NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Denosumab for hypercalcaemia of malignancy

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

Version Number:	1
Does this version include changes to clinical advice:	N/A
Date Approved:	20th March 2025
Date of Next Review:	31st March 2027
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Approval Group:	Regional Services Clinical Governance Group

Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

GUIDELINE FOR THE USE OF DENOSUMAB FOR HYPERCALCAEMIA OF MALIGNANCY

AIM/OBJECTIVE OF GUIDELINE

Denosumab is a human monoclonal antibody that can be used for the treatment of hypercalcaemia of malignancy. This guideline advises on prescribing and dosing of denosumab instead of standard treatment with zolendronic acid where the condition is refractory to bisphosphonate therapy or where bisphosphonates are contraindicated due to severe renal impairment, under the guidance of the Specialist Palliative Care Team. This guideline should be considered in conjunction with the Scottish Palliative Care Guideline on Management of hypercalcaemia.

INTRODUCTION/BACKGROUND

Hypercalcaemia is a raised level of corrected calcium in the blood. It is the commonest life-threatening metabolic disorder in cancer patients, most frequently occurring in myeloma, breast, renal, lung and thyroid cancers. Normal adjusted calcium values are 2.20 to 2.60 mmol/l. IV fluid replacement and IV bisphosphonates are treatments of choice.

In circumstances where hypercalcaemia is refractory to bisphosphonate therapy or there is a contraindication due to severe renal impairment (creatinine clearance < 30ml/min) denosumab can be considered.

Denosumab is a human monoclonal antibody that inhibits osteoclast formation, function, and survival, thereby decreasing bone resorption. The aim of treatment is to improve symptoms and reduce corrected calcium level to within the normal range. The degree of renal impairment has no effect on the pharmacokinetics of denosumab; thus dose adjustment for renal impairment is not required. There is no need for renal monitoring with denosumab dosing.

SCOPE

This guidance is for use by predominantly specialist palliative care staff with information for secondary care prescribers and healthcare professionals and is intended for use in adults only. The guidance is specifically for hypercalcaemia of malignancy. The Palliative care team should be contacted for advice before application of the guideline.

ROLES/RESPONSIBILITIES

Prescribers should ensure the patient has been managed by the Scottish Palliative Care Guideline on the Management of Hypercalcaemia before application of this guideline.

GUIDELINE

Denosumab (XGEVA) is licensed for hypercalcaemia of malignancy in the USA. The following guidance is taken from the USA licence for the product.

Indication:

Hypercalcaemia of malignancy (unlicensed indication in the UK) refractory to bisphosphonate therapy, or where bisphosphonates are contraindicated due to severe renal impairment.

Dose and Administration:

- The dose and administration is 120mg SC every 4 weeks with additional doses on days 8 and 15 of the first month if required.
- Administer by slow SC injection into the thigh, abdomen or upper arm.
- A 27-gauge needle is recommended for administration.
- No dose adjustment is required in renal impairment.

Administration notes:

- Xgeva® is for subcutaneous route only. Do not administer intravenously or intramuscularly.
- Do not shake the vial.
- Before administration, visually inspect the vial. The solution may contain trace amounts of translucent to white proteinaceous particles. Do not inject the solution if it is cloudy or discoloured.

Practice points:

- Store in a refrigerator long-term (2-8°C). May be removed and stored at room temperature, in the original container for up to 30 days.
- To reduce discomfort at the site of injection, allow the vial to reach room temperature before use. This generally takes 15 to 30 minutes. Do not warm in any other way.

Typical dosing and monitoring schedule:

- Day 1 120mg sc denosumab
- Day 5 Clinical assessment and bloods to check calcium
- Day 8 Further 120mg sc denosumab if patient remains symptomatic of a high calcium
- Day 13 Clinical assessment and bloods to check calcium
- Day 15 Further 120mg sc denosumab if patient remains symptomatic of a high calcium
- Day 20 Clinical assessment and bloods to check calcium

Additional monitoring should be considered in patients with risk factors for hypocalcaemia e.g. severe renal impairment. For patients being discharged from hospital clarity will be required around responsibility regarding organisation and follow up of further calcium blood level testing.

Cautions:

- Patients with severe renal impairment (creatinine clearance <30ml/min) or receiving dialysis are at greater risk of a prolonged hypocalcaemia.
- The safety and efficacy of Denosumab has not been studied in patients with hepatic impairment.
- Osteonecrosis of the jaw is a well-known and common side-effect in patients receiving Denosumab for hypercalcaemia of malignancy.
    - Risk factors include smoking, old age, poor oral hygiene, invasive dental procedures, comorbidities, advanced cancer, previous treatment with bisphosphonates, and concomitant treatments (including chemotherapy, anti-angiogenic biologics, corticosteroids, and radiotherapy to head and neck).
    - A dental examination and appropriate preventative dentistry is recommended as soon as possible after treatment, if appropriate with consideration to expected prognosis. However, patients treated under this guideline are likely to be those with a very limited prognosis and longer term complications such as osteonecrosis of the jaw may not be clinically relevant.

Contraindications:

- Dental or jaw conditions requiring surgery or unhealed lesions from dental or oral surgery. However, in the case of life threatening or highly symptomatic hypercalcaemia in an individual with a prognosis of short weeks, where there is no viable alternative this would be a relative contraindication.
- Hypersensitivity to active ingredient or excipients. Xgeva® contains Sorbitol, patients with rare hereditary problems of fructose intolerance should not take this medicinal product.

Side effects:

Very common (>10%): breathlessness, diarrhoea, hypocalcaemia, musculoskeletal pain.

Common (<10%, >1%): hypophosphataemia, hyperhidrosis, osteonecrosis of the jaw, tooth extraction, rash.

Rare (<0.1%, >0.01%): atypical femoral fracture.

Not known: osteonecrosis of external auditory canal.

Clinically significant hypersensitivity including anaphylaxis has been reported with use of Xgeva®.

REFERENCES

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