NHS
Pan Mersey
Area Prescribing Committee

Prescribing Support Information

Denosumab 60mg in 1ml prefilled syringe

AMBER following specialist initiation

Your patient has been identified as being suitable to receive denosumab in accordance with the indication detailed below. He/she has been started on treatment and has been reviewed to assess the adverse effects of the treatment by the specialist team. **The first two doses have been administered in secondary care at 6 monthly intervals.**

Denosumab has been considered as appropriate for prescribing in primary care and the information contained in this document has been provided to support you to prescribe it for your patient in the community.

Denosumab (Prolia® brand) is a monoclonal antibody, administered by subcutaneous injection into the thigh, abdomen or upper arm once every 6 months; it inhibits osteoclast formation, function and survival thereby decreasing bone resorption. It is licensed at this dose and frequency for the treatment of postmenopausal osteoporosis in women and in men at increased risk of fractures, and bone loss associated with hormone ablation in men with prostate cancer at increased risk of fracture. **(A high dose preparation (XGEVA® brand) administered every 4 weeks is licensed for reduction of bone damage in patients with bone metastases – this is not suitable for shared care and is NOT covered by this protocol).**

Pan Mersey Approved Indications for use
Treatment of postmenopausal osteoporosis in women and in men at increased risk of fractures, and bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures.

NICE recommend denosumab as a treatment option for the secondary prevention of osteoporotic fragility fractures only in postmenopausal women at increased risk of fractures who are unable to comply with the special instructions for administering alendronate and either risedronate or etidronate, or have an intolerance of, or a contraindication to, those treatments.

For further information, please follow the link for the NICE technology appraisal TA204 Osteoporotic fractures - denosumab: Link and NICE NG 131, Prostate Cancer: Link

Prescribing for patients with renal impairment CKD stages G4 and G5 should not be carried out by GPs and should remain the responsibility of the specialist.

Name of Drug, Form and Dose
Denosumab (Prolia® brand) 60mg in 1ml injection. Dosage is 60mg by subcutaneous injection every 6 months. **Calcium and Vitamin D must be prescribed** in conjunction with denosumab, or adequate intake should be established as hypocalcaemia has been reported.

No dosage adjustment is necessary in the elderly.

The degree of renal impairment has no effect on the pharmacokinetics of denosumab.

Specialists initiating treatment will guide all patients to register with the Prolong Patient Support Programme (Patient Education & Reminder Service) which will automatically provide a reminder every 6 months to patient and prescriber that a dose is due.

Denosumab injection may be prescribed by FP10 prescription for subsequent administration, or practices may wish to obtain supplies from a pharmaceutical wholesaler and claim reimbursement for a personally administered item. It is suitable for administration by a healthcare professional who has been suitably trained in injection techniques.

Monitoring recommendations

A pre-dose serum calcium level should be measured prior to each dose to check for hypocalcaemia. For patients predisposed to hypocalcaemia, it should be rechecked two weeks after each dose. See special warnings/cautions section.

How long the medicine should be prescribed for

Treatment with denosumab should continue long term. It is recommended that patients are referred back to the specialist service for review after 5 years of treatment to assess the need for further continuation of therapy. The specialist service must inform the GP of the date denosumab therapy was started in the clinic letter.

If at any point treatment no longer seems appropriate, please contact the specialist for advice.

Contra-indications

Severe untreated hypocalcaemia.
Unhealed lesions from dental or oral surgery
Hypersensitivity to the active substance or to any of the excipients

Adverse effects

Cellulitis is an uncommon adverse effect and patients will have been warned by the specialist at initiation to report any skin infections.
Osteonecrosis of the external auditory canal.
Osteonecrosis of the jaw – see special warnings/cautions section
Atypical femoral fractures – see special warnings/cautions section
Hypocalcaemia – see special warnings/cautions section

Commonly reported infections include:
Urinary tract infection and upper respiratory tract infection.
Sciatica and musculoskeletal pain, pain in extremity
Rash and eczema
Alopecia
Constipation and abdominal discomfort
Cataracts

This list is not exhaustive; please refer to the manufacturer's SPC and the most current BNF for full information on contraindications, warnings, side effects and drug interactions.

