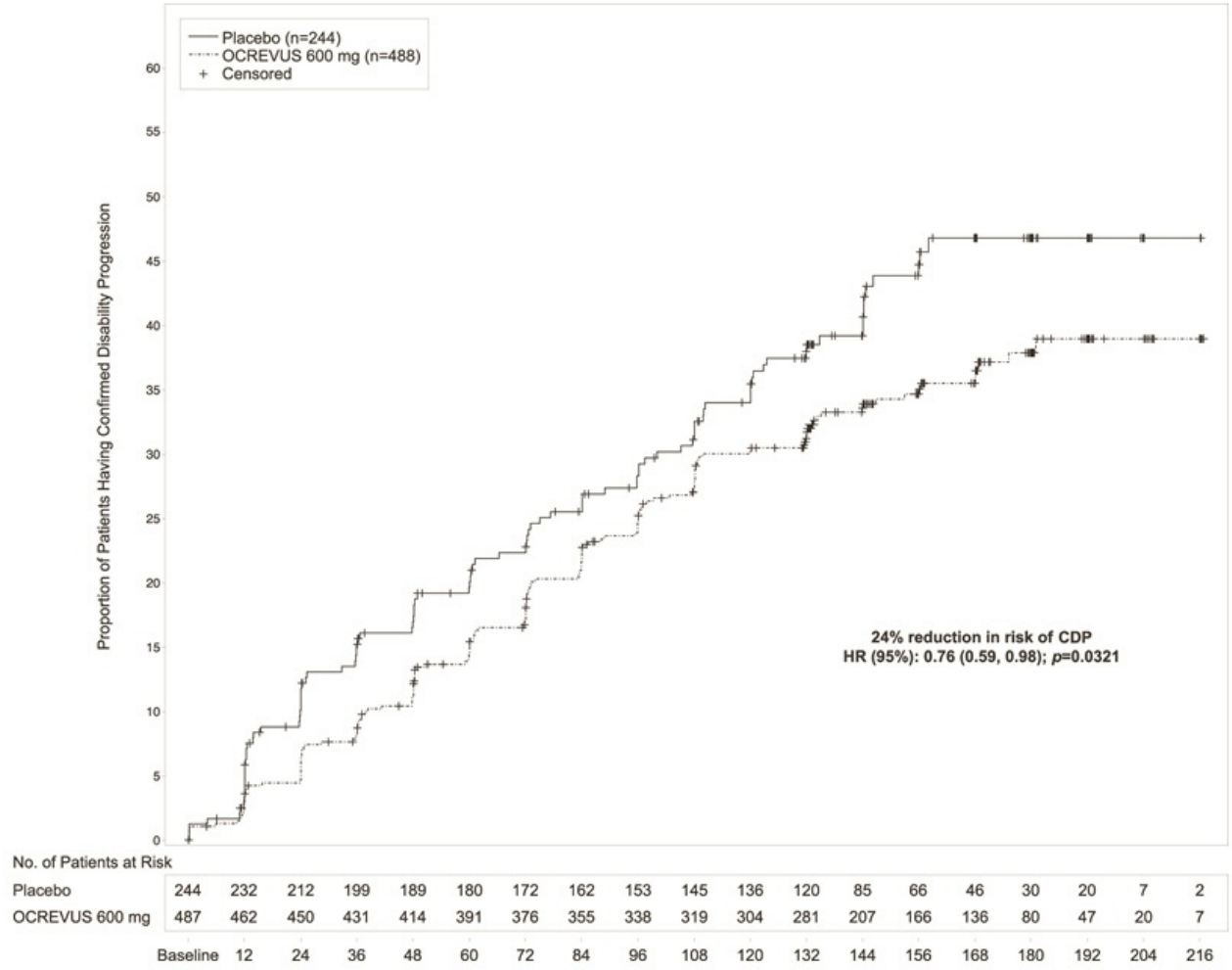
26% had one or more T1 Gd-enhancing lesions at baseline; 88% of patients had not been treated previously with a non-steroid treatment for MS. The time to onset of disability progression confirmed at 12 weeks after onset was significantly longer for OCREVUS-treated patients than for placebo-treated patients (see Figure 2). Results for Study 3 are presented in Table 7 and Figure 2.

