SHARED CARE AGREEMENT: DENOSUMAB

NHS GREATER GLASGOW AND CLYDE

NB: This document should be read in conjunction with the current Summary of Product Characteristics (SPC)

DRUG AND INDICATION:

Generic drug name:	Denosumab
Formulations:	60mg subcutaneous injection (Prolia®)
Intended indication:	**Treatment of Osteoporosis in post-menopausal women at increased risk of fracture**
Status of medicine or treatment:	**Licensed indication for licensed medicine; On GGC Total Formulary.** **GGC formulary states: Osteoporosis:** Use in the treatment of osteoporosis in postmenopausal women, restricted to use in those patients for whom oral bisphosphonates are unsuitable, contraindicated or not tolerated in accordance with local protocol.

RESPONSIBILITIES OF ACUTE CARE/SPECIALIST SERVICE (CONSULTANT):

- The specialist team will discuss the benefits and side effects of this treatment with patient (or carer) and provide Patient Information Leaflet.
- The specialist team will explain side-effects of treatment including the rare risks of osteonecrosis of the jaw and auditory canal and atypical femoral fractures and advise patients on precautions to take - see MHRA advice and BNF
- The specialist team will discuss the responsibilities of patient/carer (below) before progressing denosumab treatment plan. This will particularly include discussion around not stopping treatment unplanned without medical advice.
- The specialist team will ensure all appropriate investigations are arranged, carried out and results reviewed prior to any recommendation around initiation of therapy. Where any relevant biochemical abnormality is detected, this will be addressed by secondary care team prior to advising commencing denosumab therapy.
- The specialist team will accept re-referral of patients with hypocalcaemia/borderline hypocalcaemia.
- The specialist team will liaise with the primary care team in the event of any queries around the treatment, the finding of abnormal results or management of side-effects.
- The specialist team will provide primary care prescribers with the relevant secretary number for each service in written correspondence to facilitate seamless communication in the event of any queries.
- The specialist team will intend to treat all patients initiated on denosumab for 10 years.
- The specialist team will arrange an interim review at year 5 with DXA for all appropriate patients when denosumab is initiated
- The specialist team will advise primary care on the outcome of the Direct Access DXA service (DADS) assessment and further treatment plans.

RESPONSIBILITIES OF PRIMARY CARE TEAM

- The primary care team will ensure denosumab is added to the patient's drug record
- The primary care team will prescribe and administer denosumab therapy as soon as practicable after secondary care recommendation.
- Drug administration may be by appropriately trained healthcare professional.
- A recall is to be set up by the practice to ensure 6 monthly injections are administered. Due to a potential rebound off-effect after discontinuing denosumab, the dosing frequency of every six months plus or minus 1 month needs to be maintained.
- If a patient does not receive their planned dose within 1 month of the due date then on a first occasion this can be given late (providing no more than 12 months has elapsed). Routine injections can then continue as planned if the patient is committed to ongoing therapy. If more than 12 months treatment gap has elapsed on a first occasion or if the patient is not committed to ongoing treatment, then referral should be made back to the Mineral Metabolism clinic (as urgent

referral). If the patient fails to attend for treatment on a second occasion with a greater than 7-month interval, treatment should not be re-started, and referral should be made back to local Mineral Metabolism clinic (as urgent referral).

- At each 6-month review patients should be asked about adherence to calcium and vitamin D (or vitamin D only preparations).
- Provide monitoring as per the current Near Patient Testing NES specification.
- Primary care should not stop denosumab pending review with Mineral Metabolism clinic.
- Healthcare professionals working in Primary Care may report concerns and seek advice (preferably via SCI gateway) at any time from the secondary team around any aspect of patient care relating to bone health that is of concern.
- Discontinuation of denosumab has been associated with rebound fractures of the spine in patients that do not receive alternative ongoing treatment. Patients who discontinue denosumab should be referred to the local Mineral Metabolism clinic (as urgent referral via SCI-Gateway). Denosumab should be continued until Mineral Metabolism review has happened and a plan is in place for the patient to transition off denosumab.

Patients should be re-referred (urgently via SCI-Gateway) to the Mineral Metabolism Clinic if eGFR reduces below 20ml/min due to risk of hypocalcaemia.

