**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.

**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, and immune-mediated colitis.

For additional safety information, please see pages 15 through 18 and click here for full Prescribing Information and Medication Guide.
Attention Pharmacist: Dispense the accompanying Medication Guide to each patient.
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For additional safety information, please see pages 15 through 18 and click here for full Prescribing Information and Medication Guide.
Patient pre-infusion counseling

Advise the patient to read the FDA-approved Medication Guide. Inform patients of the following:

- **CONTRACEPTION**
  Advise female patients of childbearing potential to use effective contraception while receiving OCREVUS and for 6 months after the last infusion of OCREVUS.

- **INFUSION REACTIONS**
  Inform patients about the signs and symptoms of infusion reactions (IRs), and that IRs can occur up to 24 hours after infusion. Advise patients to contact their healthcare provider immediately for signs or symptoms of IRs.

- **PREGNANCY**
  Instruct patients that if they are pregnant or plan to become pregnant while taking OCREVUS they should inform their healthcare provider. Encourage patients to enroll in the OCREVUS Pregnancy Registry if they become pregnant while taking OCREVUS.

- **MALIGNANCIES**
  Advise patients that an increased risk of malignancy, including breast cancer, may exist with OCREVUS. Advise patients that they should follow standard breast cancer screening guidelines.

- **INFECTION**
  Advise patients to contact their healthcare provider for any signs of infection during treatment or after the last dose. Signs include fever, chills, constant cough, or signs of herpes, such as cold sores, shingles, or genital sores.

- **REDUCTION IN IMMUNOGLOBULINS**
  Inform patients that OCREVUS may cause a decrease in immunoglobulins and that their healthcare provider will do blood tests to check their blood immunoglobulin levels.

- **PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY**
  Inform patients that PML has occurred in patients who received OCREVUS and that PML is characterized by a progression of deficits and usually leads to death or severe disability over weeks or months. Instruct the patient of the importance of contacting their healthcare provider if they develop any symptoms suggestive of PML and 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.

- **VACCINATION**
  Patients should complete necessary live or live-attenuated vaccinations at least 4 weeks prior to initiation of OCREVUS and, when possible, at least 2 weeks prior for non-live vaccines. Administration of live-attenuated or live vaccines is not recommended during OCREVUS treatment and until B-cell recovery.

For additional safety information, please see pages 15 through 18 and click here for full Prescribing Information and Medication Guide.
Dose and dosing schedule

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*
  – The first subsequent dose is administered 6 months after Infusion 1 of the initial dose and is administered over the same time period as a single 600 mg intravenous infusion

• Observe the patient for at least 1 hour after the completion of the infusion

---

INITIAL DOSE

DAY 1

DAY 15

300 MG

2.5 hours

300 MG

2.5 hours

SUBSEQUENT DOSES

EVERY 6 MONTHS

600 MG

Single Infusion

2 hours or 3.5 to 4 hours

Doses of OCREVUS must be separated by at least 5 months.

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

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Helpful hint: Time spent during the infusion appointment can be used to educate your patient about OCREVUS and talk about treatment expectations over the next 6 months.

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*Infusion time may take longer if the infusion is interrupted or slowed.

For additional safety information, please see pages 15 through 18 and click here for full Prescribing Information and Medication Guide.
Premedication

Assessments prior to first dose of OCREVUS

• Hepatitis B virus screening and testing for quantitative serum immunoglobulins should be performed in all patients before initiation of treatment with OCREVUS

• Complete necessary vaccinations at least 4 weeks prior to initiation of OCREVUS for live or live-attenuated vaccines and, when possible, at least 2 weeks prior for non-live vaccines

Preparation on the day of infusion

• Determine whether there is an active infection. In case of active infection, delay infusion of OCREVUS until the infection resolves

Recommended premedication

Premedicate with 100 mg of methylprednisolone (or an equivalent corticosteroid) administered intravenously approximately 30 minutes prior to each OCREVUS infusion to reduce the frequency and severity of infusion reactions.