Table 7 Key Clinical and MRI Endpoints in Adult PPMS Patients for Study 3

Endpoints	**Study 3**	
	OCREVUS 600 mg (two 300 mg infusions two weeks apart every 24 weeks) N=488	**Placebo N=244**
Clinical Outcomes		
Proportion of patients with 12-week Confirmed Disability Progression*	32.9%	39.3%
Risk reduction	24%; p=0.0321	
MRI Endpoints		
Mean change in volume of T2 lesions, from baseline to Week 120 (cm^3)	-0.39	0.79
	p<0.0001	

* Defined as an increase of 1.0 point or more from the baseline EDSS score for patients with baseline score of 5.5 or less, or an increase of 0.5 or more when the baseline score is more than 5.5

Figure 2 Kaplan-Meier Plot of Time to Onset of Confirmed Disability Progression Sustained for at Least 12 Weeks with the Initial Event of Neurological Worsening Occurring During the Double-blind Treatment Period in Adults in Study 3*



* All patients in this analysis had a minimum of 120 weeks of follow-up. The primary analysis is based on all disability progression events accrued including 21 without confirmatory EDSS at 12 weeks.

In the overall population in Study 3, the proportion of patients with 20 percent worsening of the timed 25-foot walk confirmed at 12 weeks was 49% in OCREVUS-treated patients compared to 59% in placebo-treated patients (25% risk reduction).

In exploratory subgroup analyses of Study 3, the proportion of female patients with disability progression confirmed at 12 weeks after onset was similar in OCREVUS-treated patients and placebo-treated patients (approximately 36% in each group). In male patients, the proportion of patients with disability progression confirmed at 12 weeks after onset was approximately 30% in OCREVUS-treated patients and 43% in placebo-treated patients. Clinical and MRI endpoints that generally favored OCREVUS numerically in the overall population, and that showed similar trends in both male and female patients, included annualized relapse rate, change in T2 lesion volume, and number of new or enlarging T2 lesions.

14.3 Safety Study of 2-Hour Infusions in Adults

The safety of the 2-hour OCREVUS infusion was evaluated in Study 4 (NCT03085810), a prospective, multicenter, randomized, double-blind, controlled, parallel arm substudy in adult patients with Relapsing-Remitting Multiple Sclerosis who were naïve to other non-steroid therapies for MS and did not experience a serious infusion reaction with any previous OCREVUS infusion. The first dose of OCREVUS was administered as two 300

mg infusions (600 mg total) separated by 14 days. After enrollment in the substudy, patients were randomized in a 1:1 ratio to receive infusions over approximately 3.5-hours or 2-hours, after appropriate premedication *[see Dosage and Administration (2.2)]*, every 24 weeks. The randomization was stratified by region and the dose at which patients were first randomized.

The primary endpoint of the substudy was the proportion of patients with infusion reactions occurring during or within 24 hours following the first randomized infusion of OCREVUS. The primary analysis was performed when 580 patients were randomized, at which time 469/579 (81%) of the treated patients had received only a single randomized infusion of OCREVUS. The proportions of patients with infusion reactions occurring during or within 24 hours following the first randomized infusion in this substudy were similar between the 2-hour and 3.5-hour infusion groups (24.4% versus 23.3%, respectively). Overall, in all randomized doses, 27.1% of the patients in the 2-hour infusion group and 25.0% of the patients in the 3.5-hour infusion group reported mild or moderate infusion reactions; two infusion reactions were severe in intensity, with one severe infusion reaction (0.3%) reported in one patient in each group in this substudy *[see Warnings and Precautions (5.1)]*. There were no life-threatening, fatal, or serious infusion reactions in this substudy.

14.4 Relapsing-Remitting MS in Pediatric Patients 10 Years to less than 18 Years of Age

The efficacy and safety of OCREVUS in pediatric patients 10 years to less than 18 years of age with relapsing-remitting multiple sclerosis (RRMS) was established in a randomized, double-blind, double-dummy clinical study (Study 5; NCT05123703 with a follow-up time of at least 24 weeks. Patients were randomized 1:1 to receive either OCREVUS intravenously according to the recommended dosage regimen *[see Dosage and Administration (2.3)]* or 0.5 mg fingolimod daily by mouth. Both treatment groups received placebo, either by mouth or via infusion, respectively.

