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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 Drug Safety Monitoring Centre, National Pharmaceutical Control Bureau (NPCB), Malaysia.

In This Issue:

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 Drug Safety Monitoring Centre,
   National Pharmaceutical Control Bureau,
   Ministry of Health
   PO Box 319, Jalan Sultan,
   46730 Petaling Jaya,
   Selangor.

Telephone

03-78835400
(ext. 5542/ 8461 / 8463)

Fax

03-79567151

Zithromax®/ Zmax® (azithromycin): Risk of Potentially Fatal Irregular Heart Rhythms

A study published in the New England Journal of Medicine (NEJM) 2012 by Ray, Murray, Hall *et al.* suggested a higher risk of death from cardiovascular or other causes in patients treated with a 5-day course of oral azithromycin compared to those treated with amoxycillin, ciprofloxacin, or no antibacterial drug. In addition, a study was conducted by the product manufacturer to assess the effects of azithromycin on the QT interval in adults, with results showing that the drug prolonged the QTc interval.

The Zithromax® and Zmax® local package inserts mention the risk of developing QT interval prolongation and arrhythmias during treatment with azithromycin and other macrolides, under the sections 'Special Warnings and Precautions For Use' as well as 'Undesirable Effects'.

On 12 March 2013, the U.S. Food and Drug Administration (FDA) issued a safety announcement warning the public on the risk of azithromycin causing abnormal changes in the electrical activity of the heart which may lead to potentially fatal heart rhythms. The European Medicines Agency (EMA) is also considering strengthening the warnings about this risk in the prescribing information for azithromycin.

In Malaysia

Currently, there are 26 registered products containing azithromycin. Since the year 2000, the NPCB has received 181 reports related to azithromycin. Ten (10) reports were related to heart rate and rhythm disorders, with the following events reported: palpitation (3), tachycardia (3), arrhythmia, bradycardia, heart block, supraventricular tachycardia, and ventricular tachycardia (1 each). This issue will be monitored closely to decide if these warnings need to be further strengthened.

Advice to healthcare providers:

- The risk of *torsades de pointes* and fatal arrhythmia should be considered when choosing between azithromycin and other antibacterial drugs, especially for patients who are at higher risk of cardiovascular events.
- The potential risk of QT prolongation should be weighed against the side effects of alternative drugs, which may also cause QT prolongation or cause other significant adverse effects.
- Patients should be advised to seek immediate medical attention if they experience an irregular heartbeat, shortness of breath, dizziness or fainting while taking azithromycin.
- Any adverse event suspected to be associated with the use of azithromycin, even those which are common or well-known, should be reported to the National Drug Safety Monitoring Centre, NPCB.

Botulinum Toxin Products: Rare but Serious Risk of Distant Toxin Spread & Non-Interchangeability of Products

Botulinum toxin is a neurotoxin produced by the bacteria *Clostridium botulinum*. Two types of botulinum toxin (type A and B) are available for therapeutic and cosmetic use (upper facial rhytides, since 2010).

In Malaysia, 2 products containing botulinum toxin type A are registered, i.e. Botox® (MAL19970915A) manufactured by Allergan Pharmaceuticals Ireland, and Dysport® (MAL1998071709A) manufactured by Ipsen Biopharm Limited, United Kingdom (UK). Kindly refer to the individual package insert for detailed indications. No botulinum toxin type B is registered locally.

Distant Toxin Spread

The Drug Safety Monitoring Centre, NPCB would like to remind healthcare professionals about the rare but serious risk of distant toxin spread in the use of botulinum toxin products.

Botulinum toxin may spread from injection site to produce symptoms consistent with botulism. The symptoms that may occur include muscle weakness, aspiration/aspiration pneumonia, respiratory depression, dysphagia, dysphonia, blurred vision, ptosis and diplopia. Children treated for spasticity face higher risk for these symptoms. Nevertheless, symptoms can also occur in adults treated for spasticity and other conditions, and are treated with high doses.

Non-Interchangeability of Products

Furthermore, healthcare professionals are also reminded that botulinum toxin products are **not interchangeable** because these products differ from one another in its specific indications and strength. Their clinical doses are expressed in units. The units of one product cannot be converted into units of another product. In addition, these products are derived from different *Clostridium* strains, produced by different manufacturing processes and are obtained by different techniques.

Local Scenario

Since the year 2000, a total of 12 reports involving botulinum toxin products have been received with reported reactions of injection site pain/erythema, medication ineffectiveness, rash maculo-papular and itching. Only one reported toxin-spread related symptoms. The report involved a 4-year-old cerebral palsy boy who was given 160 IU Dysport®. Five (5) hours later, he experienced breathing difficulty and fever. At the time of reporting, patient had not recovered. The causality given was C3 (possibly-related).

Side effects related to distant toxin spread are addressed in the Botox® and Dysport® local package inserts. Healthcare professionals should report any adverse event suspected to be associated with the use of botulinum toxin to aid a better monitoring of its safe use in Malaysia.

Advice to healthcare providers:

- Botulism-like side effects may occur beyond the injection site with symptoms of swallowing and breathing difficulties which may be life-threatening.
- Botulinum toxin should be used with caution in patients with underlying neurological disorders, or a history of dysphagia and aspiration.
- Patients should be advised to seek immediate medical attention if they experience difficulty swallowing or talking, trouble breathing or muscle weakness following treatment with botulinum toxin.
- Each botulinum toxin product has its specific indications and strength. Hence, it is **not interchangeable** with other botulinum toxin products.