Effective Shared Care Agreement (ESCA)

Denosumab ▼ (Prolia)

ESCA: For the treatment of postmenopausal osteoporosis

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of denosumab for the treatment of postmenopausal osteoporosis can be shared between the specialist and general practitioner (GP). You are **invited** to participate however, if you do not feel confident to undertake this role, then you are 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.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care will be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with postmenopausal osteoporosis are usually under regular specialist follow-up, which provides an opportunity 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

Specialist responsibilities
1. Confirm the diagnosis of postmenopausal osteoporosis and assess patient suitability for denosumab in line with NICE TA 204.
2. Discuss the potential benefits, treatment side effects, and possible drug interactions with the patient.
3. Ask the GP whether he or she is willing to participate in shared care before initiating therapy so that appropriate follow on prescribing arrangements can be made.
4. Arrange for appropriate biochemistry (Baseline and prior to each injection – renal function, bone profile 25OH-vitamin D and check calcium levels). Ensure patient has good oral hygiene and if dental examination is required prior to initiating denosumab. If patient is on other osteoporosis treatment (alendronate, risedronate, ibandronate, strontium) advise patient to stop this treatment prior to initiating denosumab.
5. Initiate and administer the first and second dose of treatment with denosumab if not contraindicated. Issue patient "My Bone Passport", ensure it is updated and explain the purpose of the passport. Provide patients the patient reminder card for regarding osteonecrosis of the jaw.
6. If any calcium and vitamin D treatment is required – initiate treatment and advise patient and GP accordingly. Ensure patient is calcium and vitamin D replete before administering treatment.
7. Review the patient's condition and monitor response to treatment regularly.
8. A written summary to be sent promptly to the GP i.e. within 10 working days of a hospital outpatient review or inpatient stay.
9. Report adverse events to the MHRA.
10. Ensure clear backup arrangements exist for GPs, for advice and support (Please complete details below).

General Practitioner responsibilities						
1. Reply to the request for shared care as soon as practicable i.e. within 10 working days.						
2. Arrange for appropriate biochemistry prior to each injection – renal function, bone profile, 25OH-vitamin D and check calcium levels.						
3. Check if the patient has their "My Bone passport" and that it is up to date. Record all relevant details in the passport to support the patients care. Ensure the patient has the patient reminder card for regarding osteonecrosis of the jaw						
4. Ensure that other osteoporosis treatments (alendronate, risedronate, ibandronate, strontium etc.) are stopped and removed from the patient's repeat prescription.						
5. Prescribe and administer the third and subsequent treatment with denosumab at the dose recommended.						
6. Continue any calcium and vitamin D treatment as advised by the specialist.						
7. Ensure that the practice system is set up to recall the patient at six monthly interval (including checking patient's calcium and vitamin D status before each injection).						
8. In the patient's notes, using the appropriate Read Code listed below, denote that the patient is receiving treatment under a shared care agreement.						
GP Prescribing System	**Read Code**	**Description**		**GP Prescribing System**	**Read Code**	**Description**
EMIS and Vision	8BM5.00	Shared care prescribing		SystmOne	XaB58	Shared care
9. Monitor patient's response to treatment; make dosage adjustments if agreed with specialist.						
10. GP to arrange a DXA Scan at 5 years.						
11. Report to and seek advice from the specialist or clinical nurse specialist on any aspect of patient care that is of concern to the GP, patient or carer and may affect treatment.						
12. Refer back to specialist if condition deteriorates.						
13. Report adverse events to specialist and MHRA.						
14. Stop treatment on advice of specialist.						