The primary outcome of Study 5 was ARR. Secondary outcome measures included the annualized rate of new or enlarging T2 hyperintense MRI lesions, and the mean number of T1 gadolinium (Gd)-enhancing MRI lesions at Week 12.

In Study 5, 93 patients were randomized to the OCREVUS arm and 94 patients to the fingolimod arm. The duration of the study was variable for each patient, but all patients received double-blind treatment for at least 24 weeks. Patients were treated until the last randomized patient completed 24 weeks of double-blind treatment. The median (range) treatment duration for patients treated with OCREVUS was 72.1 (24.0-158.9) weeks and for patients treated with fingolimod was 70.9 (0.0-141.7) weeks.

The baseline demographic and disease characteristics were balanced between the two treatment groups. At baseline, the median age was 15 years (range: 11–17 years). Patients were predominantly female (69%); 66% were White, 5% were Black or African American, 5% were multiracial, and race was unknown for 19%. The median weight of patients was 63.1 kg (range: 42.3–154.2 kg). The median EDSS score was 1.5 in both arms.

In Study 5, OCREVUS demonstrated non-inferiority to fingolimod in reducing the ARR and superiority in reducing the annualized rate of new/enlarging T2 lesions during the double-blind period and reducing the number of Gd-enhancing T1 lesions at Week 12. Results for Study 5 are presented in Table 8.

Table 8 Key Clinical and MRI Endpoints in Pediatric Patients with RRMS from Study 5

Endpoints	Study 5	
	OCREVUS Intravenous Infusion* N = 93	Fingolimod 0.5 mg By Mouth N = 94†
Clinical Endpoints		
Annualized Relapse Rate (Primary Endpoint)‡	0.070	0.135
Relative Reduction	48.3%	
Rate Ratio	0.517 (95% CI: 0.193-1.329)§	
MRI Endpoints		
Annualized rate of new and/or enlarging T2 hyperintense lesions per MRI scan‡	3.778	7.235
Relative Reduction	47.8% (p=0.001)	
Mean number of T1 Gd-enhancing lesions at Week 12	0.031	0.243
Relative Reduction	87.2% (p=0.001)	

* Based on body weight *[see Dosage and Administration (2.3)]*
† Two patients were randomized to the fingolimod arm, but were not treated and did not contribute follow-up time to the estimate of the annualized relapse rate.
‡ During the double-blind treatment period
§ Based on the prespecified non-inferiority criteria, non-inferiority of ocrelizumab to fingolimod was demonstrated.

16 HOW SUPPLIED/STORAGE AND HANDLING

OCREVUS (ocrelizumab) injection is a preservative-free, sterile, clear or slightly opalescent, and colorless to pale brown solution supplied as a carton containing one 300 mg/10 mL (30 mg/mL) single-dose vial (NDC 50242-150-01).

Store OCREVUS vials at 2°C to 8°C (36°F to 46°F) in the outer carton to protect from light. Do not freeze or shake.

17 PATIENT COUNSELING INFORMATION

Advise the patient and caregiver to read the FDA-approved patient labeling (Medication Guide).

Infusion Reactions

Inform patients and caregivers about the signs and symptoms of infusion reactions, and that infusion reactions can occur up to 24 hours after infusion. Advise patients and

caregivers to contact the patient's healthcare provider immediately for signs or symptoms of infusion reactions *[see Warnings and Precautions (5.1)]*.

Infection

Advise patients and caregivers to contact the patient's healthcare provider for any signs of infection during treatment or after the last dose *[see Clinical Pharmacology (12.2)].* Signs include fever, chills, constant cough, dysuria, or signs of herpes such as cold sores, shingles, or genital sores *[see Warnings and Precautions (5.2)]*.

Advise patients and caregivers that OCREVUS may cause reactivation of hepatitis B infection and that monitoring will be required if the patient is at risk *[see Warnings and Precautions (5.2)]*.

