Indication	Prevention of skeletal-related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with bone metastases from breast cancer and from solid tumours.
Treatment Intent	Symptom management
Frequency and number of cycles	To be given every 4 weeks or alternative schedule of every 6 weeks. To continue for as long as clinically indicated or unacceptable toxicity.
Monitoring Parameters pre-treatment	• Pre-existing hypocalcaemia must be corrected prior to initiating therapy with denosumab and monitored for the first 3 months. • Monitoring of calcium levels should be conducted (i) prior to the initial dose, (ii) within two weeks after the initial dose and (iii) if suspected symptoms of hypocalcaemia occur • Patients should have U&Es, bone profile, LFTs and FBC prior to the first 3 cycles. Thereafter they can be taken at the time of treatment, treatment may proceed, and results checked when available. Patients at risk of hypocalcaemia should be monitored more frequently as necessary or if suspected symptoms of hypocalcaemia occur. • **Renal impairment:** no dose adjustment necessary, however, use with caution in patients with CrCl <30 ml/min as these patients are at greater risk of developing hypocalcaemia. • **Hepatic impairment:** no data available. • Patients should be advised to seek prompt medical attention if they develop signs or symptoms of cellulitis. • Denosumab is not recommended for use in pregnant women and women of childbearing potential not using contraception. **<u>Osteonecrosis of the jaw</u>** • A dental examination with appropriate preventive dentistry is recommended for all patients prior to the start of denosumab treatment. • Do not start treatment in patients with an active dental or jaw condition requiring surgery or in patients who have not completely recovered following oral surgery. • A minimum of 4 weeks should have passed before starting treatment following dental procedures where bone has been exposed or manipulated. • Patients should be encouraged to have regular dental check-ups whilst on treatment, at least every 6 months. • While on treatment avoid dental procedures if possible. • If patients require invasive dental procedures (ie: dental extraction, surgical dental extraction or root planing /deep scaling/root canal therapy) then the patient is required, where possible, to stop treatment 8 weeks prior, and recommence treatment when there is mucosal healing as assessed by a dental professional (there is no need to wait 8 weeks post procedure if full mucosalisation has occurred). NB Superficial dental fillings (drilling), normal hygiene appointments and the provision of dentures and routine root canal therapy are not invasive dental procedures and therefore there is no indication to stop denosumab for these. • Patients who develop osteonecrosis of the jaw should be referred to a maxillofacial surgeon. • Caution is advised when denosumab is administered with anti-angiogenic drugs (eg bevacizumab, sunitinib, pazopanib), as an increase in the incidence of ONJ has been observed in patients treated concomitantly with these medicinal products.

	• Please refer to UK chemotherapy board guidance on medication related osteonecrosis of the jaw: https://www.rcplondon.ac.uk/guidelines-policy/medication-related-osteonecrosis-jaw-guidance-oncology-multidisciplinary-team • Osteonecrosis of the external auditory canal should be considered in patients who present with ear symptoms including chronic ear infections. • During treatment patients should be advised to report any thigh, hip or groin pain and any patient presenting with such symptoms should be evaluated for an incomplete femur fracture.
References	KMCC protocol SUPP-006 KMCC protocol SUPP-003 v5

NB For funding information, refer to CDF NICE Drugs Funding List

Repeat every 4 weeks

Day	Drug	Dose	Route	Administration
1	**Denosumab Xgeva®**	**120mg**	Sub-cutaneous injection into the thigh, abdomen or upper arm	Once every 4 weeks

TTO	Drug	Dose	Route	Directions
Day 1	Calcium 600mg & colecalciferol 400iu tablets **(Adcal D3®)**	1 tablet	PO	Once daily, chewed or sucked before swallowing. Dispense 56 tablets every other cycle.

Repeat every 6 weeks

Day	Drug	Dose	Route	Administration
1	**Denosumab Xgeva®**	**120mg**	Sub-cutaneous injection into the thigh, abdomen or upper arm	Once every 6 weeks

TTO	Drug	Dose	Route	Directions
Day 1	Calcium 600mg & colecalciferol 400iu tablets **(Adcal D3®)**	1 tablet	PO	Once daily, chewed or sucked before swallowing. Dispense 56 tablets every cycle.