Roche Products (Ireland) Limited
3004 Lake Drive
Citywest
Naas Road
Dublin 24.

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

April 12th 2013

Dear Healthcare Provider,

Roche Registration Ltd. in co-operation with the European Medicines Agency (EMA) and the Irish Medicines Board (IMB) 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.

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.

Call for Reporting

Health care professionals should report any serious adverse events suspected to be associated with the use of MabThera to the Drug Surveillance Centre at Roche Products (Ireland) Limited (either by mail, telephone [01 4690700], fax [01 4690793] or e-mail [Ireland.drug_surveillance_centre@roche.com]). Alternatively, suspected adverse events should be reported to the Irish Medicines Board using the online form at www.imb.ie or by using the freepost yellow card system. The IMB can also be contacted on 01-6764971.

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 Medical Information at Roche Products (Ireland) Limited (by mail, telephone [01 4690700], fax [01 4690791] or e-mail [ireland.druginfo@roche.com]).

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

Yours sincerely,

Dr. Maria Luz Amador
Medical Director

Roche Products (Ireland) Limited
3004 Lake Drive
Citywest
Naas Road
Dublin 24
Ireland
(Registered Office)
Tel: 353-1-469 0700
Fax: 353-1-469 0790
353-1-469 0791
Registered in Ireland
No. 214337