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Reaksi

DRUG SAFETY NEWS

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.

This is a bimonthly publication by the National Pharmaceutical Regulatory Agency (NPRA), Malaysia.

TO REPORT AN ADVERSE DRUG REACTION

Online

1. Visit http://npra.moh.gov.my.
2. Click on ADR Reporting.
3. Click to report as a healthcare professional and print out the ADR form.
4. Scan and submit the completed form via email to fv@bpfk.gov.my.

Mail

1. Print out and complete the ADR form available from our website.
2. Mail or fax to:
   The National ADR Monitoring Centre, Centre for Post Registration of Products, National Pharmaceutical Regulatory Agency, Ministry of Health, PO Box 319, Jalan Sultan, 46730 Petaling Jaya, Selangor.

Telephone

03-7883 5400
(ext. 8460/ 8461/ 8463)

Fax

03-7956 7151

In This Issue:

Editor's Note: *In this issue of Reaksi, we would like to highlight safety signals which are currently under review by the NPRA. These signals involve potential safety issues which are being investigated further, and do not mean that the NPRA has concluded there is a problem with the product/ drug. These articles aim to increase awareness among healthcare professionals and stimulate ADR reporting, particularly of any reactions related to the safety issues below.*

Proton Pump Inhibitors (PPIs): Potential Long-term Safety Issues

Overview

Proton pump inhibitors (PPIs) have long been considered a safe and well-tolerated drug class. However, there are emerging concerns on the safety of PPIs, particularly associated with long-term use. **Overutilisation** of PPIs is known to occur worldwide, in both in-patient and outpatient settings.

PPIs are widely used for the treatment of gastro-oesophageal reflux disease (GERD), *Helicobacter pylori* eradication, stress ulcer prophylaxis, as well as the prophylaxis of gastrointestinal bleeding in patients on non-steroidal anti-inflammatory drugs (NSAIDS) or dual antiplatelet therapy post-percutaneous coronary intervention.

The NPRA is currently reviewing several potential safety issues which have been linked to PPI use, including the risk of subacute cutaneous lupus erythematosus (SCLE), hypomagnesaemia, fractures, dementia, and rhabdomyolysis. It should be noted that some of these issues were described in epidemiological studies, and **no causal link** has been established. The results of this review and any risk minimisation action required will be communicated once the review is completed.

Local Scenario

There are 72 products containing PPIs registered in Malaysia currently, namely 58 oral products and 14 injectables. The types of PPIs registered are omeprazole (30 products); pantoprazole (22); lansoprazole (11); esomeprazole (4); rabeprazole (3); and dexlansoprazole (2). Data from the National Medicines Utilisation Survey and IMS Health Malaysia Sdn. Bhd. revealed that omeprazole was the most commonly used PPI in Malaysia in 2014 (3.449 DDD/1000 population/day), followed by esomeprazole (1.470 DDD/1000 population/day).

Adverse Drug Reaction Reports

The NPRA Malaysian ADR database contains 468 reports (823 adverse events) suspected to be due to PPIs reported between year 2000- June 2015. Majority of the reports involved ADRs occurring within 2 weeks of starting the PPI. Only 7% (33 reports) stated a time to onset of reaction of more than 2 weeks, with ADRs including itching, maculopapular rash, abdominal discomfort, and Stevens-Johnson syndrome/ toxic epidermal necrolysis (SJS/TEN) overlap.

A search of the WHO International ADR database* revealed reported adverse events involving the potential safety issues under NPRA review, such as SCLE, hypomagnesaemia, osteoporosis fracture, *C. difficile* infection, and dementia. Details of these reports will be further considered as part of the review.

***DISCLAIMER:** The information in the WHO ADR database comes from a variety of sources, and the likelihood that the suspected adverse reaction is drug-related is not the same in all cases. This information does not represent the opinion of WHO.*

Advice for Healthcare Professionals

- Please review each individual patient's need for PPI therapy at every follow-up, use 'on-demand' or 'step-down' therapy, and discontinue any unnecessary PPIs.
- Monitor patients for possible long-term ADRs, including photosensitive dermatosis with arthralgia, cognitive impairment, falls or fractures.
- Please report all suspected ADRs associated with PPI use to the National ADR Monitoring Centre, including ADRs following long-term use.

Paliperidone Palmitate: Alert on Potential Serious Adverse Events

Overview

The NPRA would like to highlight international reports of cardiac arrest and sudden death suspected to be related to Invega Sustenna® (paliperidone palmitate), and remind healthcare professionals of the potential risk of prolonged QT interval when this product is used concomitantly with:

(i) paliperidone in other dosage forms
(ii) risperidone
(iii) other anti-psychiatric drugs

Invega Sustenna® is a long-acting injectable psychotropic agent, approved in Malaysia for the treatment of schizophrenia and for the prevention of recurrence of symptoms of schizophrenia. Paliperidone palmitate is hydrolysed to paliperidone, which is also the active metabolite of risperidone.

Background of safety concern

Cases of cardiac arrest and sudden death suspected to be related to paliperidone palmitate were highlighted by the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) and the Taiwan Food and Drug Administration (TFDA). The 'Precautions' section in the Japanese package insert has been strengthened with additional information on this safety issue.

A review by the NPRA concluded that there was currently no new safety issue identified from these cases, as the mortality reporting rates were within the expected range for the schizophrenia population. No changes to the package insert have been requested by international regulatory authorities other than PMDA.

Local Scenario

There are currently **five (5)** products containing paliperidone palmitate registered with the Drug Control Authority. Paliperidone palmitate preparations are listed in the Ministry of Health (MOH) Drug Formulary under category A* (only to be initiated by consultants for specific indications) for second or third line treatment of acute and maintenance treatment of schizophrenia in adults.

Adverse Drug Reaction Reports

Since the products were first registered in Malaysia in year 2010, the National ADR Monitoring Centre has received **45 reports** related to paliperidone palmitate with 73 adverse events. **None** of the cases involved death or serious cardiovascular adverse events.

The most frequently reported adverse events were medication ineffective, marked restlessness, and injection site reactions (pain, swelling, and erythema).

Advice for Healthcare Professionals[3]

- Use caution when Invega Sustenna® is co-administered with risperidone or oral paliperidone for extended periods of time.
- There is limited safety data on the use of Invega Sustenna® with other antipsychotics.
- Stay alert for any adverse reactions or drug interactions as the drug remains in the body for up to four (4) months after administration.
- In order to help NPRA better investigate this issue, please report all adverse events associated with paliperidone palmitate-containing products to the National ADR Monitoring Centre.

References:

1. Japan PMDA Blue Letter (2014). Fatal cases with Xeplion Aqueous Suspension for IM Injection. No. 14-01.
2. Taiwan FDA Safety Communication Letter: Paliperidone Palmitate (2016). No. 1051403185.