

INCORPORATING OCREVUS ZUNOVO™ INTO YOUR PRACTICE WORKFLOW

Considerations for the new subcutaneous route of administration for ocrelizumab

Indications

OCREVUS and OCREVUS ZUNOVO are 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

Treatment with ocrelizumab is contraindicated in patients with active hepatitis B virus infection and in patients with a history of life-threatening administration reaction to ocrelizumab. OCREVUS ZUNOVO is also contraindicated in patients with a history of hypersensitivity to ocrelizumab, hyaluronidase, or any component of OCREVUS ZUNOVO.

Please see additional Important Safety Information throughout and click here for full OCREVUS [Prescribing Information](#) and [Medication Guide](#). For OCREVUS ZUNOVO, click here for full [Prescribing Information](#) and [Medication Guide](#).

OCREVUS ZUNOVO™
ocrelizumab & hyaluronidase-ocsq
Subcutaneous injection 920mg



INTRODUCING OCREVUS ZUNOVO™

2x yearly HCP-administered OCREVUS® (ocrelizumab)—now with the choice and flexibility of 2 route-of-administration options:

- OCREVUS for intravenous use
- OCREVUS ZUNOVO (ocrelizumab and hyaluronidase-ocsq) injection, for subcutaneous use

With a shorter administration time and no split first dose, OCREVUS ZUNOVO offers scheduling flexibility for your patients and practice.

KEY ATTRIBUTES

NO split first dose

NO reconstitution

NO IV infusion-specific supplies needed

TOTAL TREATMENT TIME

	Oral Premedication	Injection	Post-injection Monitoring	Overall Time
1st Injection	At least 30 min prior	~10 min*	At least 60 min [†]	As little as 1 hr 40 min
Subsequent injections			At least 15 min [†]	As little as 55 min

- OCREVUS ZUNOVO is for subcutaneous use in the abdomen only
- OCREVUS ZUNOVO has different dosage and administration instructions than intravenous ocrelizumab
- OCREVUS ZUNOVO should be administered via subcutaneous injection by an HCP

HCP=health care professional; IV=intravenous.

*Infusion/injection time may take longer if the treatment is interrupted or slowed.

[†]For all doses, post-injection monitoring with access to appropriate medical support to manage severe injection reactions after injection is recommended.

Important Safety Information

The warnings and precautions for ocrelizumab are infusion reactions (OCREVUS) or injection reactions (OCREVUS ZUNOVO) 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.

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WHAT IS INCLUDED IN THIS WORKFLOW RESOURCE

As with any new product, there will be some updates to logistics and workflow processes for your practice associated with OCREVUS ZUNOVO™. This brochure reviews some of the unique considerations to keep in mind once your organization has decided to begin prescribing OCREVUS ZUNOVO for your patients.

1

Pre-prescription and acquisition

- EHR and practice management system updates
- Acquiring OCREVUS ZUNOVO
- Storing OCREVUS ZUNOVO
- Ancillary supplies

2

Administration logistics

- Staff training
- Scheduling
- Pretreatment counseling
- Oral premedications
- Post-dose observation

3

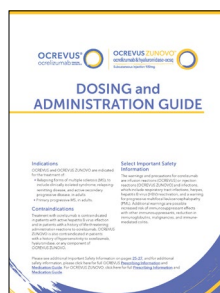
Coverage and reimbursement

- Formulary coverage
- Coding and billing

LOOKING FOR MORE INFORMATION THAT ISN'T IN THIS RESOURCE?

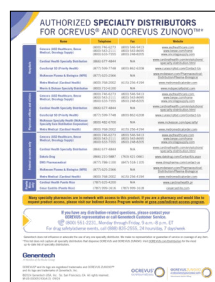
Resources are also available to go into more detail on the following topics.

Click on the links below or ask your OCREVUS® (ocrelizumab) representative to learn more.



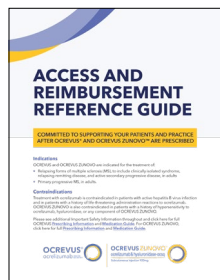
[Dosing and Administration Guide](#) →

Find detailed information about dosing and administering OCREVUS and OCREVUS ZUNOVO, from pre- to post-infusion/injection.



