SHARED CARE GUIDELINE

Drug: Denosumab 120mg injection (Xgeva®)

Indication: prevention of skeletal-related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with advanced malignancies involving bone AND treatment of adults and skeletally mature adolescents with giant cell tumour of bone that is unresectable or where surgical resection is likely to result in severe morbidity.

Please note: there is an alternative shared care guideline that must be used for denosumab 60mg injection (Prolia®) for the treatment of osteoporosis. Access via:

https://www.lancsmmg.nhs.uk/prescribing-guidance/shared-care-guidelines/

Introduction	**Indications**: Licensed: Prevention of skeletal-related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with advanced malignancies involving bone. Treatment of adults and skeletally mature adolescents with giant cell tumour of bone that is unresectable or where surgical resection is likely to result in severe morbidity. **Background:** Denosumab is a human monoclonal antibody that inhibits osteoclast formation, function, and survival, thereby decreasing bone resorption. Subcutaneous denosumab is available as two different preparations: Xgeva 120mg and Prolia 60mg injection. They are licensed for different indications and are not interchangeable. This shared care guideline refers only to Xgeva 120mg vial and only Xgeva 120mg should be prescribed under this guideline.
Form	Vial of solution for subcutaneous injection: denosumab 120mg in 1.7ml
Dose & Administration	By subcutaneous injection: 120mg every 4 weeks administered as a single subcutaneous injection into the thigh, abdomen, or upper arm. Supplementation of at least 500mg calcium and 400 units vitamin D daily is required in all patients unless hypercalcaemia is present.
Secondary Care Responsibilities	• Check for absence of pregnancy in women of child-bearing age and ensure the patient understands the importance of contraception. If pregnancy occurs despite these precautions, patient must be aware of the need to contact her Oncologist **and** GP immediately. • Discuss the benefits and side effects of treatment with the patient. Ensure that the patient understands which warning symptoms to report. • Perform pre-treatment screening: ◦ Renal function, calcium, magnesium, phosphate, and vitamin D levels should be checked prior to starting treatment. No other routine monitoring is required while

	receiving denosumab. ◦ If there is pre-existing hypocalcaemia or a deficiency in vitamin D, this should be corrected prior to recommending denosumab 120mg. ◦ Initiate prescribing of regular calcium and vitamin D. ◦ A dental examination with appropriate preventative dentistry is now recommended for all patients before starting treatment unless the benefits of starting denosumab urgently are felt to outweigh the risks of foregoing prior dental examination. ◦ Calcium and U&Es should be rechecked within two weeks of the initial dose. • Initiate treatment by prescribing and administering the first two doses. • Plan for shared care with the patient's GP. • Review the patient regularly to monitor the patient's response to therapy. • Advise the GP on when to stop treatment. • Ensure that clear backup arrangements exist for GPs (General Practitioners) to obtain advice. • Patients will be given a booklet to record their treatment plan and what has been given at each visit. If the timing of a patient's denosumab treatment coincides with their other systemic anti-cancer treatment (SACT), then the patient will be given the dose of denosumab in secondary care. If the timing does not coincide, or the patient is not on SACT, then the Shared Care agreement would be actioned, and the GP would be asked to prescribe and administer the denosumab. If SACT is resumed, then the prescribing and administration would remain with primary care to avoid confusion.
Primary Care Responsibilities	• Provide the patient with prescriptions for denosumab as well as continuing the prescribing of calcium and vitamin D supplementation. • Ensure that the patient understands their treatment and which warning symptoms to report (see adverse reactions below). • Monitor at the recommended frequencies (see MONITORING below). • Report any adverse events to the consultant or specialist nurse and stop treatment on their advice or immediately if an urgent need arises (see MONITORING below). • Report any worsening of control of the condition to the consultant or the specialist nurse. • Refer immediately if a female patient discovers she is pregnant whilst on denosumab.
Dosing adjustments in specific populations	• No dose adjustment is required in patients with renal impairment. Experience in patients on dialysis or with severe renal impairment (creatinine clearance less than 30ml/min) is limited (see monitoring). • The safety and efficacy of denosumab has not been studied in patients with hepatic impairment. • No dose adjustment is required in elderly patients. • Denosumab is not recommended in paediatric patients (age<18 years).
Common Drug Interactions	There appear to be no clinically significant drug interactions with denosumab. Patients being treated with Xgeva should not be treated concomitantly with any other denosumab containing medicinal products (for osteoporotic indication). Patients being treated with Xgeva should not be treated concomitantly with bisphosphonates.

