Specialised Medicines Service (SMS) Guideline ~ Denosumab for osteoporosis

Specialist: Please complete the letter template sending a request to GP (see bottom of the page)

GP: Please indicate whether you wish to share patient's care by completing letter and return to specialist

Aim of treatment

Denosumab is a biological medicine; it is a monoclonal antibody drug indicated for the primary prevention, and as a treatment option for the secondary prevention of osteoporotic fractures in postmenopausal women at increased risk. Denosumab is given as a single subcutaneous injection once every six months.

Please refer to NICE TA204 and consider denosumab in patients 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

Local specialists have indicated subgroups of patients for whom denosumab may be more appropriate (see under “Duration of treatment”).

Biosimilar medicines

Biological medicines are medicines that are made, or derived from, a biological source. They are large, complex molecules, with inherent variability in their structure. Variability between batches of the same product is controlled and monitored during manufacturing, to maintain this within defined and approved limits.

A biosimilar is a biological medicine which is highly similar to another biological medicine already licensed for use (the reference product). It will have been shown not to have any clinically meaningful differences from the originator biological medicine in terms of quality, safety and efficacy. Where NICE has already recommended the originator biological medicine, the same guidance will normally apply to a biosimilar of that originator, providing the licensing indications are the same. Prolia is the reference product for denosumab solution for injection pre-filled syringe 60mg/1ml.

A biosimilar product is considered interchangeable with its reference product and with other biosimilars of the same reference product. A prescriber can choose the biosimilar medicine over the reference product or vice versa and expect the same therapeutic effect in the patient.

As a result, switching patients from one product to another (reference product or biosimilar) has become clinical practice. The decision to prescribe an originator biological medicine or a biosimilar product rests with the responsible clinician in consultation with the patient. The use of biosimilars is supported by NHS England and NHS Devon; the appropriate use of biosimilars is expected to result in significant cost savings to reinvest in patient care.

Biological medicines and biosimilars must be prescribed by brand name to support on-going pharmacovigilance of the individual products

The brand specified on the prescription should be dispensed to avoid inadvertent switching. Automatic substitution of brands at the point of dispensing is not appropriate for biological medicines.

Refer to Devon formulary for a list of denosumab brands approved for use locally (N&E / S&W).

Refer also to Devon Formulary information on biological medicines and biosimilar products (N&E / S&W).

Responsibilities of clinician initiating treatment

1. Ensure that the patient meets the criteria for treatment with denosumab by checking full details of patient's medical records and medication history.
2. Pre-existing hypocalcaemia must be investigated, treated and corrected prior to initiating denosumab. It is therefore recommended that all patients have a pre-treatment eGFR and serum calcium.
3. Ensure that the patient is adequately supplemented with calcium and vitamin D before starting treatment. See Devon Formularies section 9.6.4 Vitamin D for further information and doses (N&E / S&W).
4. Check for osteonecrosis of the jaw (ONJ); the clinician should ask about dental hygiene and previous dental care especially recent root canal treatments; if concerns are raised consider referral to dentist. Please refer to the MHRA Drug Safety Update (September 2014), and also see below for further information.
5. Inform patient about the rationale and need for biosimilar switching and explain that this may happen in primary care. Obtain consent to adopt a best value denosumab in the future. The following resource may support this discussion: https://www.patients-association.org.uk/switchingtobiosimilars
6. Initiate the first dose of treatment with denosumab injection and ensure that the patient understands the plan for follow-up care. Give patients the patient reminder card for their medicine (refer to individual manufacturer's risk materials available here). **Prescribe by brand.**
7. Ensure that arrangements for continued prescribing are in place.
8. Provide the GP and patient with relevant contact information and clear arrangements for back-up advice and support.
9. Report any adverse events to the Medicines and Health Care Regulatory Agency (MHRA). For all biological medicines, adverse reaction reports should clearly state the brand name and the batch number of the suspected medicine.

Responsibilities of clinician prescribing on-going treatment

1. Prescribe and administer denosumab at the dose recommended, at six monthly intervals after initial administration (plus or minus a maximum of two weeks). **Prescribe by brand** and inform the patient of the brand administered.
2. Ensure that the practice system is set up to recall the patient regularly at six monthly intervals, with follow up for missed appointments
3. Monitor calcium levels before each dose of denosumab. Check patient is taking a calcium and vitamin D supplement
4. Seek advice from a specialist if the GP considers treatment with denosumab is no longer appropriate or the patient wishes to discontinue treatment
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 to the specialist if the patient's condition deteriorates
10. Report any adverse events to the Medicines and Health Care Regulatory Agency (MHRA). For all biological medicines, adverse reaction reports should clearly state the brand name and the batch number of the suspected medicine.