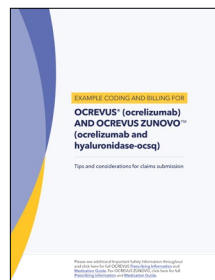
[Authorized Distributors](#) →

Find specialty distributors and pharmacies for OCREVUS and OCREVUS ZUNOVO.



[Access and Reimbursement Guide](#) →

This resource provides details about the various programs and services Genentech offers to help patients access OCREVUS and OCREVUS ZUNOVO.



[Coding and Billing Guide](#) →

This example coding information may assist you as you complete the payer forms for OCREVUS and OCREVUS ZUNOVO.

EHR=electronic health record.

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WHAT IS UNIQUE ABOUT OCREVUS ZUNOVO™ VS. OCREVUS® (ocrelizumab) [IV]?

If your practice currently administers OCREVUS [IV], there are many similarities to OCREVUS ZUNOVO. However, this resource helps walk through some of the differences and considerations for the workflow specific to OCREVUS ZUNOVO. Some of those considerations include:

	WHAT'S THE SAME?	WHAT'S UNIQUE?
Genentech support	<ul style="list-style-type: none"> • Patient Navigators • OCREVUS Access Solutions • Patient financial assistance programs* • Support program enrollment process (OCREVUS Start Form) • Patient one-on-one supplemental education 	<ul style="list-style-type: none"> • OCREVUS ZUNOVO Starter Program* • OCREVUS ZUNOVO injection training via experiential demonstration
Administration	<ul style="list-style-type: none"> • HCP administered • Premedication types 	<ul style="list-style-type: none"> • Administration method • Administration time • Post-dose observation time after the first injection • No split first dose • No reconstitution • Ancillary supplies
Scheduling	<ul style="list-style-type: none"> • Ability to administer in-office or via home health • Ability to refer to alternate treatment centers 	<ul style="list-style-type: none"> • Total treatment time • No infusion-specific setting needed • First dose is not split between two appointments
Acquisition	<ul style="list-style-type: none"> • Available via authorized distributors and specialty pharmacies 	
Benefit type	<ul style="list-style-type: none"> • Mainly covered under the medical benefit 	
Claims submission	<ul style="list-style-type: none"> • ICD-10-CM diagnosis codes • Payer forms and processes 	<ul style="list-style-type: none"> • HCPCS codes (temporary miscellaneous J-code for OCREVUS ZUNOVO) • NDCs • CPT administration codes
Payer coverage	<ul style="list-style-type: none"> • Genentech's commitment to parity access to preserve patient and provider choice 	<ul style="list-style-type: none"> • Payers may take time to establish policies for OCREVUS ZUNOVO

Correct coding is the responsibility of the provider submitting the claim for the item or service. Genentech does not make any representation or guarantee concerning reimbursement or coverage for any item or service.

CPT=Current Procedural Terminology; HCPCS=Healthcare Common Procedure Coding System; ICD-10-CM=International Classification of Diseases, 10th Revision, Clinical Modification; NDC=National Drug Code.

*Each option has its own eligibility criteria that must be met for patients to receive assistance.

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EHR AND PRACTICE MANAGEMENT SYSTEM UPDATES

As one of the key tools for decision making and process in the practice, **it is important to integrate OCREVUS ZUNOVO™ into your EHR system to enable HCPs to consider it for their appropriate patients.**



CONSIDERATIONS FOR YOUR PRACTICE

- Ensure your organization's IT staff and EHR and/or practice management systems vendors have updated your:
 - Order sets
 - Billing software
 - Appointment scheduling tools
 - Other necessary systems
-
- Notify and train appropriate staff as needed once all updates are made



ADDITIONAL CONSIDERATIONS

Consider adding OCREVUS ZUNOVO to the same dropdown fields in the EHR where OCREVUS® (ocrelizumab) [IV] appears today.

IT=information technology.

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ACQUIRING OCREVUS ZUNOVO™

OCREVUS ZUNOVO has the **same specialty distributor and specialty pharmacy networks** as OCREVUS® (ocrelizumab) [IV].



