

Guideline for the use of denosumab

This guideline has been produced to support the seamless transfer of prescribing for denosumab from secondary to primary care, and provides an information resource to support clinicians providing care to the patient. It does not replace discussion about sharing care on an individual patient basis.

This guideline was prepared using information available at the time of preparation, but users should always refer to the manufacturer's current edition of the Summary of Product Characteristics (available at <http://www.emc.medicines.org.uk>) for more details.

1.0 Status of Denosumab

Denosumab has been approved by NICE (NICE TA 204).

Denosumab has been approved by the North Central London Sector. Local practice is for the drug to be initiated in secondary care, and for the treatment to be transferred to primary care if the initial response is good with no adverse effects.

2.0 Licensed Indications and Dose

Denosumab (PROLIA[®]) is licensed for the treatment of osteoporosis in postmenopausal women at increased risk of fractures.

The recommended dose of denosumab is 60mg administered as a single subcutaneous injection once every 6 months into the thigh, abdomen or back of the arm.

Patients must be adequately supplemented with calcium and vitamin D.

NB: PROLIA[®] is also licensed for bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures; another preparation of denosumab (XGEVA[®]) is licensed for bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures. These are both outside of the scope of this guideline.

3.0 Referral Criteria and Patient Selection

Primary Prevention

Denosumab will be recommended as a treatment option for the primary 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

and

- who have a combination of T-score, age and number of independent clinical risk factors for fracture. (Independent clinical risk factors for fractures are parental history of hip fracture, alcohol intake of 4 units or more per day, and rheumatoid arthritis).

Secondary Prevention

Denosumab will be recommended 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.

4.0 Safety Issues

4.1 *Contra-indications (see BNF or SPC)*

- Hypocalcaemia
- Hypersensitivity to the active substance or to any of the excipients

4.2 *Cautions (see BNF or SPC)*

- Hypocalcaemia must be corrected by adequate intake of calcium and vitamin D before initiating therapy.
- Patients receiving denosumab may develop skin infections (predominantly cellulitis). Patients must seek prompt medical attention if they develop signs of cellulitis.
- Osteonecrosis of the jaw (ONJ) has been reported (rare). A dental examination with appropriate preventive dentistry should be considered prior to starting denosumab in patients with concomitant risk factors (a diagnosis of cancer with bone lesions, concomitant therapies {chemotherapy, corticosteroids, anti angiogenic biologics, radiotherapy to head and neck}, poor oral hygiene, dental extractions, and co-morbid disorders {pre-existing dental disease, anaemia, coagulopathy, infection} and previous treatment with bisphosphonates).
- While on denosumab treatment patients should avoid invasive dental procedures and maintain good oral hygiene.
- The needle cover of the prefilled syringe contains dry natural rubber (a derivative of latex), which may cause allergic reactions.
- Patients with rare hereditary problems of fructose intolerance should not use denosumab.

4.3 *Common Side Effects (See BNF or SPC)*

- Mild, transient decreases in serum calcium.
- Skin infections predominantly cellulitis.
- Other common undesirable effects (incidence of 1-10%) were urinary tract infection, upper respiratory tract infection, cataracts, constipation, sciatica, rash, pain in extremity.
- There have been no reports of anaphylaxis with the injection of denosumab to date.

4.4 *Drug Interactions (see BNF or SPC)*

- No interaction studies have been performed.

4.5 *Pre-treatment Assessment*

- Hypocalcaemia is a contraindication and must be corrected before administration. Clinical monitoring of calcium levels is recommended for patients predisposed to hypocalcaemia.
- Assess the patient to ensure he/she has good oral/dental hygiene. If necessary advise the patient to see a dentist before proceeding.

4.6 *Routine Safety Monitoring*

- Check that the patient is calcium and vitamin D replete.
- There are no other specific monitoring requirements for denosumab.

- Advise patients to seek prompt medical attention if they develop signs or symptoms of cellulitis.
- Refer patients for prompt medical attention if they develop signs or symptoms of hypocalcaemia (i.e. altered mental status, tetany, seizures, and QTc prolongation)

5.0 Role of Consultant

- To assess the suitability of the patient for denosumab.
- To discuss the benefits and side effects of treatment with the patient.
- Explain to the patient that the treatment is 6 monthly injections for up to 3 years.
- Discuss the shared care arrangement with the patient and ensure he/she understands the plan for their follow-up 6 monthly injections at their GP surgery.
- Explain to the patient that the GP will refer them back for a review on completion of the treatment course (as specified by the specialist).
- Ensure that the patient is taking calcium and vitamin D supplements.
- Assess the patient to ensure he/she has good oral hygiene and use clinical judgement to determine if dental examination is required prior to initiating therapy.
- Initiate first denosumab injection.
- Report any adverse events to the MHRA.
- Supply GP with a summary of the patient review and a copy of the local guidelines on use of denosumab.

6.0 Role of GP

- To ensure that denosumab is added to the patient's drug record.
- To ensure that other osteoporosis treatments (e.g. alendronate, strontium) are stopped and removed from the patient's repeat prescription.
- To ensure that calcium and vitamin D supplements are continued if appropriate.
- To ensure that additional calcium supplementation is prescribed if hypocalcaemia occurs.
- To ensure that additional monitoring of serum calcium levels is conducted in patients with severe renal impairment (creatinine clearance < 30 ml/min) or receiving dialysis.
- Ensure an account is set up to order denosumab and determine if it will come direct to the practice (more straightforward scenario for the patient). Alternatively, if the patient will need to collect their prescription from the pharmacy ensure an FP10 is written.
- Ensure that prior to injection the denosumab prefilled syringe must be kept in its outer carton, in order to protect from light, and stored in a refrigerator.
- Prescribe and administer the denosumab injection at six monthly intervals for time period as specified by the initiating specialist.
- Report any adverse events to the MHRA and discuss with the consultant if action is uncertain.
- Refer patient back to the consultant for review on completion of the treatment course, or sooner if any concerns (such as altered mental health, tetany, seizures, or QTc prolongation which may indicate severe hypocalcaemia).

<p>In line with MHRA drug safety update (February 2013) all patients newly initiated on denosumab therapy will be advised to report new or unusual thigh, hip or groin pain. Patients presenting with such symptoms to the GP should be referred for prompt medical attention for evaluation of an incomplete femoral fracture.</p>

7.0 Role of Patient

- To report any adverse events to the doctor who last administered the injection.
- To seek prompt medical attention if they develop signs or symptoms of cellulitis.
- To avoid invasive dental procedures and maintain good oral hygiene whilst on denosumab treatment.
- To continue the calcium and vitamin D supplement.
- To attend the GP surgery every 6 months for the denosumab injection.

8.0 Role of the Specialist Nurse in Rheumatology

- To ensure that the patient is calcium and vitamin D replete.
- To administer the first injection of denosumab.
- Advise the patient that their other osteoporosis treatments should stop but that they should continue with their calcium and vitamin D supplements.
- Advise the patient that their next injection will be administered at the GP surgery in 6 months.

9.0 Further Information

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10.0 Version Control

Version Control Details			
Date	Version	Description	Reason for changes
16/07/2012	1.0	New Guideline	Approved by RNOH Drugs & Therapeutics Committee
17/09/2012	1.1	Update	Further detail added to monitoring and role of GP sections; Ratified by DTC
20/05/2013	1.2	Update	Includes MHRA drug safety update (February 2013); Ratified by DTC