RESPONSIBILITIES OF PATIENT/CARER:

- Patient must engage with all hospital or GP reviews appointments. Failure to engage with appointments may result in treatment being stopped. Patient must engage for treatment review every 6 months (+/- 1 month).
- Patient/carer will report any concerns they might have around treatment. These concerns would usually be reported to the GP in the first instance.
- Patients should be encouraged to report symptoms of hypocalcaemia – as detailed in patient information leaflet supplied by the secondary care clinic. Patients should be encouraged to follow MHRA advice relating to osteonecrosis of the jaw and advise their dentist they are being treated with denosumab – as detailed in patient information leaflet supplied by the secondary care clinic. Patients should ensure they attend for regular dental check-ups.
- Patients should be encouraged to report persistent thigh pain– as detailed in patient information leaflet supplied by the secondary care clinic.
- Patient/carer will report any adverse effects of the treatment to GP or specialist team.
- Patient/carer may request specialist appointment out with anticipated timeframe via their primary care team if he/she has specific concerns.

ADDITIONAL RESPONSIBILITIES

- None

CAUTIONS:

Hypocalcaemia
It is important to identify patients at risk for hypocalcaemia. Blood calcium concentration will be assessed (and addressed if out with range) by the secondary care team prior to commencement of therapy.

Vitamin D
Vitamin D status will be assessed (and addressed if out with range) by the secondary care team prior to commencement of therapy.

Measurement of vitamin D is not routinely required once treatment has been started assuming the patient is also being treated with a calcium & vitamin D supplement (or vitamin D alone).

Renal Failure

Patients with renal failure (Creatinine Clearance <30ml/min) are at greater risk of hypocalcaemia – patients should be made aware of this risk and be made aware of the symptoms of hypocalcaemia. Where these symptoms are mild these should be discussed initially with GP. Patients with symptoms suggesting severe hypocalcaemia out of hours should contact NHS 24.

Patients with progressive deterioration in renal function should be more closely monitored. For monitoring arrangements, please refer to current Near Patient Testing NES specification.

N.B Denosumab has no adverse effect on renal function; however, patients may experience a decline in renal function as part of the normal aging process or for other patient specific reasons.

Osteonecrosis of the jaw
Although osteonecrosis of the jaw is rarely described; patients should be advised to tell their dentist they are on denosumab therapy prior to dental work. Please refer to SPC and BNF/MHRA for advice and risk factors for the development of ONJ.

Osteonecrosis of the external auditory canal Osteonecrosis of the external auditory canal has been very rarely reported with denosumab. Possible risk factors for osteonecrosis of the external auditory canal include steroid use and chemotherapy and/or local risk factors such as infection or trauma. 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. Should osteonecrosis of the external auditory canal be suspected administration of denosumab may continue, however patients should be referred to the appropriate Ear, Nose and Throat department.

Atypical fractures
Atypical (sub-trochanteric) fractures are rare with denosumab therapy and would not be expected within the first 3-5 years of treatment. Patients should be advised to report any femoral shaft bone pain. If this symptom occurs plain x-ray of femur should be arranged.

Skin Infections
Although uncommon, patients receiving denosumab may develop skin infections (predominantly cellulitis) leading to hospitalisation. Patients should be advised to seek prompt medical attention if they develop signs or symptoms of cellulitis.

Stopping Treatment
Discontinuation of denosumab has been associated with rebound fractures of the spine in patients that do not receive alternative ongoing treatment. Patients who discontinue denosumab should be referred to local Mineral Metabolism clinic (as urgent referral)

CONTRAINDICATIONS:

Uncorrected Hypocalcaemia (see above).

Hypersensitivity to the active substance or to any of the excipients - refer to Summary of Product Characteristics (link to electronic Medicines Compendium below in *Supporting Documentation* section).

TYPICAL DOSAGE REGIMENS:

Route of administration:	Subcutaneous injection
Recommended starting dose:	60mg
Titration of dose:	No titration
Maximum dose:	60mg once every 6 months
Adjunctive treatment regimen:	Calcium and vitamin D (as per NHS GGC Formulary) /Vitamin D
Conditions requiring dose adjustment:	None
Usual response time:	Within first 6 months
Duration of treatment	10 years

SIGNIFICANT DRUG INTERACTIONS:

There are no known clinically relevant drug interactions with denosumab.

