**DRUG:** Denosumab (Prolia®)  

<table>
<thead>
<tr>
<th>Introduction:</th>
<th><strong>Indication:</strong> Osteoporosis</th>
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</thead>
<tbody>
<tr>
<td><strong>Licensing Information:</strong></td>
<td>Prolia is licensed for the treatment of osteoporosis in postmenopausal women at increased risk of fractures. It significantly reduces the risk of vertebral, non vertebral and hip fractures.</td>
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<tr>
<td><strong>Formulations:</strong></td>
<td>Injection 60mg in a pre-filled syringe</td>
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<tr>
<td><strong>Dosage &amp; administration:</strong></td>
<td>60 mg administered as a single subcutaneous injection once every 6 months into the thigh, abdomen or upper arm. No dose adjustment is indicated in renal impairment and the elderly.</td>
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<tr>
<td><strong>Contraindications &amp; Warnings:</strong></td>
<td><strong>Contra-indications:</strong> Hypocalcaemia and hypersensitivity to the active substance or to any of the excipients.</td>
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<td></td>
<td><strong>Warnings:</strong> Adequate intake of calcium and vitamin D is important in all patients. MHRA safety alerts (Oct 2012 and Sept 2014) cautions about the risks of hypocalcaemia with denosumab. Patients with severe renal impairment (eGFR &lt; 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 (see monitoring, below). Patients should be asked to report symptoms of hypocalcaemia e.g. muscle spasms, cramps or tingling of fingers, toes or around mouth.</td>
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<tr>
<td></td>
<td>MHRA safety alert – Denosumab: hypocalcaemia (Oct 2012)</td>
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<tr>
<td></td>
<td>MHRA safety alert – Denosumab: Osteonecrosis of the jaw (Sept 2014)</td>
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<td>An MHRA safety alert (Feb 2013) describes rare reports of atypical femoral fractures in women with post-menopausal osteoporosis receiving long term (&gt; 2.5 years) treatment with denosumab 60mg. Patients presenting with new or unusual thigh, hip or groin pain should be evaluated for an incomplete femoral fracture. Denosumab should be discontinued if an atypical femur fracture is suspected.</td>
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<tr>
<td></td>
<td>MHRA safety alert – Denosumab: atypical femoral fracture (Feb 2013)</td>
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<td></td>
<td>Denosumab is associated with osteonecrosis of the jaw (ONJ). Patients should be assessed for ONJ risk factors before starting denosumab and those identified as at risk, a dental examination and appropriate preventative dentistry is recommended to reduce the risk of ONJ (MHRA safety alert, Sept 2014). Risk factors for ONJ include a diagnosis of cancer with bone lesions, concomitant therapies (e.g., chemotherapy, antiangiogenic biologics, corticosteroids, radiotherapy to head and neck), poor oral hygiene, dental extractions, and co-morbid disorders (e.g., pre-existing dental disease, anaemia, coagulopathy, infection) and previous treatment with bisphosphonates</td>
</tr>
<tr>
<td></td>
<td>MHRA safety alert – Denosumab: Osteonecrosis of the jaw (Sept 2014)</td>
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</table>
| | The needle cover of the pre-filled syringe contains dry natural rubber (a
### Interactions:

The current SPC does not report any significant drug interactions. Please refer to the BNF or SPC at [www.medicines.org.uk/EMC](http://www.medicines.org.uk/EMC).

### Adverse Effects:

**Common:** Infections, constipation, pain in extremity.

**Uncommon:** Cellulitis - prompt medical attention.

**Rare:** Hypocalcaemia (see “warnings” above).

**Rare:** Osteonecrosis of the jaw (ONJ) (see “warnings above”).

**Rare:** Hypersensitivity reactions.

**Rare:** Atypical femoral fractures (see “warnings” above).

For full list see BNF or SPC at [www.medicines.org.uk/EMC](http://www.medicines.org.uk/EMC).

### Responsibilities of the specialist initiating treatment:

<table>
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<tr>
<th>General:</th>
<th>Specific:</th>
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</table>
| • To assess the suitability of the patient for treatment.  
• To ensure that the patient/carer has received counselling and understands the therapy, its benefits, limitations, continued monitoring (where applicable), adverse effects, and is aware of actions to take if adverse effects are suspected.  
• Inform the GP of the information provided to the patient.  
• To review the patient at agreed intervals and copy any relevant results to the GP  
• Carry out disease and drug monitoring as listed below  
• Formally hand over to GP by letter and patient informed - send a copy (either electronically or paper copy) of the Shared Care Guideline to the GP and ask whether they are willing to participate in shared care. | • To advise the patient to stop all other osteoporosis medications but to ensure that they continue with calcium and vitamin D supplements.  
• To correct hypocalcaemia prior to first dose of denosumab and monitor patients at risk of hypocalcaemia, e.g. severe renal disease.  
• To assess the individuals risk factors for ONJ and refer for dental assessment or treatment accordingly before the first treatment with denosumab.  
• The Specialist Nurse will provide patients with information about the PROLONG patient reminder service sponsored by the pharmaceutical companies to support patient recall for dosing and education. This is a voluntary service and the patient is free to register with the service if they wish. [www.myprolong.com](http://www.myprolong.com). |

### Prescribing:

• The first dose will be administered in hospital. Subsequent doses will then be given at 6 monthly intervals in primary care for 3 years total course and then be reviewed by the referring Specialist. A calcium and vitamin D supplement will be initiated if not already prescribed and the patient is not hypercalcaemic.
Disease & drug monitoring:
- Monitor bloods according to schedule:

<table>
<thead>
<tr>
<th>Calcium levels</th>
<th>Specialist to test prior to initiation of denosumab in all patients</th>
<th>In those with eGFR&lt;30mL/min or other risk factors for hypocalcaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specialist team to recheck calcium within 7-10 days of administering the first dose and initiate/recommend any necessary treatment.</td>
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Dexa scan
- To be undertaken at the discretion of the Consultant.

