SHARED CARE ARRANGEMENT AND PRESCRIBING INFORMATION FOR DENOSUMAB 120MG INJECTION (XGEVA®) FOR PREVENTION OF SKELETAL RELATED EVENTS IN PATIENTS WITH BONE METASTASES FROM SOLID TUMOURS, EXCLUDING PROSTATE (ADULTS ONLY)

Note: This document should be read in conjunction with the current Summary of Product Characteristics (SmPC).

Patient safety is paramount. The prescriber who prescribes the medicine legally assumes clinical responsibility for the drug and the consequences of its use.

GENERIC AND BRAND NAME (formulations and strength)

Name: Denosumab (Xgeva®)

Formulation: Solution for injection

Strength: 120mg

STATUS OF MEDICINE

Licence status: Licensed

Formulary status: Approved

Black triangle medicine: **No**

Risk minimisation materials: **Yes** - link

Subcutaneous denosumab is available as two different preparations Xgeva® 120mg injection and Prolia® 60mg injection**.** They are licensed for different indications and are not interchangeable. This shared care agreement refers only to Xgeva® 120mg vial and only Xgeva® 120mg vial should be prescribed under this agreement.

CONDITION(S) TO BE TREATED

For the prevention of skeletal related events in adult patients with bone metastases from solid tumours, excluding prostate. Skeletal related events refers to pathological fracture, spinal cord compression, or the need for radiation or surgery to bones as a result of bone metastases.

TYPICAL DOSAGE REGIME	
Licensed dose	120mg every 4 weeks
Route of administration	Subcutaneously into the thigh, abdomen, or upper arm.
Recommended starting dose	120mg
Titration dose/increment	N/A
Maximum dose	120mg

TYPICAL DOSAGE REGIME	
Situations requiring dose adjustment	No dose adjustments required.
Duration of treatment	The ongoing appropriateness of denosumab should be reviewed in consultant clinics every 3-6 months and any decisions to discontinue denosumab should be communicated to the patient's GP promptly (see responsibilities below).

RESPONSIBILITY OF ACUTE CARE/SPECIALIST SERVICE

- Assess patient and establish need for denosumab 120mg treatment.
- Provide patient with information including possible adverse events and obtain consent. Provide patient reminder card. Link
- Assess baseline Urea and Electrolytes (U&Es) (including creatinine and eGFR), corrected calcium and Liver Function Tests (LFTs).
- Identify if review by a dentist and/or dental work needs to be carried out and refer if necessary.
- If pre-existing hypocalcaemia then this should be corrected prior to recommending denosumab 120mg.
- Contact the GP to invite shared care for the patient.
- Assess the continued appropriateness for denosumab 120mg (usually clinic reviews every 3 - 6 months), this should be specified in the clinic letter.
- Review any concerns from the GP regarding disease progression within 2 weeks.
- Ensure that all other professionals in the shared care team are kept informed of any changes in the patient's circumstances.

RESPONSIBILITY OF PRIMARY CARE

A Practice agreeing to prescribe Denosumab should:

- Ensure that the relevant monitoring requirements are undertaken at the correct frequency.
- Ensure that the test results are checked for any abnormality as soon as the results are available.
- Ensure abnormal results are acted upon promptly.
- Only continue to prescribe medication if it is being satisfactorily monitored.
- Contact the consultant in the event of a drug reaction, monitoring abnormality, or if you are concerned in any way regarding the current treatment regime.
- Be alert for any of the known adverse reactions.

CARE WHICH IS THE RESPONSIBILITY OF THE PRESCRIBING CLINICIAN

- Prescribe medication under guidance of consultant.
- Check before prescribing denosumab 120mg that the monitoring is up to date and that results are within the normal range. U&Es (including creatinine and eGFR), corrected calcium and LFTs should be checked prior to each denosumab 120mg administration. Administration should occur within 7 days after taking blood samples. **Note:** Bloods may have been taken up to 14 days prior to the first administration of denosumab. Calcium should be re-checked 2 weeks after the first dose of denosumab 120mg.
- Check that any recommended dentistry work has been completed prior to first dose of denosumab.
- Prescribe denosumab 120mg on a GP10 every 4 weeks and arrange for administration at the GP practice.
- When the patient attends for administration they should be given the patient information leaflet supplied with the vial of denosumab 120mg (Xgeva®) unless they already have a copy.
- Calcium and vitamin D supplements should be prescribed for all patients unless hypercalcaemic. The usual dose is 1-2 tablets daily of Accrete D3 or another equivalent alternative.
- Conduct recommended laboratory tests and contact hospital consultant to advise if results are out with range. If corrected calcium is below the normal range (less than 2.2mmol/L) denosumab 120mg should be withheld until calcium is within the normal range (between 2.2-2.6mmol/L). If corrected calcium is above the normal range (more than 2.6mmol/L) denosumab 120mg can be prescribed but the prescriber should consider withholding calcium supplements and reviewing at the next administration. Other causes for hypercalcaemia should be excluded.
- Ensure no interacting medications are prescribed in primary care.
- Refer back to the hospital consultant for review if there are signs of disease progression.
- Monitor for concordance with therapy.
- Report any adverse events to consultant and the MHRA using the Yellow Card System.
- When writing laboratory request forms always include details of the patient's medication.
- Refer back to the hospital consultant for review if there are signs of disease progression.
- Ensure that all other professionals in the shared care team are kept informed of any changes in the patient's circumstances.

Note: In addition to absolute values for haematological or biochemical indices a rapid change or a consistent upward/downward trend in any value should prompt caution and extra vigilance.

If something unexpected occurs contact consultant. Notify the consultant if denosumab is stopped.

RESPONSIBILITY OF OTHER HEALTHCARE PROFESSIONALS

Routine dental check-ups should be performed on patients receiving denosumab (Xgeva®**)**. If the patient reports any oral symptoms including dental mobility, pain or swelling then the dentist should refer the patient back to their consultant.

Dentists should liaise with the patient's GP and consultant before performing any invasive dental procedures. These should only be performed after careful consideration and avoided in close proximity to denosumab (Xgeva®**)** administration.

RESPONSIBILITY OF THE PATIENT

- Attend for the administration of medication regularly as directed by the specialist/doctor.
- Attend hospital and GP clinic appointments as requested by specialist/GP practice. Failure to attend appointments may result in medication being reviewed/stopped.
- Report any adverse effects/illness to the specialist/GP and present rapidly to specialist/GP should their condition significantly worsen.
- 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. While on treatment, patients should avoid invasive dental procedures if possible due to the risk of osteonecrosis of the jaw.

PRESCRIBING INFORMATION

For specific product information consult the current summary of product characteristics (http://emc.medicines.org.uk/), the BNF (https://www.medicinescomplete.com/mc/index.htm)

CONTRAINDICATIONS

- Hypersensitivity to the active substance or to any of the excipients.
- Severe, untreated hypocalcaemia. Pre-existing hypocalcaemia should be corrected prior to initiating denosumab therapy.
- Unhealed lesions from dental or oral surgery. A dental examination with preventive dentistry and an individual benefit-risk assessment is recommended prior to treatment with denosumab due to the risk of osteonecrosis of the jaw. Consultants should refer patients for this examination if necessary prior to initiation of treatment.
- Patients being treated with denosumab (Xgeva®) should not be treated concomitantly with other denosumab containing medicinal products.
- Patients being treated with denosumab (Xgeva®) should not be treated concomitantly with bisphosphonates.

PREGNANCY

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 with denosumab. Refer back to consultant.

BREAST-FEEDING

Should be avoided when breastfeeding. Refer back to consultant.

COMMON SIDE EFFECTS AND THEIR MANAGEMENT

Hypocalcaemia – monitor plasma calcium levels during therapy. Ensure a calcium and vitamin D_3 supplement is prescribed during therapy. Denosumab therapy should be withheld until corrected calcium is back within the normal range (2.2 - 2.6mmol/L). The risk of hypocalcaemia increases with increasing degrees of renal impairment and patients with a creatinine clearance of less than 30mL/min should be monitored closely.

Hypophosphataemia – replace as necessary. Exclude other causes.

COMMON DRUG INTERACTIONS (for a full list see SmPC)

There are no significant drug interactions.

Patients being treated with Xgeva® should not be treated concomitantly with bisphosphonates or with denosumab for other indications (e.g. osteoporosis).

ADVERSE DRUG REPORTING

If an adverse reaction should occur inform relevant medical practitioner as soon as possible.

Report to the MHRA using the Yellow Card System https://yellowcard.mhra.gov.uk/

REFERENCES

Electronic Medicines Compendium – Denosumab (Xgeva®)
https://www.medicines.org.uk/emc/product/4675/smpc [accessed 01 Feb 2023]

Grampian Medicines Management, Shared Care Policy Webpage
Denosumab - Shared Care Protocol (scot.nhs.uk) [accessed 01 Feb 2023]

Web BNF – Denosumab
Denosumab | Drugs | BNF | NICE [accessed 01 Feb 2023]

ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION

In the event of concern being raised, the primary care practitioner should contact the referring consultant via the hospital switchboard, via their secretary, by e-mail or letter, whichever is more appropriate. If the concern is urgent, and out of hours advice is required, the on call oncology consultant may be contacted via switchboard.

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