Roche

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

Date: 01 /Apr/2013

Dear Healthcare Provider,

F. Hoffmann-La Roche Ltd. would like to inform you of important new safety information on the use of MabThera® (Rituximab):

Summary

- In patients with autoimmune diseases, severe skin reactions such as Toxic Epidermal Necrolysis (TEN) and Stevens - Johnson syndrome (SJS) with fatal outcome have been reported very rarely with MabThera® (Rituximab) in the post - marketing setting.

- In patients with haematological malignancies, information on severe bullous skin reactions including fatal cases of TEN and SJS, which have been reported rarely in the post marketing setting, are already included in the MabThera® (Rituximab) product information.

- For autoimmune and oncology indications, in case of the occurrence of severe skin reactions, MabThera® (Rituximab) treatment should be discontinued. The decision to re-administer MabThera® (Rituximab) must be carefully assessed based on the individual patient`s benefit–risk profile.

Further information on the safety concern

The cases of TEN and SJS in autoimmune patients have been reported with either first time use or 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® (Rituximab) 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 TEN and SJS were given concomitantly with MabThera® (Rituximab) therapy.

The mechanism of these reactions remains unknown.

The Special Warnings and Precautions for Use and the Undesirable Effects sections of the prescribing/product information for MabThera® (Rituximab) will be updated to reflect the new safety information after requested approval of the Saudi Food and drug Authority (SFDA). As recent analysis of the cases of TEN and SJS reported in patients with haematological malignancies was consistent with the information already provided in the Undesirable Effects section of the MabThera® (Rituximab) product information, which states severe bullous skin reactions including fatal cases of TEN have been reported rarely.

Approved Indications in KSA:

- **Non-Hodgkin's lymphoma**

  Monotherapy in patients with CD20-positive follicular non-Hodgkin's lymphoma (stage III–IV) who have relapsed after, or failed to respond to, chemotherapy.

  Treatment of previously untreated patients with CD20-positive follicular non-Hodgkin's lymphoma (stage III–IV) with high tumour burden in combination with CVP or CHOP. Responders may be administered maintenance therapy with rituximab monotherapy for 2 years.

  Maintenance therapy of patients with relapsed or refractory CD20-positive follicular non-Hodgkin's lymphoma (stage III–IV) who have responded to induction therapy with CHOP with or without rituximab. Treatment of patients with CD20-positive diffuse large B-cell non-Hodgkin's lymphoma (DLBCL) in combination with standard CHOP (8 cycles of cyclophosphamide, doxorubicin, vincristine and prednisone). Use in combination with fludarabine and cyclophosphamide (R-FC) for patients requiring treatment for chronic lymphocytic leukemia (CLL). Patients previously treated with fludarabine should have responded for a period of at least 6 months.

- **Rheumatoid arthritis (RA)**

  MabThera in combination with methotrexate (MTX) is indicated for the treatment of adult patients with moderately severe to severe active rheumatoid arthritis after failure of one or more tumour necrosis factor (TNF) inhibitor therapies.

The information in this letter has been agreed with the Saudi Food and Drug Authority (SFDA).

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Call for Reporting

Health care professionals should report any serious adverse events suspected to be associated with the use of MabThera® (Rituximab) according to national reporting requirements

For further information or any questions on TEN or SJS associated with the use of MabThera® (Rituximab), please contact us on the below address.

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Najoud Centre, Gate A, 1st Floor.
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Alternatively, report this information to:

The National Pharmacovigilance & Drug safety Centre (NPC)
Saudi Food and Drug Authority (SFDA)
Fax: +966-1-2057662
Npc.drug@sfda.gov.sa

Yours Sincerely,

Hazem Al-Dajani
Local Safety Responsible
10/4/2013

Naser Al-Rajhi
Scientific office director
10. April 2013

Tamer Elmahallawy
Medical Director
10 Apr 13