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Reaksi

DRUG SAFETY NEWS

NATIONAL CENTRE FOR ADVERSE DRUG REACTION MONITORING, 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 Centre for Adverse Drug Reaction Monitoring, 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:
   National Centre for Adverse Drug Reaction Monitoring, 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:

Pradaxa® (dabigatran etexilate): Early Termination of Post-surgery Arm of the RE-ALIGN Trial

Pradaxa® (dabigatran etexilate) is an anticoagulant indicated for the primary prevention of venous thromboembolic events in adults who have undergone elective total hip replacement surgery or total knee replacement surgery. It is also indicated for reduction of the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation.

The RE-ALIGN trial (a **R**andomised, phase II study to **E**valuate the s**A**fety and pharmacokinetics of ora**L** dab**IG**atran etexilate in patients after heart valve replaceme**N**t) was started in October 2011 with the objective to validate the dosing algorithm of dabigatran compared to warfarin in post-surgical (Population A, recent surgery group) and medical patients (Population B, more than 3 months post-surgery group) with prosthetic heart valve replacement.

An interim analysis of RE-ALIGN based on the first 246 patients enrolled into the trial showed that the current dosing regimen did not achieve the projected plasma levels of dabigatran in Population A patients and there was an excess of clinical ischaemic events, especially stroke. Hence, the Population A arm of RE-ALIGN was terminated. Given that the Population B had an exposure within the projected range with the current dosing algorithm and there was no clinically important disparity of clinical ischaemic events as of the date of this communication, the Population B arm was continued in the study.

These findings do not affect the use of Pradaxa® for the current approved indications as mentioned above. As the review and follow-up of subjects is still ongoing, this issue will continue to be monitored by the NPCB and further updates will be provided in the next issue of Reaksi.

Advice for healthcare providers:

- The safety and efficacy of Pradaxa® in preventing thromboembolic complications in patients with prosthetic heart valves has not been demonstrated. Therefore, healthcare providers are reminded not to use Pradaxa® in these patients.

Gilenya® (fingolimod hydrochloride): Risk of Cardiovascular Events

Gilenya® (fingolimod hydrochloride) 0.5mg capsule is the first orally formulated drug for the treatment of patients with relapsing forms of Multiple Sclerosis (MS) to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.

Gilenya®, in controlled studies, was shown to induce a dose-dependent reduction in heart rate and has been associated with atrioventricular (AV) conduction delays including 1st or 2nd degree AV block following administration of the initial dose. However, following a post-marketing report on an unexplained sudden death of a patient in the United States within 24 hours of taking Gilenya® for the first time, it was then found that the maximum heart rate lowering effect of Gilenya® which usually occurs within 6 hours of the first dose may occur as late as 24 hours after the first dose in some patients.

For this reason, Gilenya® is now contraindicated in patients with certain pre-existing or recent (within last 6 months) heart conditions or stroke, or who are taking certain antiarrhythmic drugs.

Advice for healthcare providers:

- After the first dose of fingolimod, observe all patients for 6 hours for signs and symptoms of bradycardia with hourly pulse and blood pressure measurement. Obtain in all patients an ECG prior to dosing, and at the end of the observation period.
- Patients with some pre-existing heart conditions should have a cardiac evaluation done and, if treated with GILENYA, should be monitored overnight with continuous ECG in a medical facility after the first dose.
- Patients with a prolonged QT interval (>450 msec males, >470 msec females) before dosing or during 6 hour observation, or at additional risk for QT prolongation, or on concurrent therapy with QT prolonging drugs with a known risk of Torsades de pointes should be monitored overnight with continuous ECG in a medical facility after the first dose.
- Use with caution in patients receiving concurrent therapy with drugs that slow heart rate.
- Any adverse events suspected to be associated with the use of fingolimod should be reported to the National Centre for ADR Monitoring, NPCB.

Victrelis® (boceprevir): Drug Interactions With Ritonavir-boosted HIV Protease Inhibitors

Victrelis® 200mg capsule (boceprevir) is a protease inhibitor which is approved for the treatment of chronic hepatitis C (CHC) genotype 1 infection, in combination with peginterferon alpha (PegIFNα)/ribavirin (RBV), in adult patients (18 years and older) with compensated liver disease, including cirrhosis, who are previously untreated or who have failed previous therapy.

Based on a drug interaction study in healthy volunteers carried out by Merck Sharp and Dohme, the product holder found that blood levels of ritonavir-boosted human immunodeficiency virus (HIV) protease inhibitors (atazanavir, darunavir, lopinavir) were markedly lower than expected when given with Victrelis®. It was also found that blood levels of Victrelis® were markedly lower than expected when given with ritonavir-boosted darunavir or lopinavir, although this effect was not seen with ritonavir-boosted atazanavir. These interactions could potentially reduce the effectiveness of these drugs if used together.

Subsequently, new recommendations on the co-administration of Victrelis® with the different ritonavir-boosted HIV protease inhibitors were included in the package insert of Victrelis®.

Advice for healthcare providers:

- Avoid co-administration of Victrelis® with ritonavir-boosted darunavir or lopinavir.
- Obtain complete blood counts before treatment, at Treatment Weeks 4, 8 and 12 and closely monitor when clinically indicated.
- Any adverse events suspected to be associated with the use of boceprevir should be reported to the National Centre for ADR Monitoring, NPCB.