DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE
SHARED CARE AGREEMENT

Denosumab 60mg for the prevention of osteoporotic fractures in men and post-menopausal women

1. REFERRAL CRITERIA

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- Prescribing responsibility will only be transferred when it is agreed by the specialist and the patient's GP that the patient's condition is stable or predictable.
- Patients will only be referred to the GP once the GP has agreed in each individual case
- All patients will be given the baseline injection at the hospital and among patients with Chronic Kidney Disease (eGFR <40ml/min/1.73m^2) will have 2nd injections; further treatment will be provided and administered via the GP surgery

eGFR	Under specialist care	Further treatment
eGFR >40ml/min/1.73m^2	1st injection	Continued in primary care
eGFR <40ml/min/1.73m^2	1st & 2nd injections	Continued in primary care
Initially eGFR >40ml/min/1.73m^2, but falls below 40ml/min/1.73m^2 prior to 2nd dose	1st injection	Refer to specialist care
eGFR <30ml/min/1.73m^2	Initiate and remain under specialist care	

2. AREAS OF RESPONSIBILITY

GP responsibilities	Specialist responsibilities
1. To refer appropriate patients to secondary care for assessment **2.** To agree to prescribe for patients in line with the shared care agreement **3.** To report any adverse effects to the referring specialist and the MHRA yellow card scheme **4.** To continue to prescribe for the patient as advised by the specialist **5.** To undertake monitoring as per shared care guideline **6.** Check patient is continuing calcium & vitamin D treatment if recommended **7.** Check U&E, calcium & vitamin D levels before each dose and ensure that the adjusted calcium is not less than 2.20mmol/Land the vitamin D level is >50nmol/l prior to the injection (the patient will be given a blood form from the hospital after their 1st injection and advised to have a blood test one week before their next injection is due) **8.** To inform the specialist if the patient discontinues treatment for any reason **9.** To seek the advice of the specialist if any concerns with the patient's therapy **10.** To conduct an annual face to face medication review or more frequent if required **11.** Refer at 5 years for a review of treatment. Do not discontinue denosumab until referred and seen by specialist. **12.** Refer to specialist if eGFR status falls below 30ml/min/1.73m^2 and seek advice before any further doses are given. **13.** If eGFR<40ml/min/1.73m^2 further into treatment-continue as per SCA and only refer back to the specialist if eGFR falls below 30ml/min/1.73m^2 **14.** If delay between injections is likely to be beyond 7 months contact specialist for advice.	**1.** To discuss benefits and side effects of treatment with the patient/carer and obtain informed consent. To initiate denosumab in appropriate patients **2.** To assess tolerability of treatment in the individual **3.** To undertake baseline assessment and continued monitoring as per shared care guideline (section vi. of table below) **4.** Ensure vitamin D level is stable on current regime **5.** To prescribe the • First baseline injection for patients with eGFR >40ml/min/1.73m^2, in normal individuals • Two doses in patients with CKD (eGFR <40ml/min/1.73m^2) **6.** To contact patient's GP to request prescribing under shared care and send a link to or copy of the shared care protocol. **7.** Write to the GP to summarise treatment & follow up plans, also to include explicit evidence of meeting the NICE TAG criteria by completing the attached form **8.** To advise the GP regarding continuation of treatment, including the length of treatment **9.** To discuss any concerns with the GP regarding the patient's therapy **10.** To report any adverse effects to the MHRA yellow card scheme and GP **11.** Undertake a review at 5 years and 10 years (with re-referral)

Patient responsibilities

- Report any adverse reactions to the GP or specialist whilst receiving treatment with Denosumab
- Share any concerns in relation to treatment with Denosumab
- Report to the specialist or GP if they do not have a clear understanding of their treatment
- To seek prompt medical attention if they develop signs or symptoms of cellulitis
- To maintain good oral hygiene whilst on treatment with Denosumab
- To attend the GP surgery every 6 months for the Denosumab injection
- To ensure they have a blood test (calcium & vitamin D levels) one week prior to injection
- To continue the calcium and vitamin D supplements if prescribed.
- To seek medical attention if they develop signs of hypocalcaemia
- To inform the GP/Consultant/Specialist Nurse before considering any invasive dental treatment
- To inform their dentist they have been initiated on Denosumab at the next routine appointment
- Patients presenting with new or unusual thigh, hip or groin pain should inform the prescriber

