

START NOW with twice-yearly OCREVUS¹

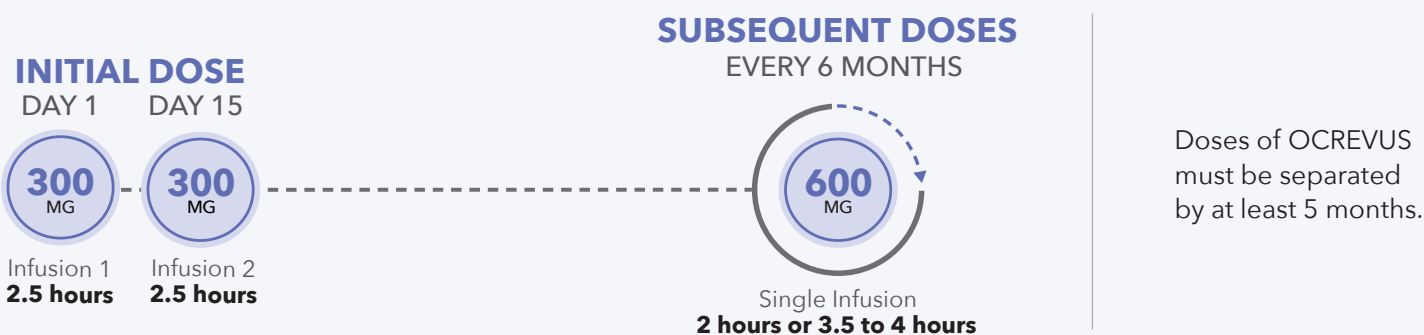


RECOMMENDED DOSE AND DOSE ADMINISTRATION

- The initial 600-mg dose is administered as 2 separate intravenous infusions given over approximately 2.5 hours: first as a 300-mg intravenous infusion followed 2 weeks later by a second 300-mg intravenous infusion
- Subsequent doses are administered as a single 600-mg intravenous infusion every 6 months, using either a 3.5- to 4-hour infusion protocol or a 2-hour shorter infusion protocol **if the patient has not had a serious infusion reaction during any previous OCREVUS infusion^a**
- Observe the patient for at least 1 hour after the completion of the infusion
- Infusion time may take longer if the infusion is interrupted or slowed. There are no differences in premedication, dose, formulation, or post-treatment monitoring between infusion timing options

^aPer the ENSEMBLE Plus study protocol, serious infusion reactions included those that were fatal or life-threatening, required or prolonged hospitalization, resulted in persistent or significant disability, or were deemed to be medically significant by the trial investigator.¹

Standard twice-yearly dosing schedule with OCREVUS



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

HCP administration may enable closer monitoring of patient adherence.^{2,3}

Indications

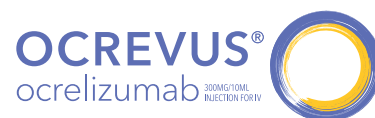
OCREVUS is indicated for the treatment of:

- 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.

Contraindications

OCREVUS is contraindicated in patients with active hepatitis B virus infection and in patients with a history of life-threatening infusion reaction to OCREVUS.

For additional safety information, please see pages [5](#), [6](#), [7](#), and [8](#) and [click here](#) for full Prescribing Information and Medication Guide.



Dosing with twice-yearly OCREVUS® — what you should know^{1,a}

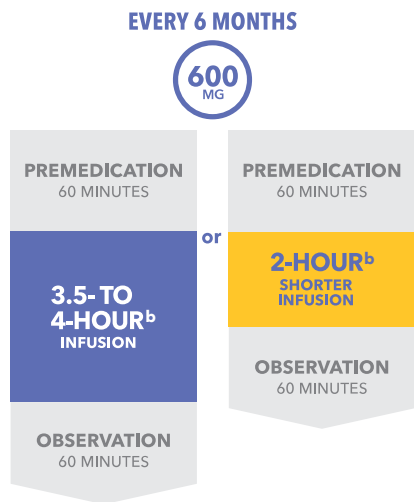


HOW TO START AND MANAGE PATIENTS ON OCREVUS

- **Prior to first dose:** Perform hepatitis B virus screening, test for quantitative serum immunoglobulins, and complete necessary vaccinations (4 weeks prior for live or live-attenuated vaccines and, when possible, 2 weeks prior for non-live vaccines). Obtain serum aminotransferases (ALT and AST), alkaline phosphatase, and bilirubin levels
- **Before each infusion:** Assess for active infection and administer premedications
- **After each infusion:** Monitor patients for 1 hour for possible infusion reactions (IRs)



AFTER THE INITIAL DOSE, THERE ARE 2 OPTIONS FOR ADMINISTERING OCREVUS, INCLUDING A SHORTER INFUSION PROTOCOL



Shorter OCREVUS infusion is available to any patient who has not had a serious infusion reaction during any previous OCREVUS infusion.

