Shared care guidance
Denosumab 60mg (PROLIA®)

Principles of Shared Care Agreements

Introduction

Good organisation of care across the interface between primary and secondary/tertiary care is crucial in ensuring that patients receive safe and high quality care – and in making the best use of clinical time and NHS resources in all care. Good professional practice requires care for patients to be seamless; patients should never be placed in a position where they are unable to obtain the medicines they need, when they need them. Lack of communication between primary and secondary/tertiary care and misunderstandings around the responsibilities of the professionals involved are often cited as reasons for patients not being able to get their medicines in a timely manner, despite effective collaborative working and communication being an important part of patient-centered professionalism.

1. Criteria for Classifying Drugs as Suitable for Shared Care

a. It is in the best interests of the patient for a primary care prescriber to take over prescribing, however, specialist involvement is required for:

- initiation of treatment
- on-going specialist monitoring and/or
- assessment to enable effectiveness and /or
- reducing risk of toxicity.

and/or

b. Medicines that are specifically suggested as suitable for shared care by the DH or NICE.

2. Shared Care Agreements

a. Treatment should be initiated by a specialist (which could include consultant, suitably trained specialist non-medical prescriber or GP with specialist interest within a secondary, tertiary, or primary care clinic). Clinical and prescribing responsibility should be transferred to primary care only when the patient's clinical condition is stable or predictable. This does not mean that the patient is discharged from specialist care.
NHSE guidance states that patients can be discharged, but need a fast track referral route in certain circumstances e.g. Adult ADHD.
As the CCG is not responsible for agreeing tertiary care shared care, there may be a need to consider treatment on a case by case basis.
The GP should agree in writing for each individual case and the secondary/tertiary provider must continue to provide prescriptions until successful transfer of responsibilities. Specialist advice should be available to primary care prescribers i.e. not requiring referral back to specialist as such.

b. The legal responsibility for prescribing lies with the doctor or health professional who signs the prescription and it is the responsibility of the individual prescriber to prescribe within their own level of competence. This includes responsibilities with supplying or administering the prescribed medicine and instructions to others.

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c. Patients should be at the centre of the shared care agreement however where patients do not have the mental capacity to make healthcare decisions involvement of carers and/or attorneys (holding the Lasting Power of Attorney for health and welfare) should be considered prior to decisions around shared care.

d. Shared care must be in accordance to the Shared Care template (Appendix 1). Communication between the specialist and the primary care prescriber should include the letters of request and agreement/refusal (Appendix 2).

e. For medicines which are prescribed under a share care arrangement, primary care prescribers should have sufficient knowledge and experience to monitor, stop, or alter the dosage of the medicine **in appropriate circumstances and have access to specialist advice to support them** (details should be made available within Share Care Agreements i.e. not requiring referral back to specialist as such). The degree of control, which they have over this prescribing, and 'a route of return' to specialist care will form part of the shared care agreement.

f. Agreements for shared care must not be used nor declined for cost shifting purposes.

g. It is the responsibility of the Joint Prescribing Committee (JPC) to ensure that adequate support, education and information is made available to primary care prescribers who "share care" of patients with a specialist in order for treatment to be managed safely in primary care.

h. GP/Primary care prescribers must seek further support from the referring specialist or CCG rather than decline shared care on the basis of lack of competence as default.

i. Explicit criteria for review need for monitoring and discontinuation of the medicine should be included; this should also be communicated to the patient.

j. Patients should never be used as a conduit for informing the GP that prescribing is to be transferred nor to inform the specialist that shared care has been declined. They should never be placed in a position where they are unable to obtain the medicines they need because of lack of communication between primary and secondary/ tertiary care.

3. Circumstances where shared care is not appropriate

In some situations the use of shared care is not appropriate and in these cases the hospital/specialist should retain responsibility for prescribing. Whilst the situations may be broad and diverse the following would be examples:

a. Patients receiving the majority of ongoing care, including monitoring, from the specialist service.

b. Where the primary care prescriber does not feel competent in taking on clinical responsibility for the prescribing of the medicine despite taking steps (as stated in point 2e above) to seek further support from the specialist.

c. Where a drug requires specialist intervention, stabilisation and monitoring on an ongoing basis.

d. Where patients have declined the shared care option following informed discussions with the specialist prescriber.

e. Where insufficient information has been provided to proceed with shared care and/or no

Shared Care Agreement or protocol exists.

f. Unlicensed medicines unsuitable for use in primary care or being used 'off-label' for an indication with no established evidence base.

