PHARMACY AND POISONS BOARD
HONG KONG
香港藥劑業及毒藥管理局

Your Ref. :
貴處檔號

Our Ref. : DH DO PRIE/1-55/1
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香港九龍南昌街382號
公共衞生檢測中心三樓

25th February 2016

To: Certificate holders of
registered pharmaceutical products

Dear Sirs / Madams,

New Safety Warnings for Denosumab and Intravenous Bisphosphonates

On 18th February 2016, the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee (the Committee) considered the latest overseas recommendations on denosumab and intravenous bisphosphonates with regard to the risk of osteonecrosis of the jaw, and decided that the sales pack labels and/or package inserts of pharmaceutical products containing denosumab and intravenous bisphosphonates should include the following new safety warnings:

a. For products containing **denosumab**:

Contraindication:

Denosumab 120mg should be contraindicated in patients with unhealed lesions from dental or oral surgery

b. For products containing **denosumab** and **intravenous bisphosphonates**

(including ibandronic acid, pamidronate disodium, and zoledronic acid):

Special warnings and precautions:

Osteonecrosis of the jaw (ONJ)

ONJ has been reported in the post-marketing setting in patients receiving [BRAND NAME].

The start of treatment or of a new course of treatment should be delayed in patients with unhealed open soft tissue lesions in the mouth. A dental examination with preventive dentistry and an individual benefit-risk assessment is recommended prior to treatment with [BRAND NAME] in patients with concomitant risk factors.

The following should be considered when evaluating a patient's risk of developing ONJ:

- Potency of the medicinal product that inhibits bone resorption (higher risk for highly potent compounds), route of administration (higher risk for parenteral administration) and cumulative dose of bone resorption therapy.

- Cancer, co-morbid conditions (e.g. anaemia, coagulopathies, infection), smoking.

- Concomitant therapies: corticosteroids, chemotherapy, angiogenesis inhibitors, radiotherapy to head and neck.

- Poor oral hygiene, periodontal disease, poorly fitting dentures, history of dental disease, invasive dental procedures, e.g. tooth extractions.

All patients should be encouraged to maintain good oral hygiene, undergo routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain or swelling, non-healing of sores or discharge during treatment with [BRAND NAME]. While on treatment, invasive dental procedures should be performed with caution and avoided in close proximity to [BRAND NAME] treatment.

The management plan for patients who develop ONJ should be set up in close collaboration between the treating physician and a dentist or oral surgeon with expertise in ONJ. Temporary interruption of [BRAND NAME] should be considered until the condition resolves and contributing risk factors are mitigated where possible.

You are therefore required to review and revise, if necessary, the sales pack labels and/or package inserts of the concerned products registered by your company to ensure that the products comply with the above requirements. The revised sales pack labels and/or package inserts should be submitted to the Committee for approval within 2 months from the date of this letter. Failing to comply with the above requirements may result in de-registration of the products by the Committee.

If you have any enquiries on the above issue, please contact the Drug Office duty officer at 2319 8458.

Yours sincerely,

(Clive CHAN)
Secretary,
Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee

c.c. 7-15/3, Product Files
SM/CC