- NO CHANGES IN:**
- Premedication
 - Dose or formulation
 - 1-hour post-treatment monitoring

The difference is the infusion rate, which could translate into less time at the infusion site for your OCREVUS patients.

^aThe first dose of OCREVUS is split between 2 treatments, for a total of 3 treatments in the first year.

^bInfusion time may take longer if the infusion is interrupted or slowed.

Rates of IRs in 2-hour infusion OCREVUS study^{1,4,c}

- When the primary analysis was performed, 81% (469/579) of the treated patients had received only a single randomized infusion of OCREVUS
- The incidence, frequency, and severity of IRs with the 2-hour OCREVUS infusion protocol were comparable to the 3.5- to 4-hour protocol
- In all randomized doses, 27.1% of patients in the 2-hour infusion group and 25% in the 3.5-hour infusion group reported mild or moderate infusion reactions. One patient in each infusion group reported an infusion reaction that was severe in intensity (0.3%)
- There were no life-threatening, fatal, or serious infusion reactions. More than 98% of all IRs resolved without sequelae in both groups

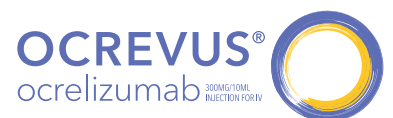
^cThe ENSEMBLE PLUS study evaluated the safety of OCREVUS shorter infusion in a prospective, multicenter, randomized, double-blind, controlled, parallel-arm substudy of 580 patients with early RRMS.

RRMS=relapsing-remitting multiple sclerosis.

Select Important Safety Information

The warnings and precautions for OCREVUS are infusion reactions and infections, which include respiratory tract infections, herpes, hepatitis B virus (HBV) reactivation, and a warning for progressive multifocal leukoencephalopathy (PML). Additional warnings are possible increased risk of immunosuppressant effects with other immunosuppressants, reduction in immunoglobulins, malignancies, immune-mediated colitis, and liver injury.

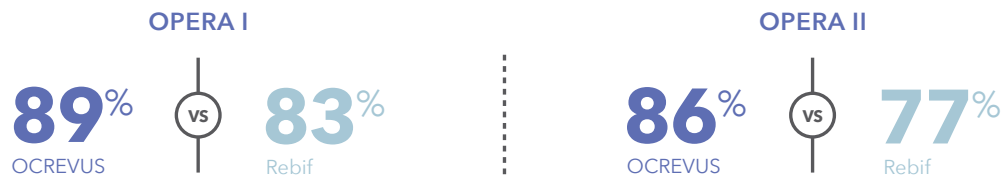
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OCREVUS® CLINICAL TRIAL COMPLETION¹

■ In the OCREVUS RMS clinical trials, the percentage of patients who completed the clinical trials at year 2 were:



OPERA I and II (RMS): Two randomized, double-blind, double-dummy, active comparator-controlled clinical trials of identical design vs Rebif® in 1656 patients (OCREVUS; OPERA I [n=410], OPERA II [n=417]; Rebif; OPERA I [n=411], OPERA II [n=418]) with RMS treated for 96 weeks. Both studies included patients who had experienced ≥1 relapse within the prior year, or 2 relapses within the prior 2 years, and had an EDSS score between 0 and 5.5. The primary outcome of both studies was the annualized relapse rate.^{1,5}



REAL-WORLD ANALYSIS OF OCREVUS AND KESIMPTA TREATED PATIENTS WITH 2 YEARS OF FOLLOW-UP⁷

■ Study design for OCREVUS real-world analysis among patients with 2 years of follow-up

OCREVUS (ocrelizumab) and Kesimpta® (ofatumumab) were studied using real-world US commercial, Medicare, and Medicaid claims data from IQVIA PharMetrics® Plus.

- Adherence and persistence over a 2-year period were evaluated in the IQVIA PharMetrics Plus Database^a
- Inclusion criteria included: patients ≥18 years of age with a diagnosis of MS who initiated OCREVUS or Kesimpta using a confirmed^b loading dose between August 20, 2020, and December 31, 2021; at least ≥12 months of continuous health plan enrollment prior to treatment initiation (index date)^c with 24 months of follow-up data
- Exclusion criteria included: patients initiating multiple DMTs on index; patients with any claims of index DMT in the prior 12 months
- In this sensitivity analysis, adjustments for overlapping days' supply were not made for either OCREVUS or Kesimpta
- **Adherence** was calculated based on proportion of days covered (PDC), with ≥80% considered adherent to the DMT initiated
 - PDC=number of days of supply or administration divided by 730 days
- **Persistence** measured the duration of time from initiation to discontinuation of therapy
 - The date of discontinuation was defined as the earliest of DMT switch date or the end supply date of last index DMT fill before treatment gap

^aIQVIA PharMetrics Plus Q2 2024 Data Delivery (fully adjudicated medical and pharmacy claims data through 2023 Q4).