CONSIDERATIONS FOR YOUR PRACTICE

- Determine how to acquire OCREVUS ZUNOVO (e.g., purchasing through a specialty distributor or specialty pharmacy)

- Stay up-to-date on your product inventory

- OCREVUS ZUNOVO is priced at annual wholesale acquisition cost (WAC) parity with OCREVUS [IV]. Please check with your distributors for the latest information on purchase pricing



ADDITIONAL CONSIDERATIONS

- Consider your organization's procedure for procuring HCP-administered injectables when determining how to acquire OCREVUS ZUNOVO
- An OCREVUS Patient Navigator can help you determine if your patient's health insurance plan requires a specific acquisition method, or if you have a choice

FOR MORE INFORMATION:



Visit [OCREVUS.com/Access](https://www.ocrevus.com/Access)



Call **(844) OCREVUS** (844-627-3887) to speak with a Patient Navigator

Published WAC information does not include negotiated discounts or rebates, or other price concessions. Actual price paid by patients, third-party payers and pharmacies may vary and may not correlate with WAC.

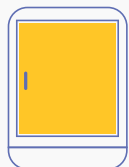
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STORING OCREVUS ZUNOVO™

OCREVUS ZUNOVO has the **same storage needs** as OCREVUS® (ocrelizumab) [IV].



Ensure you have adequate refrigeration space to accommodate the vials needed for patient treatments when they are scheduled. The carton dimensions are 53 × 64 × 87 mm (W × D × H)



Store OCREVUS ZUNOVO vials at 2 °C to 8 °C (36 °F to 46 °F) in the original carton to protect from light



If necessary, OCREVUS ZUNOVO can be removed and placed back into the refrigerator. The total combined time out of the refrigerator of the OCREVUS ZUNOVO vial must not exceed 12 hours at ≤25 °C (77 °F)

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ANCILLARY SUPPLIES

OCREVUS ZUNOVO™ requires **different supplies** from OCREVUS® (ocrelizumab) [IV]. They may also be different from other subcutaneous products you administer in your practice.

These supplies are **not co-packaged with the vial and may take time to acquire**. Contact your distributor to learn more about purchasing the injection supplies.

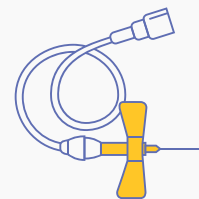
SUPPLIES NEEDED INCLUDE:



Syringe



21-gauge transfer needle



24- to 26-gauge winged infusion set

You also have the option of using a syringe pump* in lieu of the manual injection.

*The B. Braun Perfusor® Space Syringe Pump was used in the OCARINA II clinical trial. Genentech does not endorse or recommend any particular pumps. Please refer to the syringe pump manufacturer's instructions for the most up-to-date information and to ensure appropriate use of any drug or device.

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STAFF TRAINING AND TREATMENT SCHEDULING

Since administration for OCREVUS ZUNOVO™ differs from OCREVUS® (ocrelizumab) [IV] and may be different from some other subcutaneous medications, there are additional considerations for staff training and treatment scheduling.

Staff training



CONSIDERATIONS FOR YOUR PRACTICE

- Determine which medical personnel within your office will perform an injection like this for this type of product

- Ensure relevant staff are trained on appropriate subcutaneous administration of OCREVUS ZUNOVO



Experiential demonstrations of OCREVUS ZUNOVO manual administration are available from your [OCREVUS representative](#)



Treatment scheduling



WHEN SCHEDULING PATIENTS, CONSIDER:

- The need for dedicated space for administration, such as an exam room or infusion chair
 - If you have an open layout, consider ways you might accommodate the need for patient privacy when conducting an abdominal injection

- The impact of total treatment time on nurse/administration personnel bandwidth

- The number of schedule blocks available and how many patients you may be able to schedule based on total treatment time

- Whether your organization's or the payer's policies allow you to schedule administration on the same day as an office visit, and the billing documentation logistics involved

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PRETREATMENT COUNSELING

Before their OCREVUS ZUNOVO™ injection, be sure to discuss treatment with patients so they know what to expect.



TOPICS TO DISCUSS WITH PATIENTS

- Remind patients to bring their health insurance card and other documentation if needed

- Let them know they may want to bring activities to help them pass the time, as well as water, food, snacks or gum (if your facility allows them)

- Remind patients to wear loose-fitting clothing that allows for ease of access for injection into the abdomen

Important Safety Information (cont)

OCREVUS: 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.

OCREVUS ZUNOVO: Injection Reactions

Management recommendations for injection reactions depend on the type and severity of the reaction. Permanently discontinue OCREVUS ZUNOVO if a life-threatening or disabling injection reaction occurs.