Special warnings/cautions

Hypocalcaemia

All patients must have calcium checked prior to each injection of denosumab. Severe symptomatic hypocalcaemia has been reported, with most cases occurring in the first weeks of initiating therapy, but it can occur later.

Patients should also be told to report the symptoms of hypocalcaemia (e.g. muscle spasms, twitches, cramps, numbness or tingling in the fingers, toes or around the mouth). Calcium levels should be checked if patients report these symptoms.

In the event of hypocalcaemia the next dose should not be given and the relevant specialist should be contacted for advice by telephoning the number in the clinic letter.

Patients with severe renal impairment (creatinine clearance < 30 ml/min) or receiving dialysis are at greater risk of developing hypocalcaemia in the absence of calcium supplementation.

Further information: Drug Safety Update - hypocalcaemia

Osteonecrosis of the jaw (ONJ) There have been rare cases of ONJ in patients receiving denosumab 60 mg for osteoporosis in clinical practice. The most common risk factors were invasive dental procedures, history of bisphosphonate therapy, and being more than 65 years old.

During treatment with denosumab patients should avoid invasive dental procedures if possible (e.g., tooth extraction, dental implants, oral surgery), and maintain good oral hygiene. They should have regular dental check-ups and be encouraged to report any dental symptoms regularly.

A dental examination with appropriate preventive dentistry should be considered by the specialist prior to treatment with denosumab in patients with concomitant risk factors.

Patients who develop ONJ should be referred back to the specialist and treatment should be stopped until the condition resolves and contributing risk factors are mitigated.

Further Information: Drug Safety Update - updated - ONJ

Osteonecrosis of the External Auditory Canal has been reported with denosumab and this should be considered in patients who present with ear symptoms including chronic ear infections or in those with suspected cholesteatoma. Possible risk factors include steroid use and chemotherapy, with or without local risk factors such as infection or trauma. The MHRA recommends advising patients to report any ear pain, discharge from the ear, or an ear infection during denosumab treatment.

Further information: Drug Safety Update - Osteonecrosis-of-the-external-auditory-canal

Atypical femoral fractures have been reported rarely in patients with postmenopausal osteoporosis receiving long-term (≥2.5 years) treatment with denosumab 60 mg in a clinical trial. The nature of the fractures seen with denosumab 60 mg is similar to the atypical femoral fractures seen with long-term bisphosphonate therapy.

Patients should be told to report new or unusual thigh, hip or groin pain. Any patients presenting with these symptoms during denosumab treatment should be evaluated for an incomplete femoral fracture, along with examination of the contralateral femur. Discontinuation of denosumab therapy should be considered if an atypical femur fracture is suspected, while the patient is evaluated. Further information: Drug Safety Update - atypical femoral fractures

Fructose intolerance
This product contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not receive denosumab.

Latex allergy
The needle cover of the pre-filled syringe contains dry natural rubber (a derivative of latex), which may cause allergic reactions. Patients should be asked if they have an allergy to latex.

Interaction with other medicines
No drug interactions have been identified in clinical trials and interaction studies have not been performed.

Other information
Denosumab should be administered via subcutaneous injection in the upper arm, upper thigh or abdomen by a healthcare professional who has been suitably trained in injection techniques.

Denosumab should be stored in a refrigerator at 2°C – 8°C.

Patients should be given the package leaflet and the patient reminder card.

Contact details for advice
Please refer to the contact details included in the clinic letter issued by the specialist.

References
1. NICE TA 204 Denosumab for the prevention of osteoporotic fractures in postmenopausal women. NICE TA204
2. NICE NG 131 Prostate cancer: diagnosis and management. NICE NG131
3. Electronic Medicines Compendium, Prolia, accessed March 2020. SPC Denosumab (Prolia)
4. NICE BNF accessed March 2020. DENOSUMAB BNF content published by NICE