^bOCREVUS loading dose definition: 13-21 days gap between 1st and 2nd OCREVUS claim; Kesimpta loading dose definition: quantity equal to 1.2 and days' supply equal to either 28 or 30 days on 1st Kesimpta claim.

^cIndex date=OCREVUS or Kesimpta initiation date.

DMT=disease-modifying treatment; RMS=relapsing multiple sclerosis.

Trademarks are the property of their respective owners.

SELECT IMPORTANT SAFETY INFORMATION

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.

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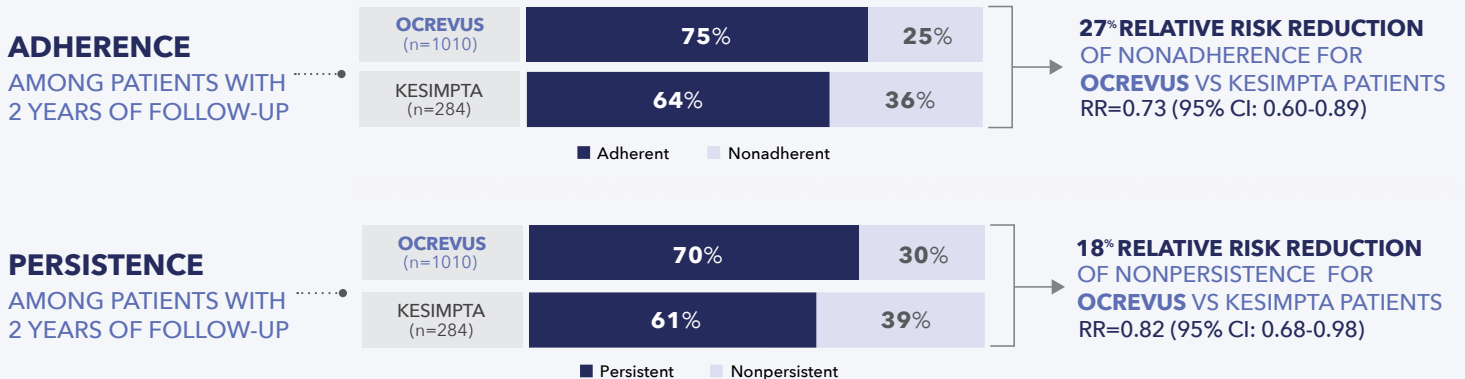


OCREVUS® REAL-WORLD ADHERENCE AND PERSISTENCE RETROSPECTIVE STUDY⁷ (cont'd)

■ Limitations for OCREVUS real-world analysis among patients with 2 years of follow-up

- Analyses using administrative pharmacy and medical claims data are dependent on the accuracy and specificity of information provided
- Adherence and persistence were calculated based on the administration schedule recommended in each product's Prescribing Information and days' supply as shown in claims for Kesimpta® (ofatumumab); instances where prescribing patterns differ from the FDA-approved administration schedules, adherence and persistence may be misclassified
- Differences in dosing and pharmacodynamics should be considered when making direct comparisons between DMTs
 - Kesimpta is a monthly subcutaneous injection, please refer to Kesimpta's PI for additional information
- Claims data have inherent limitations:
 - Unable to ascertain if patients on self-administered medications, including Kesimpta, took DMT as prescribed
 - Limited clinical information available may impact interpretation of results (eg, MS subtype, line of therapy). ICD-10 codes do not identify patients by MS subtypes
 - Lack of data on reason for discontinuation
- Data may not be generalized to all patients, including those without insurance, and may be limited to the study population of commercially insured patients in the US
- **Real-world adherence and persistence rates should not be considered as a comparison of safety and efficacy**

Real-world analysis^a of OCREVUS and Kesimpta-treated patients with 2 years of follow-up



^aResults based on a sensitivity analysis from a retrospective cohort study using fully adjudicated medical and pharmacy claims from August 2019 through December 2023 extracted from the IQVIA PharMetrics Plus Database.
PI=Prescribing Information; RR=relative risk.

SELECT IMPORTANT SAFETY INFORMATION

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 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. OCREVUS was not associated with an increased risk of serious infections in MS patients in controlled trials.