Premedicate with an antihistamine (eg, diphenhydramine) approximately 30-60 minutes prior to each OCREVUS infusion to further reduce the frequency and severity of infusion reactions. The addition of an antipyretic (eg, acetaminophen) may also be considered.

Helpful hint: It is recommended that you administer OCREVUS after the premedication has taken effect.

For additional safety information, please see pages 15 through 18 and click here for full Prescribing Information and Medication Guide.
How OCREVUS is supplied and stored¹

HOW OCREVUS IS SUPPLIED

OCREVUS injection is a preservative-free, sterile, clear or slightly opalescent, and colorless to pale brown solution.

OCREVUS is supplied as a carton containing one 300 mg/10mL (30 mg/mL) single-dose vial.

HOW OCREVUS IS STORED

Store OCREVUS vials at 2°C-8°C (36°F-46°F).

Keep the vial in the outer carton to protect from light.

Do not freeze or shake.

For additional safety information, please see pages 15 through 18 and click here for full Prescribing Information and Medication Guide.
OCREVUS must be prepared by a healthcare professional using aseptic technique.

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

Withdraw intended dose and further dilute into an infusion bag containing 0.9% sodium chloride injection, to a final drug concentration of approximately 1.2 mg/mL.

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

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

For additional safety information, please see pages 15 through 18 and click here for full Prescribing Information and Medication Guide.
Preparation and storage of the dilute solution for infusion, continued¹

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

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

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

For additional safety information, please see pages 15 through 18 and click here for full Prescribing Information and Medication Guide.
Administration¹

**OCREVUS is administered as an intravenous infusion through a dedicated line**

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.

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

For additional safety information, please see pages 15 through 18 and [click here](#) for full Prescribing Information and Medication Guide.
OCREVUS infusion options

After the initial dose, there are 2 options for administering OCREVUS, including a shorter infusion protocol. Both protocols use the same premedication, dose, formulation, and posttreatment monitoring.

**Patients who have had a serious IR during any previous OCREVUS infusion are not eligible for the shorter infusion protocol.**

### INITIAL DOSE

**DAY 1**

- **300 MG**
- **PREMEDICATION** 60 MINUTES
- **2.5-HOUR* INFUSION**
- **OBSERVATION** 60 MINUTES

**DAY 15**

- **300 MG**
- **PREMEDICATION** 60 MINUTES
- **2.5-HOUR* INFUSION**
- **OBSERVATION** 60 MINUTES

### SUBSEQUENT DOSES

**EVERY 6 MONTHS**

- **600 MG**
- **PREMEDICATION** 60 MINUTES
- **3.5- TO 4-HOUR* INFUSION**
- **OBSERVATION** 60 MINUTES

**OR**

- **PREMEDICATION** 60 MINUTES
- **2-HOUR* SHORTER INFUSION**
- **OBSERVATION** 60 MINUTES

*Available for patients without prior serious IR with any OCREVUS infusion

*Infusion time may take longer if the infusion is interrupted or slowed.

For additional safety information, please see pages 15 through 18 and [click here](#) for full Prescribing Information and Medication Guide.
**Infusion rate tables**

### INITIAL DOSE (600 MG) ADMINISTERED AS 2 INFUSIONS

<table>
<thead>
<tr>
<th>Infusion 1</th>
<th>Day 1</th>
<th>300 mg in 250 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2.5-HOUR INFUSION:</strong></td>
<td>start at a rate of 30 mL/hr. Thereafter, increase the rate by 30 mL/hr every 30 minutes to a maximum of 180 mL/hr. <strong>Each infusion will last 2.5 hours or longer.</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infusion 2</th>
<th>Day 15</th>
<th>300 mg in 250 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Start</strong></td>
<td><strong>at 30 min</strong></td>
<td><strong>at 60 min</strong></td>
</tr>
<tr>
<td>30 mL/hr</td>
<td>60 mL/hr</td>
<td>90 mL/hr</td>
</tr>
</tbody>
</table>

