JANUARY 2013, No. 9

Reaksi

DRUG SAFETY NEWS

NATIONAL DRUG SAFETY MONITORING CENTRE, NPCB

Mission: This publication provides information and recommendations to healthcare professionals to enhance communication of drug safety updates, raise awareness of adverse drug reactions reported, and stimulate additional adverse drug reaction reporting. It is a newsletter published bimonthly by the National Drug Safety Monitoring Centre, National Pharmaceutical Control Bureau (NPCB), Malaysia.

TO REPORT AN ADVERSE DRUG REACTION

Online

1. Visit www.bpfk.gov.my.
2. Click on ADR Reporting and Product Complaints.
3. Click to report as a healthcare professional via online or hardcopy.
4. Submit the form once completed.

Mail

1. Print out ADR form available on website and complete it.
2. Mail or fax to:
   The National Drug Safety Monitoring Centre, Centre for Post-Registration of Products, National Pharmaceutical Control Bureau, Ministry of Health PO Box 319, Jalan Sultan, 46730 Petaling Jaya, Selangor.

Telephone
03-78835400

Fax
03-79567151

In This Issue:

Follow-up Communication: Pradaxa® (dabigatran etexilate): New Contraindication in Patients with Prosthetic Heart Valve Replacement

In the previous issue of Reaksi (November 2012), NPCB reported that Pradaxa® (dabigatran etexilate) is not recommended for use in patients with prosthetic heart valves following the termination of the post-surgical arm of the RE-ALIGN trial (a **R**andomised, phase II study to **E**valuate the s**A**fety and pharmacokinetics of ora**L** dabI**G**atran etexilate in patients after heart valve replaceme**N**t). This warning has now been strengthened to a **contraindication**.

Boehringer Ingelheim (Malaysia) Sdn. Bhd. in discussion with NPCB issued a Direct Healthcare Professional Communication (DHPC) on this matter and the package insert will also be revised to incorporate these new safety updates.

In Malaysia:
Since its registration in 2009, 58 reports on adverse events related to dabigatran have been received. However, none reported on the use in patients with prosthetic heart valves. NPCB will continue to monitor the safety profile of dabigatran etexilate.

Advice for healthcare providers:
- Pradaxa® must not be used in patients with prosthetic heart valves requiring anticoagulant treatment.
- Assess renal function prior to initiation of Pradaxa® and monitor at every follow-up appointment. Dosage adjustment should be made in patients with renal impairment.
- Counsel patients to seek medical attention immediately if they have signs or symptoms of bleeding, or any other adverse effect that bothers them.
- The guideline and checklist on prescribing and dispensing dabigatran should be used by all Ministry of Health facilities (Reference: KKM-55/BPF/104/001/02 JLD. 13(8), 14 November 2012).

MabThera® (rituximab)-Associated Toxic Epidermal Necrolysis (TEN) and Stevens-Johnson Syndrome (SJS)

MabThera® is a monoclonal antibody indicated for the treatment of non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukaemia (CLL), and severe active rheumatoid arthritis.

In January 2013, Roche (Malaysia) Sdn. Bhd. in discussion with NPCB issued a Direct Healthcare Professional Communication (DHPC) to alert and update healthcare professionals on the association of MabThera® with severe skin reactions such as Toxic Epidermal Necrolysis (TEN) and Stevens-Johnson Syndrome (SJS). The 'Special Warnings and Precautions For Use' as well as 'Undesirable Effects' sections of the local package insert for Mabthera® is also being updated with this new information.

Cases of TEN and SJS, some fatal, have been reported rarely in patients treated with MabThera® for haematological malignancies and autoimmune disorders, with first-time use or with subsequent infusions. The onset of reaction ranged from the day of dosing up to four months after the dose. Four of the cases reported occured on or the day after MabThera® dosing.

In Malaysia:
The NPCB has received 39 reports consisting of 74 adverse events related to rituximab since 2004. However, there were no reports on TEN or SJS. 9 reports (23%) and 17 events involved skin reactions (rash, itching and erythema). All these reactions occurred within 1 hour to 2 days post-infusion with doses ranging from 500-700mg.

Advice for healthcare providers:
- If severe skin reactions occur during MabThera® treatment, the drug should be discontinued.
- Patients should be counseled to seek medical attention immediately if they suffer from any adverse effect.

Tredaptive®/ Pelzont®/ Trevaclyn® (nicotinic acid/ laropiprant): Suspension of Dyslipidaemia Drug in the European Union

On 11 January 2013, the European Medicines Agency (EMA) recommended the suspension of Tredaptive®, Pelzont®, and Trevaclyn® following study results which indicate the benefits of taking this product no longer outweigh the risks.

Tredaptive®, Pelzont®, and Trevaclyn® are identical products marketed by Merck Sharp & Dohme (MSD) Ltd. under these different trade names in Europe.

This product is an extended-release tablet containing 1000mg nicotinic acid and 20mg laropiprant, for the treatment of dyslipidaemia particularly in patients with combined mixed dyslipidaemia or primary hypercholesterolaemia.

The HPS2-THRIVE study (**H**eart **P**rotection **S**tudy **2**-**T**reatment of **H**DL to **R**educe the **I**ncidence of **V**ascular **E**vents) involved over 25,000 patients aged between 50-80 years with a history of heart disease, stroke, or other circulatory disease. It was conducted in almost 250 hospitals in 6 countries, with the aim of assessing the effect of adding nicotinic acid / laropiprant to simvastatin (with or without ezetimibe) on a composite endpoint of major vascular events such as heart attack, stroke, and revascularisation.

Results from this study showed that taking nicotinic acid / laropiprant together with a statin did not significantly reduce the risk of major vascular events compared with statin therapy alone. In addition, non-fatal but serious side effects occurred more frequently in patients taking this product, such as bleeding, infections, and new-onset diabetes.

MSD Ltd. has taken measures to suspend the availability of nicotinic acid / laropiprant worldwide, including recommending that physicians stop prescribing the drug, and review patients currently on this drug to discontinue the treatment in a timely manner. The company also advised patients to consult their doctor to review their treatment.

In Malaysia:
This product is **not registered** in Malaysia. The registration application in 2008 was rejected due to insufficient data on efficacy and long-term safety, including cardiovascular risks, hepatic injury and psychiatric adverse events. An appeal in 2010 was also rejected by the Minister of Health, Malaysia.