Wye Valley NHS Trust

Shared Care Guidelines

DENOSUMAB
In osteoporosis

INTRODUCTION

Denosumab is included in Herefordshire joint formulary as a second line agent. It is recommended as a treatment option for the primary 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 **and**
- Who have a combination of T-score (as detailed in NICE TA204), age and number of independent clinical risk factors for fracture.

DOSE AND ADMINISTRATION

Denosumab **60mg** pre-filled syringe [Prolia®] is administered as a single subcutaneous injection into the thigh, abdomen or upper arm, once **every 6 months**.

- Patient must be calcium and vitamin D replete on initiation of therapy
- No dose adjustment is required in elderly patients or patients with renal impairment
- The patient will be given the package leaflet and patient reminder card in clinic, on administration of the first dose.

The first injection will be given at Wye Valley Trust. The patient's GP will then prescribe and administer the second and subsequent injections at 6 month intervals. The GP will be sent written confirmation of administration of the initial injection (and the patient offered a copy).

After 3 years' treatment, patient should have a DEXA scan then be referred back to the consultant for review of ongoing need for treatment.

ADVERSE EFFECTS

- **Very common:** musculoskeletal pain and pain in the extremities
- **Common:** Urinary tract infections, upper respiratory tract infections, sciatica, constipation, abdominal discomfort, rash and eczema.
- Advise patient to seek prompt medical attention if they develop signs or symptoms of:
  - **Osteonecrosis of the jaw (ONJ)** (rare) - Temporary interruption of treatment should be considered until the condition resolves and contributing risk factors are mitigated where possible. A future management plan should be set up in close collaboration between the treating physician and a dentist or oral surgeon with expertise in ONJ
  - **Hypocalcaemia** (rare) – correct before administration of denosumab
  - **Cellulitis** (uncommon)
  - **New or unusual thigh, hip or groin pain**: may be a symptom of atypical femoral fracture which has been reported rarely. Discontinue denosumab therapy if atypical femur fracture is suspected while patient is investigated
  - **Hypersensitivity** (rare).

See BNF and Summary of Product Characteristics for comprehensive list.

CAUTIONS

- 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. Regular calcium monitoring is especially important in these patients
- A dental examination with appropriate preventive dentistry is recommended prior to starting denosumab in patients with concomitant risk factors for ONJ (see Summary of Product Characteristics). This is the responsibility of the clinician initiating therapy. All patients should be encouraged to maintain good oral hygiene, receive routine dental check-ups, immediately report any oral symptoms and avoid any invasive dental procedures during treatment
- Patients receiving denosumab may rarely develop skin infections (predominantly cellulitis).

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- The needle cover of the pre-filled syringe contains dry natural rubber (latex derivative) which may cause allergic reactions
- Inform the patient of possible symptoms of hypocalcaemia e.g. paraesthesias or muscle stiffness, twitching, spasms and muscle cramps.

CONTRAINDICATIONS

- Hypocalcaemia
- Hypersensitivity to the active substance or to any of the excipients
- Patients with rare hereditary problems of fructose intolerance (excipients include sorbitol).

PREGNANCY AND BREAST FEEDING

Not recommended for use in pregnant women.
Unknown whether excreted in human breast milk – see SmPC for more information: www.medicines.org.uk.

DRUG INTERACTIONS

- Study data indicates denosumab should not affect drugs metabolized by CYP3A4
- Should NOT be administered alongside bisphosphonates.

MONITORING STANDARDS FOR DENOSUMAB

Pre-treatment Monitoring	Baseline calcium and vitamin D: • Correct insufficiency with adequate intake of calcium and vitamin D before initiation of denosumab • If predisposed to hypocalcaemia re-check levels within two weeks of initial dose.	
Subsequent Monitoring	Calcium	• Before each dose of denosumab (every 6 months) • If suspected symptoms of hypocalcaemia occur • Monitoring especially important in severe renal impairment (see above)
	U&E	Before each dose of denosumab (every 6 months)
	Dental check-ups	Due to the rare side effect of ONJ, patients should have routine dental check-ups while on denosumab
	Ongoing indication	After 3 years' treatment, DEXA scan then refer back to the consultant for review

ACTION AND ADVICE FOR GP'S IN RESPONSE TO BLOOD MONITORING/SIDE-EFFECTS

Blood Test Results	**Action**
Calcium: abnormal	Refer to consultant
U&E: abnormal	Refer to consultant

Symptoms	**Action**
Suspected signs or symptoms of hypocalcaemia	Check calcium level
Osteonecrosis of the jaw (ONJ)	Refer to consultant
New/ unusual thigh, hip or groin pain	Refer to consultant

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SHARED CARE RESPONSIBILITIES

Consultant and/or Specialist Nurse

1. Advise patient of benefits, adverse reactions, method of administration and treatment interval.
2. Ensure patient is calcium and vitamin D replete before initiation of therapy.
3. Prescribe and administer first dose.
4. Write to the GP requesting shared care for the patient.
5. Provide written confirmation of the first dose to the GP and provide any relevant clinical information.
6. Provide information to GP regarding monitoring.
7. Provide denosumab patient reminder card to the patient on initiation of treatment[1].
8. A dental examination with appropriate preventive dentistry is recommended prior to starting denosumab in patients with concomitant risk factors for ONJ.
9. Provide on-going support and advice to GP and patient regarding any complications or adverse events.
10. Review ongoing indication for treatment at regular intervals and inform GP if treatment to cease.

General Practitioner

1. To prescribe and administer the second and subsequent injections at 6 month intervals.
2. Ensure denosumab is added to the patient's medication record.
3. Ensure other osteoporosis treatments (e.g. bisphosphonates, strontium) are stopped and removed from repeat prescription.
4. Ensure that calcium and vitamin D supplements are continued as appropriate and check adherence to treatment at least annually.
5. Regular monitoring in line with recommendations above.
6. Review any complications or adverse events and report to the hospital specialist and MHRA, where appropriate and MHRA.
7. After 3 years' therapy, review treatment as detailed above.
8. Refer back to the consultant for review if any concerns.

CONTACT NUMBERS FOR ADVICE AND SUPPORT

Wye Valley NHS Trust	
Dr David Rees, Consultant Rheumatologist	david.rees@wvt.nhs.uk 01432 355444
Liz Watkins, Osteoporosis and Fracture Liaison Practitioner http://nww.herefordshire.nhs.uk/Osteoporosis/tabid/3501/Default.aspx	Elizabeth.Watkins@wvt.nhs.uk 01432 35544 ext. 5790
Medicines Information, WVT Pharmacy	01432 364017
Other	
National Osteoporosis Society	www.nos.org.uk 0808 800 0035

This document should be read in conjunction with the BNF: http://evidence.nhs.uk/formulary/bnf/current, the Summary of Product Characteristics: https://www.medicines.org.uk/emc/ and relevant NICE guidance http://www.nice.org.uk/guidance/ta204/chapter/1-guidance

[1] Reminder cards can be ordered via Amgen Medical Information at gbinfoline@amgen.com or call 01223 420305. Alternatively can be downloaded from the 'Risk Materials' section of the denosumab SPC: www.medicines.org.uk.