

30th August 2012

Direct Healthcare Communication

Reports of symptomatic hypocalcaemia, including fatal cases reported in patients treated with XGEVA (denosumab)

Dear Healthcare Professional,

This letter is sent to remind you of the risk of severe symptomatic hypocalcaemia associated with the use of denosumab and to inform about the risk of late onset of hypocalcaemia. Hypocalcaemia can occur at any time during therapy.

Summary of the issue

- Severe symptomatic hypocalcaemia, including fatal cases, has been reported in patients treated with denosumab
- Hypocalcaemia can occur at any time during therapy with denosumab
- Signs and symptoms of these cases included altered mental status, tetany, seizures and QTc prolongation,

Healthcare Professionals are reminded of the following recommendations to minimise this risk:

- Pre-existing hypocalcaemia must be corrected prior to initiating therapy
- Supplementation of calcium and vitamin D is required in all patients unless hypercalcaemia is present.
- If hypocalcaemia occurs, additional calcium supplementation may be necessary.
- Patients with severe renal impairment (creatinine clearance < 30 ml/min) or receiving dialysis are at greater risk of developing hypocalcaemia. Monitoring of calcium levels in these patients is recommended.

This letter is sent in agreement with the European Medicines Agency and the Irish Medicines Board

Further information on the safety concern

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

The risk of severe hypocalcaemia associated with denosumab use is known and is reflected in the current product information and includes the above recommendations on risk minimisation. Following receipt of adverse drug reaction reports, the warnings in the product information have been updated to inform prescribers that severe fatal cases have been reported in the post-marketing period. The product information has also been updated with information on the risk of late onset of hypocalcaemia,

Hypocalcaemia can occur at any time during therapy with denosumab. Most commonly it occurs within the first 6 months of dosing

For more information regarding denosumab refer to the product details available on the EMA website: <http://www.ema.europa.eu>

Call for reporting

Any suspected adverse reactions with XGEVA should be reported to the Irish Medicines Board. The IMB can be contacted on (01) 676 4971. Suspected adverse reactions may also be reported to Amgen Europe B.V by contacting 1800 585 160 or +44 (0) 1223 436712

Contact details

Should you have any questions or require additional information regarding the use of XGEVA, please contact Amgen UK, Medical Information on +44 (0)1223 436712

Yours sincerely,

A handwritten signature in blue ink, appearing to read 'S Bellamy', with a horizontal line underneath.

Dr Steven Bellamy MBChB
Medical Director, UK & Ireland

Annex: Revised copy of the XGEVA Summary of Product Characteristics (SPC).