

衛生署藥物辦公室  
藥物註冊及進出口管制部

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(來函請註明此檔案號碼)  
(IN REPLY PLEASE QUOTE THIS FILE REF.)

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

Dear Dr. LI,

**Bisphosphonates: very rare reports of osteonecrosis of the external auditory canal**

Your attention is drawn to the Medicines and Healthcare products Regulatory Agency's (MHRA) announcement regarding very rare reports (fewer than 1 in 10 000 patients) of osteonecrosis of the external auditory canal associated with the use of bisphosphonates.

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 have different indications.

Benign idiopathic osteonecrosis of the external auditory canal is a rare condition that can occur in the absence of antiresorptive therapy and is sometimes associated with local trauma.

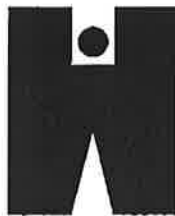
Evidence from the clinical literature and from cases reported to medicines regulators, including one report received via the UK Yellow Card scheme, supports a causal association between bisphosphonates and osteonecrosis of the external auditory canal. Product information is being updated to include advice for healthcare professionals and patients.

A total of 29 reports indicative of osteonecrosis of the external auditory canal in association with bisphosphonates have been identified worldwide, including 11 cases reported in the clinical literature. Cases have been reported with use of both intravenous or oral bisphosphonates for both cancer-related or osteoporosis indications; there is currently insufficient evidence to determine whether there is any increased risk with higher doses used for cancer-related conditions. Most cases were associated with long-term bisphosphonate therapy for 2 years or longer, and most cases had possible risk factors including: steroid use; chemotherapy; and possible local risk factors such as infection, an ear operation, or cotton-bud use. Bilateral osteonecrosis of the external ear canal was reported in some patients, as was osteonecrosis of the jaw.

The number of cases of osteonecrosis of the external auditory canal reported in association with bisphosphonates is low compared with the number of cases reported of bisphosphonate-related osteonecrosis of the jaw, a well-established side effect of bisphosphonates.

The available data do not support a causal relation between osteonecrosis of the external auditory canal and denosumab. However, this possible risk is being kept under close review, given that denosumab is known to be associated with osteonecrosis of the jaw.

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DEPARTMENT OF HEALTH  
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BY FAX

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Advice for healthcare professionals is as follows:

- The possibility of osteonecrosis of the external auditory canal should be considered in patients receiving bisphosphonates who present with ear symptoms, including chronic ear infections, or in patients with suspected cholesteatoma.
- Possible risk factors include steroid use and chemotherapy, with or without local risk factors such as infection or trauma.
- Patients should be advised to report any ear pain, discharge from the ear, or an ear infection during bisphosphonate treatment.

Please refer to the MHRA's website for details:

<https://www.gov.uk/drug-safety-update/bisphosphonates-very-rare-reports-of-osteonecrosis-of-the-external-auditory-canal>

In Hong Kong, there are 63 registered pharmaceutical products containing bisphosphonates, including 28 alendronic acid/alendronate products, 6 ibandronic acid products, 4 pamidronate disodium products, 12 risedronate sodium products, 1 clodronate disodium product, and 12 zoledronic acid products. All these products are prescription-only medicines. So far, the Department of Health (DH) has received four adverse drug reaction (ADR) cases related to alendronic acid, but none of them was related to osteonecrosis. No ADR case has been received on other bisphosphonates. In view of the above MHRA announcement, the matter will be discussed by 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](mailto: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,



(Grant NG)

for Assistant Director (Drug)