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(來函請註明此檔案號碼) DH DO DIMC/7-30/1  
(IN REPLY PLEASE QUOTE THIS FILE REF.)

18 May 2022

Dear Healthcare Professionals,

**Denosumab 60mg (Prolia): should not be used in patients under 18 years due to the risk of serious hypercalcaemia**

Your attention is drawn to the United Kingdom Medicines and Healthcare products Regulatory Agency's (MHRA) announcement that serious and life-threatening hypercalcaemia has been reported with denosumab 60mg (Prolia) in children and adolescents in clinical trials for osteogenesis imperfecta and during off-label use. Denosumab 60mg (Prolia) is authorised for use in adults with osteoporosis and other bone loss conditions, it should not be used in children and adolescents younger than 18 years.

Cases of serious and life-threatening hypercalcaemia requiring hospitalisation and complicated by acute renal injury have been reported in children and adolescents younger than 18 years receiving 60mg denosumab in clinical trials. These clinical trials were investigating treatment with denosumab in patients younger than 18 years with osteogenesis imperfecta. Osteogenesis imperfecta is a group of rare inherited conditions that cause very fragile bones. Worldwide, MHRA is also aware of 20 suspected adverse event reports of hypercalcaemia reported up to 26 Aug 2021, during off-label treatment with Prolia in children and adolescents younger than 18 years. Reports included cases in paediatric patients with osteogenesis imperfecta, as well as in those with various other conditions. There were also a small number of reports of hypercalcaemia in patients younger than 18 years after stopping treatment (rebound hypercalcaemia). Symptoms of hypercalcaemia include excessive thirst, excessive urination, drowsiness, confusion, loss of concentration, feeling or being sick, constipation, and muscle weakness. Severe hypercalcaemia can cause serious kidney problems (acute renal injury), coma, heart rhythm abnormalities and cardiac arrest.

A recent European review assessed these cases of severe hypercalcaemia and recommended stronger warnings against use of Prolia in children and adolescents younger than 18 years. MHRA has considered this review together with the safety data and agrees that the product information should be updated. The Summary of Product Characteristics for Prolia has been updated to advise that denosumab 60mg should not be used in children and adolescents younger than 18 years because of safety concerns about serious hypercalcaemia. There

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are also existing warnings that inhibition of RANK/RANK ligand (RANKL) in animal studies may be associated with inhibition of bone growth and lack of tooth eruption.

Advice for healthcare professionals:

- Denosumab 60mg (Prolia) is authorised for use only in adults (aged 18 years and older) for treatment of osteoporosis and other bone loss conditions.
- Serious and life-threatening hypercalcaemia has been reported with denosumab 60mg use in children and adolescents in clinical trials and during off-label use.
- Hypercalcaemia cases occurred during treatment or in the weeks to months after the last dose.
- Denosumab 60mg (Prolia) should not be used in children and adolescents younger than 18 years.

Please refer to the following website in MHRA for details:

<https://www.gov.uk/drug-safety-update/denosumab-60mg-prolia-should-not-be-used-in-patients-under-18-years-due-to-the-risk-of-serious-hypercalcaemia>

In Hong Kong, Prolia Solution For Injection In Pre-filled Syringe 60mg/ml (USA) (HK-60588) and Prolia Solution For Injection In Pre-filled Syringe 60mg/ml (The Netherlands) (HK-60589) are registered by Amgen Hong Kong Limited. Both products are prescription-only medicines. So far, the Department of Health (DH) has received 59 cases of adverse drug reaction related to denosumab, but these cases were not related to hypercalcaemia. Related news on hypercalcaemia after cessation of treatment with denosumab in paediatric patients and monitoring in those patients with growing skeletons was previously issued by Singapore Health Sciences Authority, and was posted on the Drug Office website on 15 Aug 2015. In light of the above MHRA's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Please note that this letter serves as a means for the DH to communicate important new safety information about registered pharmaceutical products with healthcare professionals in Hong Kong and is not intended to serve as guidelines or to replace professional clinical judgement. 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 Adverse Drug Reaction 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 faithfully,



(Terence MAN)

for Assistant Director (Drug)