3. COMMUNICATION AND SUPPORT

i. Hospital contacts:	**ii. Out of hours contacts and procedures:**
Royal Derby Hospital (University Hospitals of Derby and Burton, UHDB, NHS Foundation Trust) Osteoporosis Nurse Specialist **Telephone No:** 01332 785649 **Email:** dhft.osteoporosisservice@nhs.net **Chesterfield Royal Hospital Foundation Trust** Julianna Sharp, Osteoporosis Nurse Specialist **Telephone No:** 01246 277271 **Email:** julianna.sharp@nhs.net	Pharmacy, UHDB, ask for on-call pharmacist via switchboard: 01332 340131 Contact the on-call Medic for the relevant speciality via switchboard: 01246 277271

iii. Specialist support/resources available to GP including patient information:
National Osteoporosis Society leaflet on "Drug Treatments for Osteoporosis"
https://nos.org.uk/media/1602/denosumab-prolia.pdf

4. CLINICAL INFORMATION

i. Prescribed indications	For the treatment of osteoporosis in men and postmenopausal women at increased risk of fractures, and for the treatment of bone loss associated with hormone ablation in men with prostate cancer. Not relevant to this section Alendronic acid remains the first line treatment for osteoporosis in accordance with NICE guidance. Approximately 25% of patients cannot be treated with alendronic acid because of side effects, inability to comply with dosing instructions or malabsorption leading to inefficacy. Risedronate should also be tried if appropriate before Denosumab is considered. Denosumab provides another option for those patients also unable to take risedronate and has been recommended by NICE in this context. The guidance is available at http://guidance.nice.org.uk/TA204.
ii. Therapeutic summary	Denosumab is a human monoclonal antibody (IgG2) that targets and binds with high affinity and specificity to RANKL, preventing activation of its receptor, RANK, on the surface of osteoclast precursors and osteoclasts. Prevention of the RANKL/RANK interaction inhibits osteoclast formation, function and survival, thereby decreasing bone resorption in cortical and trabecular bone.
iii. Dose & Route of administration	60mg administered as a single subcutaneous injection once every 6 months into the thigh, abdomen or back of arm. Patients must be calcium and vitamin D replete and in most cases advice will be given to provide supplementation with calcium and vitamin D (daily dosage: calcium 1g and colecalciferol 800 units). No dosage adjustment is required in patients with renal impairment.
iv. Duration of treatment	Contact specialist after 5 years of treatment to determine if treatment should continue. There is a risk of rebound fractures, especially vertebral fractures, with the cessation of treatment. Bone mineral density is also likely to return back to prior to commencing denosumab.
v. Adverse effects	**Common (≥ 1/100 to < 1/10):** urinary tract infection, upper respiratory tract infection, sciatica, abdominal discomfort, constipation, rash and pain in extremity. **Uncommon (≥ 1/1000 to < 1/100):** diverticulitis, cellulitis, ear infection. Skin infections requiring hospitalisations **Rare (≥ 1/10,000 to < 1/1,000)**: atypical femur fracture, osteonecrosis of the jaw (ONJ), hypocalcaemia (< 1.88 mmols/l), The above details are not a complete list and the current BNF and the SPC should be consulted.
vi. Monitoring Requirements	**Prior to initiation of therapy** 1) Vitamin D deficiency and hypocalcaemia must be corrected before initiation of therapy. 2) A dental examination should be considered prior to treatment with Denosumab in patients with concomitant risk factors (refer to SPC)

Subsequent monitoring

1) Monitoring of calcium levels prior to each injection is recommended **ensuring that the adjusted calcium is not less than 2.20mmol/L and the vitamin D level is >50nmol/l prior to the injection**
2) Patients receiving denosumab may develop skin infections (predominantly cellulitis) leading to hospitalisation and thus should be advised to seek prompt medical attention if they develop signs or symptoms of cellulitis.
3) While on treatment, patients should delay invasive dental procedures if possible until just prior to their next 6 monthly injection but these procedures are not contra-indicated and should go ahead if urgent. Good oral hygiene practices should be maintained during treatment with Denosumab.

Summary of monitoring

- **Baseline (0 months) – specialist/nurse practitioner**
- Baseline assessment
- Ensure calcium & vitamin D replete
- Patient information given
- First injection

- **6 months – nurse practitioner/specialist among patients with Chronic Kidney Disease (eGFR <40ml/min/1.73m^2)**
- Check calcium & vitamin D level
- Check patient is taking calcium and vitamin D as advised at baseline
- Administer second injection
- Agreement established with GP for on-going treatment administration. Write to the GP to summarise treatment and follow-up plans, also to include NICE TA compliance

- **6months - GP surgery (second injection onwards) for patients with eGFR>40ml/min/1.73m2**
- Check calcium & vitamin D level
- Check patient is taking calcium and vitamin D as advised at baseline
- Administer second injection via GP surgery
- Treatment should be administered within a 1 month window around each 6-monthly time-point

