Health and Social Care

Department of Health
An Roinn Sláinte
Männystrie O Poustie
www.health-ni.gov.uk

Interface Pharmacist Network Specialist Medicines

Denosumab (Prolia®)
Shared care guideline

Specialist details	Patient identifier
Name: _____	
Location: _____	
Tel: _____	**Date:** _____

Introduction

Generic medicine name:	Denosumab
Formulations:	60mg/1mL subcutaneous injection (Prolia®). Should be stored between 2 - 8 °C. Other preparations of denosumab are not covered by this guideline
Intended Indication:	Treatment of Osteoporosis in **post-menopausal women** at increased risk of fracture (see NICE TA204). **This is the only licensed indication currently approved for use in Northern Ireland**. Refer to Northern Ireland Managed Entry website for status of any other indications

Hypocalcaemia or vitamin D deficiency must be corrected by adequate intake of calcium and/or vitamin D before initiating therapy. Even normocalcaemic patients could be at risk of hypocalcaemia following administration of denosumab if they are vitamin D deficient. Severe symptomatic hypocalcaemia has been reported in patients predisposed to hypocalcaemia receiving denosumab.

Corrected calcium levels should be checked and confirmed to be within normal limits of lab:

- before each dose (e.g. one to three weeks before each dose is given)
- within two weeks after the initial dose in patients with risk factors for hypocalcaemia (eg, eGFR < 30 mL/min/1.73m^2). This is not required with subsequent doses (unless advised otherwise by specialist)
- if suspected symptoms of hypocalcaemia occur or if otherwise indicated based on the clinical condition of the patient.

[a] It is important that all patients know to report symptoms of hypocalcaemia to their doctor (eg, muscle spasms, twitches, or cramps; numbness or tingling in the fingers, toes or around the mouth).

Adult dosage and administration

The recommended dose of denosumab is 60mg administered as a single subcutaneous injection once every 6 months into the thigh, abdomen or upper arm. No dose adjustment is required in renal impairment or elderly.

In some circumstances, denosumab is suitable for self-administration by a patient or carer. In these instances, training will be arranged by the hospital specialist who initiates the drug. A protocol on how to self-administer the injection and a patient support programme (Prolong®) is available from the pharmaceutical company if required www.prolia.co.uk

Pathways

A number of different pathways for prescribing and administration (with agreement between GP and Hospital Specialist) are covered by this shared care guideline and are outlined in summary below. See Hospital Specialist, and GP responsibilities sections for detail.

Pathway 1: First dose in secondary care with ongoing prescribing and administration in primary care

Pathway 2: First dose in secondary care with ongoing prescribing in primary care – patient to self-administer

Pathway 3: First dose in primary care with subsequent prescribing and administration in primary care

Hospital specialist responsibilities

- Assess patient suitability for denosumab (as per NICE TA204) and ensure other antiresorptives (e.g. bisphosphonates) are discontinued prior to starting denosumab
- Provide patient/carer with relevant written information on use (including Prolia® patient alert card), side effects and need for monitoring of medication
- Assess risk factors for hypocalcaemia. Ensure patients are aware that they should report symptoms of hypocalcaemia [a)]
- Ensure patients are adequately supplemented with calcium and vitamin D – this is especially important in patients with severe renal impairment
- Evaluate patients for Osteonecrosis of the Jaw (ONJ) risk factors [b)] prior to treatment. A dental exam with appropriate preventative dentistry is recommended in patients with concomitant risk factors. Explain to the patient about the risk of ONJ and advise patients to:
  - tell their doctor if they have any problems with their mouth or teeth before starting or during treatment (e.g. loose teeth, pain, swelling, non-healing sores or discharge)
  - if they wear dentures they should make sure their dentures fit properly before starting treatment
  - maintain good oral hygiene and get routine dental check-ups during treatment
  - tell their doctor and dentist that they are receiving denosumab if they need dental treatment or dental surgery
- Explain to the patient about the risk of osteonecrosis of the external auditory canal [c)]. Advise patients to:
  - report any ear pain, discharge from the ear, or an ear infection during denosumab treatment
- Ensure corrected calcium and renal function is checked before each dose of denosumab is administered in secondary care
- Arrange shared care with GP:
  - Decide which pathway for prescribing and administration best suits patient and agree plans for prescribing and administration of denosumab therapy with the patient's GP specifying brand (Prolia®) to be prescribed
  - Discuss the shared care arrangement with the patient to ensure he/she understands the plans for follow-up care
  - Indicate if patient/carer has been trained and will self-administer
  - If patient/carer cannot self-administer, ongoing administration in primary care will be required
- Communicate baseline results and clearly state who is responsible for ongoing monitoring and acting on test results
- For patients on pathway 1 or 2, administer the first denosumab injection in secondary care
- For patients on pathway 2, provide training on self-administration and disposal of sharps box.
- For those patients predisposed to hypocalcaemia, arrange check of corrected calcium within two weeks after the first dose and ensure GP and patient are aware of the need for this
- Continue to review the patient at agreed specified intervals to monitor disease response to treatment and need to continue therapy. The optimal duration of denosumab treatment for osteoporosis has not been established; re-evaluate the need for continued treatment periodically based on the expected benefits and potential risks of denosumab on an individual patient basis, particularly after 5 or more years of use.
- Review results of safety monitoring, request additional tests if required and send a written summary to the GP
- Provide any other advice or information for the GP if required
- Report adverse drug reactions to usual bodies (e.g. MHRA).