Patient's role
1. Report to the specialist, clinical nurse specialist or GP if she does not have a clear understanding of the treatment.
2. Share any concerns in relation to treatment with denosumab – immediately report any adverse events to the doctor who last administered denosumab, particularly if patient develops a swollen, red area of skin, most commonly in the lower leg, that feels hot and tender (cellulitis); symptoms of fever, muscle aches, dizziness and any dental problems. Report symptoms of hypocalcaemia to their doctor (eg, muscle spasms, twitches, or cramps; numbness or tingling in the fingers, toes, or around the mouth).
3. Maintain good oral hygiene; undertake to have regular dental check-ups. Tell their doctor and dentist that they are receiving denosumab or an intravenous bisphosphonate if they need dental treatment or dental surgery.
4. Adhere to any calcium and vitamin D treatment prescribed.
5. Respond in timely manner to specialist or GP's recall for appointment for blood test and administration of denosumab to ensure treatment is received on a six-monthly interval.
6. Keep a record of treatment ensuring "My Bone passport" is updated at 6-monthly visit for denosumab injection.
7. Report any adverse effects to the specialist or GP whilst taking denosumab.
8. Tell their doctor and dentist immediately if they have any problems with their mouth or teeth during treatment (eg loose teeth, pain, swelling, non-healing sores or discharge)

BACK-UP ADVICE AND SUPPORT

	Contact details	Telephone No.	Email address:
Trust	Consultant:-		
	Specialist Nurse		

Based on MTRAC template
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Interface Lead Pharmacist
Birmingham CrossCity CCG

SUPPORTING INFORMATION

Indication	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.
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.
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.
Renal Impairment	No dose adjustment is required
Hepatic impairment	Denosumab has not been tested in patients with hepatic impairment.
Contra-indications / Special precautions	**Contraindications** • Hypocalcaemia • Hypersensitivity to the active substance or to any of the excipients listed **Cautions** <u>Calcium and Vitamin D supplementation</u> Adequate intake of calcium and vitamin D is important in all patients. <u>Precautions for use</u> <u>*Hypocalcaemia*</u> It is important to identify patients at risk for hypocalcaemia. Hypocalcaemia must be corrected by adequate intake of calcium and vitamin D before initiating therapy. Clinical monitoring of calcium levels is recommended before each dose and, in patients predisposed to hypocalcaemia within two weeks after the initial dose. If any patient presents with suspected symptoms of hypocalcaemia during treatment calcium levels should be measured. Patients should be encouraged to report symptoms indicative of hypocalcaemia. In the post-marketing setting, severe symptomatic hypocalcaemia has been reported, with most cases occurring in the first weeks of initiating therapy, but it can occur later. <u>*Skin Infections*</u> 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. <u>*Osteonecrosis of the Jaw (ONJ)*</u> ONJ has been reported rarely in clinical studies and in the post marketing setting in patients receiving denosumab at a dose of 60 mg every 6 months for osteoporosis. ONJ has been reported commonly in clinical studies in patients with advanced cancer treated with denosumab at the studied dose of 120 mg administered monthly. Known risk factors for ONJ include previous treatment with bisphosphonates, older age, poor oral hygiene, invasive dental procedures (e.g. tooth extractions, dental implants, oral surgery), and co-morbid disorders (e.g. pre-existing dental disease, anaemia, coagulopathy, infection), smoking, a diagnosis of cancer with bone lesions, concomitant therapies (e.g., chemotherapy, antiangiogenic biologics, corticosteroids, radiotherapy to head and neck). It is important to evaluate patients for risk factors for ONJ before starting treatment. A dental examination with appropriate preventive dentistry is recommended prior to treatment with denosumab in patients with concomitant risk factors. All patients should be encouraged to maintain good oral hygiene, receive routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain or swelling during treatment with denosumab. While on treatment, patients should avoid invasive dental procedures if possible. For patients who develop ONJ while on denosumab therapy, dental surgery may exacerbate the condition. The management plan of the individual patients who develop ONJ should be set up in close collaboration between the treating physician and a dentist or oral surgeon with expertise in ONJ. Temporary interruption of treatment should be considered until the condition resolves and contributing risk factors are mitigated where possible <u>*Atypical fractures of the femur*</u> Atypical femoral fractures have been reported in patients receiving denosumab. Atypical femoral fractures may occur with little or no trauma in the subtrochanteric and diaphyseal regions of the femur. Specific radiographic findings characterise these events. Atypical femoral fractures have also been reported in patients with certain comorbid conditions (e.g. vitamin D deficiency, rheumatoid arthritis, hypophosphatasia) and with use of certain pharmaceutical agents (e.g. bisphosphonates, glucocorticoids, proton pump inhibitors). These events have also occurred without antiresorptive therapy. Similar fractures reported in association with bisphosphonates are often bilateral; therefore the contralateral femur should be examined in denosumab -treated patients who have sustained a femoral shaft fracture. Discontinuation of denosumab therapy in patients suspected to have an atypical femur fracture should be considered pending evaluation of the patient based on an individual benefit risk assessment. During denosumab treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Patients presenting with such symptoms should be evaluated for an incomplete femoral fracture. *Concomitant treatment with other denosumab-containing medicinal products* Patients being treated with denosumab should not be treated concomitantly with other denosumab-containing medicinal products (for prevention of skeletal related events in adults with bone metastases from solid tumours). <u>*Renal impairment*</u> Patients with severe renal impairment (creatinine clearance < 30 ml/min) or receiving dialysis are at greater risk of developing hypocalcaemia. The risks of developing hypocalcaemia and accompanying parathyroid hormone elevations

