DENOSUMAB (Xgeva®)

Indication: An option for the prevention of skeletal-related events in adult patients with bone metastasis from breast cancer and solid tumours other than prostate cancer, if biphosphonates would otherwise be prescribed. (NICE TA265)

Regimen details: Denosumab 120mg subcutaneous

Administration: single subcutaneous injection into the thigh, abdomen or upper arm

Frequency: every 4 weeks

Supportive medicines: At least 500mg calcium and 400IU vitamin D daily unless hypercalcaemic or low vitamin D levels (see comments below)

Low vitamin D levels must be corrected before administration. Please see Trust guidance.

Main Toxicities: hypocalcaemia (may be severe and potentially fatal), hypophosphataemia, diarrhoea, dyspnoea, osteonecrosis of the jaw (see comments), skin infections (cellulitis), hyperhidrosis (abnormal perspiration), atypical fracture of the femur (see comments)

Investigations: Dental check Baseline
Vitamin D level Baseline (see comments)
Corrected Ca\(^2+\) Before every dose (see comments)
Phosphate Before every dose
Magnesium If low calcium reported
U&Es Baseline, then periodically (the risk of hypocalcaemia is greater if CrCl < 30ml/min)

NB. FBC Not needed

Comments:

Electrolyte abnormalities:
Any pre-existing hypocalcaemia or low vitamin D levels must be corrected before treatment with denosumab is given.
If corrected calcium is < 2.0mmol/l, withhold treatment until hypocalcaemia has resolved
If vitamin D < 35nmol/L withhold treatment until has had at least 2 weeks of high-dose repletion. See Trust guidelines on replacement of vitamin D
Ensure maintenance vitamin D supplements (with added calcium unless hypercalcemic) have been prescribed for all patients.
Measure serum magnesium in hypocalcaemic patients to determine whether magnesium replacement is required.
Prescribe phosphate supplementation in hypophosphataemia.

Patients with fructose intolerance should not receive Xgeva

Adequate contraception methods to be applied during the therapy.
Osteonecrosis of the jaw is a rare but potentially serious side effect of denosumab. All patients SHOULD undergo baseline dental check and appropriate preventative dentistry before starting denosumab. The MHRA state that denosumab MUST NOT be started in patients with a dental or jaw condition requiring surgery, or in patients who have not recovered following oral surgery. All non-urgent invasive dental procedures should be avoided whilst on treatment. For patients who develop ONJ, dental surgery may exacerbate the condition and should only be performed by a dental surgeon skilled in managing these patients.

Atypical fracture of the femur is a further rare but serious side effect of denosumab therapy. During treatment patients should be advised to report any thigh, hip or groin pain. Discontinuation of therapy in patients suspected to have an atypical femur fracture should be considered pending evaluation of the patient, based on an individual risk benefit assessment.

**Dose Modifications**

There are no dose adjustments required. Withhold treatment for any Grade 3 or 4 adverse events.

**Renal Impairment:**
No dose adjustment is required in patients with renal impairment. Experience in patients on dialysis or with severe renal impairment (creatinine clearance < 30 ml/min) is limited. Risk of hypocalcaemia is greater when CrCl < 30ml/min, close monitoring required. Consider the individual risk-benefit profile.

**Hepatic impairment:**
The safety and efficacy of denosumab have not been studied in patients with hepatic impairment. Denosumab is not thought to be eliminated via hepatic mechanisms.

**Drug interactions:**
Concomitant biphosphonates contra-indicated

**References:**
- [www.medicines.org.uk](http://www.medicines.org.uk) (accessed May 14)
- [www.micromedex.com](http://www.micromedex.com) (accessed May 14)
- NICE TA265. October 2012