GP responsibilities

- Prescribe denosumab 60mg (by brand name Prolia®) subcutaneously every six months as advised by the initiating specialist. Prescribe a sharps box where needed
- Ensure practice systems are in place for prescribing (and administration if needed) every six months and inform initiating specialist if any missed treatments are identified. The Prolia® ProActive service can support clinicians in primary care with this and is available at www.prolia.co.uk
- Patients should not stop denosumab without specialist review.
- GP to identify and confirm who will be responsible for administering the denosumab injection (i.e. the GP, nurse or in some cases, the patient/carer (as advised by initiating specialist)
- Ensure corrected calcium levels and renal function are checked before every dose (e.g. one to three weeks before each dose is administered). These should also be checked two weeks after each dose for those patients who require it as advised by specialist. If any results are abnormal or if any concerns, withhold denosumab and contact initiating specialist for advice.
- Ensure calcium and vitamin D preparations are prescribed as advised by specialist (see also NI formulary for preferred choices) and encourage patient compliance
- Ensure other antiresorptives (e.g. bisphosphonates) are discontinued prior to starting denosumab
- Ensure no drug interactions with other medicines
- Reiterate to patient the importance of maintaining good oral hygiene - recommending regular dental check-ups. Refer to Prolia® patient alert card
- Report adverse drug reactions to initiating specialist and usual bodies (e.g. MHRA)
- Refer the patient back to the initiating specialist if their condition deteriorates and/or they experience any adverse reactions

Adverse effects, precautions and contraindications

Side effects listed as common include urinary tract infection, upper respiratory tract infection, sciatica, cataracts, constipation, abdominal discomfort, musculoskeletal pain, rash and pain in extremities.

Hypocalcaemia with denosumab most commonly occurs within the first 6 months of treatment, but it can occur at any time during treatment.

Skin infections: patients receiving denosumab may develop skin infections (predominantly cellulitis) leading to hospitalisation. Prompt medical attention is required if signs or symptoms of cellulitis develop.

Pregnancy: Denosumab is not recommended for use in pregnant women.

Osteonecrosis of the jaw (ONJ) has been reported in patients treated with denosumab or bisphosphonates, another class of anti-resorptive agents. For patients who develop ONJ while on denosumab therapy, dental surgery may exacerbate the condition. If ONJ occurs during treatment with denosumab, use clinical judgment and guide the management plan of each patient based on individual benefit/risk evaluation. Temporary interruption of treatment should be considered until the condition resolves and contributing risk factors are mitigated, where possible. While on treatment with denosumab, patients with risk factors for ONJ should avoid invasive dental procedures if possible.

[b)] Risk factors for ONJ include: smoking; old age; poor oral hygiene; invasive dental procedures; comorbidity (eg, dental disease, anaemia, coagulopathy, infection) ; advanced cancer ; previous treatment with bisphosphonates; concomitant treatments (e.g., chemotherapy, anti-angiogenic biologics, corticosteroids, radiotherapy to head and neck)

Osteonecrosis of the external auditory canal has been reported rarely and should be considered in patients who present with ear symptoms including chronic ear infections or in those with suspected cholesteatoma. Possible risk factors [c)] include steroid use and chemotherapy, with or without local risk factors such as infection or trauma.

Atypical femoral fractures have been reported rarely. Patients presenting with new or unusual thigh, hip or groin pain should be evaluated for an incomplete femoral fracture. Discontinuation of denosumab therapy should be considered if an atypical femur fracture is suspected, while the patient is evaluated.

Increased risk of multiple vertebral fractures after stopping or delaying ongoing treatment has been reported in patients within 18 months of stopping or delaying ongoing denosumab treatment for osteoporosis. Patients with a previous vertebral fracture may be at highest risk. Patients should not stop denosumab without specialist review

Latex Allergy: the needle cover of the pre-filled syringe contains dry natural rubber (a derivative of latex), which may cause allergic reactions.

Denosumab is contraindicated in hypocalcaemia and in any patients who have hypersensitivity to active substance or to any of the excipients listed in the SPC.

Patients being treated with Prolia® should not be treated concomitantly with other denosumab-containing medicinal products.

Common drug interactions

No significant drug interactions have been reported.

Communication

For any queries relating to this patient's treatment with denosumab, please contact the specialist named at the top of this document.

This information is not inclusive of all prescribing information and potential adverse effects.
Please refer to full prescribing data in the SPC at www.medicines.org.uk or the BNF

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