### SUBSEQUENT DOSES† (600 MG) ONCE EVERY 6 MONTHS

<table>
<thead>
<tr>
<th>Single infusion</th>
<th>600 mg in 500 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>3.5- TO 4-HOUR INFUSION:</strong></td>
<td>start at a rate of 40 mL/hr. Thereafter, increase the rate by 40 mL/hr every 30 minutes to a maximum of 200 mL/hr. <strong>Each infusion will last 3.5 hours or longer.</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Start</th>
<th>at 30 min</th>
<th>at 60 min</th>
<th>at 90 min</th>
<th>at 120 min</th>
<th>after 120 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 mL/hr</td>
<td>80 mL/hr</td>
<td>120 mL/hr</td>
<td>160 mL/hr</td>
<td>200 mL/hr</td>
<td>continue 200 mL/hr</td>
</tr>
</tbody>
</table>

**2-HOUR SHORTER INFUSION**

Available for patients without prior serious IR with any OCREVUS infusion

**Start at a rate of 100 mL/hr. Thereafter, increase the rate as shown below to a maximum of 300 mL/hr. **Each infusion will last 2 hours or longer.**

<table>
<thead>
<tr>
<th>Start</th>
<th>at 15 min</th>
<th>at 30 min</th>
<th>at 60 min</th>
<th>after 60 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 mL/hr</td>
<td>200 mL/hr</td>
<td>250 mL/hr</td>
<td>300 mL/hr</td>
<td>continue 300 mL/hr</td>
</tr>
</tbody>
</table>

*Infusion time may take longer if the infusion is interrupted or slowed.*

†Administer the first subsequent dose 6 months after Infusion 1 of the initial dose.

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.

For additional safety information, please see pages 15 through 18 and [click here](#) for full Prescribing Information and Medication Guide.
IRs associated with OCREVUS

**RATES OF IRs DURING THE OPERA TRIALS²**

<table>
<thead>
<tr>
<th>Percentage of Patients With IRs (n=825)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion 1</td>
</tr>
<tr>
<td>Mild/Moderate</td>
</tr>
<tr>
<td>Severe</td>
</tr>
<tr>
<td>Life-threatening or Disabling</td>
</tr>
<tr>
<td>0.1</td>
</tr>
<tr>
<td>1.7</td>
</tr>
<tr>
<td>25.7</td>
</tr>
<tr>
<td>Infusion 2</td>
</tr>
<tr>
<td>4.7</td>
</tr>
<tr>
<td>13.4</td>
</tr>
<tr>
<td>0.4</td>
</tr>
</tbody>
</table>

**RATES OF IRs IN THE ENSEMBLE PLUS STUDY¹,³**

<table>
<thead>
<tr>
<th>3.5- TO 4-HOUR INFUSION</th>
<th>24.6% had IRs</th>
<th>2-HOUR INFUSION</th>
<th>0.3% (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of patients</td>
<td>76.9% (223)</td>
<td>75.4% (218)</td>
<td></td>
</tr>
</tbody>
</table>

**IRs were highest with first infusion.**

Of OCREVUS patients participating in the ORATORIO clinical trial, 20.2% reported having a mild IR following their first dose, 6.4% of patients reported having a moderate IR, and 0.8% of patients reported having a severe IR. There were no reported life-threatening or fatal IRs. All reported IRs declined significantly after administration of the second dose.

The 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.

- 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 infusion protocol were comparable to the 3.5- to 4-hour infusion protocol.
- There were no life-threatening, fatal, or serious IRs. More than 98% of all IRs resolved without sequelae in both groups.

*One severe IR (grade 3) occurred in the shorter infusion group: fatigue at first randomized dose.

For additional safety information, please see pages 15 through 18 and click here for full Prescribing Information and Medication Guide.
IRs associated with OCREVUS\(^1\) (continued)

**Symptoms of IRs include, but are not limited to\(^1\):**

- PRURITUS
- RASH
- URTICARIA
- ERYTHEMA
- BRONCHOSPASM
- DYSPNEA
- PHARYNGEAL OR LARYNGEAL EDEMA
- THROAT IRRITATION
- OROPHARYNGEAL PAIN
- HYPOTENSION
- FLUSHING
- PYREXIA
- FATIGUE
- HEADACHE
- DIZZINESS
- NAUSEA
- TACHYCARDIA
- ANAPHYLAXIS

