PRAC recommends further measures to minimise risk of osteonecrosis of the jaw with bisphosphonates

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Information on Zolendronic acid

Zolendronic acid belongs to a class of medications called bisphosphonates; used to treat osteoporosis and bone loss. A known side effect called osteonecrosis of the jaw has been reported very rarely in patients treated with zolendronic acid and denosumab. In patients treated for osteoporosis, the risk is very small compared to patients treated with higher doses for cancer related conditions. The risk seems also to be greater when parenteral formulations are used.

It is essential that osteonecrosis of the jaw is prevented from developing as it can be painful and difficult to treat.

Active Ingredients	Product Name	Pharmaceutical Form	Classification	Authorisation Number	MAH/license holder
Hydroxyzine Dihydrochloride 2mg/ml	Atarax syrup	SYRUP	PoM	MA030/00101	UCB Pharma SA
Hydroxyzine Dihydrochloride 25mg	Atarax	FILM-COATED TABLET	PoM	MA030/00102	UCB Pharma SA

Information from the European Medicines Agency (EMA) about the safety concern

During a periodic review of Aclasta (zolendronic acid), the EMA recommended some measures to further minimise this risk with this medicine. EMA is planning similar recommendations for other parenteral formulations of bisphosphonate medicines and denosumab at their next periodic reviews over the course of 2015/2016.

In Malta

For Healthcare Professionals

Healthcare professionals should follow the following recommendations for Aclasta (zoelndronic acid):

- Delay the start of treatment or a new course of treatment in patients with unhealed open soft tissue lesions in the mouth that may require dental or oral procedures.
- Ensure patients have a dental examination and an individual benefit-risk assessment before starting treatment in patients with concomitant risk factors.
- Consider the following when evaluating a patient's risk of developing osteonecrosis of the jaw:
  - 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.

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- Cancer, co-morbid conditions (e.g. anaemia, coagulopathies, infection) and smoking.
- Concomitant therapies: corticosteroids, chemotherapy, angiogenesis inhibitors and radiotherapy to head and neck.
- Poor oral hygiene, periodontal disease, poorly fitting dentures and a history of dental disease, invasive dental procedures, e.g. tooth extractions.

- Encourage patients 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 zoledronic acid. While patients are on treatment, invasive dental procedures should be performed with caution and these procedures should be avoided close to their treatment.
- Managing patients who develop osteonecrosis of the jaw should involve close collaboration between the treating physician and a dentist or oral surgeon with expertise in osteonecrosis of the jaw. Consider interrupting treatment temporarily until the condition resolves and the contributing risk factors are mitigated, where possible.

For more information please visit **www.ema.europa.eu**

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on bisphosphonates including Zolendronic acid. Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form or online at **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Prof. John J Borg PhD (Bristol)
Post-licensing Director

Healthcare professionals and patients are encouraged to regularly check the Medicine Authority website for product safety updates as these are issued on an ongoing basis.

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