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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.

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:
   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

Volibris® (ambrisentan): Contraindication In Patients With Idiopathic Pulmonary Fibrosis (IPF)

Volibris® (ambrisentan) is a selective endothelin A (ET_A) receptor antagonist indicated for the treatment of patients with pulmonary arterial hypertension (PAH) classified as WHO functional class II and III, to improve exercise capacity. Efficacy has been shown in idiopathic PAH (IPAH) and in PAH associated with connective tissue disease.

The product holder of Volibris®, GlaxoSmithKline Pharmaceuticals Sdn Bhd distributed a Direct Healthcare Professional Communication (DHPC) letter in discussion with NPCB regarding the new contraindication of Volibris® in patients with idiopathic pulmonary fibrosis (IPF), with or without secondary pulmonary hypertension.

The decision was based on the result of a prematurely discontinued study (ARTEMIS-IPF) conducted to evaluate safety and effectiveness of ambrisentan in IPF as the predetermined primary efficacy endpoint could not be met. Evaluation of the primary endpoint components indicated that there were higher rates of respiratory hospitalisations, mortality events and decreases in respiratory function in the ambrisentan group versus placebo. This safety update will be included in the package insert.

In Malaysia:
Currently, there are 2 ambrisentan-containing products registered in Malaysia, i.e. Volibris® film-coated tablets at the strength of 5mg and 10mg. Since its registration in March 2010, the National Centre for ADR Monitoring has received only 1 report related to ambrisentan with the adverse drug reaction reported as increased hepatic enzymes.

Advice for healthcare providers:
- Ambrisentan is contraindicated in patients with idiopathic pulmonary fibrosis (IPF), with or without secondary pulmonary hypertension.
- Any adverse events suspected to be associated with the use of ambrisentan should be reported to the National Centre for ADR Monitoring, NPCB.

Prolia® (denosumab): Risk of Atypical Femoral Fracture

Prolia® (denosumab) is indicated for the treatment of osteoporosis in postmenopausal women at increased risk of fracture. In postmenopausal women with osteoporosis, Prolia® increases bone mineral density (BMD) and reduces the incidence of hip, vertebral and non-vertebral fractures. Prolia® is also indicated for the treatment of bone loss in patients undergoing hormone ablation for prostate cancer or aromatase inhibitor treatment for breast cancer. In patients with prostate cancer, Prolia® reduces the incidence of vertebral fractures.

GlaxoSmithKline Pharmaceuticals Sdn Bhd, the product holder, issued a Direct Healthcare Professional Communication (DHPC) letter in discussion with NPCB to inform on the cases of atypical femoral fractures. These were identified in participants of an ongoing open-label extension study of the pivotal phase 3 trial in postmenopausal osteoporosis (FREEDOM). However, these events have occurred *very rarely (<1/10,000)* based on 31,266 subject-years exposed to Prolia® in bone loss studies. This safety update will be included in the package insert.

In Malaysia:
There are 2 denosumab-containing products registered in Malaysia, i.e. Prolia® solution for injection 60mg vial and 60mg prefilled syringe. It was approved on February 23, 2012 and no ADR report has been received to date.

Advice for healthcare providers:
- Atypical femoral fractures have been reported in patients receiving Prolia®.
- Educate patients to report new or unusual thigh, hip or groin pain.
- Evaluate patients presenting with such symptoms for an incomplete femoral fracture and examine the contralateral femur.
- Any adverse events suspected to be associated with the use of denosumab should be reported to the National Centre for ADR Monitoring, NPCB.

Case Report: Zometa® (zoledronic acid) Associated Osteomyelitis

A 37-year old female received Zometa® 4mg every 3 weekly for breast cancer with bone metastasis. She had a history of exposure to chemotherapy drugs including doxorubicin, cyclophosphamide, trastuzumab, paclitaxel and anastrozole. After receiving Zometa® for approximately one and a half years, she complained of growth in her upper gums. Upon referral to a dentist, she was diagnosed with osteomyelitis of the jaw and assessed as possibly due to Zometa®. The patient recovered 4 months after discontinuation of Zometa®. Causality assessment by the MADRAC was possibly-related.

Osteonecrosis of the jaw (ONJ) is a known serious adverse drug reaction which has been reported predominantly in cancer patients treated with bisphosphonates, including Zometa®. Secondary events such as dental infection, injection of local anaesthetics with vasoconstrictors and trauma can add further complications to the disease process and chronic non-pus forming bone infection osteomyelitis can also be associated with ONJ.

In Malaysia:
There are no reports for Zometa®-associated ONJ. However, 2,508 reports on osteonecrosis of the jaw and 913 reports on osteomyelitis associated with Zometa® have been reported to the WHO Uppsala Monitoring Centre, Sweden*.

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

Advice for healthcare providers:
- Patients must be informed to seek medical attention if they develop toothache, jaw pain, loosening of teeth, gum swelling or any signs of mouth infection.
- Educate patients to maintain good oral hygiene and regular dental check-ups.
- Consider patients with concomitant risk factors (e.g. cancer, chemotherapy, corticosteroids, and poor oral hygiene) for dental examination, with appropriate preventive dentistry, before initiating bisphosphonate treatment.
- During bisphosphonate treatment, patients with concomitant risk factors should avoid invasive dental procedures if possible. For patients who develop ONJ during bisphosphonate treatment, dental surgery may exacerbate the condition.