BOURNEMOUTH, DORSET AND POOLE PRESCRIBING FORUM

SHARED CARE GUIDELINE FOR PRESCRIBING DENOSUMAB (PROLIA ®)

INDICATION

This shared care guideline has been prepared to support healthcare professionals in the implementation of shared care management of patients who have been prescribed denosumab (Prolia®) for the prevention of fragility fractures.

Denosumab is recommended as an option for the treatment of osteoporosis in **postmenopausal women** at increased risk of fractures.

This document should be used alongside guidance published by the National Institute for Health and Clinical Excellence (Technology Appraisal 204 "Denosumab for the prevention of osteoporotic fractures in post menopausal women", October 2010[1]).

Denosumab is recommended as a treatment option for the primary prevention of osteoporotic fragility fractures 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[1], age and number of independent clinical risk factors for fracture as indicated in the following table.

Table 1: T-scores at (or below) which denosumab is recommended when oral bisphosphonates are unsuitable

	Number of independent clinical risk factors for fracture		
Age (years)	**0**	**1**	**2**
65–69	– [a]	−4.5	−4.0
70–74	−4.5	−4.0	−3.5
75 or older	−4.0	−4.0	−3.0

[a] Treatment with denosumab is not recommended.

For the purposes of the NICE guidance, independent clinical risk factors for fracture are parental history of hip fracture, alcohol intake of 4 or more units per day, and rheumatoid arthritis.

Denosumab is also 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.

AREAS OF RESPONSIBILITY FOR SHARED CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of denosumab can be shared between the consultant and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the consultant. If the consultant asks the GP to prescribe this drug, the GP must reply to this request as soon as practicable confirming whether or not they are happy to do so.

Sharing of care assumes communication between the consultant, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

Shared Care is only appropriate if it provides the optimum solution for the patient.

Note, the doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

CONSULTANT RESPONSIBILITIES	
1	To assess the patient and establish/confirm the diagnosis
2	To determine a management strategy and ensure follow-up in conjunction with the GP

3	To initiate denosumab treatment including:
	• Ensuring the suitability of the patient for denosumab treatment in accordance with NICE TA 204
	• Completing retrospective notification form for denosumab treatment and forwarding this to the relevant PCT
	• Discussing and agreeing the management strategy with the patient including:
	  ○ informing them of possible side-effects to the treatment and ensuring they are aware of who to contact in this instance
	  ○ whether the patient would be happy to administer subsequent denosumab injections themselves (this may be appropriate for patients who are already self administering parenteral therapy such as anti-TNF treatment, methotrexate etc)
	• Giving the initial injection of denosumab (including teaching the patient how to self administer the injection if they are to perform subsequent injections themselves)
	• Ensuring the patient understands the proposed plan for follow-up
	• Writing to the patient's GP advising them of the treatment commenced, including appropriate prescribing information and ongoing need for calcium and vitamin D, requesting written confirmation of their agreement to 'share care' and administer further denosumab injections (unless the patient is going to self administer the injection), and advising them of duration of therapy and arrangements for follow-up

4	To be available for advice if the patient's condition changes and to arrange for the patient to be followed up in the out-patient clinic as necessary

GENERAL PRACTITIONER RESPONSIBILITIES	
1	To confirm, in writing, without delay, their agreement or otherwise to participate in shared care
2	Where shared care is agreed, to prescribe and administer denosumab at six-monthly intervals after the initial administration by the specialist. [Note: a protocol on how to administer the injection is available from the pharmaceutical company if required]
3	To ensure practice system is set up to recall patient at six monthly intervals for repeat injections
4	Ensure account is set up to order denosumab and determine if it will come direct to the practice or if the patient will need to collect their prescription from the pharmacy. If the latter, ensure a reminder letter is sent to patient with the relevant instructions.
5	To monitor side effects of treatment and seek advice from the consultant if necessary
6	Report any adverse events to the Committee on Safety of Medicines (CSM) at the Medicines and Health Care Regulatory Agency (MHRA)
7	To liaise with the consultant regarding any complications of treatment or the discontinuation of treatment
8	To ensure the patient continues to take calcium and vitamin D (unless replete) and to deal with general health issues of the patient
9	To check for possible drug interactions when newly prescribing concurrent medication

Patient's role (or that of carer)	
1	Report to the specialist or GP if he/she does not have a clear understanding of the treatment and to report any concerns
2	Attend appropriate consultant and GP appointments
3	To have any required monitoring/tests carried out at regular intervals, as appropriate
4	Report any adverse events to the doctor who last administered their injection.