g. Where drugs are being used as part of a hospital-initiated clinical trial.

h. Where the drug is new, only available through hospitals or has not been approved for addition to the current primary care formulary.

i. The indication for prescribing is contrary to NICE guidance and the use of the drug has not been approved on an 'exceptional basis'.

j. A medicine for which the JPC considers there to be poor evidence base or lack of cost effectiveness compared to alternative commissioned treatments.

k. Black Triangle Medicines (unless there is a large body of evidence supporting use e.g. BNF, NICE).

l. There is a NICE recommendation that the medicine should not be prescribed on the NHS for the condition specified.

m. Medicines subject to High-tech Hospital at Home guidance (EL (95)5).

n. All other treatments funded by NHS England unless specifically agreed to be provided through a shared care prescribing agreement, or other process as agreed by the JPC.

o. There is a clear NHSE/I Specialised Commissioning or JPC decision to not routinely fund usage of the medicine or NHSE considers the drug not suitable for shared care.

p. Shared care should not be approved with non-NHS funded providers as no guarantee patients will continue to fund themselves.

4. Funding Issues

a. Each shared care protocol submission must include an estimate of the number of patients affected.

b. Commissioners should take account of the operational and resource implications of shared care, and of the fact that this should also extend to the requirements and sustainability of hospitals in situations where shared care is not accepted.

c. If the treatment is likely to produce significant cost pressures (i.e. it cannot be managed within the existing prescribing budget), then agreement needs to be reached with JPC and if supported, appropriate funds identified.

d. All appropriate monitoring requirements (e.g. phlebotomy, ECG, height/weight checks) must be fulfilled. The person delivering that aspect of the shared care agreement should ensure that the resources to do this are in place in the clinical setting in which they are delivered (for example within a Primary Care Network (PCN)).

e. The requirement for the appropriate resource will need to be considered by

commissioners, based on the likely workload implications of the transfer of care i.e. from secondary/tertiary to primary care.

5. Approval and Review of Shared Care protocols

a. Consultation with primary/secondary/tertiary care prescribers must be sought when developing or reviewing a shared care protocol or supporting prescribing guideline.

b. The JPC must recommend the approval of all shared care protocols before they can be distributed for use between primary and secondary care.

c. A shared care protocol or supporting prescribing guideline will usually be approved for two years after which time an up-dated version should be submitted by the author for re-approval. Any major changes in national guidance or any significant issue that arises should prompt a review of the shared care protocol or supporting prescribing guideline at an earlier date.

References

- Responsibility for Prescribing between Primary and Secondary/Tertiary Care. NHS England. Jan 2018.
- SPS - Shared Care Guidance - A Standard Approach - Regional Medicines Optimisation Committee (RMOC) October 2019 V2
- Good Practice in Prescribing and Managing Medicines and Medical Devices. General Medical Council Guidance. 2013.

Appendix 1

Shared Care Protocol

Denosumab 60mg (PROLIA®)

AREAS OF RESPONSIBILITY FOR SHARED CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of **denosumab** can be shared between the specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so *(please refer to Principles of Shared Care Agreements in point 2h)*. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. Refer to Principles of Shared Care document for full details, in summary:

- Transfer of monitoring and prescribing to primary care is normally after the patient has had the first injection with satisfactory investigation.
- The duration of treatment will be determined by the specialist based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the GP/primary care clinician
- Termination of treatment will be the responsibility of the specialist.
- Shared care for denosumab involves the first dose to be administered within secondary care and subsequent doses administered in primary care. Primary care clinicians should refer back to secondary care after 3 to 5 years of treatment for review as stated in the treatment plan. **Do not stop treatment until discussed with the specialists.**

PRESCRIBING INFORMATION

1. Background

Osteoporosis is a disease characterised by low bone mass and progressive deterioration of bone tissue leading to increased fragility and a consequent susceptibility to fracture. Risk factors for fragility fractures include: reduced bone mineral density (BMD), the use of oral or systemic glucocorticoids, age, sex, previous fractures, a family history of osteoporosis, premature menopause and hormonal therapies such as aromatase inhibitors and anti-androgens.

Denosumab is a monoclonal antibody that inhibits osteoclast formation, function and survival thereby decreasing bone resorption.

Denosumab 60mg injection (PROLIA®) is licensed for:

- The treatment of osteoporosis in postmenopausal women and in men at increased risk of fractures.
- Treatment of bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures.
- Treatment of bone loss associated with long-term systemic glucocorticoid therapy in adult patients at increased risk of fracture.

