November 8th 2013

MabThera (rituximab): screen for hepatitis B virus before treatment

Dear Healthcare Provider,

Roche Products (Ireland) Limited would like to inform you of the updated recommendation for hepatitis B virus (HBV) screening before treatment with MabThera (rituximab).

Summary

- **Screen all patients for HBV before starting treatment with MabThera (rituximab).**
- **Patients with active hepatitis B disease should not be treated with MabThera (rituximab).**
- **Refer patients with positive hepatitis B serology (but no active disease) to a liver disease expert before starting treatment with MabThera (rituximab). These patients should be monitored and managed following local medical standards to prevent HBV reactivation.**

Further information

MabThera (rituximab) has been associated with HBV reactivation in clinical practice for the oncology and rheumatoid arthritis indications. These cases included fulminant hepatitis, some of which were fatal.

A recent analysis showed that MabThera (rituximab) is associated with HBV reactivation in people with positive HB surface antigen (HBsAg+ve) and those with negative HB surface antigen and positive anti-HB core antibody (HBsAg-ve/HBcAb+ve), particularly when administered in combination with steroids or chemotherapy.

Therefore HBV screening is now recommended in all patients (not just those at risk of HBV infection) before starting treatment with MabThera (rituximab) in all indications. Anyone with positive HBV serology should be referred to a liver disease specialist before the start of treatment with MabThera (rituximab). During treatment, they should be monitored and managed to prevent HBV reactivation.

The product information for MabThera (rituximab) has been updated to include this new recommendation (see Annex overleaf).

Call for Reporting

Healthcare professionals should report any suspected side effects of MabThera (rituximab) to the Roche Drug Surveillance Centre by mail, telephone (01 4690700), fax (01 4690793) or email (ireland.drug_surveillance_centre@roche.com). Alternatively, suspected adverse reactions should be reported to the Irish Medicines Board (IMB) using a Yellow Card obtained either from the IMB, or electronically via the website at www.imb.ie. Alternatively adverse reactions can be reported by calling (01) 6764971.

Company contact point

For further information or any questions please contact Roche Medical Information by mail, telephone (01 4690700), fax (01 4690791) or email (ireland.druginfo@roche.com).

Please distribute this communication further within your team.

Yours sincerely,

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Annex

New updated recommendation for Hepatitis B as set out in the Special warnings and precautions for use of MabThera Product Information (CHMP opinion 24 October 2013, Commission Decision pending).

Cases of hepatitis B reactivation have been reported in subjects receiving MabThera including fulminant hepatitis with fatal outcome. The majority of these subjects were also exposed to cytotoxic chemotherapy. Limited information from one study in relapsed/refractory CLL patients suggests that MabThera treatment may also worsen the outcome of primary hepatitis B infections. Hepatitis B virus (HBV) screening should be performed in all patients before initiation of treatment with MabThera. At minimum this should include HBsAg-status and HBcAb-status. These can be complemented with other appropriate markers as per local guidelines. Patients with active hepatitis B disease should not be treated with MabThera. Patients with positive hepatitis B serology (either HBsAg or HBcAb) should consult liver disease experts before start of treatment and should be monitored and managed following local medical standards to prevent hepatitis B reactivation.