Dear Healthcare Professionals,

**Denosumab (Xgeva) for giant cell tumour of bone: risk of clinically significant hypercalcaemia following discontinuation**

Your attention is drawn to the Medicines and Healthcare products Regulatory Agency’s (MHRA) announcement that cases of rebound hypercalcaemia have been reported up to 9 months after cessation of treatment. Healthcare professionals should monitor patients for signs and symptoms of hypercalcaemia after discontinuation of denosumab treatment for giant cell tumour of bone.

Cases of clinically significant hypercalcaemia requiring hospitalisation and complicated by acute renal injury have been reported in a clinical trial of adults and skeletally mature adolescents with giant cell tumour of bone. Cases of rebound hypercalcaemia were reported up to 9 months after discontinuation of denosumab. Cases have also been through some national adverse drug reaction reporting schemes. No Yellow Cards have been received of this suspected adverse drug reaction with denosumab in the UK, but continued vigilance is recommended.

The Summary of Product Characteristics for Xgeva has been updated to include risk of hypercalcaemia following discontinuation of treatment for giant cell tumour of the bone. This adverse event is thought to occur uncommonly, with an estimated frequency of occurring in fewer than 1 in every 100 patients receiving denosumab. Symptoms of hypercalcaemia include excessive thirst, fatigue, drowsiness, confusion, loss of concentration, depression, nausea, vomiting, constipation, and muscle and/or bone pain.

Clinically significant hypercalcaemia is a known risk after stopping denosumab treatment in patients with growing skeletons; denosumab is not recommended in this patient group.
Healthcare professionals are advised:

- cases of clinically significant hypercalcaemia (rebound hypercalcaemia) have been reported up to 9 months after discontinuation of denosumab treatment for giant cell tumour of bone
- monitor patients for signs and symptoms of hypercalcaemia after discontinuation, consider periodic assessment of serum calcium, and re-evaluate the patient’s calcium and vitamin D supplementation requirements
- advise patients to report symptoms of hypercalcaemia
- denosumab is not recommended in patients with growing skeletons
- report any suspected adverse reactions to denosumab or other medicines on a Yellow Card

Please refer to the following website in MHRA for details:

In Hong Kong, Xgeva Solution for Injection 120mg (HK-61163) is a pharmaceutical product registered by Amgen Asia Holding Limited (Amgen), and is a prescription-only medicine. So far, the Department of Health (DH) has received 15 cases of adverse drug reaction related to denosumab, but these cases were not related to hypercalcaemia.

In Jun 2018, Amgen submitted an application for update of the product insert to include the safety information on hypercalcaemia following treatment discontinuation in patients with giant cell tumour of bone, and the application is currently being processed. The DH will remain vigilant on safety update of the product issued by other overseas drug regulatory authorities. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under “ADR Reporting”: http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office’s website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Joseph LEE)
for Assistant Director (Drug)

We build a healthy Hong Kong and aspire to be an internationally renowned public health authority