Denosumab has been approved by NICE for the prevention of osteoporotic fractures in postmenopausal women (NICE TA204).

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NB: Another preparation of denosumab 120mg injection (XGEVA®) is licensed for bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures. This is outside the scope of this guideline.

The guidance in this document should be read in conjunction with the Summary of product characteristics (SmPC) and current British National Formulary (BNF).

IV bisphosphonates should also be considered as treatment options but Denosumab can be used ahead of these if clinically appropriate. The Royal Osteoporosis society recommends utilising treatments that allow patients to be treated within primary care.

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.

2. Indications (*Please state whether licensed or unlicensed)*

- The prevention of osteoporotic fractures in men and postmenopausal women (Licensed).

Duration of Treatment

The need for continued treatment should be re-evaluated periodically based on the benefits and potential risks of denosumab on an individual patient basis, particularly after 5 or more years of use.

3. Pharmaceutical aspects

Route of administration: Subcutaneous injection

Formulation: Solution for injection

Administration details: 60mg administered as a single subcutaneous injection once every 6 months into the thigh, abdomen or upper arm.

Other important information: Store in a refrigerator (+2°c to +8°c)

4. Exclusions or contraindications

Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.

Exclusions

- Patients on combination therapy
- Unstable disease state
- Patient does not consent to shared care
- Creatinine clearance <30ml/min
- Patients under the age of 18 years
- Patients prescribed denosumab 120mg (Xgeva®)
- Indications outside of the shared care guidance
- Patients not registered with a GP in the Kent and Medway CCG area
- Patients unwilling or likely to be unable to be compliant with the service
- Non- NHS patients

Contraindications

- Hypocalcaemia - hypocalcaemia must be corrected by adequate intake of calcium and vitamin D before initiating therapy.
- Hypersensitivity to the active substance or to any of the excipients
- Latex allergy
- Hereditary fructose intolerance

For further information refer to the current BNF and SPC: www.medicines.org.uk/emc

5. Initiation and ongoing dose regime (by specialist)

Note -

- *Transfer of monitoring and prescribing to Primary care is normally **after the patient is stable on a regular dose** and with satisfactory investigation results for period of time as agreed by the specialist.*
- *The duration of treatment will be determined by the specialist based on clinical response and tolerability.*
- *Specialist to specify the length of treatment supplied to the patient in order to indicate to primary care when new supply will be required for forward planning.*
- *All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician*
- *Termination of treatment will be the responsibility of the specialist.*

6. Specialist responsibilities for monitoring (including frequency)

At initiation:

- To assess the patient, establish and confirm the diagnosis.
- Review prior treatments for osteoporosis, concomitant medical problems and allergies (including latex)
- Evaluate individual factors for benefits and risks before initiating treatment with denosumab, particularly in those with previous vertebral fracture and patients at increased risk of vertebral fractures.
- Discuss with patient the benefits and possible side-effects of treatment as listed in the patient information leaflet including the risk of cellulitis, eczema and advice on dental treatment.
- Ensure patients have been assessed by their dentist prior to initiating therapy. This should involve informing the patient that they require a dental examination prior to commencing denosumab therapy. A dental examination within the preceding 6 months is sufficient. The patient should inform their dental practitioner that they are due to commence denosumab therapy. This could have an impact on how the dental practitioner manages treatment for the patient. The initiating specialist should communicate with the dental practitioner directly should any complications or concerns arise.
- Baseline monitoring of U&Es, creatinine clearance, corrected calcium and vitamin D levels.
- Advise on calcium supplementation and symptoms of hypocalcaemia.
- Monitor corrected calcium concentration within two weeks after the initial dose of denosumab in patients with risk factors for hypocalcaemia e.g. severe renal impairment.
- Unless contraindicated patients should be given vitamin D supplementation between 1000units to 2000units daily.

- To initiate denosumab treatment by a specialist with an osteoporosis interest including:
    - Ensure the suitability of the patient for denosumab treatment in accordance with guidelines.
    - Discuss and agree the management strategy with the patient including
        - Informing them of possible side effects to the treatment and ensuring that they are aware who to contact in this instance.
        - Explain to the patient that the treatment is 6 monthly injections for up to 5 years.
        - Explaining the plan of treatment to the patient including the proposed plan for follow up
        - Explain the risk of hypocalcaemia, what symptoms to watch out for and to seek medical advice as soon as possible.
- To administer the first injection of denosumab.