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ORAL PREMEDICATIONS

Although patients must take the **same types of premedications** as they do for OCREVUS® (ocrelizumab) [IV], the premedications for OCREVUS ZUNOVO™ are **administered orally**.



**Administer at least 30 minutes
before each OCREVUS ZUNOVO
administration**

20 mg dexamethasone (or equivalent corticosteroid)

An antihistamine (e.g., desloratadine)

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

Oral premedications can be taken at home or in office, subject to the prescribing physician's discretion. Consider how the patient has been instructed to take the premedications by their prescriber prior to the scheduled visit.



If at home, be sure to warn patients that antihistamines may cause them to be drowsy, dizzy or less alert than normal



If in your office, consider where patients will wait during this time and the effect on scheduling

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POST-DOSE OBSERVATION

For the initial dose, monitor the patient for at least one hour post-injection. For subsequent doses, monitor the patient for at least 15 minutes post-injection.



CONSIDERATIONS FOR YOUR PRACTICE

- Identify where the patient will wait during the post-dose observation—this may be in the same room as the administration or another area depending on your office setup

- Monitor for injection reactions, including but not limited to:
 - Local reactions such as erythema, pain, swelling or pruritus
 - Systemic reactions such as headache or nausea

- Ensure access to and provide appropriate supportive or symptomatic treatment as necessary

Please note: In the clinical trial (OCARINA II), all injection reactions were of mild or moderate severity. Most injection reactions required no treatment and all that occurred were resolved.

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PAYER COVERAGE

Genentech supports **parity coverage** for OCREVUS ZUNOVO™ and OCREVUS® (ocrelizumab) to **enable you to choose** the option that's right for your patients and practice.



IMPORTANT POINTS TO REMEMBER

- OCREVUS ZUNOVO is available for Medicare Fee-for-Service patients based on MAC guidance
- Commercial payers may take up to 6 to 8 months to establish policies, but may allow for coverage on a case-by-case basis through their medical exception process. **Check with individual payers to understand their requirements**
- Your OCREVUS representative can help keep you up-to-date on the evolving payer policies for OCREVUS ZUNOVO
- Patients awaiting a health insurance coverage determination for >5 business days may be eligible to receive free medicine through the OCREVUS Starter Program*



To apply for the OCREVUS Starter Program, complete the [OCREVUS Start Form](#).



MAC=Medicare Administrative Contractor.

*Subject to eligibility requirements and terms and conditions. This program is void where prohibited by law and may not be used in or by residents of restricted states, if applicable.

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CODING AND BILLING

While OCREVUS ZUNOVO™ and OCREVUS® (ocrelizumab) use **the same ICD-10-CM diagnosis code, the drug-specific and administration coding is different**. Be sure to check with individual payers for specific requirements.

In particular, OCREVUS ZUNOVO will use a miscellaneous HCPCS code (J-code) at first.



IMPORTANT POINTS TO REMEMBER ABOUT USING MISCELLANEOUS HCPCS CODES

- CMS issues new HCPCS codes each quarter, and practices should routinely check the updated CMS HCPCS lists for new codes. **A permanent J-code for OCREVUS ZUNOVO is expected in the first half of 2025**
- When billing for OCREVUS ZUNOVO soon after FDA approval, check with the payer that the medication is known and loaded in their system, and provide the approved Prescribing Information
- Check any contracts you may have with the payer to understand any specific terms and reimbursement rates for miscellaneous J-codes
- **Some additional information might be needed when submitting claims, including:**
 - A Letter of Medical Necessity
 - Pricing information
 - Full Prescribing Information
 - Peer-reviewed articles
 - FDA approval letter
 - Patient records
- Keeping track of the miscellaneous code billing and coding policies for the payers that are billed frequently will help make the process easier
- **Your Field Reimbursement Manager (FRM)** can provide you with additional considerations for billing with a miscellaneous J-code, and you can download a [detailed coding and billing guide](#)

CMS=Centers for Medicare & Medicaid Services; FDA=US Food and Drug Administration; HCPCS=Healthcare Common Procedure Coding System; ICD-10-CM=International Classification of Diseases, 10th Revision, Clinical Modification.

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EXAMPLE CODING FOR OCREVUS ZUNOVO™

This coding information may assist you as you complete the payer forms for OCREVUS ZUNOVO.

