County Durham & Tees Valley
Area Prescribing Committee

GP clinical information sheet to support the prescribing and monitoring of Denosumab (Prolia®)

General information

Denosumab is licensed for the treatment of osteoporosis in postmenopausal women and in men at increased risk of fractures.

The recommended dose of denosumab is 60mg administered as a single subcutaneous injection once every 6 months into the thigh, abdomen or upper arm.

No dose adjustment is required in elderly patients or patients with mild to moderate renal impairment (see below for recommendations relating to monitoring of calcium).
No data is available in patients with long-term systemic glucocorticoid therapy and severe renal impairment (GFR < 30 mL/min). The safety and efficacy of denosumab have not been studied in patients with hepatic impairment

The patient must have been supplied with the contact details for the initiating specialist team (e.g. Rheumatology Department or secondary care physician with special interest in metabolic bone disease) and a patient information leaflet.

Precautions for use

Patients must be adequately supplemented with calcium and vitamin D.

Additional risk factors for hypocalcaemia:

- untreated vitamin D deficiency
- severe renal impairment and dialysis
- concomitant glucocorticoid treatment

All patients should be encouraged to maintain good oral hygiene, receive routine dental check-ups, and immediately report any oral symptoms. While on treatment, invasive dental procedures should be performed only after careful consideration and be avoided in close proximity to denosumab administration.

The Prolia® needle cover of the pre-filled syringe contains dry natural rubber (a derivative of latex), which may cause allergic reactions.

Treatment with denosumab should not be stopped without specialist review due to developing an increased risk of multiple vertebral fractures (MHRA Drug Safety Update August 2020).

Monitoring

The following blood tests should be carried out prior to *each dose* (i.e. every six months):

- serum calcium and adjusted calcium levels (should be normal)
- vitamin D levels (should be > 50 nmol/L)
- U&Es
- Patient assessment with regards to tolerability (any issues with last dose?) and any emerging safety issues such as:
    - symptomatic hypocalcaemia (see MHRA Drug Safety Update 2014)
    - skin infections
    - osteonecrosis of the jaw (see MHRA Drug Safety Update 2015)
    - osteonecrosis of the the external auditory canal (see MHRA Drug Safety Update 2017)
    - atypical fractures of the femur (see MHRA Drug Safety Update 2013)

  Please see the Summary of Product Characteristics for more information on potential side effects.
- Provide routine counselling incl. good oral hygiene and regular dental check-ups
- The patient should also be reminded to maintain their calcium and vitamin D supplementation throughout treatment with denosumab

Ideally, the blood tests should be done two weeks prior to the next dose but tests within 3 months may be acceptable.
Please contact the initiating specialist team (e.g. Rheumatology Department) if any of these are out of range, or if the prescriber has any questions.

If the patient has renal impairment (eGFR < 30/min), then serum calcium also needs to be measured 1-2 weeks post-dose. Also monitor calcium levels if the patient presents with symptoms indicative of hypocalcaemia.

Repeat DEXA scan at 3-5 years (as indicated by specialist) and copy the results to the initiating specialist team for review.

Treatment duration and next steps

The MHRA advise that the optimal duration of denosumab treatment for osteoporosis has not been established. The need for continued treatment should be re-evaluated periodically (normally after 3-5 years) based on the expected benefits and potential risks of denosumab on an individual patient basis (MHRA Drug Safety Update August 2020) and, in some cases, treatment may be continued for up to 10 years.

Re-referral to secondary care

While the patient is receiving their denosumab doses and monitoring in primary care, the patient may not always require ongoing regular reviews by secondary care although specifics will be set out by the referring specialist. At any point, the GP may contact the referring specialist for advice or refer into secondary care for an unplanned review.

In order to reduce the risk of rebound bone loss and fracture, it is essential that the patient is reviewed by a specialist clinician prior to stopping denosumab so that treatment cessation and alternative treatment initiation (if any) can be planned.