- Initiating specialist to organise corrected calcium level check 2 weeks after first injection for patients with creatinine clearance 15-30ml/min and manage as necessary.
- Initiating specialist will review patient after the first injection to assess for possible adverse effects.
    - If, following the initial review, the patient is stable and free from adverse reactions initiating specialist will contact the primary care clinician to arrange transfer of care.
    - **The initiating specialist should provide a clear treatment plan for the primary care clinician detailing recommended length of treatment, frequency of DEXA scans, arrangements for follow up and any other relevant information.**
    - The due date for the second injection, and any recommended blood investigations must be stated clearly on the letter from the initiating specialist to the primary care clinician and patient.
    - To determine need and frequency of monitoring of any further diagnostic tests e.g. DEXA and/or bone turnover markers and to organise such tests and communicate any resulting change in treatment plan with the patient and their primary care clinician in a timely manner.
    - Request shared care with the patient's primary care clinician using approved template letter and shared care protocol.
    - Writing to the primary care clinician to confirm the prescribing information (including brand of Denosumab -Prolia) and ongoing need for calcium and vitamin D and inform the primary care clinician of the duration of therapy
    - Ensure appropriate follow-up in conjunction with the primary care clinician or instruction of referral back to secondary care once planned treatment is completed.
    - Review concurrent medication for potential interactions.
    - Provide patient information leaflet and encourage patient to enroll on the PROLONG patient support programme by post/phone (03008088686) Emails prolong-support@nhs.net to access further support and to ensure that they are reminded when their next injection is due.
    - If the primary care clinician does not accept shared care, the total clinical responsibility for the patient for the diagnosed condition, remains with the initiating specialist.
    - Check for risk factors for osteonecrosis of the jaw before starting denosumab 60mg. A dental examination and appropriate preventative dentistry is necessary prior to treatment with denosumab in patients with risk factors:

- Smoking
- Old age
- Poor oral hygiene
- Invasive dental procedures (including tooth extractions, dental implants and oral surgery)
- Comorbidity (including dental disease, anaemia, coagulopathy and infection)
- Advanced cancer
- Previous treatment with bisphosphonates
- Concomitant treatments including chemotherapy, antiangiogenic biologics, corticosteroids, radiotherapy to head and neck.

- Ensure patient is calcium and vitamin D replete (adjusted calcium between 2.2-2.6mmol/L and 25(OH) vitamin D > 50nmol/L)

At review:

- Review patient according to treatment plan - at 3 or 5 years.
- Re-evaluate the need for continued treatment after 3 or 5 years based on the expected benefits and potential risks of denosumab on an individual patient basis.
- Evaluate any reported adverse effects by primary care clinician or patient.
- Inform the primary care clinician after each clinic attendance if there is any change to treatment or monitoring.
- Advise primary care clinician on review, duration or discontinuation of treatment.
- To be available for advice if the patient's condition changes.
- To ensure that primary care clinicians have access to rapid re-referral of the patient should the need arise. This includes providing a clear treatment plan for the patient and contact details for the initiating specialist.
- Inform primary care clinician of patients who do not attend review appointment and any changes to treatment plan.
- To provide advice to the patient/carer when requested.

7. GP responsibility

- Notify the initiating specialist in writing of decision regarding shared care within two weeks of request from initiating specialist.
- Prescribe and administer treatment as requested and in accordance with the shared care guidelines. The treatment should be prescribed by brand (Prolia) and not generically.
- Ensure that other osteoporosis treatments (e.g. alendronate) are stopped and removed from the patient's repeat prescription.
- Ensure that denosumab is added to the patient's medication record.
- Prescribe vitamin D or calcium & vitamin D as required.

Monitoring (including frequency):

- Arrange blood tests for corrected calcium, Vitamin D and creatinine clearance 4 weeks before every Denosumab injection. All patients must have normal corrected calcium and creatinine clearance greater than 30 ml/min, 4 weeks before dose is given in primary care. If creatinine clearance < 30 ml/min, contact the specialist for advice and guidance.
- Maintain Vitamin D levels at >50 nmol/L.