	increase with increasing degree of renal impairment. Adequate intake of calcium, vitamin D and regular monitoring of calcium is especially important in these patients, see above. *Dry natural rubber* The needle cover of the pre-filled syringe contains dry natural rubber (a derivative of latex), which may cause allergic reactions.
Side Effects Common	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 has black triangle (▼) status. All suspected reactions (including those considered not to be serious and even where the causal link is uncertain) should be reported to the MHRA*
Monitoring	<table><tr><td rowspan="3">Secondary care</td><td>Pre-treatment Assessment</td><td>Baseline renal function, bone profile, 25OH-vitamin D and check calcium levels</td></tr><tr><td>Prior to 2nd injection</td><td>Renal function, bone profile 25OH-vitamin D and check calcium levels</td></tr><tr><td>Primary care</td><td>Prior to 3rd and each subsequent injection</td><td>Renal function, bone profile 25OH-vitamin D and check calcium levels</td></tr></table> • Clinical monitoring of calcium levels is recommended for patients predisposed to hypocalcaemia • Osteonecrosis of the jaw (ONJ) - dental examination with appropriate preventive dentistry should be considered prior to treatment with denosumab in patients with concomitant risk factors Advise patients of good oral hygiene practices should be maintained during treatment. • Patients should be advised to seek prompt medical attention if they develop signs or symptoms of signs or symptoms of infection (i.e. cellulitis, UTI, chest infection, etc.) • During treatment with denosumab, patients should be advised to report new or unusual thigh, hip, or groin pain
Post Administration	• Check blood pressure, pulse, temperature, and respiration rate before discharging the patient home. • Check that the injection site is not bleeding or not showing any signs of inflammation. • Provide contact numbers of the department or advise patient to contact GP and/or attend their local Accident and Emergency Department in the event of a serious adverse reaction. • Arrange the necessary follow-up including blood test prior to next 6 monthly injection.
Drug Interactions	There is low potential for drug-drug interactions (see SmPC). 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

- MTRAC Commissioning guidance sheet for denosumab, January 2014
- TA204 Denosumab for the prevention of osteoporotic fractures in postmenopausal women. NICE 2010
- Amgen Limited. Prolia.Summary of Product Characteristics 2013.
- Cellulitis – acute http://cks.nice.org.uk/cellulitis-acute
- Denosumab: fatal cases of severe symptomatic hypocalcaemia, and risk of hypocalcaemia at any time during treatment - monitoring recommended. MHRA 2012
- Denosumab 60 mg (Prolia): rare cases of atypical femoral fracture with long-term use. MHRA 2013
- Denosumab: minimising the risk of osteonecrosis of the jaw; monitoring for hypocalcaemia—updated recommendations - MHRA Sept 2014
- Denosumab (Xgeva▼, Prolia); intravenous bisphosphonates: osteonecrosis of the jaw—further measures to minimise risk - MHRA DSU July 2015

I agree to participate in this shared care agreement for the treatment of the below named patient with denosumab for the treatment of postmenopausal osteoporosis

General Practitioner
Name (please print)_____Signature _____Date_____

Hospital Specialist/Consultant
Name (please print)_____Signature_____Date_____

Patient's name	Date of birth	Sex	Home Address	Hospital Number
				NHS Number

Please keep a copy of this agreement for your own records and forward the original to the above named Consultant at: