Denosumab (Prolia®) Guidance for Primary Care Clinicians; where patients have been previously initiated on Denosumab (Prolia®) as Shared Care by Barnsley Osteoporosis Service (patients are no longer under hospital supervision)

Barnsley Hospital has a combination of people requiring treatment for osteoporosis:

- Traditionally those people with rheumatological conditions have had their osteoporosis addressed by rheumatology (including follow ups for osteoporosis).

- Those without rheumatological conditions have previously been assessed at the community osteoporosis service and orthogeriatrics service at the hospital. *Both services have now been discontinued*.

The purpose of this document is to advise primary care physicians on the safe use of denosumab when people receiving it are not under an osteoporosis service or rheumatology. It outlines when a referral would be necessary.

Denosumab remains third line for treatment of osteoporosis and it needs to be recommended and initiated by an osteoporosis service. Refer to the Management of Osteoporosis and Fragility Fracture Risk Barnsley Guideline. Once the first subcutaneous injection has been received and tolerated, it is safe to proceed to primary care administration (and monitoring) on a six-monthly basis.

- Denosumab cannot be administered when hypocalcaemia is present. Those with severe renal impairment have a high risk of hypocalcaemia. eGFR, vitamin D and calcium profile check is mandatory within two weeks prior to the administration of each denosumab dose.

- Calcium and vitamin D supplementation are required for people taking denosumab but may need to be optimised prior to each dose of denosumab.

- Any concerning results can be discussed (ideally via Advice and Guidance service) with the rheumatology team, giving information about comorbidities, coprescriptions, indication for treatment, fracture status and relevant blood tests.

- Denosumab administration cannot be delayed due to a significant risk of rebound bone mineral density loss. Injections are required within a month from the six-monthly scheduled date. It is strongly recommended that a robust recall system is in place.

- Treatment holidays are not appropriate for denosumab due to this risk of rebound bone mineral density loss. Therefore it is expected that the treatment will be long term, unless side effects or further fractures occur. These are indications for referral to an osteoporosis service or rheumatology.

- A bone density scan (DEXA scan) (ideally in the same machine as the previous one for meaningful comparison) is recommended at 5 years (in the absence of new fractures, in which case it can be expedited for a full assessment of next treatment option).

  Treatment failure is described as the occurrence of either two/more new fractures or significant bone mineral density loss and one new fracture. A mild loss of bone mineral density does not call for change in treatment in the absence of new fractures. A concerning loss calls for FRAX assessment. If the risk of fracture has then increased to very high risk category, a treatment review by an osteoporosis service or rheumatology is recommended.

Summary of actions required:

- If DEXA at 5 years shows improved bone density, continue denosumab.
- If DEXA at 5 years shows mild deterioration in bone density and no new fractures, continue denosumab.
- If DEXA at 5 years shows significant deterioration in bone density, putting FRAX into a very high fracture risk category, refer to the osteoporosis service or rheumatology.
- If new fracture or cannot tolerate denosumab, refer to the osteoporosis service or rheumatology.

- Significant (though rare) side effects from denosumab include cellulitis and recurrent episodes call for a treatment review.

- Jaw osteonecrosis and atypical femoral subtrochanteric fractures are rare but incidence increases over time.

- People taking denosumab are recommended to report any new hip/upper thigh pain to exclude an early subtrochanteric fracture via x-ray (subtrochanteric cortex "bump" rather than traditional fracture lines/true fractures can be seen).

- Pre-treatment dental check, ongoing pristine dental health and regular dental checks are strongly recommended as the best way to reduce the risk of jaw osteonecrosis.

The following are extracts from relevant bodies to inform the above guidelines:

Summary of product characteristics states that indications for treatment with denosumab are:

- 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.

https://www.medicines.org.uk/emc/product/568/smpc

NICE guidelines for the use of Denosumab state that:

> 1.1Denosumab is recommended as a treatment option for the primary prevention of osteoporotic fragility fractures only in postmenopausal women at increased risk of fractures:
>
> - who are unable to comply with the special instructions for administering alendronate and either risedronate or etidronate, or have an intolerance of, or a contraindication to, those treatments **and**
>
> - who have a combination of T-score[1], age and number of independent clinical risk factors for fracture (see section 1.3).
>
> 1.2Denosumab is recommended as a treatment option for the secondary prevention of osteoporotic fragility fractures only in postmenopausal women at increased risk of fractures who are unable to comply with the special instructions for administering alendronate and either risedronate or etidronate, or have an intolerance of, or a contraindication to, those treatments.

1.3For the purposes of this guidance, independent clinical risk factors for fracture are parental history of hip fracture, alcohol intake of 4 or more units per day and rheumatoid arthritis.

1.4People currently receiving denosumab for the primary or secondary prevention of osteoporotic fragility fractures who do not meet the criteria specified in recommendations 1.1 or 1.2 should have the option to continue treatment until they and their clinician consider it appropriate to stop.

https://www.nice.org.uk/guidance/ta204/chapter/1-Guidance

The **National Osteoporosis Guideline Group** states the following:

1. Before starting denosumab, ensure a long-term personalised osteoporosis management plan is in place and that both the patient and the primary care practitioner are made aware that denosumab treatment should not be stopped or delayed without discussion with a healthcare professional (Strong recommendation).
2. Avoid unplanned cessation of denosumab because it can lead to increased vertebral fracture risk, hence it must not be stopped without considering an alternative therapy (Strong recommendation).
3. If denosumab therapy is stopped, intravenous infusion of zoledronate is recommended 6 months after the last injection of denosumab (Conditional recommendation).

https://www.nogg.org.uk/

Note that it was previously agreed to adopt the Sheffield Denosumab 60mg/mL Injection (Prolia®) prescribing guidelines:
https://best.barnsleyccg.nhs.uk/clinical-support/prescribing-guidelines/denosumab/16227?UNLID=36830404020229219139