TYPE	CODE	DESCRIPTION
Diagnosis: ICD-10-CM	G35	Multiple sclerosis
Drug: HCPCS	J3490	Unclassified drugs
	J3590	Unclassified biologics
	J9999	Not otherwise classified, antineoplastic drugs
	C9399	Unclassified drugs or biologicals (generally for hospital outpatient use)
Home Injection: HCPCS	G0069	Professional services for the administration of subcutaneous immunotherapy or other subcutaneous infusion drug or biological for each infusion drug administration calendar day in the individual's home, each 15 minutes
HCPCS Modifier*	JZ	Zero drug amount discarded/not administered to any patient
Drug: NDC	10-digit	Ocrelizumab 920 mg and hyaluronidase 23,000 units single-dose vial
	50242-554-01	
	11-digit	
50242-0554-01		
Administration Procedures: CPT	96401	Chemotherapy administration, subcutaneous or intramuscular; non-hormonal anti-neoplastic

*The JZ modifier is required on claims for all single-dose containers or single-use drugs when no drug is discarded/administered to any patient as of July 1, 2023. For more information on the JZ modifier, visit [CMS.gov](https://www.cms.gov).

These codes are not all-inclusive; appropriate codes can vary by patient, setting of care and payer. Correct coding is the responsibility of the provider submitting the claim for the item or service. Please check with the payer to verify codes and special billing requirements. Genentech does not make any representation or guarantee concerning reimbursement or coverage for any service or item.

Many payers will not accept unspecified codes. If you use an unspecified code, please check with your payer.

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INDICATIONS AND IMPORTANT SAFETY INFORMATION

Indications

OCREVUS and OCREVUS ZUNOVO are 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

Treatment with ocrelizumab is contraindicated in patients with active hepatitis B virus infection and in patients with a history of life-threatening administration reactions to ocrelizumab.

OCREVUS ZUNOVO is also contraindicated in patients with a history of hypersensitivity to ocrelizumab, hyaluronidase, or any component of OCREVUS ZUNOVO.

Warnings and Precautions

Injection Reactions (OCREVUS ZUNOVO) OR Infusion Reactions (OCREVUS)

OCREVUS ZUNOVO can cause injection reactions, which can be local or systemic. Common symptoms of local injection reactions reported by patients treated with OCREVUS ZUNOVO in multiple sclerosis (MS) clinical trials included erythema, pain, swelling, and pruritus. Common symptoms of systemic injection reactions reported by patients included headache and nausea. In an open-label, active-controlled trial, injection reactions were more frequently reported with the first injection; 49% of patients experienced an injection reaction with the first injection.

In OCREVUS MS clinical trials, the incidence of infusion reactions in patients [who received methylprednisolone (or an equivalent steroid) and possibly other pre-medication to reduce the risk of infusion reactions prior to infusion] was 34% to 40%, with the highest incidence with the first infusion. There were no fatal infusion reactions, but 0.3% of intravenous ocrelizumab-treated MS patients experienced infusion reactions that were

serious, some requiring hospitalization. Symptoms of infusion reactions 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.

Monitor OCREVUS ZUNOVO patients during and after injections. 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 administration reactions can occur during or within 24 hours of treatment.

Reducing the Risk and Managing Injection or Infusion Reactions

For OCREVUS ZUNOVO, administer oral pre-medication (e.g., dexamethasone or an equivalent corticosteroid, and an antihistamine) at least 30 minutes prior to each OCREVUS ZUNOVO injection to reduce the risk of injection reactions. The addition of an antipyretic (e.g., acetaminophen) may also be considered.

For OCREVUS, 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.

Management recommendations depend on the type and severity of the reaction. For life-threatening reactions, immediately and permanently stop OCREVUS ZUNOVO or OCREVUS and administer appropriate supportive treatment. For less severe OCREVUS ZUNOVO injection reactions, the injection should be interrupted immediately, and the patient should receive symptomatic treatment. The injection should be completed at the healthcare provider's discretion and only after all symptoms have resolved. For less severe OCREVUS infusion reactions, management may involve temporarily stopping the infusion, reducing the infusion rate, and/or administering symptomatic treatment.

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INDICATIONS AND IMPORTANT SAFETY INFORMATION (CONT)

Infections

Serious, including life-threatening or fatal, bacterial, viral, parasitic and fungal infections have been reported in patients receiving ocrelizumab. 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 was not associated with an increased risk of serious infections in MS patients in controlled trials.

