衞生署
藥物註冊組
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本署檔號 OUR REF.: DH PS PRIE/7-30/15
(來函請敍明此檔案號碼)
(IN REPLY PLEASE QUOTE THIS FILE REF.)

BY FAX

26 May 2011

Dr. Raymond LIANG
President
Hong Kong Academy of Medicine
(Fax Number: 2505 5577)

Dear Dr. LIANG,

Association of MabThera (Rituximab) with Fatal Infusion Related Reactions in Patients with Rheumatoid Arthritis

Your attention is drawn to the important new safety information on the use of rituximab in rheumatoid arthritis (RA). The Department of Health has been informed by Roche Hong Kong Ltd. of such information.

According to Roche HK Ltd., there are 4 cases of spontaneous post marketing reports of fatal infusion related reactions. In light of the incidence, the Dosage and Administration and Special Warnings and Precautions for Use sections of the prescribing information for rituximab would be updated to reflect the new safety information.

For details, please refer to the attached letter issued by Roche HK Ltd. to healthcare professionals.

In Hong Kong, MabThera (rituximab) is registered as Injection 500mg/50ml (HK-46231), Injection 100mg/10ml (HK-46232), Concentrate for Solution for Infusion 100mg/10ml (HK-59248) and Concentrate for Solution for Infusion 500mg/50ml (HK-59249) by Roche HK Ltd. and are prescription medicines. The package inserts are being updated to include the appropriate warnings.

Please remind your members to report any adverse events caused by the drug to the Adverse Drug Reaction Monitoring Unit of Department of Health (tel. no.: 2319 8633, fax: 2147-0457 or email: adr@dh.gov.hk). For details, please refer to the website: http://www.psdh.gov.hk at Pharmaceutical Service under "Reporting an Adverse Drug Reaction".

Yours sincerely,

(Ms Pamela LI)
for Chief Pharmacist

Roche

26 May 2011

Our Ref.: 110530

Direct Healthcare Professional Communication on the association of MabThera (Rituximab) with fatal infusion related reactions in patients with Rheumatoid arthritis

Dear Healthcare Professional:

The Roche group would like to inform you of important new safety information on the use of rituximab in rheumatoid arthritis (RA).

Since the marketing approval of rituximab in RA, fatal infusion related reactions in patients with rheumatoid arthritis treated with rituximab have been reported in the post marketing setting.

Summary

- Healthcare professionals must be vigilant for signs of hypersensitivity or anaphylaxis in all patients receiving rituximab, both during and following its administration.
- Premedication consisting of analgesic/anti-pyretic (*e.g. paracetamol*) and an anti-histaminic drug (*e.g. diphenhydramine*) should always be administered before each infusion of rituximab.
- Premedication with glucocorticoids should also be administered in order to reduce the frequency and severity of infusion related reactions.
- Medicinal products for the treatment of hypersensitivity reactions (*e.g. epinephrine, antihistamines and glucocorticoids*), should be available for immediate use in the event of an allergic reaction during administration of rituximab.
- If anaphylaxis or any other serious hypersensitivity/infusion reaction occurs,
  - administration of rituximab should be stopped immediately, and
  - appropriate medical management should be initiated
- Patients with pre-existing cardiac conditions and those who experienced prior cardiopulmonary adverse reactions should be closely monitored.
- The prescribing information for MabThera is being updated to include this information

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Further information on the safety concern

Available details of the spontaneous post marketing reports of fatal infusion related reactions are presented below:

- A 62 yr old male with a history of pericardial effusion and sleep apnoea syndrome developed shortness of breath and weakness in his extremities after the fifth course of rituximab. The patient progressed into cardiorespiratory arrest. CPR was unsuccessful. The patient was pronounced dead at the hospital.

- A 51 yr old female with a history of aortic valve incompetence experienced an anaphylactic reaction during the second infusion of the first course of rituximab. The patient was transferred to the ICU where her medical condition temporarily improved. However she subsequently developed possible gastrointestinal or lung bleeding with hemodynamic decompensation. The patient died the same day.

- Two other patients (a 46 yr old female and a 29 yr old male) died on the day of a rituximab infusion. Although no symptoms suggestive of an anaphylactic reaction were reported for either patient, based on the temporal relationship of the infusion and death, infusion related reactions could not be ruled out.

Information regarding severe infusion related reactions associated with treatment with rituximab for RA previously has been provided in the prescribing information.

The Dosage and Administration and Special Warnings and Precautions for Use sections of the prescribing information for rituximab is being updated to reflect the new safety information.

In the Dosage and Administration section, specific information on pre-medication for RA patients will be added:

- Premedication consisting of an analgesic/anti-pyretic (*e.g. paracetamol*) and an anti-histaminic drug (*e.g. diphenhydramine*) should always be administered before each infusion of MabThera.

- Premedication with glucocorticoids should also be administered in order to reduce the frequency and severity of infusion-related reactions. Patients should receive 100 mg IV methylprednisolone to be completed 30 minutes prior to each MabThera infusion

In the Warnings and Precautions for Use Section, information on reports of fatal infusion reactions in the post marketing setting, as well as clarifications for use of pre-medication prior to infusion of rituximab for RA, will be added.

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Call for Reporting

Please report any suspected adverse events occurring with the use of rituximab to the Adverse Drug Reaction Monitoring Unit of the Hong Kong Department of Health by phone at 2319-8633, by facsimile at 2147-0457, by e-mail to adr@dh.gov.hk or mailed to the Department of Health, 392 Nam Cheong Street, Kowloon, Hong Kong.
Alternatively, suspected adverse events may be reported to Roche at 2733-4711.

For further information or any questions on anaphylactic or serious hypersensitivity reactions associated with the use of rituximab, please contact our sales representatives.

Thank you for your kind attention.

Yours sincerely,
For and on behalf of
Roche Hong Kong Limited

Anny Lau
Director, Specialty Business Unit

Qingyong Dai
Medical Director