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 subcutaneous denosumab injections for postmenopausal women with 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. **If a specialist asks the GP to prescribe and administer denosumab injection, 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 will be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and agree with it. Patients on denosumab injection 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 osteoporosis and assess patient suitability for denosumab in line with NICE CG146, NICE QS149 and NICE TA204 (please complete appendix 2)
2. Discuss the potential benefits, treatment side effects, and possible drug interactions with the patient.
3. Ask the GP whether they are willing to participate in shared care and confirm with the GP that the specialist will discuss the shared arrangement with the patient.
4. Arrange for appropriate biochemistry (baseline and prior to each injection – bone profile, 25OH-vitamin D and albumin adjusted serum calcium levels).
5. Ensure patient is calcium and vitamin D replete before administering denosumab injection.
6. If any calcium and vitamin D supplementation is required – initiate treatment and advise patient and GP accordingly regarding the dosage, frequency and duration.
7. Ensure patient has good oral hygiene and required dental examination/treatment is completed prior to initiating denosumab treatment.
8. Ensure patient has no ear pain, discharge from the ear, or an ear infection.
9. If patient is on other osteoporosis treatment (alendronate, risedronate, ibandronate, strontium ranelate) advise patient to stop this treatment prior to initiating denosumab.
10. Initiate and administer the first dose of treatment with denosumab if not contraindicated.
11. Issue patient "My Bone Passport*", ensure it is updated and explain the purpose of the passport. Provide patients the patient reminder card regarding osteonecrosis of the jaw and the importance of good oral hygiene.
12. 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.
13. Review the patient's condition and monitor response to treatment regularly including follow-up DXA scan (at 3 and 5 years then 3 yearly thereafter if treatment is to continue long-term).
14. A written summary to be sent promptly to the GP i.e. within 10 working days of a hospital outpatient review or inpatient stay.
15. Report adverse events to the Medicines and Healthcare Products Regulatory Agency (MHRA) and GP.
16. Ensure clear backup arrangements exist for GPs to obtain 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. Following discussion with the specialist and agreement with shared care, prescribe and administer the second and subsequent treatments with denosumab as agreed and at the dose recommended.
3. Arrange for appropriate biochemistry within 4 weeks prior to each denosumab injection – bone profile and albumin adjusted serum calcium levels.
4. 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 regarding osteonecrosis of the jaw. Ensure patient does not have chronic ear pain, discharge or ear infection.
5. Ensure that other osteoporosis treatments (alendronate, risedronate, ibandronate, strontium ranelate etc.) are stopped and removed from the patient's repeat prescription.
6. Continue any calcium and vitamin D treatment as advised by the specialist.
7. Ensure that the practice system is set up to ensure denosumab injection is prescribed and administered to the patient at six monthly intervals (including checking patient's calcium status before each injection) and within 4 weeks of the due date, without delay.
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	SNOMED Code	Description
EMIS and Vision	8BM5.00	415522008	Shared care prescribing
SystmOne	XaB58		Shared care

9. To make sure patient is taking calcium and vit. D, or vit. D alone at least 800 units daily if good dietary calcium intake. Monitor patient's response to treatment; make dosage adjustments if required.
10. GP to arrange a DXA scan at 3 and/or 5 years (if initial DXA scan was arranged by primary care clinician to ensure scan is carried out in the same centre for appropriate comparison).
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. Stop treatment on the advice of specialist or immediately if an urgent need to stop treatment arises.
14. Report adverse events to specialist and MHRA.

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 to the specialist, clinical nurse specialist or GP.
3. Inform specialist or GP of any other medication being taken, including over-the-counter products

4.	Report any adverse events to the specialist or GP particularly if patient develops a swollen, red area of skin, most commonly in the lower leg, that feels hot and tender (cellulitis); symptoms of urine infection; any unusual groin, hip or thigh pain, and chronic ear infection.
5.	Report symptoms of hypocalcaemia to their specialist or GP (e.g. muscle spasms, twitches, or cramps; numbness or tingling in the fingers, toes, or around the mouth).
6.	Maintain good oral hygiene and undertake to have regular dental check-ups. Seek prompt dental consultation if they have any problems with their mouth or teeth during treatment (e.g. loose teeth, pain, swelling, non-healing sores or discharge). Tell their doctor and dentist that they are receiving denosumab treatment if they need dental treatment or dental surgery.
7.	Adhere to any calcium and vitamin D treatment prescribed.
8.	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.
9.	Keep a record of treatment ensuring "My Bone passport*" is updated at 6-monthly visit for denosumab injection.

