NHS
Telford and Wrekin
Clinical Commissioning Group

Denosumab (Prolia®▼ 60 mg)
Effective Shared Care Agreement
For the treatment of Osteoporosis

Section 1: Shared care arrangements and responsibilities
Section 1.1 Agreement for transfer of prescribing to GP

Patient details

Name: _____

Address: _____

Date of Birth: _____

NHS number: _____

Specialist:
Address:

Email:

Contact number:

GP
Address:

Email:

Contact number:

Agreement to shared care, to be signed by GP and Specialist before prescribing is transferred to GP

Specialist Signature:

_____

Date:

GP Signature:

_____

Date:

Section 1.2: Shared Care responsibilities

This shared care agreement outlines suggested ways in which the prescribing responsibilities can be shared between the specialist and GP. GPs are invited to participate. If the GP feels that undertaking the roles outlined in the shared care agreement is outside their area of expertise or have clinical concerns about the safe management of the drug in primary care, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient's health remains with the specialist. If a specialist asks the GP to prescribe, the GP should reply to this request as soon as practicable. Sharing of care assumes communication between specialist, GP and patient.

If a specialist asks the GP to prescribe, the GP should reply to this request within 2 weeks.

The prescriber of the medication legally assumes clinical responsibility for the drug and the consequences of its use.

Responsibilities of the specialist initiating treatment

- To assess the patient and establish/confirm the diagnosis.
- Discuss with the patient, options for treatment and the suitability of denosumab.
- Pre-existing hypocalcaemia must be corrected prior to initiating denosumab. Calcium levels should be checked within 2 weeks of the initial dose in patients with risk factors (e.g. severe renal impairment, creatinine clearance <30ml/min)
- Ensure that a dental examination and appropriate preventative dentistry is completed for patients with risk factors for osteonecrosis of the jaw[1].
- Discuss the potential benefits and side effects of treatment with the patient.
- To initiate denosumab treatment including:
    - Ensuring the suitability of the patient for denosumab treatment in accordance with NICE TA 204.
    - Completing the NICE template form for denosumab treatment and forwarding this to NHS T&W CCG Medicines Management Team.
    - Discussing and agreeing the management strategy with the patient including:
        - informing them of possible side-effects to the treatment and ensuring that 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 on-going 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.

- Ensure agreed signed shared care form has been received back from GP to indicate that the GP is in agreement with prescribing and monitoring.

- Regular follow-up of patient (at least annually)

- Communicate promptly with the GP when treatment is changed.

- Advise GP when and how to stop treatment.

- Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition and ensure that clear backup arrangements exist for GPs to obtain advice and support.

- Report adverse events to the MHRA (via Yellow Card)

Responsibilities of the General Practitioner

- To confirm, without delay (within 2 weeks), their agreement or otherwise to participate in shared care.

- Prescribe and administer denosumab at six-monthly intervals after the initial administrations by the specialist.

- Check calcium levels at least two weeks before each dose.

- Ensure practice system is set up to recall patient at six monthly intervals for repeat injections.

- To monitor side effects of treatment and seek advice from the specialist if necessary.

- To liaise with specialist regarding any complications of treatment or the discontinuation of treatment.

- To check for possible drug interactions when newly prescribing concurrent treatment.

- To ensure the patient continues to take calcium and vitamin D and to deal with general health issues of the patient.

- Tell all patients to maintain good oral hygiene, receive routine dental check-ups and immediately report any oral symptoms such as dental mobility, pain or swelling.

- Report adverse events to the MHRA (via Yellow Card)

Section 2: General Information on Denosumab

Indication[2]

Denosumab (Prolia®▼ 60 mg/ml) 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, age and number of independent clinical risk factors for fracture as indicated in the following table.

Age (Years)	Number of independent clinical risk factors for fracture		
	0	1	2
65-69	*	-4.5	-4.0
70-74	-4.5	-4.0	-3.5
75 or older	-4.0	-3.5	-3.0

*Denosumab is not recommended.

Denosumab is 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.

Dosage and administration[3 4]

The recommended dose of 60mg denosumab is administered as a single subcutaneous injection once every 6 months into the thigh, abdomen or upper arm. Administration should be performed by an individual who has been adequately trained in injection techniques

Patients must be adequately supplemented with calcium and vitamin D.

No dose adjustment is required in patients with renal impairment

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

No dose adjustment is required in elderly patients.

Contraindications

Hypocalcaemia. - Denosumab should not be used in patients with hypocalcaemia, regardless of severity.

Hypocalcaemia is a known risk with denosumab use, especially in patients with severe renal impairment (creatinine clearance <30 mL/min; estimated glomerular filtration rate [eGFR] 15 – 29 mL/min/1.73 m^2) or receiving dialysis. Severe symptomatic hypocalcaemia has been reported in patients at increased risk of hypocalcaemia receiving denosumab 60 mg[5].

Pre-existing hypocalcaemia must be corrected prior to initiating denosumab, and adequate intake of calcium and vitamin D is important in all patients receiving 60mg denosumab

Ensure that a dental examination and appropriate preventative dentistry is completed for patients with risk factors for osteonecrosis of the jaw.

Atypical femoral fractures have been reported rarely in patients with postmenopausal osteoporosis receiving long term (≥2.5 years) treatment with denosumab. During treatment, 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.[6]

Patients with severe renal impairment (creatinine clearance <30 mL; eGFR 15 – 29 mL/min/1.73m2) or receiving dialysis are at greater risk of developing hypocalcaemia, and monitoring of calcium levels in these patients is recommended.

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

Patients with rare hereditary problems of fructose intolerance should not use denosumab due to nature of excipients.

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 new-born /infant and the benefit of denosumab 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

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. Most cases have been in cancer patients; however some have occurred in patients with osteoporosis.

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.).

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[1] MHRA Drug Safety Update Vol 8 Issue 2 Sept 2014

[2] Denosumab for the prevention of osteoporotic fractures in post-menopausal women (October 2010), National Institute for Health and Clinical Excellence (Technology Appraisal 204)

[3] Summary of Product Characteristics for Prolia® (Denosumab). www.medicines.org.uk

[4] BNF 64 September 2012

[5] MHRA Drug Safety Update Vol 6 Issue 3 Oct 2012.

[6] MHRA Drug safety Update Vol 6 Issue 7 Feb 2013.