Monitoring

Monitoring of calcium levels should be conducted prior to each dose of denosumab, and within two weeks after the initial dose in patients predisposed to hypocalcaemia (e.g. patients with severe renal impairment, creatinine clearance <30 ml/min), or if suspected symptoms of hypocalcaemia occur or if otherwise indicated.

Patients should be advised to report symptoms of hypocalcaemia.

Duration of treatment

The need to continue treatment with denosumab, as with all other anti-resorptive agents, should be reviewed after a maximum of 5 years.

Review requires a re-evaluation of the patient's fracture risk, normally including a repeat DXA scan.

Atypical femoral fractures have been reported in association with denosumab treatment. An increased risk of multiple vertebral fractures has been reported in patients within 18 months of stopping or delaying ongoing denosumab 60mg treatment for osteoporosis. Current guidance indicates that denosumab should not be stopped without considering alternative treatment to prevent rapid bone mineral density loss and a potential rebound in vertebral fracture risk

Local specialists have indicated that denosumab may therefore be more appropriate for patients who:

- have very high risk of fragility fracture and likely to require treatment for at least 10 years (e.g. patients with a history of hip fracture or multiple vertebral fractures)
- are elderly, as patients over the age of 75 are less likely to be suitable for drug holidays **or**
- are unable to attend for IV bisphosphonate treatment due to limited mobility or geographic reasons.

Patient/patient carer responsibilities

1. Report to the doctor if there is not a clear understanding of the treatment and share any concerns in relation to treatment.
2. If you have any questions about denosumab or biosimilars, please speak to a member of your clinical or pharmacy team.
3. Report any adverse effects or warning symptoms whilst on treatment with denosumab
4. Adhere to any calcium and vitamin D treatment prescribed
5. Inform specialist or GP of any medication being taken, including over-the-counter products
6. Ensure good oral hygiene

Dosage & Administration

60mg of denosumab (in a 1ml solution) administered by subcutaneous injection into the thigh, abdomen or back of arm once every 6 months. Administration should be performed by an individual who has been adequately trained in injection techniques.

Refer to Devon formulary for a list of denosumab brands approved for use locally (N&E / S&W).

Storage

Refer to SmPC: https://www.medicines.org.uk/emc/search?q=denosumab

Supporting Information

This guideline highlights significant prescribing issues, not all prescribing information and potential adverse effects are listed.

- Please refer to SmPC/data sheet for full prescribing data: https://www.medicines.org.uk/emc/search?q=denosumab
- National Osteoporosis Guideline Group: Osteoporosis Clinical guideline for prevention and treatment: http://www.shef.ac.uk/NOGG/NOGG_Executive_Summary.pdf

MHRA Drug Safety Updates

MHRA Drug Safety Update (October 2012) and MHRA Drug Safety Update (September 2014): Denosumab: monitoring recommended. Fatal cases of severe symptomatic **hypocalcaemia**, and risk of hypocalcaemia at any time during treatment.

a. The following precaution should be followed to minimise the risk of hypocalcaemia with denosumab:
   i. Denosumab 60mg (for osteoporosis indications) should not be used in patients with hypocalcaemia, regardless of severity (the contraindications vary between the two doses, because their indications are different)
b. Refer to the MHRA alerts for further information and advice including suggested monitoring

MHRA Drug Safety Update (February 2013): **Atypical femoral fractures** have been reported rarely in patients with postmenopausal osteoporosis receiving long-term (2.5 years or longer) treatment with denosumab 60mg in a clinical trial. During denosumab treatment, patients presenting with new or unusual thigh, hip or groin pain should be evaluated for an incomplete femoral fracture. Discontinuation of denosumab therapy should be considered if an atypical femur fracture is suspected, while the patient is evaluated

MHRA Drug Safety Update (July 2015), MHRA Drug Safety Update (December 2015) and MHRA Drug Safety Update (June 2017):

a. Denosumab is associated with a risk of **osteonecrosis of the jaw**, **osteonecrosis of the external auditory canal has also been reported with denosumab**
b. Before prescribing denosumab or intravenous bisphosphonates:
   i. give patients the patient reminder card for their medicine
   ii. explain the risk of osteonecrosis of the jaw, and osteonecrosis of the external auditory canal, and advise patients on precautions to take
   iii. advise patients to report any problems with their mouth or teeth, any ear pain, discharge from the ear, or an ear infection during denosumab treatment

MHRA Drug Safety Update (August 2020): Denosumab 60mg (**Prolia**): **increased risk of multiple or vertebral fractures after stopping or delaying ongoing treatment**

a. an increased risk of multiple vertebral fractures has been reported in patients within 18 months of stopping or delaying ongoing denosumab 60mg treatment for osteoporosis
b. patients with a previous vertebral fracture may be at highest risk
c. if a patient misses a prescribed dose of denosumab, the missed injection should be administered as soon as possible
d. patients should not stop denosumab without specialist review
e. re-evaluate the need for continued treatment periodically, particularly after 5 or more years of use

MHRA Drug Safety Update (May 2022): Denosumab 60mg (**Prolia**): **should not be used in patients under 18 years** due to the risk of serious hypercalcaemia

Version 1

Date ratified: November 2016 (Biosimilar prescribing update January 2026)

This guideline has been reviewed by stakeholders across Devon and is intended for use in accordance with locally commissioned services.