Please enter Specialist contact details and patient specific information in Appendix 2

SUPPORTING INFORMATION

<table>
<tr><td>Indication as per NICE guidance (TA204 and CG146) (see appendix 1 and 2)</td><td colspan="3">Primary prevention of 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 defined in guidance. In postmenopausal women, denosumab significantly reduces the risk of vertebral, non-vertebral and hip fractures.</td></tr>
<tr><td>Age range</td><td colspan="3">Adults 65 or older.
Denosumab (Prolia) is not recommended in paediatric patients (age < 18)</td></tr>
<tr><td rowspan="2">Dosage and Administration</td><td colspan="3">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.</td></tr>
<tr><td colspan="3">Patients must be adequately supplemented with calcium and vitamin D.</td></tr>
<tr><td>Renal Impairment</td><td colspan="3">No dose adjustment is required</td></tr>
<tr><td>Hepatic impairment</td><td colspan="3">Denosumab has not been tested in patients with hepatic impairment.</td></tr>
<tr><td>Contra-indications / Special precautions</td><td colspan="3">Hypocalcaemia, Renal impairment, Skin infections, Osteonecrosis of the Jaw (ONJ), Osteonecrosis of the external auditory canal, Atypical fractures of the femur, Long-term antiresorptive treatment, Concomitant treatment with other denosumab-containing medicinal products, Dry natural rubber, Warnings for excipients.
For further information refer to: https://www.medicines.org.uk/emc/product/568/smpc</td></tr>
<tr><td>Side Effects</td><td colspan="3">As above, for further information refer to: : https://www.medicines.org.uk/emc/product/568/smpc</td></tr>
<tr><td rowspan="4">Monitoring</td><td>Secondary care</td><td>Pre-treatment assessment</td><td>Baseline renal function (only at baseline), 25OH-vitamin D and albumin-adjusted serum calcium levels</td></tr>
<tr><td>Primary care</td><td>Prior to 2nd and each subsequent injection</td><td>Check bone profile including albumin and adjusted serum calcium levels, and U&Es.</td></tr>
<tr><td colspan="3">• Clinical monitoring of serum calcium level 1-2 weeks after administration of denosumab injection is recommended for patients predisposed to hypocalcaemia (e.g. patient with renal disease). The specialist will give clear advice regarding the need for calcium monitoring. In majority of the cases, patients with renal disease who are at high risk of hypocalcaemia following denosumab treatment, will be managed in secondary care for their on-going denosumab treatment. Where these patients are receiving denosumab injections in primary care it is important that they have their monitoring blood test 2 weeks before and 1-2 weeks after the injection to avoid any complication of hypocalcaemia. If patient is found to have hypocalcaemia before injection, it needs to be corrected before patient can receive their denosumab injection. GP should discuss such cases with patient's renal team/rheumatologist.
• Osteonecrosis of the jaw (ONJ) - Patient advice on importance of good oral hygiene practices and regular dental consultation should be reiterated throughout the treatment. Patients with dental problem should be advised to seek prompt dental consult or treatment before receiving their next denosumab injection.
• Osteonecrosis of the external auditory canal- patients should be advised to report any ear pain, discharge from the ear, or an ear infection during denosumab treatment.
• Patients should be advised to seek prompt medical attention if they develop 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.</td></tr>
<tr><td colspan="3">Actions to be taken:</td></tr>
<tr><td colspan="2">Adjusted serum calcium levels below the normal range</td><td>Withhold until discussed with specialist team.</td></tr>
<tr><td colspan="2">Osteonecrosis of the jaw (ONJ)</td><td>Withhold until discussed with specialist team.</td></tr>
<tr><td colspan="2">Osteonecrosis of the external auditory canal</td><td>Withhold until discussed with specialist team.</td></tr>
<tr><td colspan="2">Signs or symptoms of infection (i.e. cellulitis, UTI, chest infection, etc.)</td><td>Withhold until discussed with specialist team.</td></tr>
<tr><td colspan="2">New or unusual thigh, hip, or groin pain</td><td>Withhold until discussed with specialist team. Arranging a plain X-ray of bilateral hip and pelvis is usually recommended.</td></tr>
<tr><td>Post Administration</td><td colspan="3">• 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.</td></tr>
<tr><td>Drug Interactions</td><td colspan="3">Please refer to SPC</td></tr>
</table>

References

- MTRAC Commissioning Support for denosumab (Prolia), November 2019.
- NICE CG146. Osteoporosis: Assessing the risk of fragility fracture. NICE 2012 (updated: February 2017).
- NICE QS149. Osteoporosis- Quality Standard. NICE 2017.
- NICE TA204. Denosumab for the prevention of osteoporotic fractures in postmenopausal women. NICE 2010.
- Amgen Limited. Prolia 60mg solution for injection in pre-filled syringe. Summary of Product Characteristics 2020.
- NICE CKS 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
- Denosumab (Prolia, Xgeva▼): reports of osteonecrosis of the external auditory canal - MHRA DSU June 2017

*My Bone Passport' is developed by Amgen as part of the PROLONG programme.
Amgen issue the trusts with regular supplies which will be issued to patients during their first injection.