General and Prescribing:
- To reply to the request for shared care within 2 weeks of receipt of the Consultant letter.
- Monitor, prescribe and administer as recommended by the specialist. The GPs will be asked to prescribe and administer subsequent injections at 6 monthly intervals.
- To prescribe a calcium and vitamin D supplement in accordance with local joint primary and secondary care formulary.
- Notify Consultant if treatment with denosumab is discontinued.
- Ensure there are no drug interactions or contraindications with any other medications initiated in primary care.

Responsibilities of other prescribers (GP):
- Discuss shared care arrangement with patient.
- Support and advise GPs as required.

Disease & drug monitoring:
- Carry out drug monitoring as listed – and communicate abnormal results to the Specialist.
- Refer back to the Specialist if the patient’s condition deteriorates.
- Stop treatment on the advice of the Specialist
- Urgent drug discontinuation/ referral to specialist as clinically appropriate
- Identify adverse effects if the patient presents with any signs and liaise with the hospital Specialist where necessary. Report adverse effects to the Specialist and where appropriate to the Commission on Human Medicines/MHRA (Yellow Card scheme).

Unless otherwise stated by the secondary care Specialist, apply the following monitoring frequencies following handover from secondary care:
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<tr>
<th></th>
<th>Baseline (prior to treatment and at 7-10 days as indicated above)</th>
<th>In those with eGFR &gt; 30mL/min</th>
<th>In those with eGFR &lt; 30mL/min or other risk factors for hypocalcaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium monitoring</td>
<td>By initiating specialist for all patients</td>
<td>GP to recheck calcium before each subsequent injection.</td>
<td>GP to recheck calcium before each subsequent injection or sooner if suspected symptoms of hypocalcaemia occur.</td>
</tr>
</tbody>
</table>

If the patient is found to be hypocalcaemic, assess compliance and review calcium and vitamin D supplementation where appropriate.

**Responsibilities of the Patient / Carer:**

**General:**
- Report any possible side effects to their GP.
- Ensure they continue to take a calcium and vitamin D supplement unless instructed to stop. To stop all other osteoporosis medication.
- Attend appointments.
- Patients identified at risk of ONJ should visit their dentist for a dental examination and appropriate preventative dentistry before treatment with denosumab where this is advised. (MHRA safety alert, Sept 2014)
- Maintain good oral hygiene. Attend regular dental check ups and seek dental advice for any oral symptoms like pain, swelling or loose teeth.

**Disease & drug monitoring:**
As above – contact GP or initiating team if side effects develop (see adverse effects) and attend appointments including those for routine blood tests/investigations

**Communication:**

**Specialist to GP:**
- The specialist will inform the GP when they have initiated denosumab and when there are any subsequent changes in treatment – standard clinic letter.
- Send a copy (either electronically or paper copy) of the Shared Care Guideline to the GP and ask whether they are willing to participate in shared care.
- Inform the GP of the information provided to the patient

**GP to Specialist:**
- To reply to the request for shared care within 2 weeks of receipt of the Consultant letter.
- Irrespective of whether you accept prescribing responsibility or not, you should inform the consultant of relevant medical information.
regarding the patient and any changes to the patient’s medication regime irrespective of indication.

- Notify Consultant if treatment with denosumab is discontinued.

**Contact names & details:**
If you have any concerns regarding individual patients, see consultant letter for medical contact details or contact one of the following:

<table>
<thead>
<tr>
<th>Name</th>
<th>Title/Location</th>
<th>Telephone / Bleep</th>
</tr>
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<tbody>
<tr>
<td>Carol Anne Keaney</td>
<td>Hip fracture nurse specialist</td>
<td>01904 724013</td>
</tr>
<tr>
<td>Ottilia Buch</td>
<td>Endocrine Specialist Nurse</td>
<td>01904 726807</td>
</tr>
</tbody>
</table>

**Cost:**
Denosumab (Prolia) injection 60mg/mL pre-filled syringe:
Can be ordered direct to the GP practice from Movianto, which may be the most cost effective option, or provided for patients through a pharmacy by prescribing on an FP10.

**References:**
Summary of Product Characteristics (SPC), Prolia. Date of last amendment 30.04.12. www.medicines.org.uk/emc
MHRA safety alert. Denosumab 60mg (Prolia): Rare cases of atypical femoral fracture with long term use (Feb 2013)

**Document Control:**
This information is not inclusive of all prescribing information and potential adverse effects. Please refer to the SPC (data sheet) or BNF for further prescribing information.

The original Microsoft Word file of this document is located on:
York Teaching Hospital NHS Foundation Trust Pharmacy Department X:\MEDICINES INFORMATION\Shared Care Guidelines\Approved Shared Care Guidelines\DENOSUMAB Shared Care Guideline V2.0

Shared Care Guidelines are also available electronically via [http://www.yorkandscarboroughformulary.nhs.uk/](http://www.yorkandscarboroughformulary.nhs.uk/)

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Diane Tomlinson (Pharmacist NY & Humber Commissioning Support Unit)
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