Roche

Direct Healthcare Professional Communication on the management of Hepatitis B reactivation in patients treated with MabThera (rituximab)

16/7/2013

Dear Healthcare Provider,

Hoffmann-La Roche Ltd. would like to inform you on an update in the management of hepatitis B reactivation in patients treated with MabThera (rituximab).

Summary

As described in the current product information, the use of MabThera (rituximab) has been associated with cases of hepatitis B reactivation in the post -marketing setting for oncology and rheumatoid arthritis indications. These cases included reports of fulminant hepatitis, some of which were fatal. Hepatitis B virus (HBV) screening was initially recommended in patients at risk for HBV infection before initiation of treatment with MabThera.

A recent analysis of the events of hepatitis B reactivation revealed that the use of rituximab has been associated with hepatitis B reactivation in patients with positive HB surface antigen (HBsAg+ve) as well as negative HB surface antigen and positive anti-HB core antibody (HBsAg-ve/HBcAb+ve), particularly when administered in combination with steroids or chemotherapy. As of August 2012, the crude reporting rates of hepatitis B reactivation were 0.017% and 0.006% in hemato-oncology and in auto-immune diseases, respectively.

Information For Health Care Providers

Based on the current data and following the updated new clinical guidelines, Hoffmann-La Roche Ltd. thus recommends HBV screening in all patients before the initiation of treatment with MabThera (rituximab) in all indications, and the HBV screening should be done for those with high risk of HBV infection.Those patients with positive HBV serology should consult with a liver disease specialist before start of treatment. Those patients should be monitored and managed following local standards to prevent hepatitis B reactivation.

The existing information on Hepatitis B reactivation presented in Special Warnings and Precautions for Use of the Product information for MabThera is being updated to reflect the new management recommendations, as follows:

Hepatitis B virus (HBV) screening should be performed in all patients before initiation of treatment with MabThera as per institutional guidelines. Patients with active hepatitis B disease should not be treated with MabThera. Patients with positive hepatitis B serology should consult liver disease experts before start of treatment and should be monitored and managed following local medical standards to prevent hepatitis B reactivation.

The new management recommendations will be added in Product information on 15/10/2013.

Indications:

- 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.

- ANCA-associated vasculitis (AAV)

- MabThera is indicated in combination with corticosteroids for the treatment of patients with severe active ANCA-associated vasculitis (granulomatosis with polyangiitis [also known as Wegener's granulomatosis] and microscopic polyangiitis).

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

Call for Reporting:

Healthcare professionals should report any serious adverse events suspected to be associated with the use of MabThera according to national reporting requirements.

For further information or any questions on the management of Hepatitis B reactivation associated with the use of MabThera please contact:

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Yours Sincerely,

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Local Safety Responsible	Scientific office director	Medical Director
30/7/2013	31. July. 2013	30/07/2013