- Mild IRs are asymptomatic or have mild symptoms
- Moderate IRs are minimal, local, and do not require invasive intervention
- Severe IRs are medically significant but not immediately life threatening
- Life-threatening IRs put a patient at immediate risk of death at the time of the event. Urgent intervention is needed\(^4\)

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**IRs can occur up to 24 hours after infusion.**

For additional safety information, please see pages 15 through 18 and [click here](#) for full Prescribing Information and Medication Guide.
Rate modifications because of IRs

Modify the infusion rate in response to the severity of the reaction

For IRs that are not life threatening, the change in infusion rate will increase the duration of the infusion but not the total dose.

<table>
<thead>
<tr>
<th>MILD TO MODERATE</th>
<th>SEVERE</th>
<th>LIFE-THREATENING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduce the infusion rate to half the rate at the onset of the IR and maintain the reduced rate for at least 30 minutes. If this rate is tolerated, increase the rate as described in the Infusion Rate Tables on page 10. This change in rate will increase the total duration of the infusion but not the total dose.</td>
<td>Immediately interrupt the infusion and administer appropriate supportive treatment, as necessary. 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 IR. If this rate is tolerated, increase the rate as described in the Infusion Rate Tables on page 10. This change in rate will increase the total duration of the infusion but not the total dose.</td>
<td>Immediately stop and permanently discontinue OCREVUS if there are signs of a life-threatening or disabling IR. Provide appropriate supportive treatment.</td>
</tr>
</tbody>
</table>

Reminder: Premedication can reduce the frequency and severity of IRs.

For additional safety information, please see pages 15 through 18 and click here for full Prescribing Information and Medication Guide.
The proposed mechanism of action for OCREVUS\textsuperscript{1} is directed against CD20-expressing B cells.  

OCREVUS is a recombinant humanized monoclonal antibody directed against CD20-expressing B cells. Lymphoid stem cells and plasma cells do not express CD20 and therefore are not directly targeted by OCREVUS.\textsuperscript{4} 

The precise mechanisms through which OCREVUS exerts its therapeutic clinical effects in RMS and PPMS are not fully elucidated but are presumed to involve immunomodulation through selective binding to CD20-expressing B cells. Following cell surface binding to B lymphocytes, OCREVUS results in antibody-dependent cellular cytolysis and complement-mediated lysis.

**Helpful hint:** Help your patient understand that OCREVUS is an infused monoclonal antibody and there may be potential for IRRs. Explain to your patients how premedication can help lower the risk of experiencing an IR.
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

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
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. 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.

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 16 through 18 and click here for full Prescribing Information and Medication Guide.
**Important Safety Information (continued)**

**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 should consider assessing vaccine immune responses, including consultation with a qualified specialist, to assess whether a protective immune response was mounted.

For additional safety information, please see pages 17 through 18 and click here for full Prescribing Information and Medication Guide.
Important Safety Information (continued)

Progressive Multifocal Leukoencephalopathy (PML)

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 prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins. 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 (continued)**

**Use in Specific Populations**

**Pregnancy**

**Pregnancy Exposure Registry**

There is a pregnancy exposure registry that monitors pregnancy and fetal/neonatal/infant outcomes in women exposed to OCREVUS during pregnancy. Physicians are encouraged to register patients and pregnant women are encouraged to register themselves by calling 1-833-872-4370 or visiting www.ocrevuspregnancyregistry.com.

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.

**Most Common Adverse Reactions**

**RMS:** The most common adverse reactions in RMS trials (incidence ≥10% and >REBIF) were upper respiratory tract infections (40%) and infusion reactions (34%).

**PPMS:** The most common adverse reactions in PPMS trials (incidence ≥10% and >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](http://www.fda.gov/medwatch). You may also report side effects to Genentech at (888) 835-2555.

For additional safety information, please see pages 15 through 17 and [click here](#) for full Prescribing Information and Medication Guide.

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**References:**

1. OCREVUS [prescribing information]. South San Francisco, CA: Genentech, Inc; 2022.