מרץ 2023

Ocrevus® 300 mg/10 ml
ocrelizumab
Concentrate for solution for infusion

רופא/ה יקר/ה, רוקח/ת יקר/ה,

חברת רוש פרמצבטיקה (ישראל) בע"מ מבקשת להודיעכם על עדכונים שבוצעו בעלון לרופא של התכשיר אוקרווא‌ס.

בהודעה זו מצוינים רק עדכונים מהותיים.

ההתוויות הרשומות לתכשיר בישראל:

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

הסבר:
טקסט עם קו תחתי מציין טקסט שהוסף לעלון.
~~טקסט עם קו חוצה~~ מציין טקסט שהוסר מן העלון.

למידע נוסף יש לעיין בעלון לרופא כפי שנשלח למשרד הבריאות.

העלון המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס ע"י פנייה לבעל הרישום: רוש פרמצבטיקה (ישראל) בע"מ, ת.ד 6391 , הוד השרון 4524079
טלפון 09-9737777. כתובתנו באינטרנט: www.roche.co.il.

ב ב ר כ ה,

בתאור צפרי-חג'ג'
מחלקת רישום

לביא עמי-עד
רוקח ממונה

עדכונים מהותיים בעלון לרופא

בסעיף 2 Dosage and Administration עודכן המידע הבא:

2.3 Recommended Dosage and Dose Administration

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

		Amount and Volume[1]	Infusion Rate and Duration[3]
Initial Dose (two infusions)	Infusion 1	300 mg in 250 mL	• Start at 30 mL per hour • Increase by 30 mL per hour every 30 minutes • Maximum: 180 mL per hour • Duration: 2.5 hours or longer
	Infusion 2 (2 weeks later)	300 mg in 250 mL	
~~**Subsequent Doses** (one infusion)~~ **Subsequent Doses** (one infusion) every 6 months)[2]	~~One infusion every 6 months[2]~~ Option 1 Infusion of approximately 3.5 hours duration[3]	600 mg in 500 mL	• Start at 40 mL per hour • Increase by 40 mL per hour every 30 minutes • Maximum: 200 mL per hour • Duration: 3.5 hours or longer
	OR		
	Option 2 (If no prior serious infusion reaction with any previous OCREVUS infusion)[4] Infusion of approximately 2 hours duration[3]	600 mg in 500 mL	• Start at 100 mL per hour for the first 15 minutes • Increase to 200 mL per hour for the next 15 minutes • Increase to 250 mL per hour for the next 30 minutes • Increase to 300 mL per hour for the remaining 60 minutes Duration: 2 hours or longer

[1] Solutions of Ocrevus for intravenous infusion are prepared by dilution of the drug product into an infusion bag containing 0.9% Sodium Chloride Injection, to a final drug concentration of approximately 1.2 mg/mL.
[2] Administer the first Subsequent Dose 6 months after Infusion 1 of the Initial Dose.
[3] Infusion time may take longer if the infusion is interrupted or slowed *[see Dosage and Administration (2.5)]*.
[4] *[see Adverse Reactions (6.1) and Clinical Studies (14.3)].*

בסעיף 6 Adverse Reactions עודכן המידע הבא:

6.1 Clinical Trials Experience

Adverse Reactions in Patients who Received 2-hour Infusions

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

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6.3 Postmarketing Experience

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Skin: Pyoderma gangrenosum

בסעיף 12 Clinical Pharmacology עודכן המידע הבא:

12.3 Pharmacokinetics

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

בסעיף 14 Clinical Studies עודכן המידע הבא:

14.3 Safety Study of 2-Hour Infusions

The safety of the 2-hour OCREVUS infusion was evaluated in Study 4 (NCT03085810), a prospective, multicenter, randomized, double-blind, controlled, parallel arm substudy in patients with Relapsing-Remitting Multiple Sclerosis who were naïve to other non-steroid therapies for MS and did not experience a serious infusion reaction with any previous OCREVUS infusion. The first dose of OCREVUS was administered as two 300 mg infusions (600 mg total) separated by 14 days. After enrollment in the substudy, patients were randomized in a 1:1 ratio to receive infusions over approximately 3.5-hours or 2-hours, after appropriate premedication *[see Dosage and Administration (2.2)]*, every 24 weeks. The randomization was stratified by region and the dose at which patients were first randomized.

The primary endpoint of the substudy was the proportion of patients with infusion reactions occurring during or within 24 hours following the first randomized infusion of OCREVUS. The primary analysis was performed when 580 patients were randomized, at which time 469/579 (81%) of the treated patients had received only a single randomized infusion of OCREVUS. The proportions of patients with infusion reactions occurring during or within 24 hours following the first randomized infusion in this substudy were similar between the 2-hour and

3.5-hour infusion groups (24.4% versus 23.3%, respectively). Overall, in all randomized doses, 27.1% of the patients in the 2-hour infusion group and 25.0% of the patients in the 3.5-hour infusion group reported mild or moderate infusion reactions; two infusion reactions were severe in intensity, with one severe infusion reaction (0.3%) reported in one patient in each group in this substudy *[see Warnings and Precautions (5.1)]*. There were no life-threatening, fatal, or serious infusion reactions in this substudy.