Refer to Summary of Product Characteristics (link to electronic Medicines Compendium below in *Supporting Documentation* section).

UNDESIRABLE EFFECTS:

Refer to current SPC for more detailed information

- ADR classification - very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000) and very rare (< 1/10,000) based on crude incidence rates.

Refer to Summary of Product Characteristics (link to electronic Medicines Compendium below in *Supporting Documentation* section).

ADR details (where possible indicate if common, rare or serious)	**ADR details** (where possible indicate if common, rare or serious)	**Management of ADR**
Pain in extremity	Very common	Treat as appropriate
Musculoskeletal pain	Very common	Treat as appropriate
Urinary tract infection	Common	Treat as appropriate
Upper respiratory tract infection	Common	Treat as appropriate
Sciatica	Common	Treat as appropriate
Constipation	Common	Treat as appropriate
Abdominal discomfort	Common	Treat as appropriate
Rash	Common	Treat as appropriate
Eczema	Common	Treat as appropriate
Diverticulitis	Uncommon	Treat as appropriate
Cellulitis	Uncommon	Treat as appropriate; Contact appropriate secondary care team
Ear infection	Uncommon	Treat as appropriate
Osteonecrosis of the jaw	Rare	Contact appropriate secondary care team
Osteonecrosis of the external auditory canal	Unknown but very rare	Contact appropriate department of Ear, Nose & Throat
Atypical femoral fractures	Rare	Contact appropriate secondary care team
Drug hypersensitivity	Rare	Contact appropriate secondary care team
Anaphylactic reaction	Rare	Treat as appropriate; Contact appropriate secondary care team
Hypocalcaemia	Rare	Contact appropriate secondary care team **Patients should be re-referred (urgently via SCI-Gateway) to the Mineral Metabolism Clinic if eGFR reduces below 20ml/min due to risk of hypocalcaemia.**

BASELINE INVESTIGATIONS:

- Patients who might be considered appropriate for denosumab should have bone density measured and be seen through a GGC Mineral Metabolism Clinic or have the treatment recommended following assessment via the Direct Access DXA Service or the Fracture Liaison Service.
- All necessary baseline investigations will be arranged by secondary care teams as above.

MONITORING (PRIMARY CARE):

- For monitoring arrangements, please refer to current Near Patient Testing NES specification which can be found here.

MONITORING (ACUTE SECTOR):

- The following monitoring is to be undertaken in Acute Care

Monitoring Parameters	Frequency
DXA	DXA will be carried out before treatment commenced. Repeat DXA measure should be considered after 5 years denosumab therapy (patients can be referred for this via DADS)

PHARMACEUTICAL ASPECTS:

- Shelf life 3 years if stored in a refrigerator (2°C – 8°C).
- Denosumab injection may be stored at room temperature (up to 25°C) for up to 30 days in the original container. It must be used within this 30-day period.

COST:

- 60mg/ml solution in pre-filled syringe (Prolia®), 1ml = £183.00.

INFORMATION FOR COMMUNITY PHARMACIST:

- Store in a refrigerator (2°C – 8°C).
- Do not freeze.
- Keep the container in the outer carton in order to protect from light

ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION:

Name	Designation	Acute Site	Department phone number
Dr Maria Talla	Consultant Physician Endocrinology & Mineral Metabolism	QEUH	**0141 451 5845**
Dr Chris Sainsbury	Consultant	WG ACH	**0141 451 6188**
Dr Maurizio Panarelli	Consultant Clinical Biochemist	Stobhill	**0141 232 0830**
Dr Clare Harrow	Consultant - Diabetes & Endocrinology	RAH	**0141 314 7202**
Dr Lisa Hutton	Consultant	IRH	**01475 504 771**
Amy Brown	Advanced Pharmacist Diabetes and Endocrinology	GRI	**0141 211 4000**

SUPPORTING DOCUMENTATION:

- Summary of Product characteristics: can be accessed via https://www.medicines.org.uk/emc
- Manufacturers Patient Information leaflet: can be accessed via https://www.medicines.org.uk/emc
- *Information about Denosumab (Prolia)* patient leaflet developed by NHSGGC Acute Services Division is located in the shared care agreement section of the GGC prescribing website.