Specialised Medicines Service (SMS) Guideline Agreement Letter - Specialist Request to GP

To	**GP name**	
	Practice address	
Patient name		
Hospital number		
NHS number		
Date of birth		
Address		

GPs are invited to participate in SMS Guideline agreements, but if the GP is not confident to undertake these roles then they are under no obligation to do so. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs."

This patient is now suitable for prescribing to move to primary care. The patient fulfils criteria within this SMS guideline therefore I am writing to request your agreement to continue their care according to the Guideline.

I have discussed and agreed the following treatment with the patient.:

	Specialist to complete
Denosumab 60mg (State brand administered)	
Indication (Indicate licensing status)	
Date first dose administered	
GP to undertake prescribing and calcium monitoring in line with the SMS Guideline from (insert date)	
Next dose due date	

I can confirm that the following have occurred with regard to this treatment:

	Specialist to complete (YES/NO)
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	
The patient has agreed to this arrangement, understands the need for ongoing calcium monitoring, and has agreed to attend all necessary appointments	
The roles of the Specialist / GP / Patient have been explained and agreed	
The risks and benefits of treatment have been explained to the patient	
Patient has been informed about the rationale and need for biosimilar switching and understands that this may happen in primary care. Consent has been obtained to adopt a best value denosumab in the future.	
The patient has been provided with relevant contact information and clear arrangements for advice and support.	
Baseline investigation and monitoring as set out in the SMS Guideline have been completed and were satisfactory	
I have enclosed a copy of the SMS Guideline which covers this treatment. The guideline can also be found here	
I have included with this letter copies of the information the patient has received	

The results of baseline tests, early monitoring and any additional supportive information are included below and/or attached.

GP please sign response letter and return promptly (where possible this should be within 14 days of the request being made).

Specialist signature		**Date**	
Specialist name, role, speciality			
Daytime telephone number			
Email address			
Alternative contact e.g. clinic or specialist nurse			
Out of hours contact details e.g. duty doctor			

Remember to keep a copy of this letter for the patient's records.

Specialised Medicines Service (SMS) Agreement Letter – GP Acceptance Letter to Specialist

To	Specialist name	

Patient name	
Hospital number	
NHS number	
Date of birth	
Address	

GPs are invited to participate in SMS Guideline agreements, but if the GP is not confident to undertake these roles then they are under no obligation to do so. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs."

Thank you for your request for me to accept prescribing responsibility for this patient and to provide densosumab 60mg subcutaneous injections once every 6 months.

I can confirm that **I am willing to take on this responsibility** from: ……

I will maintain the prescribing and monitoring responsibilities as set out in the SMS Guideline.

GP signature		**Date**	
GP name			
Practice address			
Telephone number			
Email address			

Remember to keep a copy of this letter for the patient's records. If this letter is not returned sharing of the care for this patient will not commence.

Specialised Medicines Service (SMS) Agreement Letter – GP Refusal Letter to Specialist

To	Specialist name	

Patient name	
Hospital number	
NHS number	
Date of birth	
Address	

GPs are invited to participate in SMS Guideline agreements, but if the GP is not confident to undertake these roles then they are under no obligation to do so. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs."

In the interest of patient safety NHS Devon, in conjunction with local acute trusts ongoing prescribing of denosumab requires a number of conditions to be met before transfer can be made to primary care.

Thank you for your request for me to accept prescribing responsibility for this patient. I regret to inform you that in this instance **I am unable to take on responsibility** due to the following:	**Tick all applicable**
The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing the agreement. As the patients GP I do not feel clinically confident to manage this patient's condition. I have consulted with other GPs in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given below.**	

The condition does not fall within the criteria defined within the SMS Guideline. As the condition requested to be treated is not included on the locally recognised list of indications in the SMS Guideline, I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this condition is identified within the SMS guideline the responsibility for providing this patient with their medication remains with you.**	
Initiation and optimisation by the initiating specialist. First dose must be administered by specialist team. As the patient has not been initiated on this medication, I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. **Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.**	
Other (GP to complete if there are other reasons why the request cannot be accepted):	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this patient as soon as possible.

GP signature		**Date**	
GP name			
Practice address			
Telephone number			
Email address			

Remember to keep a copy of this letter for the patient's records.