Ocrelizumab increases the risk for upper respiratory tract infections, lower respiratory tract infections, skin infections, and herpes-related infections. Delay administration of ocrelizumab in patients with an active infection until the infection has resolved.

Respiratory Tract Infections

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

Herpes

In active-controlled (RMS) clinical trials, herpes infections were reported more frequently in OCREVUS-treated patients than in REBIF-treated patients, including herpes zoster (2.1% vs. 1.0%), herpes simplex (0.7% vs. 0.1%), oral herpes (3.0% vs. 2.2%), genital herpes (0.1% vs. 0%), and herpes virus infection (0.1% vs. 0%). Infections were predominantly mild to moderate in severity. 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 ocrelizumab. Serious herpes virus infections may occur at any time during treatment with ocrelizumab. Some cases were life-threatening.

If serious herpes infections occur, treatment with ocrelizumab should be discontinued or withheld until the infection has resolved, and appropriate treatment should be administered.

Hepatitis B Virus Reactivation

Hepatitis B virus (HBV) reactivation has been reported in MS patients treated with ocrelizumab 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 ocrelizumab. Do not administer ocrelizumab 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.

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INDICATIONS AND IMPORTANT SAFETY INFORMATION (CONT)

Possible Increased Risk of Immunosuppressant Effects With Other Immunosuppressants

When initiating treatment with ocrelizumab after an immunosuppressive therapy or initiating an immunosuppressive therapy after ocrelizumab-containing products, consider the potential for increased immunosuppressive effect. Treatment with ocrelizumab 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 ocrelizumab treatment for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of ocrelizumab treatment for non-live vaccines. Ocrelizumab may interfere with the effectiveness of non-live vaccines. The safety of immunization with live or live-attenuated vaccines following treatment with ocrelizumab 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 Ocrelizumab Products During Pregnancy

In infants of mothers exposed to ocrelizumab 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.

Progressive Multifocal Leukoencephalopathy

Cases of progressive multifocal leukoencephalopathy (PML) have been reported in patients with MS treated with ocrelizumab in the postmarketing setting. PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically occurs only in patients who are immunocompromised, and that usually leads to death or severe disability. PML has

occurred in ocrelizumab-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 ocrelizumab 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 treatment with ocrelizumab-containing products 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 ocrelizumab should be discontinued.

Reduction in Immunoglobulins

As expected with any B-cell depleting therapy, decreased immunoglobulin levels are observed with ocrelizumab 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 treatment with ocrelizumab and after discontinuation of treatment, until B-cell repletion, and especially in the setting of recurrent serious infections. Consider discontinuing treatment with ocrelizumab- in patients with serious opportunistic or recurrent serious infections, and if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins.

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INDICATIONS AND IMPORTANT SAFETY INFORMATION (CONT)

Malignancies

An increased risk of malignancy with ocrelizumab 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 ocrelizumab 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 ocrelizumab 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.

Use in Specific Populations

Pregnancy

There are no adequate data on the developmental risk associated with use of ocrelizumab in pregnant women. There are no data on B-cell levels in human neonates following maternal exposure to ocrelizumab-containing products. However, transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other anti-CD20 antibodies during pregnancy. Ocrelizumab 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 or hyaluronidase 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 ocrelizumab and any potential adverse effects on the breastfed infant from ocrelizumab or from the underlying maternal condition.

Females and Males of Reproductive Potential

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

Most Common Adverse Reactions

In patients treated with OCREVUS:

- **RMS:** The most common adverse reactions ($\geq 10\%$ and $> \text{REBIF}$): upper respiratory tract infections and infusion reactions.
- **PPMS:** The most common adverse reactions ($\geq 10\%$ and $> \text{placebo}$): upper respiratory tract infections, infusion reactions, skin infections, and lower respiratory tract infections.

The most common adverse reaction observed with OCREVUS ZUNOVO in patients with RMS and PPMS was injection reactions (incidence of 49%).

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.

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Call **(844) OCREVUS** (844-627-3887) to speak with a **Patient Navigator**, Monday through Friday, 9 a.m. to 8 p.m. ET

- Help is available in English and Spanish



Contact your [OCREVUS representative](#)

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