SUPPORTING INFORMATION[2,3]

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 back of arm. Administration should be performed by an individual who has been adequately trained in injection techniques.

Patients must be calcium and vitamin D replete during treatment with denosumab.

Dosage adjustments in specific patient populations

Patients with liver impairment
The safety and efficacy of denosumab have not been studied in patients with hepatic impairment.

Patients with kidney impairment
No dose adjustment is required in patients with renal impairment.

Elderly patients
No dose adjustment is required in elderly patients.

Contraindications

Denosumab is contraindicated in:

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

Special Warnings

Hypocalcaemia must be corrected by adequate intake of calcium and vitamin D before initiating therapy. Patients with severe renal impairment (creatinine clearance < 30 ml/min) or receiving dialysis are at greater risk of developing hypocalcaemia. Clinical monitoring of calcium levels is recommended for patients predisposed to hypocalcaemia.

Patients receiving denosumab may develop skin infections (predominantly cellulitis) leading to hospitalisation. Patients should be advised to seek prompt medical attention if they develop signs or symptoms of cellulitis.

Osteonecrosis of the jaw (ONJ) has been reported in patients treated with denosumab or bisphosphonates, another class of anti-resorptive agents. Most cases have been seen in cancer patients, however, some have occurred in patients with osteoporosis. ONJ has been reported rarely in clinical studies in patients receiving denosumab at a dose of 60mg every 6 months for osteoporosis. Known risk factors for ONJ include a diagnosis of cancer with bone lesions, concomitant therapies (e.g chemotherapy, antiangiogenic biologics, corticosteroids, radiotherapy to head & neck), poor oral hygiene, dental extractions, and co-morbid disorders (e.g pre-existing dental disease, anaemia, coagulopathy, infection) and previous treatment with bisphosphonates.

As with bisphosphonates, a dental examination with appropriate preventative dentistry should be considered prior to treatment with denosumab in patients with concomitant risk factors. While on treatment, these patients should avoid invasive dental procedures if possible. Good oral hygiene practices should be maintained during treatment with denosumab. 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.

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

Patients with rare hereditary problems of fructose intolerance should not take denosumab.

Pregnancy and breastfeeding

Denosumab is not recommended for use in pregnant women. It is unknown whether denosumab is excreted in human milk. A decision on whether to abstain from breast-feeding or to abstain from treatment with denosumab should be made, taking into account the benefit of breast-feeding to the newborn/infant and the benefit of denospumab therapy to the woman.

Drug interactions

No interaction studies have been performed. There are no clinical data on the co-administration of denosumab and hormone replacement therapy (oestrogen), however, the potential for a pharmacodynamic interaction is considered to be low.

In postmenopausal women with osteoporosis the pharmacokinetics and pharmacodynamics of denosumab were not altered by previous alendronate therapy, based on data from a transition study (alendronate to denosumab).

Side Effects

Common side effects include: urinary tract infection, upper respiratory tract infection, sciatica, cataracts, constipation, rash, pain in extremity.

This list is not exhaustive – the manufacturer's summary of product characteristics (SPC) and the most current edition of the British National Formulary (BNF) should be consulted for full information on contra-indications, warnings, side-effects and drug interactions.

Cost

Annual treatment cost at 60mg every 6 months: £366 (MIMMS February 2011)

References

1. Denosumab for the prevention of osteoporotic fractures in post menopausal women (October 2010), National Institute for Health and Clinical Excellence (Technology Appraisal 204)
2. Summary of product characteristics for Prolia® (Denosumab). Amgen. October 2010
3. BNF 60 (September 2010)

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