**Denosumab** DRAFT

ESCA: For the treatment of osteoporosis

Specialist details:

Name:

Tel:

Hospital Pharmacy Dept:

Other:

Patient details:

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of subcutaneous denosumab in people with osteoporosis can be shared. 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 specialist. **If a specialist asks the GP to prescribe and administer this drug, the GP should reply to this request as soon as practicable.**

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients on denosumab are under regular follow-up, which provides opportunities to discuss drug therapy*.*

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

**RESPONSIBILITIES and ROLES**

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| **Specialist responsibilities** |
| 1. Assess patient suitability for denosumab in line with NICE CG146.
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| 1. Discuss the benefits and side effects of treatment with the patient.
2. Ask the GP whether he or she is willing to participate in shared care, and agree with the GP as to whom will discuss the shared care arrangement with the patient.
3. Arrange for appropriate initial haematology/biochemistry.
4. Initiate and administer the first dose of treatment with denosumab if not contraindicated.
5. Agree with the GP who will be responsible for a) following up the patient’s response to treatment and b) administering the second dose; this may be dependent on any prior history of hypocalcaemia (see All Wales Medicines Strategy Group Shared care protocol for denosumab).
6. Report adverse events to the Medicines and Healthcare Products Regulatory Agency (MHRA) and GP.
7. Ensure that clear backup arrangements exist for GPs to obtain advice and support.
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| **General Practitioner responsibilities** |
| 1. Reply to the request for shared care as soon as practicable.
2. Following discussion with the specialist, prescribe and administer the second or third and subsequent treatments with denosumab as agreed and at the dose recommended.
3. Ensure that the practice system is set up to recall the patient after a six-month interval.
4. To undertake monitoring of calcium levels as recommended (see contraindications)
5. Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment.
6. Refer back to specialist if the patient’s condition deteriorates, as advised.
7. Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
8. Report adverse events to the specialist/specialist nurse and MHRA.
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| **Patient's role** |
| 1. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
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| 1. Share any concerns in relation to treatment with denosumab.
2. Adhere to any calcium and vitamin D treatment prescribed.
3. Inform specialist or GP of any other medication being taken, including over-the-counter products.
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| 1. Report any other adverse effects or warning symptoms to the specialist or GP whilst receiving denosumab. Especially, any signs or symptoms of cellulitis, any unusual groin, hip or thigh pain, or chronic ear infections (further details on page 2).
2. Maintain good oral hygiene, with regular dental review if appropriate. Inform dentist that denosumab treatment has been received.
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**SUPPORTING INFORMATION**

**NICE guidance (TA204)**

For **primary prevention** of osteoporosis, denosumab is an option in women for whom alendronate or risedronate are unsuitable **and** who have an appropriate combination of T-score, age and independent clinical risk factors for fracture (parental history of hip fracture, alcohol intake of 4 or more units per day, or rheumatoid arthritis). As **secondary prevention**, denosumab is recommended as a treatment option in women at increased risk of fractures if alendronate or risedronate are unsuitable.

**Licensed indications**

Denosumab is licensed for the treatment of osteoporosis in postmenopausal women, and in men at increased risk of fractures. In postmenopausal women, denosumab significantly reduces the risk of vertebral, non-vertebral and hip fractures.

**Dosage and Administration**

The recommended dose of denosumab is 60 mg administered as a single subcutaneous injection once every 6 months into the thigh, abdomen or upper arm.

*Patients must be adequately supplemented with calcium and vitamin D.*

No dose adjustment is required in elderly patients, or in those with renal impairment. Denosumab has not been tested in patients with hepatic impairment. The need for continued treatment should be re-evaluated periodically based on the benefits and potential risks of denosumab on an individual patient basis, particularly after five or more years of use.

**Contraindications and cautions for use**

Denosumab is contraindicated in patients with hypersensitivity to denosumab or to any of the excipients. Caution is advised in patients with known hypersensitivity to other bisphosphonates.

*Hypocalcaemia (MHRA guidance available; see references):* must be corrected by an adequate intake of calcium and vitamin D before initiating therapy with denosumab. 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. According to the SPC concomitant glucocorticoid treatment is an additional risk factor for hypocalcaemia.

*Skin Infections (cellulitis leading to hospitalisation):* Signs and symptoms include: red, painful, hot, swollen and tender skin that spreads rapidly, that may be accompanied or preceded by fever, malaise, nausea, shivering, and rigors.

*Osteonecrosis of the Jaw (ONJ)*: has been reported with denosumab and bisphosphonate treatment. A dental examination with appropriate preventive dentistry should be considered before treatment with denosumab.

*Atypical fractures of the femur (see MHRA reference below):* Discontinuation of denosumab therapy should be considered if patient reports any new or unusual thigh, hip, or groin pain, pending evaluation of the patient for an atypical femoral fracture, based on an individual benefit risk assessment.

**Therapeutic Use**

Refer to the MTRAC Commissioning Support guidance on denosumab.

**Side Effects**

Infections of the urinary tract and upper respiratory tract are listed as common in the SPC; along with sciatica, cataracts, constipation, rash, and pain in the extremities. For adverse effects other than those described under contraindications, please see the SPC.

*Denosumab was launched in 2010 and no longer has black triangle* (▼) *status. Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the MHRA..*

**Drug Interactions**

There is low potential for drug-drug interactions (see SPC). 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).

**References**

[Prescribing of Denosumab (Prolia®) in Wales: Review – Shared care protocol All Wales Medicines Strategy Group](http://www.awmsg.org/awmsgonline/docs/awmsg/medman/Prescribing%20of%20denosumab%20%28Prolia%29%20in%20Wales%20%28Review%29.pdf)

MTRAC Commissioning guidance sheet for denosumab, updated June 2019

[CG146 Osteoporosis: assessing the risk of fragility fracture](https://www.nice.org.uk/guidance/cg146)

[TA204 Denosumab for the prevention of osteoporotic fractures in postmenopausal women. NICE 2010](http://publications.nice.org.uk/denosumab-for-the-prevention-of-osteoporotic-fractures-in-postmenopausal-women-ta204)

Amgen Limited[. Prolia. Summary of Product Characteristics 2018.](http://www.medicines.org.uk/emc/medicine/23127/SPC/Prolia/)

Cellulitis – acute <http://cks.nice.org.uk/cellulitis-acute>

[Denosumab: monitoring recommended](https://www.gov.uk/drug-safety-update/denosumab-monitoring-recommended)

[Denosumab (Xgeva▼, Prolia); intravenous bisphosphonates: osteonecrosis of the jaw—further measures to minimise risk. MHRA (2015](https://www.gov.uk/drug-safety-update/denosumab-xgeva-prolia-intravenous-bisphosphonates-osteonecrosis-of-the-jaw-further-measures-to-minimise-risk))

[Denosumab 60 mg (Prolia): rare cases of atypical femoral fracture with long-term use. MHRA 2013](https://www.gov.uk/drug-safety-update/denosumab-60-mg-prolia)

[Denosumab (Prolia, Xgeva▼): reports of osteonecrosis of the external auditory canal MHRA (2017)](https://www.gov.uk/drug-safety-update/denosumab-prolia-xgeva-reports-of-osteonecrosis-of-the-external-auditory-canal)