- For further information refer to the British National Formulary and Denosumab summary of product characteristics (www.medicines.org.uk/emc)
- Do not postpone treatment with denosumab in patients with suspected/confirmed COVID-19.
- To carry out blood test and monitor patients as detailed in the shared care protocol.
- Patients must be on vitamin D or calcium and vitamin D supplements and actually taking them or a specialist decision made, not to give them with an established vitamin D level of > 50nmol/l on the regime being followed . Primary care clinician to prescribe any necessary vitamin D or calcium and vitamin D.
- Monitor for any side effects to treatment and seek advice from the initiating specialist if necessary; and liaise with specialist regarding any complications of treatment and/or need to discontinue treatment.
- To check for possible drug interactions when newly prescribing concurrent medication.

Review/follow up:

- Treatments must be given at **6 monthly intervals**. If there is anticipated deviation from the protocol this must be discussed with the initiating specialist.
- Patients should not stop denosumab without initiating specialist review even if the patient has been receiving treatment for 3 to 5 years.
- Refer patients for a review as specified in the treatment plan.
- If the specialist has not specified duration of treatment, patient should be referred back to the specialist at 3 years. **Do not stop treatment unless advised by specialist. Maintain the responsibility until patient is seen by the specialist.**
- Report to and seek advice from the initiating specialist on any aspect of patient care that is of concern to the primary care clinician and may affect treatment via available advice and guidance digital platforms such as KINESIS in your local areas.
- Report adverse events to the MHRA on a Yellow Card www.mhra.gov.uk/yellowcard and to the specialist team.
- Refer back to the initiating specialist if a new fracture occurs whilst on denosumab. If the fractures are multiple, e.g. multi-level vertebral fractures or multiple rib fractures, treatment failure may be suspected.
- In line with MHRA drug safety update (February 2013) all patients newly initiated on denosumab therapy will be advised to report new or unusual thigh, hip or groin pain. Patients presenting with such symptoms to the primary care clinician should be referred for prompt medical attention for evaluation of an incomplete femoral fracture.
- Patients must continue treatment until specialists indicate other wise
- Encourage patients to maintain good oral hygiene and to attend regular checkups/monitoring as advised by dental practitioner.
- Refer patient back to the initiating specialist for review on completion of the treatment course according to patient's treatment plan. This should be completed as soon as the final injection is administered to avoid treatment delays. Cessation of Denosumab can cause rapid bone loss and rebound fractures. Referrals can be made sooner if any concerns (such as anti-resorptive related osteonecrosis of the jaw, altered mental health, tetany, seizures, or QTc prolongation which may indicate severe hypocalcaemia)

8. Dose Management (by primary care)

Result	Action
Corrected calcium ≤ 2.2 mmol/ L despite patient adherence with supplementation	Contact specialist team for advice and guidance via local digital platform
Vitamin D levels < 50 nmol/L despite patient adherence with supplementation	Contact specialist team for advice and guidance via local digital platform. See appendix 3 for Vitamin D repletion.
Creatinine clearance < 30ml/min or receiving dialysis	Refer patient back to the specialist.

Combination therapy:
If combination therapy is required and recommended by an expert specialist consultant then this will remain the responsibility of secondary care. This cannot be passed over to primary care for management.

Monotherapy:

- No dose adjustment is required in elderly patients
- No dose adjustment is required in patients with renal impairment
- No data is available in patients with long-term systemic glucocorticoid therapy and severe renal impairment (GFR < 30ml/min)
- The safety and efficacy of denosumab have not been studied in patients with hepatic impairment.

For further information refer to the current BNF and SPC: www.medicines.org.uk/emc

9. Significant medicine interactions – *prescriber must consider interactions with any and all repeat medication the patient is taking at the time of initiation*

- Study data indicates denosumab should not affect drugs metabolized by CYP3A**.**

For further information refer to current BNF and SPC: www.medicines.org.uk/emc

10. Adverse effect management

Specialist to detail action to be taken upon occurrence of a particular adverse event as appropriate. Most serious toxicity is seen with long-term use and may therefore present first to GPs.

- Hypocalcaemia – Denosumab is associated with a risk of hypocalcaemia. This risk increases with the degree of renal impairment. Hypocalcaemia usually occurs in the first weeks of denosumab treatment but it can also occur late in the treatment.
- Musculoskeletal pain, pain in the extremities, urinary tract infections, upper respiratory tract infections.
- Associated with a risk of atypical femoral fracture.
- Associated with a risk of osteonecrosis of the jaw (ONJ)

- Associated with a risk of osteonecrosis of the external auditory canal
- MHRA/CHM advice: Denosumab: reports of osteonecrosis of the external auditory canal (June 2017)
- MHRA/CHM advice: Denosumab: osteonecrosis of the jaw—further measures to minimise risk (July 2015)
- MHRA/CHM advice: Denosumab: atypical femoral fractures (February 2013)
- MHRA/CHM advice: Denosumab 60mg (Prolia): Increased risk of multiple vertebral fractures after stopping or delaying ongoing treatment (August 2020)

