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Ofatumumab (ARZERRA) – screen all patients for hepatitis B virus before treatment

Dear Healthcare Professional,

GlaxoSmithKline in agreement with the European Medicines Agency and The Irish Medicines Board, would like to inform healthcare professionals of updated recommendations for hepatitis B virus screening (HBV) before treatment with ofatumumab.

Summary:

- **Following cases of HBV infection and reactivation in patients treated with anti-CD20 monoclonal antibodies, it is now recommended that all patients should be screened for HBV infection before starting treatment with ofatumumab.**

- **Patients with active/current hepatitis B infection should not be treated with ofatumumab.**

- **For patients with positive hepatitis B serology (but no active/current disease), a liver disease expert should be consulted regarding monitoring and initiation of HBV antiviral therapy.**

- **In patients who develop reactivation of HBV while receiving ofatumumab, ofatumumab and any concomitant chemotherapy should be interrupted immediately, and appropriate treatment instituted.**

Further information:

A recent United States Food and Drug Administration (FDA) and relevant pharmaceutical sponsor review of anti-CD20 monoclonal antibodies has showed that HBV infection and reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, has occurred in patients treated with drugs classified as CD20-directed cytolytic antibodies, including ofatumumab.

Cases have been reported in patients who are hepatitis surface antigen (HBsAg) positive and also in those who are hepatitis B core antibody (anti-HBc) positive but HBsAg negative. Reactivation also has occurred in patients who appear to have resolved hepatitis B infection (i.e., HBsAg negative, anti-HBc positive, and hepatitis B surface antibody positive).

HBV screening is now recommended in all patients (not just those at risk of HBV infection) before starting treatment with ofatumumab in all indications. For patients who show evidence of prior HBV

infection, a liver disease expert should be consulted regarding monitoring and initiation of HBV antiviral therapy.

The product information for Arzerra has been updated to include this new recommendation (Annex).

Call for reporting:
All healthcare professionals should report any suspected sides effects of Arzerra to GlaxoSmithKline (Ireland) Ltd., Stonemasons Way, Rathfarnham, Dublin 16 (Free phone 1800 244 255, Fax 01 4938839 or e-mail ireland.drugsurveillance@gsk.com).

Healthcare professionals can also report suspected adverse reactions to the IMB using a Yellow Card obtained either from the IMB, or electronically via the website at www.imb.ie. Adverse reactions can also be reported to the IMB by calling (01) 676 4971.

Company contact point:
Further information can be obtained from:
GlaxoSmithKline (Ireland) Ltd., Stonemasons Way, Rathfarnham, Dublin 16 (Freephone 1800 244 255).

Yours sincerely,

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Annex: Summary of Product Characteristics

Extract from the SmPC, section 4.4 special warnings and precautions for use:

Hepatitis B

Hepatitis B virus (HBV) infection and reactivation, in some cases resulting in fulminant hepatitis, hepatic failure and death, has occurred in patients treated with drugs classified as CD20-directed cytolytic antibodies, including Arzerra. Cases have been reported in patients who are hepatitis B surface antigen (HBsAg) positive and also in those who are hepatitis B core antibody (anti-HBc) positive but HBsAg negative. Reactivation has also occurred in patients who appear to have resolved hepatitis B infection (i.e. HBsAg negative, anti-HBc positive, and hepatitis B surface antibody [anti-HBs] positive).

HBV reactivation is defined as an abrupt increase in HBV replication manifesting as a rapid increase in serum HBV DNA level or detection of HBsAg in a person who was previously HBsAg negative and anti-HBc positive. Reactivation of HBV replication is often followed by hepatitis, i.e., increase in transaminase levels and, in severe cases, increase in bilirubin levels, liver failure, and death.
All patients should be screened for HBV infection by measuring HBsAg and anti-HBc before initiation of Arzerra treatment. For patients who show evidence of prior (HBsAg negative, anti-HBc positive) hepatitis B infection, physicians with expertise in managing hepatitis B should be consulted regarding monitoring and initiation of HBV antiviral therapy. Arzerra treatment should not be initiated in patients with evidence of current hepatitis B infection (HBsAg positive) until the infection has been adequately treated.

Patients with evidence of prior HBV infection should be monitored for clinical and laboratory signs of hepatitis or HBV reactivation during treatment with and for 6-12 months following the last infusion of Arzerra. HBV reactivation has been reported up to 12 months following completion of therapy. Discontinuation of HBV antiviral therapy should be discussed with physicians with expertise in managing hepatitis B.

In patients who develop reactivation of HBV while receiving Arzerra, Arzerra and any concomitant chemotherapy should be interrupted immediately, and appropriate treatment instituted. Insufficient data exist regarding the safety of resuming Arzerra in patients who develop HBV reactivation. Resumption of Arzerra in patients whose HBV reactivation resolves should be discussed with physicians with expertise in managing hepatitis B.

Section 4.8 Undesirable effects:

This has been updated to include Hepatitis B infection and reactivation as a rare side effect under the MedDRA body system organ class, Infections and Infestations