Denosumab 120mg Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
For the prevention of skeletal related events in adult patients with malignancies involving bone.	C79.5	00741a	CDS

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Denosumab is administered as a single subcutaneous injection once every 28 days into the thigh, abdomen or upper arm. Treatment should continue at the discretion of the treating consultant until unacceptable toxicity or no longer deriving clinical benefit.

The treatment frequency maybe increased at the discretion of the treating consultant.

Day	Drug	Dose	Route	Cycle
1	Denosumab	120mg	SC (thigh, abdomen or upper arm)	Every 28 days

ELIGIBILITY:

- Indications as above

EXCLUSIONS:

- Hypersensitivity to denosumab or any of the excipients
- Hypocalcaemia
- Unhealed lesions from dental or oral surgery
- Pregnancy

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist or Consultant Haematologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Calcium, magnesium, phosphate and Vitamin D
- Dental examination

Regular tests:

- FBC, renal and liver profile prior to each treatment
- Calcium (within 2 weeks of initial dose, prior to each treatment and periodically if hypocalcaemia suspected).
- Magnesium, phosphate and Vitamin D prior to each treatment
- Dental examination as clinically indicated

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.

Renal and Hepatic Impairment:

Table 1: Dose modification of denosumab in renal and hepatic impairment

Renal Impairment	Hepatic Impairment
No dose modifications necessary	The safety and efficacy of denosumab has not been studied in patients with hepatic impairment

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: None

PREMEDICATIONS: None required

OTHER SUPPORTIVE CARE:

- Supplementation of at least 500 mg calcium and 400 IU vitamin D daily is required in all patients, unless hypercalcaemia is present.
- Denosumab is not recommended for use in pregnant women and women of child-bearing potential not using contraception. Women should be advised not to become pregnant during and for at least 5 months after treatment.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Hypocalcaemia:** Pre-existing hypocalcaemia must be corrected prior to initiating therapy with denosumab. Monitoring of calcium levels should be conducted, prior to the initial dose, within two weeks after the initial dose and if suspected symptoms of hypocalcaemia occur. Additional monitoring of calcium level should be considered during therapy in patients with risk factors for hypocalcaemia.
- **Renal impairment:** Patients with severe renal impairment (creatinine clearance < 30 mL/min) or receiving dialysis are at greater risk of developing hypocalcaemia. The risk of developing hypocalcaemia and accompanying elevations in parathyroid hormone increases with increasing degree of renal impairment. Regular monitoring of calcium levels is especially important in these patients.
- **Osteonecrosis of the jaw (ONJ):** ONJ has been reported commonly in patients receiving denosumab. The start of treatment/new treatment course should be delayed in patients with unhealed open soft tissue lesions in the mouth. A dental examination with preventive dentistry is recommended prior to treatment with denosumab. All patients should be encouraged to maintain good oral hygiene, receive routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain or swelling, or non-healing of sores or discharge during treatment with denosumab. Temporary interruption of denosumab treatment should be considered until the condition resolves.
- **Osteonecrosis of the external auditory canal:** Osteonecrosis of the external auditory canal has been reported with denosumab. Possible risk factors include steroid use and chemotherapy 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 including chronic ear infections.
- **Atypical fractures of the femur**: Atypical femoral fractures have been reported in patients receiving denosumab and may occur with little or no trauma in the subtrochanteric and diaphyseal regions of the femur. Discontinuation of denosumab therapy in patients suspected to have an atypical femur fracture should be considered. During denosumab treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Patients presenting with such symptoms should be evaluated for an incomplete femoral fracture.
- **Hypercalcaemia following treatment discontinuation in patients with giant cell tumour of bone and in patients with growing skeletons:** Clinically significant hypercalcaemia complicated by acute renal injury has been reported in denosumab-treated patients with giant cell tumour of bone weeks to months following treatment discontinuation. After treatment is discontinued, monitor patients for signs and symptoms of hypercalcaemia.

DRUG INTERACTIONS:

- Patients being treated with denosumab should not be treated concomitantly with other denosumab containing medicinal products (for osteoporosis indications) or bisphosphonates.
- Current drug interaction databases should be consulted for more information.

COMPANY SUPPORT RESOURCES/Useful Links:

Please note that this is for information only and does not constitute endorsement by the NCCP
https://www.xgeva.com/

Patient reminder card:
https://www.hpra.ie/img/uploaded/swedocuments/22149db5-51e7-4036-9c05-79212a63fd4c.pdf

REFERENCES:

1. Stopeck, A. T., A. Lipton, J. J. Body, et al. 2010. "Denosumab compared with zoledronic acid for the treatment of bone metastases in patients with advanced breast cancer: a randomized, double-blind study." J Clin Oncol 28(35):5132-5139
2. Denosumab (Xgeva®) Summary of Product Characteristics Accessed August 2023. Available at https://www.ema.europa.eu/en/documents/product-information/xgeva-epar-product-information_en.pdf

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1	13/04/2022		Prof Maccon Keane
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Comments and feedback welcome at oncologydrugs@cancercontrol.ie.