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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 National 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 National Drug Safety Monitoring Centre, Centre for Post-Registration of Products, National Pharmaceutical Control Bureau, Ministry of Health
   P O Box 319, Jalan Sultan,
   46730 Petaling Jaya,
   Selangor.

Telephone
03-78835400

Fax
03-79567151

Prolia® and Xgeva® (denosumab): Association with Risk of Anaphylactic Reactions and Atypical Femoral Fractures

Denosumab is a human IgG2 monoclonal antibody that inhibits nuclear factor kappa-B ligand (RANKL). In blocking RANKL on the surface of osteoclasts, denosumab inhibits the formation, function, and survival of osteoclasts which leads to decreased bone resorption and increased bone mass and strength in the cortical and trabecular bone. In addition, osteoclasts affect bone pathology in solid tumors with osseous metastases.

Prolia® (denosumab 60mg) is registered for the indication of postmenopausal osteoporosis and bone loss in patients undergoing hormone ablation for cancer. At a higher strength, Xgeva® (denosumab 120mg) is indicated for the prevention of skeletal related events in patients with bone metastases from solid tumours.

In March 2013, Dear Healthcare Professional Communication (DHPC) letters were issued regarding spontaneous reports on the risk of anaphylactic reaction and atypical femoral fracture.

Risk of Anaphylactic Reactions
In worldwide postmarketing settings, two cases of anaphylactic reactions were identified in patients taking Prolia® and five for Xgeva®. All were considered causally related to Prolia® or Xgeva®. No fatal outcomes were observed.

Risk of Atypical Femoral Fracture
Atypical femoral fractures are subtrochanteric or proximal diaphyseal fractures that occur with little or no trauma determined by specific radiographic findings.

For Xgeva®, a single case of atypical femoral fracture has been reported in the open label extension phase of an ongoing clinical trial of Xgeva® in men with hormone-refractory prostate cancer.

In Malaysia:
The National Drug Safety Monitoring Centre has not received any reports for both Prolia® and Xgeva®. The safety profile of denosumab-containing products will continuously be monitored.

Advice for healthcare providers:
- Hypersensitivity to denosumab is a contraindication for use of Prolia® and Xgeva®.
- Advice patients to report new or unusual thigh, hip, or groin pain.
- Evaluate patients presenting with such symptoms for an incomplete femoral fracture, and the contralateral femur should also be examined.
- Any adverse events suspected to be associated with the use of denosumab should be reported to the National Drug Safety Monitoring Centre, NPCB.

Invirase® (saquinavir): Removal of Paediatric Dosing Recommendation Due To Potential for QT and PR Interval Prolongation

Invirase® (Saquinavir) is available as both film-coated tablet 500mg and hard-gelatin capsule 200mg. It is a protease inhibitor indicated for the treatment of HIV-1-infected adult patients which should only be given in combination with ritonavir and other antiretroviral medicinal products

The product holder, Roche had voluntarily removed paediatric dosage recommendations and the references to paediatric use from the United States prescribing information. The decision followed paediatric clinical trials with Invirase® boosted with ritonavir.

Although no cases of QT prolongation were observed during paediatric studies, saquinavir steady-state exposures observed in paediatric patients in the trial were substantially higher than historical data in adults where both dose- and exposere- QTc and PR prolongation was shown.

Modeling and simulation assessment of pharmacokinetic/ pharmacodynamic (PK/PD) relationships in paediatric subjects suggest that reducing the Invirase® dose to minimise risk of QT prolongation is likely to reduce antiviral efficacy. In addition, no clinical efficacy data are available at Invirase® doses less than 50mg per kg in paediatric subjects.

Therefore, paediatric dose recommendations that are both reliably effective and below thresholds of concern with respect to QT and PR prolongation could not be determined.

In Malaysia:
Invirase® is indicated for adults and adolescents **over the age of 16** years. To date, no ADR reports on Invirase® have been received.

Advice for healthcare providers:
- **Do not** prescribe Invirase® in paediatric patients below 16 years of age.
- Ritonavir-boosted Invirase® is **contraindicated**:
  - in patients with congenital or documented acquired QT prolongation, and electrolyte disturbances particularly uncorrected hypokalemia.
  - with some drugs (eg. amiodarone, flecainide, propafenone) that have both pharmacokinetic interactions and prolong the QT and/or PR interval.
- Any adverse events suspected to be associated with the use of Invirase® should be reported to the National Drug Safety Monitoring Centre, NPCB.