Advise patients and caregivers that herpes infections, including serious herpes infections affecting the central nervous system, skin, and eyes, have occurred during treatment with OCREVUS. Advise patients and caregivers to promptly contact the patient's healthcare provider if any signs or symptoms of herpes infections occur, including oral or genital symptoms, fever, skin rash, pain, itching, decreased visual acuity, eye redness, eye pain, headache, neck stiffness, or change in mental status *[see Warnings and Precautions (5.2)].*

Vaccination

Advise patients and caregivers that any age-appropriate live or live-attenuated vaccinations should be completed at least 4 weeks and, whenever possible, age-appropriate non-live vaccinations at least 2 weeks prior to initiation of OCREVUS. Administration of live-attenuated or live vaccines is not recommended during OCREVUS treatment and until B-cell recovery *[see Warnings and Precautions (5.2)]*.

Progressive Multifocal Leukoencephalopathy

Inform patients and caregivers that PML has occurred in patients who received OCREVUS. Inform the patient and caregiver that PML is characterized by a progression of deficits and usually leads to death or severe disability over weeks or months. Instruct the patient and caregiver of the importance of contacting the patient's healthcare provider if any symptoms suggestive of PML develop. Inform the patient and caregiver that 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 *[see Warnings and Precautions (5.3)].*

Malignancies

Advise patients and caregivers that an increased risk of malignancy, including breast cancer, may exist with OCREVUS. Advise patients and caregivers that they should follow standard breast cancer screening guidelines *[see Warnings and Precautions (5.5)]*.

Immune-Mediated Colitis

Advise patients and caregivers to promptly contact the patient's healthcare provider if any signs and symptoms of colitis, including diarrhea, abdominal pain, and blood in stool occur while taking OCREVUS *[see Warnings and Precautions (5.6)].*

Liver Injury

Inform patients and caregivers that liver injury has been reported with anti-CD20 B-cell

depleting therapies, including OCREVUS. Instruct patients and caregivers to promptly report any symptoms that may indicate liver injury, including fatigue, anorexia, nausea, vomiting, right upper abdominal discomfort, dark urine, or jaundice. A blood test should be obtained before patients start therapy, and during treatment as clinically indicated *[see Warnings and Precautions (5.7)]*.

Contraception

Females of childbearing potential should use effective contraception while receiving OCREVUS and for 6 months after the last infusion of OCREVUS *[see Clinical Pharmacology (12.3)]*. Instruct patients and caregivers that if a pregnancy occurs or is planned while taking OCREVUS, the patient's healthcare provider should be informed *[see Use in Specific Populations (8.1)]*.

OCREVUS® [ocrelizumab]

Manufactured by:
Genentech, Inc.
A Member of the Roche Group
1 DNA Way
South San Francisco, CA 94080-4990

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MEDICATION GUIDE
OCREVUS® (oak-rev-us)
(ocrelizumab)
injection,
for intravenous use

This information does not take the place of talking to your healthcare provider about your medical condition or your treatment. If you are the parent or guardian of a child who is being treated with OCREVUS, the following information applies to your child.

What is the most important information I should know about OCREVUS?
OCREVUS can cause serious side effects, including:

- **Infusion reactions**: Infusion reactions are a common side effect of OCREVUS, which can be serious and may require you to be hospitalized. You will be monitored during your infusion and for at least 1 hour after each infusion of OCREVUS for signs and symptoms of an infusion reaction. Tell your healthcare provider or nurse if you get any of these symptoms:

  - itchy skin
  - rash
  - hives
  - tiredness
  - coughing or wheezing
  - trouble breathing
  - throat irritation or pain
  - feeling faint
  - fever
  - redness on your face (flushing)
  - nausea
  - headache
  - swelling of the throat
  - dizziness
  - shortness of breath
  - fatigue
  - fast heart beat

These infusion reactions can happen for up to 24 hours after your infusion.

It is important that you call your healthcare provider right away if you get any of the signs or symptoms listed above after each infusion.
If you get infusion reactions, your healthcare provider may need to stop or slow down the rate of your infusion.

- **Infection:**
  - Infections are a common side effect. OCREVUS increases your risk of getting upper respiratory tract infections, lower respiratory tract infections, skin infections, and herpes infections. Serious infections can happen with OCREVUS, which can be life-threatening or cause death**.** Tell your healthcare provider if you have an infection or have any of the following signs of infection including fever, chills, a cough that does not go away, or painful urination. Signs of herpes infection include:

    - cold sores
    - shingles
    - genital sores
    - skin rash
    - pain
    - itching

    Signs of a more serious herpes infection include:

    - changes in vision
    - eye redness or eye pain
    - severe or persistent headache
    - stiff neck
    - confusion

    Signs of infection can happen during treatment or after you have received your last dose of OCREVUS. Tell your healthcare provider right away if you have an infection. Your healthcare provider should delay your treatment with OCREVUS until your infection is gone.

