EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation

International non-proprietary name:

zoledronic acid (indicated for cancer and fractures)

Procedure No. EMEA/H/C/PSUSA/00003149/201408

Period covered by the PSUR: 01.September 2013 – 31 August 2014

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR for zoledronic acid (indicated for cancer and fractures), the scientific conclusions of CHMP are as follows:

With regards to the risk of Osteonecrosis of the jaw (ONJ), it is recommended that the product information is revised to reflect the current knowledge on ONJ and to optimize risk minimisation.

In addition, although the risk for ONJ may be well known for the prescribers, further awareness on such risk is needed for the patients. Thus, it is considered warranted to implement a patient reminder card as an additional risk minimisation measure for ONJ. The following wording for the reminder card has been agreed by the PRAC:

This reminder card contains important safety information that you need to be aware of before and during treatment with zoledronic acid *(relevant product name)* injections for cancer-related conditions

Your doctor has recommended that you receive zoledronic acid *(relevant product name)* injections to help prevent bone complications (e.g. fractures) caused by bone metastases, or bone cancers < *and additional indications as appropriate, using the same wording as in the approved package leaflet*>.

A side effect called osteonecrosis of the jaw (ONJ) (bone damage in the jaw) has been reported <*frequency from product information*> in patients receiving zoledronic acid *(relevant product name)* injections for cancer-related conditions. ONJ can also occur after stopping treatment.

In order to reduce the risk of developing osteonecrosis of the jaw, there are some precautions you should take:

Before starting treatment:

- Ask your doctor to tell you about ONJ before you start treatment
- Check with your doctor whether a dental examination is recommended before you start treatment with zoledronic acid *(relevant product name).*
- Tell your doctor/nurse (health care professional) if you have any problems with your mouth or teeth.

Patients undergoing dental surgery (e.g. tooth extractions), who do not receive routine dental care or have gum disease, are smokers, who get different types of cancer treatments or who were previously treated with a bisphosphonate (used to treat or prevent bone disorders) may have a higher risk of developing ONJ.

While being treated:

- You should maintain good oral hygiene, make sure your dentures fit properly and receive routine dental check-ups
- If you are under dental treatment or will undergo dental surgery (e.g. tooth extractions), inform your doctor and tell your dentist that you are being treated with zoledronic acid *(relevant product name).*

- Contact your doctor and dentist immediately if you experience any problems with your mouth or teeth such as loose teeth, pain or swelling, non-healing of sores or discharge, as these could be signs of osteonecrosis of the jaw

Read the package leaflet for further information.

Therefore, in view of available data regarding zoledronic acid (indicated for cancer and fractures), the PRAC considered that changes to the product information and conditions of the marketing authorisation were warranted.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds recommending the variation to the terms of the Marketing Authorisation

On the basis of the scientific conclusions for zoledronic acid (indicated for cancer and fractures) the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing zoledronic acid (indicated for cancer and fractures) is favourable subject to the proposed changes to the product information

The CHMP recommends that the terms of the Marketing Authorisation(s) should be varied.