Shared Care Agreement
Denosumab (Prolia®▼)
For the treatment of osteoporosis in adults

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, 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 a GP to prescribe, the GP should respond to this request within 2 weeks.

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

### Specialist’s information

<table>
<thead>
<tr>
<th>Consultant name:</th>
<th>Consultant’s signature:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultant Trust:</td>
<td></td>
</tr>
<tr>
<td>Contact number:</td>
<td></td>
</tr>
<tr>
<td>Email address:</td>
<td>Date:</td>
</tr>
</tbody>
</table>

### Patient’s information

<table>
<thead>
<tr>
<th>Patient’s name:</th>
<th>Patient’s signature:</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHS Number:</td>
<td></td>
</tr>
<tr>
<td>Date of Birth:</td>
<td>Date:</td>
</tr>
<tr>
<td>Contact number:</td>
<td></td>
</tr>
</tbody>
</table>

### General Practitioner’s information

<table>
<thead>
<tr>
<th>GP name:</th>
<th>General Practitioner’s signature:</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP Surgery:</td>
<td></td>
</tr>
<tr>
<td>Contact number:</td>
<td></td>
</tr>
<tr>
<td>Email address:</td>
<td>Date:</td>
</tr>
</tbody>
</table>

Signing indicates agreement with the responsibilities suggested in this document, and that the patient has been informed of the need to report any issues with their treatment to their doctor.

### Introduction

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, age and number of independent clinical risk factors for fracture (parental history of hip fracture, alcohol intake of 4 or more units per day and rheumatoid arthritis) as indicated in the following table.
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.

**Adult dosage and administration**

- 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 but for patients with an eGFR < 30mL/min there is an increased risk of hypocalcaemia.
- The safety and efficacy of denosumab have not been studied in patients with hepatic impairment.
- No dose adjustment is required in elderly patients.

**Available as:** 60 mg solution for injection in a pre-filled syringe (Prolia® ▼ 60 mg/ml)

### Specialist responsibilities

- To assess the patient and establish/confirm the diagnosis.
- Discuss with the patient/carer options for treatment and the suitability of denosumab.
- Correct pre-existing hypocalcaemia prior to initiating denosumab.
- Check calcium levels:
  - before each dose
  - within two weeks after the initial dose in patients with risk factors for hypocalcaemia (e.g. severe renal impairment, creatinine clearance <30 ml/min)
  - if suspected symptoms of hypocalcaemia occur.
- Tell all patients to report symptoms of hypocalcaemia to their doctor (e.g. muscle spasms, twitches, cramps, numbness or tingling in the fingers, toes or around the mouth).
- Check for interactions with other medicines.
- Discuss with the patient the potential benefits and side effects of treatment and their responsibilities under shared care.
- Check for ONJ risk factors before starting denosumab 60 mg. A dental examination and appropriate preventive dentistry is recommended for patients with risk factors. Tell all patients to maintain good oral hygiene, receive routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain, swelling, non-healing sores or discharge to a doctor and a dentist.
- 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 Shropshire 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 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 and the second injection at 6 months (including teaching the patient how to self-administer the injection if they are to perform subsequent injections themselves). The patient should be given the package leaflet and patient reminder card.
  - Ensuring the patient understands the proposed plan for follow-up
Prehypocalcaemia has been reported in patients at increased risk of hypocalcaemia receiving denosumab 60 mg (creatinine clearance <30 mL/min; estimated glomerular filtration rate [eGFR] 15–29 mL/min/1.73m2) or receiving dialysis.

Hypocalcaemia is a known risk with denosumab use, especially in patients with severe renal impairment with symptoms such as dizziness, muscle cramps, twitching, weakness, numbness or tingling in the fingers, toes, or around the mouth. Patients receiving denosumab can 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.

Ensure that a dental examination and appropriate preventative dentist follow-up is recommended (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.

Ensure this has been discussed with patient, and that patient has signed Shared Care form.

Regular follow-up of patient (at least annually)

Communicate promptly with the GP when treatment is changed.

Advise GP on 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)

### Primary Care responsibilities

- To confirm, within 2 weeks of receipt, their agreement or otherwise to participate in shared care.
- Prescribe and administer denosumab at six-monthly intervals after the initial administrations by the specialist. The patient should be given the package leaflet and patient reminder card ii, iv.
- 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.
- Check calcium levels at least every six months - this should be at least two weeks before each dose and if suspected symptoms of hypocalcaemia occur. ii
- Tell all patients to report symptoms of hypocalcaemia to their doctor (e.g. muscle spasms, twitches, cramps, numbness or tingling in the fingers, toes, or around the mouth).
- To ensure the patient continues to take calcium and vitamin D and to deal with general health issues of the patient.
- Remind patients to maintain good oral hygiene, receive routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain, swelling, non-healing sores or discharge to a doctor and a dentist.
- Report adverse events to the MHRA (via Yellow Card)

### Patient responsibilities

- To receive (or administer, if appropriately trained) the prescribed medication every 6 months unless advised by GP or specialist
- To attend scheduled appointments with specialist and GP and for monitoring as detailed in this document
- Report any adverse effects to the specialist or GP, particularly cellulitis
- Share any concerns in relation to treatment
- Report to the specialist or GP if they do not have a clear understanding of the treatment
- Inform their doctor and dentist that they are receiving denosumab if they require dental treatment or surgery

### Adverse effects and precautions

- Patients receiving denosumab can 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.
- Ensure that a dental examination and appropriate preventative dentistry is completed for patients with risk factors for osteonecrosis of the jaw.
- Common side effects include: urinary tract infection, upper respiratory tract infection, sciatica, cataracts, constipation, abdominal discomfort, rash, eczema, musculoskeletal pain, pain in extremity.
- 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/1.73m2) or receiving dialysis. Monitoring of calcium levels in these patients is recommended as severe symptomatic hypocalcaemia has been reported in patients at increased risk of hypocalcaemia receiving denosumab 60 mg.
- Pre-existing hypocalcaemia must be corrected prior to initiating denosumab.
• Adequate intake of calcium and vitamin D is important in all patients receiving 60 mg denosumab.
• 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 fracture is suspected, while the patient is evaluated vi.

Contra-indications

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

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.

Common Drug Interactions

An interaction study with midazolam, which is metabolised by cytochrome P450 3A4 (CYP3A4), demonstrated that denosumab did not affect pharmacokinetics, indicating that denosumab should not alter the pharmacokinetics of drugs metabolised by CYP3A4.

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).

Live vaccines should not be given to patients receiving monoclonal antibodies vi. Examples of live vaccines include MMR, BCG, Shingles, yellow fever, oral polio, rotavirus, childrens nasal flu vaccine. (Please note this list is not exclusive).

Communication

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

Adapted with kind permission from work by MG, NHS Telford and Wrekin CCG, Medicines Management

References
i. NICE Technology Appraisal TA204, denosumab for the prevention of osteoporotic fractures in postmenopausal women. Available at https://www.nice.org.uk/guidance/ta204/chapter/1-Guidance