衞生署藥物辦公室
藥物註冊及進出口管制部
香港九龍南昌街 382 號公共衞生檢測中心三樓
2319 8458
電話號碼 Tel. No.:
詢問處 Enquiries (852) 2319 8456
傳真號碼 Faxline No. (852) 2803 4962
本署檔號 OUR REF.: DH DO PRIE/7-30/15
(來函請註明此檔案號碼)
(IN REPLY PLEASE QUOTE THIS FILE REF.)

DEPARTMENT OF HEALTH
DRUG OFFICE
DRUG REGISTRATION AND
IMPORT/EXPORT CONTROL DIVISION
3/F., Public Health Laboratory Centre,
382 Nam Cheong Street, Kowloon, Hong Kong

BY FAX

21 July 2015

Dr. Donald LI
President
Hong Kong Academy of Medicine
(Fax Number: 2505 5577)

Dear Dr. LI,

Denosumab (Xgeva, Prolia); intravenous bisphosphonates: osteonecrosis of the jaw - further measures to minimise risk

Your attention is drawn to the Medicines and Healthcare products Regulatory Agency's (MHRA) announcement regarding further measures to minimise risk of osteonecrosis (ONJ) of the jaw.

MHRA and other European Union (EU) medicines regulators have reviewed measures to minimise the risk of ONJ in patients taking denosumab or bisphosphonates.

Denosumab and bisphosphonates are used to treat osteoporosis, Paget's disease, and as part of some cancer regimens, particularly for metastatic bone cancer and multiple myeloma. Individual bisphosphonates and denosumab-containing medicines have different indications.

Osteonecrosis of the jaw (ONJ) is a known side effect of denosumab and bisphosphonates. To date, the MHRA has received 45 Yellow Card reports of ONJ in people taking denosumab (all doses) and 323 reports in people taking a bisphosphonate. In patients treated for osteoporosis (regardless of route of administration), the risk of ONJ is small compared with that in patients treated with the higher doses used for cancer-related conditions. Other drug-specific risk factors for ONJ include drug potency (higher risk for highly potent compounds such as zoledronate, pamidronate and denosumab), route of administration (higher risk for parenteral administration) and cumulative dose.

The review recommended introducing patient reminder cards for denosumab and intravenous bisphosphonates to inform patients of the risk of ONJ and precautions to take before and during treatment. The review of ONJ and denosumab also recommended that denosumab 120 mg should be contraindicated in patients with unhealed lesions from dental or oral surgery.

Healthcare professionals are advised of the following before prescribing denosumab or intravenous bisphosphonates:

- give patients the patient reminder card for their medicine
- explain the risk of osteonecrosis of the jaw and advise patients on precautions to take—advise patients to:
  - tell their doctor if they have any problems with their mouth or teeth before starting treatment; if they wear dentures they should make sure their dentures fit properly before starting treatment
  - maintain good oral hygiene and get routine dental check-ups during treatment
  - tell their doctor and dentist that they are receiving denosumab or an intravenous bisphosphonate if they need dental treatment or dental surgery

- tell their doctor and dentist immediately if they have any problems with their mouth or teeth during treatment (eg loose teeth, pain, swelling, non-healing sores or discharge)

- do not prescribe denosumab 120 mg (cancer indication) to patients with unhealed lesions from dental or oral surgery

Please refer to the MHRA's website for details:

https://www.gov.uk/drug-safety-update/denosumab-xgeva-prolia-intravenous-bisphosphonates-osteonecrosis-of-the-jaw-further-measures-to-minimise-risk

In Hong Kong, there are 3 registered pharmaceutical products containing denosumab, and 18 registered pharmaceutical products containing intravenous bisphosphonates, including 3 products containing ibandronic acid, 4 products containing pamidronate disodium, and 11 products containing zoledronic acid. All these products are prescription-only medicines.

News related to denosumab and zoledronic acid (which is a bisphosphonate) had been issued by the European Medicines Agency, and was posted on the Drug Office website on 14 and 28 March 2015. On 30 March 2015, DH issued letters to inform local healthcare professionals on the new risks of the products. So far, DH has received 3 cases of adverse drug reactions (ADR) related to denosumab, including 1 case with the adverse effect of osteonecrosis. DH has not received any ADR case related to intravenous bisphosphonates. In view of the MHRA announcement related to the new findings with denosumab 120 mg (which is now contraindicated in patients with unhealed lesions from dental or oral surgery), and with intravenous bisphosphonates, the matter will be discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board. 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 sincerely,

(Lilly HO)

for Assistant Director (Drug)