Appendix 1

NICE QS149 – Osteoporosis

Quality statement 2: Starting drug treatment

Adults at high risk of fragility fracture are offered drug treatment to reduce fracture risk.

Women with a prior fragility fracture (particularly hip or vertebral fracture) and men and women with a 10-year probability of a major osteoporotic fracture derived from FRAX, above the upper assessment threshold, should be considered for treatment (see table 1). Men and women with a 10-year probability between the upper and lower assessment threshold should be referred for bone mineral density measurement and their fracture probability reassessed. If their 10-year fracture probability is above the intervention threshold after reassessment (see table 1), treatment should be offered.

Table 1. Lower and upper assessment thresholds and intervention thresholds for major osteoporotic fracture probability based on fracture probabilities derived from FRAX (BMI set to 25 kg/m^2)

	10-year probability of a major osteoporotic fracture (%)		
Age (years)	Lower assessment threshold	Upper assessment threshold	Intervention threshold
40	2.6	7.1	5.9
45	2.7	7.2	6.0
50	3.4	8.6	7.2
55	4.5	11	9.4
60	5.9	14	12
65	8.4	19	16
≥70	11	24	20
Reproduced with permission from McCloskey et al. (2015) FRAX-based assessment and intervention thresholds – an exploration of thresholds in women aged 50 years and older in the UK. Osteoporosis International 26 (8), 2091–9			

[Adapted from National Osteoporosis Guideline Group's Clinical guideline for the prevention and treatment of osteoporosis, section 11, recommendation 7]

Drugs that can be prescribed to prevent fragility fractures include bisphosphonates (alendronate, ibandronate, risedronate and zoledronic acid) and non-bisphosphonates (raloxifene, **denosumab**, teriparatide, calcitriol and hormone replacement therapy).

NICE TA204 - Denosumab for the prevention of osteoporotic fractures in postmenopausal women

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

T-scores (SD) at (or below) which denosumab is recommended when alendronate and either risedronate or etidronate are unsuitable

	Number of independent clinical risk factors for fracture		
Age (years)	**0**	**1**	**2**
65-69		−4.5	−4.0
70-74	−4.5	−4.0	−3.5
75 or older	−4.0	−4.0	−3.0
■ treatment with denosumab is not recommended.			

Denosumab is recommended as a treatment option for the secondary 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.

Appendix 2:

Effective Shared Care Agreement (ESCA)

Denosumab▼ (Prolia)

ESCA: For the treatment of postmenopausal osteoporosis

Please refer to BSSE APC formulary website for complete document.

NICE CG146, NICE QS149 and NICE TA204 criteria (To be completed by Specialist team)	
Patient is at high risk of fragility fracture for whom drug treatment to reduce fracture risk is indicated.	
Patient is intolerant or unable to comply with instructions for administering oral bisphosphonate (e.g. alendronate, risedronate or etidronate) , or oral bisphosphate is contraindicated for patients (e.g. gastric pathology or allergy). *List agent(s) please->*	*List agent(s) please*
AND	
T-score *List T-Score please->*	
Age *List age please->*	
FRAX Score for major osteoporotic fracture	
FRAX Score for hip fracture	
Independent clinical risk factors for fracture (tick all that apply)	
• parental history of hip fracture	
• alcohol intake of 4 or more units per day	
• rheumatoid arthritis	
• medication (e.g. steroid, aromatase inhibitor, androgen deprivation therapy)	
• Others	

BACK-UP ADVICE AND SUPPORT (To be completed by Specialist team)

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

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

Hospital Specialist/Consultant

Name (please print)_____Signature_____Date_____

To be completed by the General Practitioner:

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

General Practitioner

Name (please print)_____Signature _____Date_____

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

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	SNOMED Code	Description
EMIS and Vision	8BM5.00	415522008	Shared care prescribing
SystmOne	XaB58		Shared care

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