Cautions	• Osteonecrosis of the jaw is a well-known and common side-effect. Risk factors include smoking, old age, poor oral hygiene, invasive dental procedures (including tooth extractions, dental implants, oral surgery), comorbidity (including dental disease, anaemia, coagulopathy, infection), advanced cancer, previous treatment with bisphosphonates, and concomitant treatments (including chemotherapy, anti-angiogenic biologics, corticosteroids and radiotherapy to head and neck). • Osteonecrosis of the external auditory canal has been reported with denosumab. Risk factors include steroid use and SACT and/or local risk factors such as infection or trauma. The possibility of osteonecrosis of the external auditory canal should be considered in patients receiving denosumab who present with ear symptoms. This includes a presentation as chronic ear infection. • Atypical femoral fractures have been reported in patients receiving denosumab. • Denosumab is associated with a risk of hypocalcaemia. This risk increases with the degree of renal impairment
Contra-indications	• Hypersensitivity to denosumab or any of the excipients • Severe, untreated hypocalcaemia. • Do not start denosumab in patients with a dental or jaw condition requiring surgery, or in patients who have unhealed lesions from dental or oral surgery.
This guidance does not replace the SPC's, which should be read in conjunction with this guidance.	
Monitoring and Adverse Effects	Baseline renal function, bone profile and magnesium should be checked in Secondary Care before treatment commences so that any underlying hypocalcaemia can be corrected. Renal function and bone profile should be rechecked in Secondary Care within two weeks of the initial dose. Monitoring of calcium levels is recommended for those patients who are predisposed to hypocalcaemia, or who develop symptoms of hypocalcaemia. Patients with severe renal impairment (creatinine clearance less than 30ml/min) or receiving dialysis are at greater risk of developing hypocalcaemia. **No other routine monitoring is required while receiving denosumab.** • If corrected calcium is below the normal range (less than 2.2mmol/l) denosumab should be withheld until calcium is within the normal range • If corrected calcium is above the normal range (greater than 2.6mmol/l) denosumab can be prescribed but the GP should consider withholding calcium supplements and reviewing at the next administration. Other causes of hypercalcaemia should be excluded. • If patient presents with jaw pain denosumab should be stopped and patient referred back to the specialist • Patients presenting with unusual pain in the thigh, hip or groin should be evaluated for an incomplete femoral fracture. Discontinuation of denosumab therapy should be considered if an atypical femur fracture is suspected, while the patient is evaluated. **Other adverse effects:** • Abdominal discomfort which may present as constipation or diarrhoea. • Dyspnoea • Musculoskeletal pain • Hypocalcaemia and / or hypophosphataemia • Dental or jaw problems • Osteonecrosis of the external auditory canal – advise patients to report any ear pain, discharge from the ear or ear infection during treatment with denosumab • Hyperhidrosis **This list is not exhaustive, please refer to SPCs and BNF**

References:

1. Summary of product characteristics, Xgeva 120 mg solution for injection. Amgen Ltd. Last updated on the EMC 3rd March 2023.
2. National Institute for Health and Care Excellence. NICE TA 265: Denosumab for the prevention of skeletal-related events in adults with bone metastases from solid tumours. 24th October 2012. Accessed via www.nice.org.uk/ta265

Please note: the 'Optional Shared Care Agreement form' can be accessed via https://www.lancsmmg.nhs.uk/media/1681/generic-shared-care-agreement-ag-review-june-2019-unlocked.docx