- **12 months onwards – GP surgery (third injection onwards)**
- Check calcium & vitamin D level
- Check patient is continuing calcium & vitamin D treatment if recommended (if has stopped supplements check calcium levels prior to treatment)
- 6 monthly SC injection administered via GP surgery
- Treatment should be administered within a 1 month window around each 6-monthly time-point

- **5 years – specialist review**
- Decision whether to continue treatment
- Continue treatment via GP surgery if appropriate

Osteonecrosis of the jaw

Discontinuation of denosumab treatment should be considered if an ONJ is suspected/diagnosed or if there is an unhealed wound following an invasive dental procedure. An individual assessment of the benefits and risks should be performed.
Drug Safety Update volume 8 issue 12 July 2015: 1.
Drug Safety Update volume 8 issue 2, September 2014: A2

Atypical femoral fracture

Rare cases of atypical femoral fracture with long-term use of denosumab has been reported. 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 and consider discontinuation of treatment. An individual assessment of the benefits and risks should be performed.
MHRA Drug Safety Update vol. 6 Issue 7 February 2013

Osteonecrosis of the external auditory canal

Osteonecrosis of the external auditory canal has been reported very rarely (fewer than 1 in 10 000 patients) with bisphosphonates, mainly in association with long-term therapy (2 years or longer). The possibility of osteonecrosis of the external auditory canal should be considered in patients receiving denosumab who present with ear symptoms including chronic ear infections or in those with suspected cholesteatoma.

		Drug Safety Update volume 10 issue 11, June 2017: 1 **Drug Safety Update volume 9 issue 5 December 2015: 3** **Increased risk of multiple vertebral fractures after stopping or delaying ongoing treatment** **Patients should not stop denosumab without specialist review.** Since 2015 and upto and including June 2020, 44 cases of vertebral fracture, including multiple fractures, have been reported in the UK in post-marketing settings in patients after stopping or delaying ongoing treatment with denosumab. Where reported, these fractures occurred within 18 months of stopping or delaying denosumab treatment, with some in the first 9 months. These fractures were described as life-changing in some cases. **Drug Safety Update volume 14 issue 1 August 2020**
vii.	**Clinically relevant drug interactions**	No drug interactions have been described. Pharmacokinetics and pharmacodynamics were not altered by previous alendronate therapy.
viii.	**Contraindications**	1) Hypocalcaemia 2) Hypersensitivity to the active substance or to any of the product excipients: • Latex Allergy: The needle cover of the pre-filled syringe contains dry natural rubber (a derivative of latex). • Fructose Intolerance: Patients with rare hereditary problems of fructose intolerance should not use denosumab • Hypocalcaemia is a known risk factor with denosumab use, especially in patients with severe renal impairment (Cr Cl <30mL/min: estimated eGFR<30ml/min/1.73m^2). These will be excluded from shared care -treatment for these patients will remain under the specialist unless otherwise agreed with the GP
ix.	**Supply of ancillary equipment**	Not required
x.	**Supply, storage and reconstitution instructions**	Denosumab must not be mixed with other medicinal products. Store in a refrigerator (2°C - 8°C). Denosumab may be exposed to room temperature (up to 25ºC) for a maximum single period of up to 30 days in its original container. Once removed from the refrigerator must be used within this 30 day period. Do not freeze. Keep the pre-filled syringe in the outer carton in order to protect from light. Do not shake excessively. To avoid discomfort at the site of injection, allow the pre-filled syringe to reach room temperature (up to 25°C) before injecting and inject slowly. Inject the entire contents of the pre-filled syringe.
xi.	**Prepared by** **In consultation with**	The Shared Care Guideline Group, UHDB Dr Michelle Hui (MH), Consultant Rheumatologist, UHDB Dr Antonia Ugur (AU), Consultant Endocrinologist, UHDB Dr Lit-Hiang Lee (LHL), Consultant Rheumatologist, UHDB Sue Hind (SH), Lead Osteoporosis Nurse Specialist, UHDB Mel Calvert (MC), Lead Osteoporosis Nurse Specialist, UHDB Sarah Broadhurst (SB), Fracture Liaison Nurse Specialist, UHDB Gemma O'Hara (GO), Fracture Liaison Nurse Specialist, UHDB Derbyshire Medicines Management Guideline & Shared Care Group MH, AU, LHL, SH, MC, SB, GO, UHDB Julianna Sharp, Osteoporosis Nurse Specialist, Chesterfield Royal Hospital NHS Foundation Trust
	Reviewed by	Dr Kevin Fairburn, Consultant Rheumatologist, Chesterfield Royal Hospital NHS Foundation Trust

This does not replace the SPC, which should be read in conjunction with it.