For further information refer to the current BNF and SPC: www.medicines.org.uk/emc
Report adverse drug reactions to: www.yellowcard.mhra.gov.uk

11. Advice to patients and carers

The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice

- Before shared care is put in place the patient must be fully informed of the plan and must be in agreement with it.
- Seek help urgently if side effects are suspected, or are otherwise unwell.
- Adhere to the treatment plan agreed with the initiating specialist.
- Attend clinic appointments every 6 months for the denosumab injection.
- Do not stop denosumab without initiating specialist review.
- Report to the initiating specialist and primary care clinician if they do not have a clear understanding of their treatment.
- Report any concerns relating to treatment with denosumab with the primary care clinician and initiating specialist.
- Attend initiating specialist and primary care clinician follow up appointments and co-operate with assessments.
- Ensure they have a blood test (kidney function, calcium & vitamin D levels) four weeks prior to denosumab injection.
- If you miss a prescribed dose of denosumab, the missed injection should be administered as soon as possible. After this, your next injection will be scheduled 6 months from the date of your last injection.
- Report any adverse reactions to the primary care clinician and initiating specialist whilst receiving treatment with denosumab.
- Seek prompt medical and dental attention if they develop signs of osteonecrosis of the jaw: Any oral symptoms such as dental mobility, pain, or swelling, jaw pain, osteomyelitis, osteitis, bone erosion, tooth/periodontal injection, toothache, gingival ulceration/erosion. Dental practitioner should inform the primary care clinician and initiating specialist should any issues arise. Patient to also inform primary care clinician and initiating specialist.
- Seek prompt medical attention if they develop signs or symptoms of severe infection, cellulitis or ear infections.
- Seek medical attention if they develop signs of hypocalcaemia: muscle spasms, twitches, cramps, numbness or tingling in the fingers, toes, or around the mouth.
- Report new or unusual thigh, hip or groin pain to the primary care clinician and initiating specialist.
- Inform the initiating specialist or the primary care clinician of any medication being taken, including herbal or over the counter products.
- It is important patient maintains good oral hygiene and regular checkups/monitoring as advised by your dental practitioner. Patients should seek dental advice should any issues occur.
- To inform their dentist they have been initiated on denosumab at the next routine appointment.

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- To inform the primary care clinician, initiating specialist or specialist nurse before considering invasive dental treatment.

12. Pregnancy and breast feeding

It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the GP and the specialist.

Manufacturer advises avoid.

Ensure effective contraception in women of child bearing potential, during treatment and for at least 5 months after stopping treatment (BNF)

13. Specialist contact information

This section has been redacted to maintain confidentiality.
Please contact your local medicines optimisation team for the full version.

14. Additional information

- Denosumab should be stored at +2ºC to +8ºC (in a refrigerator).
- Once removed from the refrigerator, Prolia may be stored at room temperature (up to +25°C) for a maximum single period of up to 30 days in the original container. It must be used within this 30 days period.
- Do not freeze.
- For subcutaneous use only. Administration should be performed by an individual who has been adequately trained in subcutaneous injection techniques.
- The injection solution should not be used if it contains particles, or is cloudy or discoloured.
- It must not be mixed with other medicinal products.
- Do not shake.
- To avoid discomfort at the site of injection, the pre-filled syringe should be allowed to reach room temperature (up to maximum of 25°C) before injecting slowly.
- The needle cover of the pre-filled syringe contains dry natural rubber (a derivative of latex), which may cause allergic reactions.

Applications such as MDCalc provide the ability to use adjusted body weight, ideal body weight, or actual bodyweight as appropriate when calculating the Cockcroft-Gault CrCl value.

For a full list of cautions, refer to the Summary of Product Characteristics (www.medicines.org.uk).

