

April 2013

Direct Healthcare Professional Communication on the association of MabThera[®] (rituximab) with Toxic Epidermal Necrolysis and Stevens-Johnson-Syndrome

Dear Healthcare Provider,

Roche Registration Ltd. in co-operation with the European Medicines Agency (EMA) and the Medicines Authority would like to inform you of important new safety information on the use of MabThera (rituximab):

Summary

- Cases of severe skin reactions such as toxic epidermal necrolysis (TEN) and Stevens-Johnson Syndrome (SJS) have been very rarely reported in patients with autoimmune diseases. They include one case of TEN with fatal outcome
- Severe bullous skin reactions, including fatal cases, of TEN have been reported very rarely in patients with haematological malignancies. This information is already included in the MabThera product information.
- If severe skin reactions occur, MabThera treatment should be permanently discontinued.

Roche Products Limited

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April 2013**

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Further information on the safety concern

Cases of TEN and Stevens- Johnson syndrome in autoimmune patients have been reported with both first-time use and with later infusions. Some of the cases occurred on the day of dosing or within a few days of dosing. In other cases, the event occurred weeks or up to four months after the dose.

Four of the cases in autoimmune patients had a close association in time to MabThera dosing (starting on the day of dosing or the next day), of which one case of TEN had a fatal outcome.

In several of the cases in autoimmune patients, treatments known to be possibly associated with Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome were given concomitantly with MabThera therapy.

The mechanism of these reactions remains unknown.

The product information (SmPC) for MabThera is being updated to reflect the new safety information, as follows:

4.4 Special warnings and precautions for use

Non-Hodgkin's lymphoma and chronic lymphocytic leukaemia **Rheumatoid arthritis**

Skin reactions:

- Severe skin reactions such as Toxic Epidermal Necrolysis (Lyell's Syndrome) and Stevens-Johnson Syndrome, some with fatal outcome, have been reported (see section 4.8). In case of such an event, treatment should be permanently discontinued.

4.8 Undesirable effects

Experience from Rheumatoid Arthritis

Skin and subcutaneous tissue disorders:

- Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome, some with fatal outcome, have been reported very rarely.

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Call for Reporting

Healthcare professionals should report any adverse event suspected to be associated with the use of MabThera to Roche by phone on +44 (0)1707 367554, by fax on+44 (0)1707 367582 or e-mail at welwyn.uk_dsc@roche.com.

Any suspected adverse reaction should also be reported via the national Adverse Drug Reactions (ADRs) reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Company contact point

For further information or any questions on Toxic Epidermal Necrolysis or Stevens-Johnson Syndrome associated with the use of MabThera, please contact Roche Medical Information by phone on +44 (0)800 328 1629 or via e-mail medinfo.uk@roche.com

Detailed information on MabThera is available on the European Medicines Agency web site: <http://www.ema.europa.eu>.

Yours sincerely,



Zoe Conway
Head of UK Medical Services & UK Local Safety Responsible

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