Date Prepared: October 2012 **Reviewed:** March 2019 **Review Date**: February 2022

References

Denosumab for the Primary and Secondary Prevention of Osteoporotic Fractures in Postmenopausal Women, Technology Appraisal, October 2010. http://guidance.nice.org.uk/TA204.
Prolia Summary of Product Characteristics www.medicines.org.uk/EMC/medicine/23127/SPC/Prolia/
MHRA volume 6 Issue 3 October 2012
MHRA volume 6 Issue 7 February 2013 Denosumab 60 mg (Prolia▼): rare cases of atypical femoral fracture with long-term use
MHRA volume 14 issue 1 August 2020: Denosumab 60mg (Prolia): increased risk of multipal vertebral fractures after stopping or delaying treatment

Protocol for primary care management of patients prescribed PROLIA® (Denosumab) for prevention of fractures

Step 1: before the patient is administered Denosumab

- Determine stocking process for the injection –ideally it will be stored in the practice refrigerator (2°C - 8°C); where this is not possible, work with local pharmacy/pharmacies to agree process for collection. The injection may be stored at room temperature (25°C) for up to 30 days. Once removed from the refrigerator it must be used within a 30 day period.
- Ensure Movianto account is set-up for ordering / ensure pharmacy has stock. Denosumab can be delivered to your practice within 24 hours – to order, contact Movianto on 01234 248631 (product code 900320).
- Ensure the practice system is set-up to recall patients on a six-monthly interval.
- Ensure you are familiar with the product SPC –including the shelf life and storage instructions (sections 6.3 & 6.4)
- Check U&E, calcium & vitamin D level prior to each injection.
- Ensure the patient is continuing calcium & vitamin D treatment if recommended (if stopped supplements check vitamin D & calcium prior to treatment)

Step 2: administering Denosumab

- Before administration, inspect the solution. Do not inject the solution if it contains particles, or is cloudy or discoloured. Do not shake excessively
- To avoid discomfort at the site of injection, allow the pre-filled syringe to reach room temperature (up to 25°C) before injecting and inject slowly (company leaflet is available with specific instructions for administration) .
- Inject the entire contents of the pre-filled syringe and dispose of any medicinal product remaining in the pre-filled syringe
- Any unused product or waste material should be disposed of in accordance with local requirements
- Record batch number and site of injection on patient's notes
- Instruct patient to report any adverse events to the practice so these can in turn be reported to the MHRA

Step 3: follow-up care and administration

- Patient should have been recalled six months after last administration of Denosumab
- Check that patient was satisfied that there were no AEs following the last administration of Denosumab

Useful Contact Information

Amgen UK medical information: 01223 436441 or gbinfoline@amgen.com

UK Adverse Event Reporting: 01223 436712

Movianto: 01234 248631 or customercare.uk@movianto.com

THIS PROTOCOL HAS BEEN ADAPTED FROM THE AMGEN & GLAXOSMITHKLINE PROTOCOL TO SUPPORT PRIMARY CARE PROFESSIONALS IN THE APPROPRIATEUSE OF DENOSUMAB

Sample Transfer Letter

Hospital No: «HOSPITAL_NUMBER»
NHS No: «NHS_NUMBER»

{Insert date}

PRIVATE & CONFIDENTIAL
«GP_TITLE» «GP_INITIALS» «GP_SURNAME»
«GP_ADDRESS_1»
«GP_ADDRESS_2»
«GP_ADDRESS_3»
«GP_ADDRESS_4»
«GP_POSTCODE»

DERBYSHIRE JAPC SHARED CARE AGREEMENT LETTER

Dear «GP_TITLE» «GP_SURNAME»

«FORENAME_1» «SURNAME» «DATE_OF_BIRTH»
«CURRENT_ADDRESS_1» «CURRENT_ADDRESS_2» «CURRENT_ADDRESS_3»
«CURRENT_ADDRESS_4» «CURRENT_POSTCODE»

Your patient was seen on ***{Insert date}*** with a diagnosis of ***{Insert diagnosis}***. I have initiated the following medication ***{Insert drug name}*** and am writing to ask you to participate in the shared care for this patient.

This medication has been accepted as suitable for shared care by the Derbyshire Joint Area Prescribing Committee (JAPC). I agree to the secondary care responsibilities set out in the shared care agreement for this medication (available from www.derbyshiremedicinesmanagement.nhs.uk/clinical_guidelines/shared_care_guidelines). I am therefore requesting your agreement to share the care of this patient. Where preliminary tests are set out in the agreement I have carried these out and results are below.