15. References

- National Osteoporosis Guideline Group (NOGG) 2017. Clinical guideline for the prevention and treatment of osteoporosis. Updated July 2019.
- CG146 Osteoporosis: assessing the risk of fragility fracture. *NICE* 2012. https://www.nice.org.uk/guidance/cg146.
- Denosumab for the Primary and Secondary Prevention of Osteoporotic Fractures in Postmenopausal Women, Technology Appraisal, October 2010.
- http://guidance.nice.org.uk/TA204.
- Summary of product characteristics www.medicines.org.uk/emc
- COVID-19 rapid guideline: rheumatological autoimmune, inflammatory and metabolic bone disorders NG 167. https://www.nice.org.uk/guidance/ng167
- Prescribing medicines in renal impairment. Drug Safety Update October 2019
- British National Formulary

Appendix 2 – Monitoring Standards

MONITORING STANDARDS FOR DENOSUMAB		
Pre-treatment Monitoring	Baseline corrected 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	Corrected Calcium	• Four weeks before each dose of denosumab injection (every 6 months). May be more frequent in patients with severe renal impairment (specialist to advise) • If suspected symptoms of hypocalcaemia occur
	Vitamin D	• Four weeks before each dose of denosumab injection (every 6 months). • Correct insufficiency with adequate intake of vitamin D before administering denosumab. • See Appendix 3 for Vitamin D repletion.
	U&Es including eGFR	Four weeks before each dose of denosumab injection (every 6 months).
	Dental check-ups	Due to the rare side effect of ONJ, patients should have routine dental check-ups as advised by dental practitioner whilst on denosumab. Patients should seek advice of a dentist in the event of any dental problems.
	Ongoing indication	To review therapy, DEXA scan at 3 or 5 years as stated in treatment plan

ACTION AND ADVICE FOR GP'S IN RESPONSE TO SIDE-EFFECTS	
Symptoms/Side effects	**Action**
Suspected signs or symptoms of hypocalcaemia	Check corrected calcium level and contact specialist for advice and guidance
Osteonecrosis of the jaw (ONJ)	Refer to dental surgeon and inform the specialist
New/ unusual thigh, hip or groin pain (Undertake femoral and pelvic x-ray first to assess for atypical femoral fracture or other causes, prior to referral).	Contact specialist for advice and guidance
Vertebral fractures in patients whose treatment with Denosumab has been interrupted or stopped.	Contact specialist for advice and guidance

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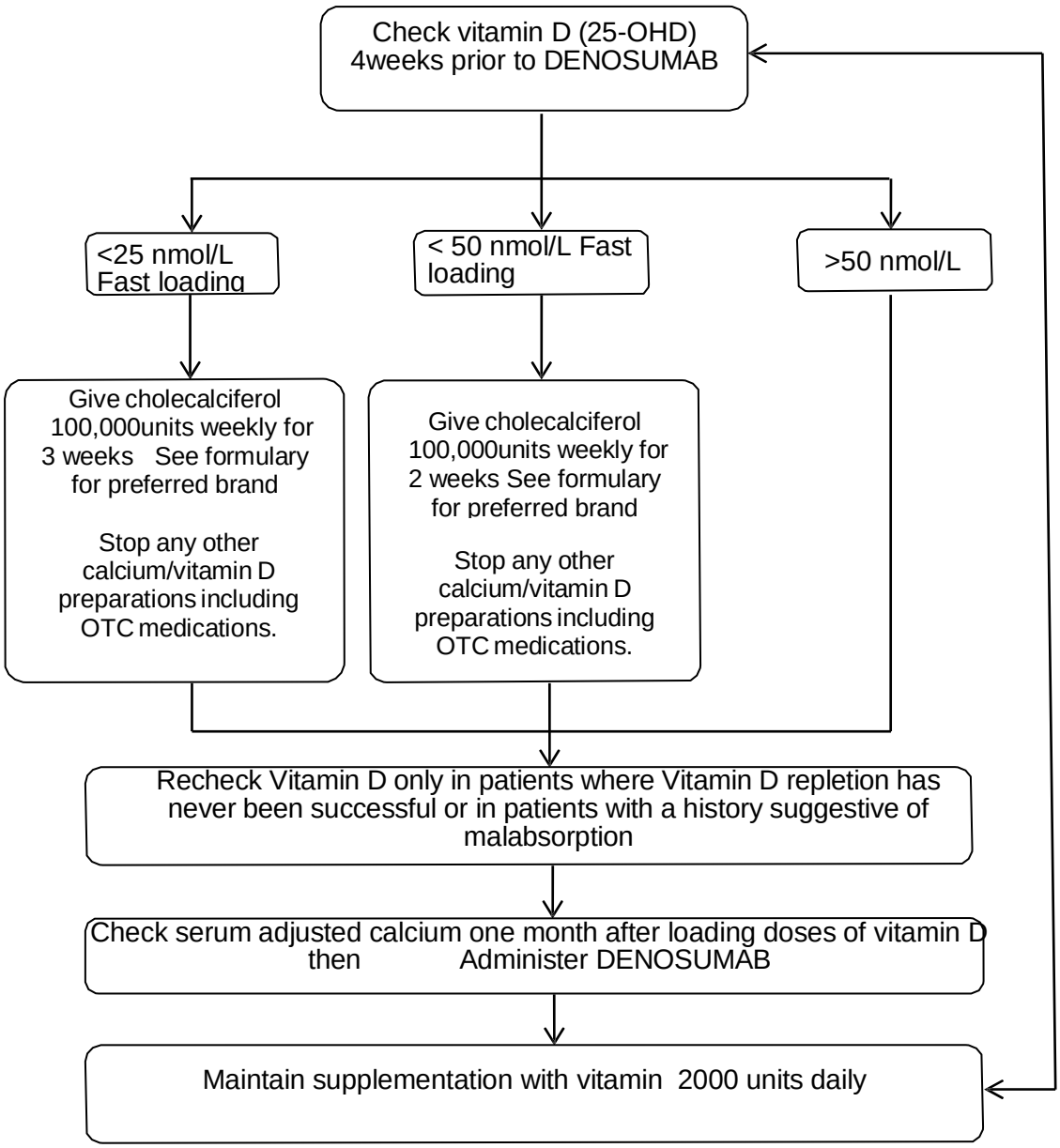
Appendix 3 – Vitamin D repletion



