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Denosumab (XGEVA▼) and risk of osteonecrosis of the jaw: new contraindication and introduction of a patient reminder card to minimize the risk

Dear Healthcare Professional,

Amgen Ltd, in agreement with the European Medicines Agency and the Health Products Regulatory Authority, would like to inform you of a new contraindication in patients with unhealed lesions from dental or oral surgery, revised warnings and precautions and the introduction of a patient reminder card, to minimise the risk of osteonecrosis of the jaw (ONJ) during treatment with XGEVA▼.

Summary

- **XGEVA▼ is now contra-indicated in patients with unhealed lesions from dental or oral surgery.**
- **A patient reminder card is introduced to increase patients' awareness for the risk of ONJ and the necessary precautions to minimize this risk.**
- **Patients treated with XGEVA▼ should be given this patient reminder card with information on ONJ, as well as the package leaflet.**

Further information on the safety concern

ONJ is a common side effect in patients treated with XGEVA▼ (may affect up to 1 in 10 people).
The product information is being updated to reflect the current knowledge on ONJ and to optimize risk minimisation. Changes to the product information include the addition of a contraindication in patients with unhealed lesions from dental or oral surgery to ensure that treatment is not initiated when the patient is in this situation. A dental examination with preventive dentistry is recommended prior to treatment with XGEVA▼.
The management plan of any 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.

Why these changes are being introduced

The European Medicines Agency (EMA) recently undertook a review of the effectiveness of risk minimisation measures regarding the risk of osteonecrosis of the jaw (ONJ) with bisphosphonates and denosumab. This has resulted in a recommendation that reinforced safety messages be reflected in the product information (which contains the SmPC and package leaflet) for these products, as well as introduction of a patient reminder card, giving details of precautions to take to minimise the risk for ONJ.

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Place of Registration: Ireland
Company Registration Number: 379345
Directors: Michael Byrne, Thomas Dittrich (German), Rolf Hoffman (German), John Kearney (British)

The card will remind patients about important safety information that they need to be aware of before and during treatment with denosumab (XGEVA▼) injections for cancer-related conditions, including:

- to tell their doctor/nurse if they have any problems with their mouth or teeth before starting treatment;
- to maintain good oral hygiene and receive routine dental check-ups during treatment;
- to inform their doctor and tell their dentist that they are being treated with denosumab (XGEVA▼) if they are under dental treatment or will undergo dental surgery
- to contact their doctor and dentist immediately if they experience any problems with their mouth or teeth such as loose teeth, pain or swelling, non-healing of sores or discharge

You will receive 10 copies of the patient reminder card with this letter.

Further information on the product

XGEVA▼ is indicated for:

- the prevention of skeletal related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with bone metastases from solid tumours.
- treatment of adults and skeletally mature adolescents with giant cell tumour of bone that is unresectable or where surgical resection is likely to result in severe morbidity

Call for reporting

Suspected adverse reactions should be reported to the Health Products Regulatory Authority (HPRA) using a Yellow Card obtained either from the HPRA, or electronically via the online reporting system at www.hpra.ie. Adverse reactions can also be reported to the Health Products Regulatory Authority by calling on (01) 676 4971.

Reports can also be made to Amgen Europe B.V. by contacting Amgen UK/Ireland Drug Safety Department directly on +44 1223 436712.

▼ This medicinal product is subject to additional monitoring.

Contact details

Should you have any questions or require additional information regarding the use of XGEVA▼, or to request additional copies of the patient reminder card, please contact Amgen UK/Ireland Medical Information at:

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Milton Road
Cambridge
CB4 0WD
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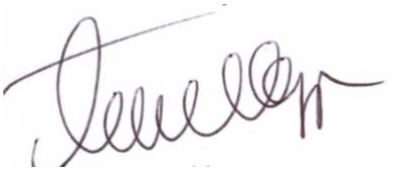
Annex:
Patient reminder card regarding osteonecrosis of the jaw

Yours sincerely,



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Prescribing information for XGEVA can be accessed at http://www.medicines.ie/medicine/15078/SPC/XGEVA/ (Summary of Product Characteristics) and http://www.medicines.ie/medicine/15079/PIL/XGEVA/ (Package Leaflet)