Dose Regimen	Date ***{Insert medicine name}*** started	Date for GP to start prescribing ***{Insert medicine name}*** from
The most recent test results are (if applicable): **See overleaf for initiation criteria.**		

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	*Yes / No*
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	*Yes / No*
The risks and benefits of treatment have been explained to the patient	*Yes / No*
The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed	*Yes / No*
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	*Yes / No*
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here	*Yes / No*

(insert electronic/ web link)	
I have included with the letter copies of the information the patient has received	*Yes / No*
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

I confirm I have explained to the patient: the risks and benefits of treatment, the baseline tests conducted the need for monitoring, how monitoring will be arranged, and the roles of the consultant / nurse specialist, GP and the patient in shared care. I confirm the patient has understood and is satisfied with this shared care arrangement at this time.

If you do **NOT** wish to participate in shared care for this patient, usually under clinical grounds, please complete the attached form.

Yours sincerely

{Consultant name}

To be completed by Osteoporosis Nurse/Consultant when treatment is initiated:

Criteria			**Yes**	**No**
Was denosumab given for the **primary/secondary*** prevention of osteoporotic fragility fractures?			☐	☐
Was the patient postmenopausal (or greater than 50 years age if male)?			☐	☐
Was the patient at increased risk of fractures?			☐	☐
Did the patient also meet one of the following criteria:				
	unable to comply with special instructions for:	intolerance of:	Treatment with this drug is contraindicated	
Alendronate **and**	☐	☐	☐	
Risedronate	☐	☐	☐	

Please tick in the following table to indicate the age of the patient and the T-score **(to be completed for primary prevention of osteoporotic fragility fractures only)**:

	T-Score		
Age	−3.0 to −3.5	−3.6 to −4.0	−4.1 to −4.5
65–69			
70–74			
75 +			

Does the patient have any of the following independent clinical risk factors:		
• parental history of hip fracture	☐	☐
• alcohol intake of 4 or more units per day	☐	☐
• rheumatoid arthritis	☐	☐

*delete as appropriate

GP RESPONSE TO SHARED CARE (only complete & send if **NOT** participating in shared care)

Shared care is produced by GPs and specialists knowledgeable in the field of that drug usage. The shared care has been approved by the JAPC. This allows a more convenient service to the patient and cost effective use of NHS resources.

Patient:	NHS No:
Consultant:	Medicine requested for shared care:

I will **NOT** be undertaking the GP responsibilities as described in the agreed shared care guideline. My clinical reasons for declining shared care for this patient are listed in the box below:

		Tick which apply
1.	**The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care** As the patients primary care prescriber I do not feel clinically confident to manage this patient's condition because *[insert reason]*. I have consulted with other primary care prescribers 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 above.**	
2.	**The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement** As the medicine requested to be prescribed is not included on the national list of shared care drugs as identified by RMOC or is not a locally agreed shared care medicine I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this medicine is identified either nationally or locally as requiring shared care the responsibility for providing this patient with their medication remains with you**	
3.	**A minimum duration of supply by the initiating clinician** As the patient has not had the minimum supply of medication to be provided by the initiating specialist 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 has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.***	
4.	**Initiation and optimisation by the initiating specialist** As the patient has not been optimised 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.***	
5.	**Shared Care Protocol not received** As legal responsibility for clinical care lies with the clinician who signs the prescription, I need to ensure that I am in possession of sufficient clinical information for me to be confident to prescribe this treatment for my patient and it is clear where each of our responsibilities lie to ensure the patient is safely managed. For this reason I am unable to take clinical responsibility for prescribing this medication at this time, therefore would you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.***	
6.	**Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted)**	

Yours sincerely

{GP name}
{Surgery}

Please send a copy of this response to:

1. The specialist/consultant requesting shared care
2. **AN ANONYMISED COPY OF THIS FORM ONLY** to the Medicines Management and Clinical Policies and Decisions Team, 1st Floor East Point, Cardinal Square, 10 Nottingham Road, Derby, DE1 3QT or E-MAIL: ddccg.medicinesmanagement@nhs.net

(Sending a copy of this form to the Medicines Management and Clinical Policies and Decisions Team will help to identify any inappropriate requests for shared care e.g. indication not covered, hospital monitoring requirements not fulfilled. It will also help to inform the CCG prescribing group of the reasons shared care is not being undertaken allowing for changes to be made in future updates to improve patient care).