University Hospitals of Morecambe Bay NHS Foundation Trust

Document Type: **Guideline**	**Unique Identifier:** SCG/013
Document Title: **Denosumab (Xgeva) – Shared Care Guideline**	**Version Number:** 1.1
	Status: Ratified
Scope: All clinical staff prescribing Denosumab	**Classification:** Departmental
Author / Title: Andrea Scott, Medicines Management Pharmacist	**Responsibility:** Oncology
Replaces: V1 Denosumab (Xgeva) – Shared Care Guideline	**Head of Department:** David Eaton
Validated By: Lancashire North CCG	**Date:** 16/05/2017
Ratified By: Medicines Management, Drug & Therapeutics Sub-Committee	**Date:** 12/06/2017
Review dates may alter if any significant changes are made	**Review Date:** 01/12/2020 – Review date extended (Form 172/2019)

Which Principles of the NHS Constitution Apply? 1-7	**Which Staff Pledges of the NHS Constitution Apply? 1-7**

Does this document meet the requirements of the Equality Act 2010 in relation to Race, Religion and Belief, Age, Disability, Gender, Sexual Orientation, Gender Identity, Pregnancy & Maternity, Marriage and Civil Partnership, Carers, Human Rights and Social Economic Deprivation discrimination? **Yes**

Document for Public Display: No

Evidence Search Completed by……Not Applicable ……

To be completed by Library and Knowledge Services Staff

SHARED CARE GUIDELINE

Drug: Denosumab (Xgeva)

Introduction	**Indications**: Licensed: Prevention of skeletal related events in patients with bone metastases from solid tumours (other than prostate). **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. Supplementation of at least calcium 500mg and vitamin D 400units daily should also be taken unless hypercalcaemia is present. Injection should be into the thigh, abdomen or upper arm.
Secondary Care Responsibilities	• Check for absence of pregnancy in women of child-bearing age and ensure the patient understands the importance of contraception. • 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: ◦ U&Es (including calcium, magnesium and phosphate) and creatinine if patient has severe renal impairment. No other routine monitoring s required while receiving denosumab. ◦ A dental examination with appropriate preventative dentistry is now recommended for all patients before starting treatment. ◦ Calcium should be rechecked within two weeks of the initial dose. • If there is pre-existing hypocalcaemia, this should be corrected prior to recommending denosumab 120mg. • Initiate prescribing of regular calcium and vitamin D. • Initiate treatment by prescribing and administering the first two doses. • Make arrangements 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 to obtain advice. • Ensure patient understands the need to keep a record of doses as some doses may be given in secondary care (if it corresponds with chemotherapy treatment dates) while some doses may be given in primary care.

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 (CrCl<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). • 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 • 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 and corrected calcium level should be checked before treatment commences so that any underlying hypocalcaemia can be corrected. Monitoring of calcium levels is recommended for those patients who are predisposed to hypocalcaemia. Patients with severe renal impairment (creatinine clearance < 30ml/min) or receiving dialysis are at greater risk of developing hypocalcaemia. • 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 • Hyperhidrosis This list is not exhaustive, please refer to SPCs and BNF.

References

1. http://www.medicines.org.uk/emc/medicine/24755/SPC/XGEVA
2. https://www.nice.org.uk/guidance/ta265/documents/bone-metastases