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Indications

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Contraindications

OCREVUS is contraindicated in patients with active hepatitis B virus infection and in patients with a history of life-threatening infusion reaction to OCREVUS.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

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. 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 34-40%, 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. 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. 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.

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 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. OCREVUS was not associated with an increased risk of serious infections in MS patients in controlled trials. 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.

For additional safety information, please see pages [6](#), [7](#), and [8](#) and [click here](#) for full Prescribing Information and Medication Guide.



IMPORTANT SAFETY INFORMATION

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. 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%).

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.

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 effect. OCREVUS has not been studied in combination with other MS therapies.

Vaccinations

Administer all 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. 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.

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.

You may administer non-live vaccines, as indicated, prior to recovery from B-cell depletion, but you should consider assessing vaccine immune responses, including consultation with a qualified specialist, to assess whether a protective immune response was mounted.

IMPORTANT SAFETY INFORMATION

Progressive Multifocal Leukoencephalopathy (PML)

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 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.

Magnetic resonance imaging (MRI) findings may be apparent before clinical signs or symptoms of PML. Monitoring with MRI for signs 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.

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

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) 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.

Malignancies

An increased risk of malignancy with OCREVUS may exist. In controlled trials, malignancies, including breast cancer, occurred more frequently in OCREVUS-treated patients. Breast cancer 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.

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.

IMPORTANT SAFETY INFORMATION

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 3x the upper limit of normal (ULN) with serum total bilirubin greater than 2x ULN are potentially at risk for severe drug-induced liver injury.

Obtain liver function tests prior to initiating treatment with OCREVUS, 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.

Use in Specific Populations

Pregnancy

There are no adequate data on the developmental risk associated with use of OCREVUS in pregnant women. There are no data on B-cell levels in human neonates following maternal exposure to OCREVUS. However, transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other anti-CD20 antibodies during pregnancy. OCREVUS is a humanized monoclonal antibody of an immunoglobulin G1 subtype and immunoglobulins are known to cross the placental barrier.

Lactation

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.

Females and Males of Reproductive Potential

Women of childbearing potential should use effective contraception while receiving OCREVUS and for 6 months after the last infusion of OCREVUS. Instruct patients that if they are pregnant or plan to become pregnant while taking OCREVUS, they should inform their healthcare provider.

Most Common Adverse Reactions

RMS: The most common adverse reactions in RMS trials (incidence $\geq 10\%$ and $> \text{REBIF}$) were upper respiratory tract infections (40%) and infusion reactions (34%).

PPMS: The most common adverse reactions in PPMS trials (incidence $\geq 10\%$ and $> \text{placebo}$) were upper respiratory tract infections (49%), infusion reactions (40%), skin infections (14%), and lower respiratory tract infections (10%).

You may report side effects to the FDA at **(800) FDA-1088** or www.fda.gov/medwatch. You may also report side effects to Genentech at **(888) 835-2555**.

References: **1.** OCREVUS [prescribing information]. South San Francisco, CA: Genentech, Inc. 2025. **2.** The importance of medication adherence in patients with chronic hematologic malignancies. *J Oncol Navig Surviv.* 2019;10. <https://jons-online.com/special-issues-and-supplements/2019/best-practices-in-hematologic-malignancies-december-2019-vol-10/2729-the-importance-of-medication-adherence-in-patients-with-chronic-hematologic-malignancies> **3.** Morillo Verdugo R, Ramírez Herráiz E, Fernández-Del Olmo R, Roig Bonet M, Valdivia García M. Adherence to disease-modifying treatments in patients with multiple sclerosis in Spain. *Patient Prefer Adherence.* 2019;13:261-272. doi:10.2147/PPA.S187983 **4.** Hartung HP; ENSEMBLE Steering Committee members and study investigators. Ocrelizumab shorter infusion: primary results from the ENSEMBLE PLUS substudy in patients with MS. *Neurol Neuroimmunol Neuroinflamm.* 2020;7(5):e807. doi:10.1212/NXI.0000000000000807 **5.** Hauser SL, Bar-Or A, Comi G, et al; OPERA I and OPERA II Clinical Investigators. Ocrelizumab versus interferon beta-1a in relapsing multiple sclerosis. *N Engl J Med.* 2017;376(3):221-234. doi:10.1056/NEJMoa1601277 **6.** Data on file. Genentech, Inc. **7.** Pineda ED, Miller A, Patel A, Pardo G. Real-world adherence and persistence to ocrelizumab vs ofatumumab among people with multiple sclerosis over 24 months. Poster presented at the ACTRIMS Forum 2025; February 27-March 1, 2025; West Palm Beach, Florida, USA, and virtual. Poster P406.

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