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Direct Healthcare Professional Communication

16 May 2018

Xgeva▼ (denosumab): risk of new primary malignancy

Dear Healthcare Professional,

Amgen, in agreement with the European Medicines Agency (EMA) and the MHRA, would like to inform you of the following:

Summary

- **New primary malignancies were reported more frequently in clinical studies in patients with advanced malignancies treated with Xgeva (denosumab) compared to zoledronic acid.**
- **The cumulative incidence of new primary malignancies at one year was 1.1% for denosumab treated patients compared to 0.6% for zoledronic acid treated patients.**
- **No treatment-related pattern in individual cancers or cancer groupings was apparent.**

Background on the safety concern

Xgeva (denosumab) is indicated for:

- Prevention of skeletal related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with advanced malignancies involving bone.
- 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

In a pooled analysis from four phase III studies in patients with advanced malignancies involving bone, new primary malignancy was reported more frequently in patients treated with Xgeva (denosumab 120 mg once monthly) compared to zoledronic acid (4 mg once monthly) during the primary double-blind treatment phases of these studies. New primary malignancy occurred in 54/3691 (1.5%) of patients treated with XGEVA (median exposure of 13.8 months; range: 1.0–51.7) and in 33/3688 (0.9%) of patients treated with zoledronic acid (median exposure of 12.9 months; range: 1.0-50.8). The cumulative incidence at one year was 1.1% for denosumab and 0.6% for zoledronic acid, respectively. No treatment-related pattern in individual cancers or cancer groupings was apparent.

The product information for Xgeva will be updated to include this information.

Call for Reporting
Healthcare professionals are reminded to continue to report suspected adverse reactions (ADRs) to the MHRA through the Yellow Card Scheme.

It is easiest and quickest to report ADRs online via the Yellow Cards website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gov.uk
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- or by downloading and printing a form from the Yellow Card section of the MHRA website

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name. As Xgeva is a biological product, the product name and batch details should also be reported.

▼ Xgeva is subject to additional monitoring. This will allow quick identification of new safety information.

Company contact point
Should you have any questions or require additional information regarding the use of Xgeva, please contact Amgen UK/Ireland Medical Information on 01223 436441 or by email to gbinfoline@amgen.com

Yours sincerely,

Dr Anthony Patrikios
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