FOLLOW UP

- Check serum adjusted calcium one month after treating with loading doses of vitamin D. Vitamin D repletion may unmask primary hyperparathyroidism
- Note: in the presence of CKD4/ eGFR<30ml/min/1.732 and vitamin D < 50nmol/L **do not administer dose. Refer patient back to specialists.**

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Appendix 4
REQUEST TO SHARE CARE AND AGREEMENT FORM

Denosumab 60mg (PROLIA®)

The expectation is that this information, along with the full shared care protocol, provides sufficient information to enable GP* to be confident to take on clinical and legal responsibility for prescribing and monitoring. GP* must review and respond to provider trust request to share care within 2 weeks, using form provided.
*****_This may be any primary care prescribing clinician._

For completion by specialist (with shared care agreement form)			
Patient name			
DOB			
NHS Number			
Patient weight (kg)			
Drug (s) Dose, frequency, and route at handover			
Diagnosis (please indicate if unlicensed or "off-label"			
Date of first prescription by specialist			
Date of the next blood monitoring review date			
Estimated date for prescribing responsibility to be with GP* (at least 28 days after first prescribing)			
Special prescribing advice for this patient, to include any other medication patient is taking for same condition			
KEY PRIMARY CARE INFORMATION (refer to full shared care guideline for full details)			
GP* Responsibilities			
MONITORING (as per Shared Care document unless stated below)			
Frequency of GP* monitoring			
Frequency of specialist review			
TEST	NORMAL RANGE	Pre-Treatment Baseline Result (specialist responsibility)	Initiation of treatment Result (specialist responsibility)
ACTION TO BE TAKEN IF ABNORMAL RESULT			
TEST	RESULT	ACTION	

SHARED CARE AGREEMENT FORM

This form is used to agree shared care between specialist, patient and GP*.

Specialist and patient agreement

By signing below we accept:

- The Kent and Medway CCG shared care principles
- The requirements and responsibility defined in this drug specific shared care protocol
- To provide medication for the transition period (at least 28 days)

Specialist name:	Patient name:
Designation:	DOB:
Provider Trust:	NHS number:
Direct telephone number:	
Email:	
Specialist signature:	Patient signature:
Date:	Date:

GP* response to shared care request

Please return to specialist within **2 weeks** of receipt of request to share.
This form is to be completed by the GP* who is requested to share care.

I agree to accept shared care as set out in this shared care protocol and KMCCG shared care principles. ☐

I have not received adequate support to take over prescribing therefore I do not accept shared care for this patient. ☐

My reasons for not accepting are:

Please note that GP agreement is voluntary, with the right to decline to share care if for any reason you do not feel confident in accepting clinical responsibility.

GP* name	
Designation	
Direct telephone number	
Email	
Practice address	
GP* signature	
Date	

Specialist to retain a copy in the patients' hospital notes
Copy to be given to patient
GP* to retain a copy in primary care notes.

Approved by JPC, KMMOC and Clinical Cabinet
Approved Date: By Clinical Cabinet December 2020
Review date: December 2022