Genentech
A Member of the Roche Group

August 2025

Subject: Risks with Use of OCREVUS® (ocrelizumab) and OCREVUS ZUNOVO® (ocrelizumab and hyaluronidase-ocsq): Liver Injury

Dear Health Care Provider:

The purpose of this letter is to inform you of updated safety information in the United States Prescribing Information (USPI) for OCREVUS® (ocrelizumab) and OCREVUS ZUNOVO® (ocrelizumab and hyaluronidase-ocsq) regarding clinically significant liver injury, without findings of viral hepatitis. Both OCREVUS® and OCREVUS ZUNOVO® are CD20-directed cytolytic antibodies indicated for the treatment of adults with relapsing forms of multiple sclerosis and primary progressive multiple sclerosis.

Risk of Liver Injury With Use of OCREVUS® and OCREVUS ZUNOVO®

The FDA has become aware of post-marketing reports of clinically significant liver injury, without findings of viral hepatitis, for anti-CD20 monoclonal antibodies approved for the treatment of multiple sclerosis, including OCREVUS® and OCREVUS ZUNOVO®.

A review of available data concerning liver injury with OCREVUS® and OCREVUS ZUNOVO® identified 13 cases of clinically significant liver injury. Some cases were severe and life-threatening, and some had markedly elevated serum aminotransferases with elevated total bilirubin. In a few cases, patients were temporarily added to the transplant list. These cases showed evidence of a temporal association with the first or second dose of ocrelizumab. Recovery was reported in 6 cases, with a median time to recovery of 6 weeks (with a range up to 9 months) following treatment cessation. In one case, the patient died of another cause after liver injury had improved. Recovery information was not reported in 6 cases.

Cases were reported mainly in the post-marketing setting, so the incidence cannot be accurately calculated. In coordination with the FDA, we have updated the US Prescribing information and Medication Guides for OCREVUS® and OCREVUS ZUNOVO®.

Prescriber Action

- Counsel patients about the risks and benefits of OCREVUS® and OCREVUS ZUNOVO®, including that clinically significant liver injury, without findings of viral hepatitis, is a newly identified risk.
- Obtain liver function tests, including serum aminotransferases, alkaline phosphatase, and bilirubin levels, before initiating treatment with OCREVUS® or OCREVUS ZUNOVO®, and during treatment as clinically indicated.
- Counsel patients regarding potential symptoms of liver injury (e.g., new or worsening fatigue, anorexia, nausea, vomiting, right upper abdominal discomfort, dark urine, or jaundice) that should be promptly reported.
- Monitor patients for signs and symptoms of liver injury during treatment.
- Perform liver function tests promptly in patients who report signs or symptoms that may indicate liver injury.
- If liver injury is present and an alternative etiology is not identified, discontinue OCREVUS® or OCREVUS ZUNOVO®.

Reporting Adverse Events / Product Complaints and Company Contact

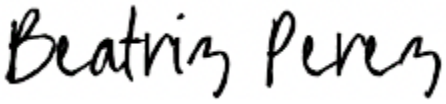
Health Care Providers should report any adverse events suspected to be associated with the use of OCREVUS® or OCREVUS ZUNOVO® to Genentech at 1-888-835-2555. Alternatively, this information may be reported to FDA's MedWatch reporting system by phone (1-800-FDA-1088) or online (www.fda.gov/medwatch).

Please report any product complaint suspected to be associated with the use of OCREVUS® or OCREVUS ZUNOVO® to Genentech at (800) 334-0290.

Should you have any questions about the information in this letter or the safe and effective use of OCREVUS® or OCREVUS ZUNOVO®, please feel free to contact us at: Genentech Medical Information/Communications Department at (800) 821-8590.

This letter is not intended as a complete description of the benefits and risks related to the use of OCREVUS® or OCREVUS ZUNOVO®. Please refer to the enclosed full prescribing information for OCREVUS® or OCREVUS ZUNOVO®.

Sincerely,



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