DENOSUMAB

An option for the prevention of skeletal-related events in adults with bone metastases from breast cancer and solid tumours other than prostate cancer, if bisphosphonates would otherwise be prescribed.
NICE approved Oct 2012
Due to its relative high cost, reserved for use only in patients with poor renal function (CrCl < 30ml/min), or patients intolerant of zoledronic acid (including deteriorating renal function)

Drug/Dosage:	Denosumab 120mg s/c bolus	
Administration:	subcutaneous bolus injection into the thigh, abdomen or upper arm	
Other drugs:	at least 500mg calcium and 400iu Vitamin D supplements is required daily unless patient is hypercalcaemic e.g. Calceos tablets, one to be chewed daily.	
Frequency:	once every 4 weeks for as long as the patient is receiving benefit. For patients receiving 3-weekly chemotherapy, denosumab may be administered every 6 weeks for practical purposes[1]. Once the chemotherapy course is completed, denosumab should be given once every 4 weeks.	
Main Toxicities:	hypocalcaemia (may be severe and potentially fatal); hypophosphataemia; diarrhoea; dyspnoea; osteonecrosis of the jaw (see Comments); hyperhidrosis (abnormal perspiration)	
Regular Investigations:	Corrected Ca^{2+} }	before every dose for 6 doses, then every 1 – 3 months, according to individual case and Consultant preference (the required frequency of monitoring after 6 doses must be clearly specified in the patient records)
	Phosphate }	
	Magnesium	if low calcium reported (see Comments)
	U&Es	baseline, then every 3 – 6 months (the risk of hypocalcaemia is greater if CrCl < 30ml/min)
	Baseline dental check-up	ideally recommended before 1st dose given

Comments: Any pre-existing hypocalcaemia **must** be corrected before treatment with denosumab may begin.

Osteonecrosis of the jaw has been reported in patients on denosumab. For this reason;

- a baseline dental check is advised before initiating denosumab.
- all non-urgent invasive dental procedures should be avoided whilst on treatment
- For patients requiring urgent dental procedures, there are no data available to suggest whether discontinuation of denosumab treatment reduces the risk of osteonecrosis of the jaw. Clinical judgement of the treating physician should guide the management plan of each patient based on individual benefit/risk assessment. It is recommended that any unavoidable dental extractions are performed in hospital by a maxillofacial surgeon.
- For patients who develop osteonecrosis of the jaw, dental surgery may exacerbate the condition.

Reason for Update: restricted use added to indication	Approved by Medical Oncology Consultant: Dr A Michael
Version: 3	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 2	Date: 22.7.14
Prepared by: S Taylor	Checked by: C Tucker

Dose Modifications There are no dose adjustments required.

Withhold treatment for any Grade 3 or 4 adverse events, or for osteonecrosis of the jaw.

Electrolyte abnormalities: If corrected calcium is < 2.0 mmol/l, withhold the denosumab until hypocalcaemia resolved.

There is no standard agreed practice for the management of hypocalcaemia. The deficiency is usually asymptomatic, but ensure that the patient is taking the daily calcium and vitamin D supplements, as specified above. Increase the dose if necessary. Also, **serum magnesium** should be measured in these patients to determine whether magnesium replacement is required.
If in doubt, discuss with Consultant.

There is also no standard advice regarding management of hypophosphataemia, but short-term supplemental therapy with Sandophos may be advised to correct the deficiency while denosumab treatment continues. If in doubt, discuss with the prescriber.

Renal Impairment: No dosage adjustment is required in renal impairment.
Experience in patients on dialysis or with CrCl < 30ml/min is limited, but the risk of hypocalcaemia is greater in patients with CrCl < 30ml/min, and so these patients should be monitored more closely.

Hepatic Impairment: Denosumab has not been studied in patients with hepatic impairment, but it is not thought to be eliminated via hepatic mechanisms.

References:
Stopeck, AT et al; JCO 2010; 28: 5132–5139
Henry, DH et al; JCO 2011; 29: 1125 – 1132
[1]No evidence, but local agreement