

03 September 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 MHRA

#### 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**

Please report suspected adverse reactions with any medicine or vaccine to the MHRA through the Yellow Card Scheme online at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard).

Alternatively, prepaid Yellow Cards for reporting are available:

- upon request by mail: "FREEPOST YELLOW CARD"
- at the back of the British National Formulary (BNF)
- by telephoning the Commission of Human Medicines (CHM) free phone line: 0800 731 6789
- or by electronic download through the MHRA website ([www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard))

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset and treatment dates.

Any suspected adverse reactions with XGEVA may also be reported to Amgen Europe B.V by contacting +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,



Dr Steven Bellamy MBChB  
Medical Director, UK & Ireland

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