  - **Hepatitis B virus (HBV) reactivation**: Before starting treatment with OCREVUS, your healthcare provider will do blood tests to check for hepatitis B viral infection. If you have ever had hepatitis B virus infection, the hepatitis B virus may become active again during or after treatment with OCREVUS. Hepatitis B virus becoming active again (called reactivation) may cause serious liver problems including liver failure or death. Your healthcare provider will monitor you if you are at risk for hepatitis B virus reactivation during treatment and after you stop receiving OCREVUS.
  - **Weakened immune system**: OCREVUS taken before or after other medicines that weaken the immune system could increase your risk of getting infections.

- **Progressive Multifocal Leukoencephalopathy (PML):** PML is a rare brain infection that usually leads to death or severe disability, and has been reported with OCREVUS. Symptoms of PML get worse over days to weeks. It is important that you call your healthcare provider right away if you have any new or worsening neurologic signs or symptoms that have lasted several days, including problems with:

  - thinking
  - eyesight
  - strength
  - balance
  - weakness on 1 side of your body
  - using your arms or legs

- **Decreased immunoglobulins:** OCREVUS may cause a decrease in some types of antibodies. Your healthcare provider will do blood tests to check your blood immunoglobulin levels.

See **"What are the possible side effects of OCREVUS?**" for more information about side effects.

What is OCREVUS?

OCREVUS is a prescription medicine used to treat:

- relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.
- primary progressive MS, in adults.
- relapsing-remitting MS, in children 10 years of age and older who weigh 55 pounds (25 kg) or more.

It is not known if OCREVUS is safe and effective in children younger than 10 years of age or who weigh less than 55 pounds (25 kg).

Who should not receive OCREVUS?

Do not receive OCREVUS if you:

- have an active hepatitis B virus (HBV) infection.
- have had a life-threatening allergic reaction to OCREVUS. Tell your healthcare provider if you have had an allergic reaction to OCREVUS or any of its ingredients in the past. See **"What are the ingredients in OCREVUS?"** for a complete list of ingredients in OCREVUS.

Before receiving OCREVUS, tell your healthcare provider about all of your medical conditions, including if you:

- have or think you have an infection. See **"What is the most important information I should know about OCREVUS?"**
- have ever taken, take, or plan to take medicines that affect your immune system, or other treatments for MS. These medicines could increase your risk of getting an infection.
- have ever had hepatitis B or are a carrier of the hepatitis B virus.
- have a history of inflammatory bowel disease or colitis.
- have a history of liver problems.
- have had a recent vaccination or are scheduled to receive any vaccinations.
  - **You should receive any age-appropriate 'live' or 'live-attenuated' vaccines at least 4 weeks before you start treatment with OCREVUS.** You **should not receive** 'live' or 'live-attenuated' vaccines while you are being treated with OCREVUS and until your healthcare provider tells you that your immune system is no longer weakened.
  - **When possible, you should receive any age-appropriate 'non-live' vaccines at least 2 weeks before you start treatment with OCREVUS.** If you would like to receive any non-live (inactivated) vaccines, including the seasonal flu vaccine, while you are being treated with OCREVUS, talk to your healthcare provider.
  - If you have a baby and you received OCREVUS during your pregnancy, it is important to tell your baby's healthcare provider about receiving OCREVUS so they can decide when your baby should be vaccinated.
- are pregnant, think that you might be pregnant, or plan to become pregnant. It is not

known if OCREVUS will harm your unborn baby. You should use birth control (contraception) during treatment with OCREVUS and for 6 months after your last infusion of OCREVUS. Talk with your healthcare provider about what birth control method is right for you during this time. Tell your healthcare provider if you become pregnant while receiving OCREVUS.
- are breastfeeding or plan to breastfeed. It is not known if OCREVUS passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take OCREVUS.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive OCREVUS?
- OCREVUS is given through a needle placed in your vein (intravenous infusion) in your arm.
- Before treatment with OCREVUS, your healthcare provider will give you a corticosteroid medicine and an antihistamine to help reduce infusion reactions (make them less frequent and less severe). You may also receive other medicines to help reduce infusion reactions. See **"What is the most important information I should know about OCREVUS?"**
- Your first full dose of OCREVUS will be given as 2 separate infusions, 2 weeks apart. Each infusion will last about 2 hours and 30 minutes.
- Your next doses of OCREVUS will be given as 1 infusion every 6 months. These infusions will last about 2 hours to 3 hours and 30 minutes depending on the infusion rate prescribed by your healthcare provider.

What are the possible side effects of OCREVUS?
OCREVUS may cause serious side effects, including:
- see "**What is the most important information I should know about OCREVUS?"**
- **risk of cancers (malignancies) including breast cancer.** Follow your healthcare provider's instructions about standard screening guidelines for breast cancer.
- **Inflammation of the colon, or colitis:** Tell your healthcare provider right away if you have any symptoms of colitis, such as:
  - Diarrhea (loose stools) or more frequent bowel movements than usual
  - Stools that are black, tarry, sticky or have blood or mucus
  - Severe stomach-area (abdomen) pain or tenderness
- **Liver damage.** OCREVUS may cause liver damage. Your healthcare provider will do blood tests to check your liver before you start OCREVUS and while you take OCREVUS if needed. Tell your healthcare provider right away if you have any symptoms of liver damage, such as:
  - yellowing of the skin and eyes (jaundice)
  - nausea
  - vomiting
  - unusual darkening of the urine
  - feeling tired or weak
  - loss of appetite
  - discomfort in the upper right area of your stomach (abdomen)

These are not all the possible side effects of OCREVUS.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of OCREVUS.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your pharmacist or healthcare provider for information about OCREVUS that is written for health professionals.

What are the ingredients in OCREVUS?

Active ingredient: ocrelizumab.

Inactive ingredients: glacial acetic acid, polysorbate 20, sodium acetate trihydrate, trehalose dihydrate.

Manufactured by: Genentech, Inc., A Member of the Roche Group, 1 DNA Way, South San Francisco, CA 94080-4990

U.S. License No. 1048

For more information, go to www.OCREVUS.com or call 1-844-627-3887.

This Medication Guide has been approved by the U.S. Food and Drug Administration

Revised: 5/2026

Representative sample of labeling (see the HOW SUPPLIED section for complete listing):

PRINCIPAL DISPLAY PANEL - 300 mg/10 mL Vial Carton

NDC 50242-150-01

Ocrevus®
(ocrelizumab)
Injection

300 mg/10 mL
(30 mg/mL)

For Intravenous Infusion.
Must Be Diluted.

Single-Dose Vial.
Discard Unused Portion.

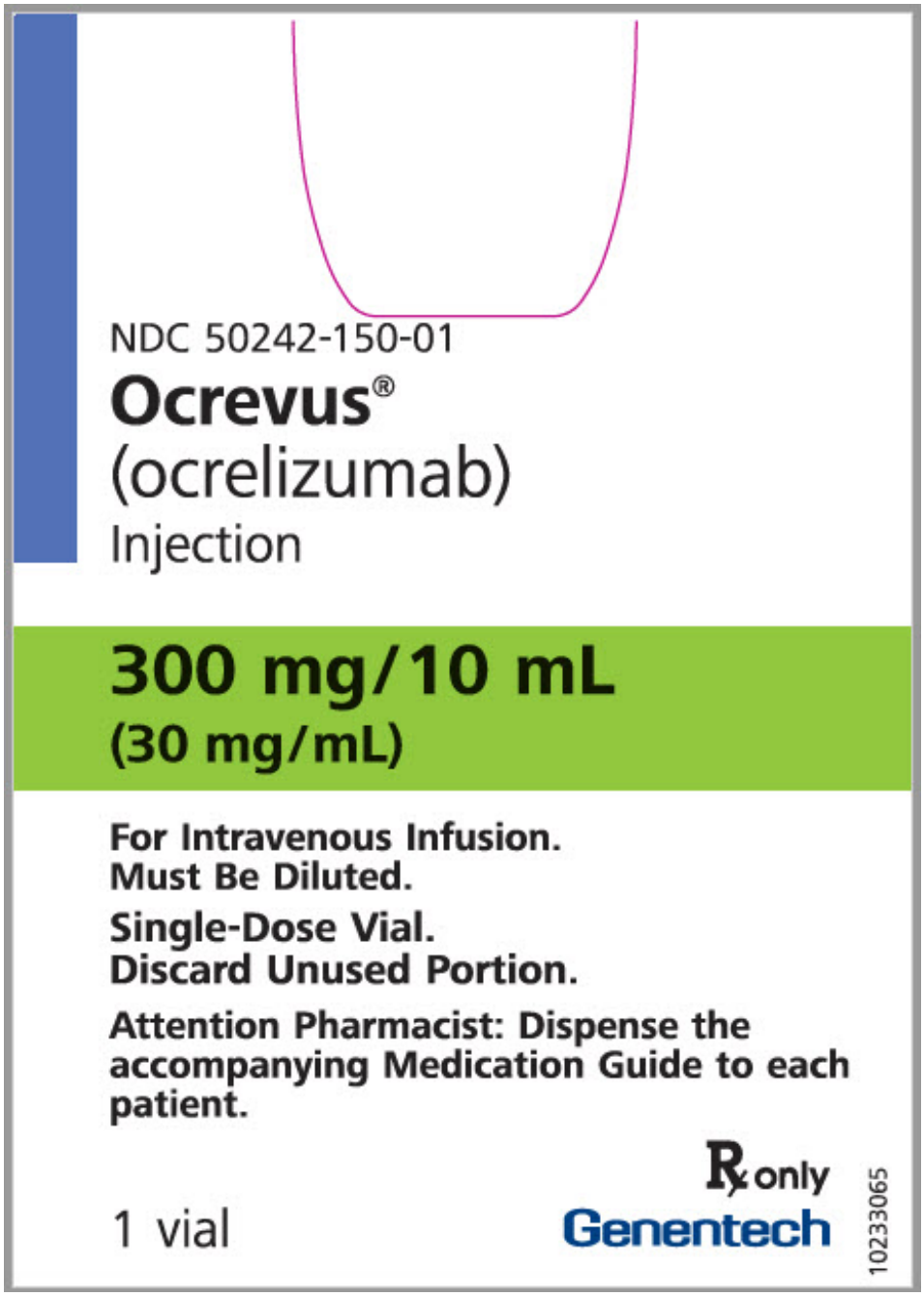
Attention Pharmacist: Dispense the accompanying Medication Guide to each patient.

Rx only

1 vial

Genentech

10233065



OCREVUS

ocrelizumab injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:50242-150
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
OCRELIZUMAB (UNII: A10SJL62JY) (OCRELIZUMAB - UNII:A10SJL62JY)	OCRELIZUMAB	300 mg in 10 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM ACETATE (UNII: 4550K0SC9B)	21.4 mg in 10 mL
ACETIC ACID (UNII: Q40Q9N063P)	2.5 mg in 10 mL
TREHALOSE DIHYDRATE (UNII: 7YIN7J07X4)	400 mg in 10 mL
POLYSORBATE 20 (UNII: 7T1F30V5YH)	2 mg in 10 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50242-150-01	1 in 1 CARTON	03/28/2017	
1		10 mL in 1 VIAL, SINGLE-USE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761053	03/28/2017	

Labeler - Genentech, Inc. (080129000)

Registrant - Genentech, Inc. (080129000)

Establishment

Name	Address	ID/FEI	Business Operations
F. Hoffmann-La Roche AG		485244961	ANALYSIS(50242-150) , MANUFACTURE(50242-150) , PACK(50242-150) , LABEL(50242-150)

Establishment

Name	Address	ID/FEI	Business Operations
Roche Diagnostics GmbH		315028860	ANALYSIS(50242-150) , MANUFACTURE(50242-150) , PACK(50242-150) , LABEL(50242-150)

Establishment

Name	Address	ID/FEI	Business Operations
Roche Diagnostics		323105205	ANALYSIS(50242-150)

Establishment

Name	Address	ID/FEI	Business Operations
Genentech, Inc.		080129000	ANALYSIS(50242-150)

Establishment

Name	Address	ID/FEI	Business Operations
Genentech, Inc. (Oceanside)		146373191	ANALYSIS(50242-150)