INFORMATION ON DENOSUMAB (PROLIA)

- Denosumab is an effective drug for osteoporosis.[1-3]
- Drug holidays are not possible with this drug. Discontinuation is associated with a precipitous loss of BMD and the potential development of multiple spontaneous vertebral compression fractures.[4-6]
- For this reason, Osteoporosis Canada recommends denosumab as a second-line therapeutic option for patients who have contraindications, substantial intolerance or barriers to bisphosphonates.[7]

- Given the difficulties in discontinuing denosumab, it should be reserved for patients who are recommended for long term, uninterrupted therapy. Particularly careful consideration is needed before starting denosumab in younger patients.

- Denosumab is given at a dose of 60 mg SQ every 6 months. Hypocalcemia is an absolute contraindication. A calcium level should be checked prior to each dose, preferably within no more than 2-4 weeks prior to the injection. A 25-hydroxyvitamin D level ≥ 75 nmol/L is advisable when using denosumab, specifically to avoid precipitating hypocalcemia.

- Side-effects can include:
    - An increased risk of infection. In particular, there is a small but significant increased risk of bladder infections and cellulitis.
    - An increased risk of eczema and a very small increase in cholesterol level.
    - Remote possibility of osteonecrosis of the jaw (ONJ).
    - Remote possibility of developing atypical femoral fractures.

- Denosumab is not renally excreted and can be given without any change in dose to patients with reduced renal function. However, patients with eGFR < 30 are at increased risk of developing significant hypocalcemia post-dose. In such patients, a repeat calcium level should be done 10-14 days post-initial dose. If that initial post-dose calcium level remains normal, then further monitoring of the post-dose calcium level can be done after every few doses.

- The injection schedule of every 6 months should not be delayed by more than one month because of the rapid bone loss and rebound vertebral fractures that may occur.[4-6] Consequently, denosumab should be avoided for any patients who may be unreliable in adhering to the strict Q6month schedule.

- Should it become advisable to stop denosumab, transition to an alternate antiresorptive (a bisphosphonate) is strongly recommended. However, this may provide only partial protection from the rapid bone loss and rebound vertebral fractures that can happen following denosumab discontinuation.

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- When discontinuing denosumab, Osteoporosis Canada recommends:
    - If discontinuing after ≤ 4 doses, transition to a bisphosphonate, initiated 6 months after the last dose of denosumab. Duration of bisphosphonate treatment should be one year, then reassess the ongoing need for transition therapy.[7]
    - If discontinuing after ≥ 5 doses, it is strongly recommended that advice be sought from an osteoporosis specialist to help manage this challenging transition.[7]

- Denosumab is an exception status drug on the Nova Scotia Seniors' Pharmacare Program. The below is cut and pasted from their Appendix III – Criteria for Coverage of Exception Status Drugs:

***DENOSUMAB** *(Prolia 60mg/mL Prefilled Syringe)*

- For the treatment of osteoporosis in postmenopausal women and in men who meet the following criteria:
    - Have a contraindication to oral bisphosphonates; and
    - High risk for fracture, or refractory or intolerant to other available osteoporosis therapies.

Clinical Notes:

- Refractory is defined as a fragility fracture or evidence of a decline in bone mineral density below pre-treatment baseline levels, despite adherence for one year to other available osteoporosis therapies.
- High fracture risk is defined as:
    - Moderate 10-year fracture risk (10% to 20%) as defined by the Canadian Association of Radiologists and Osteoporosis Canada (CAROC) tool or the World Health Organization's Fracture Risk Assessment (FRAX) tool with a prior fragility fracture; or
    - High 10-year fracture risk (≥ 20%) as defined by the CAROC or FRAX tool.

- More information on this medication can be obtained from the denosumab product monograph.

References:

1. Cummings SR, San Martin J, McClung MR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. N Engl J Med 2009; 361(8): 756-65.
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3. Langdahl BL, Teglbjaerg CS, Ho PR, et al. A 24-month study evaluating the efficacy and safety of denosumab for the treatment of men with low bone mineral density: results from the ADAMO trial. J Clin Endocrinol Metab 2015; 100(4): 1335-42.
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6. Cummings SR, Ferrari S, Eastell R, et al. Vertebral Fractures After Discontinuation of Denosumab: A Post Hoc Analysis of the Randomized Placebo-Controlled FREEDOM Trial and Its Extension. J Bone Miner Res; 2018; 33(2): 190-8.
7. Morin SN, Feldman S, Funnell L, et al. Clinical practice guideline for the management of osteoporosis and fracture prevention in Canada: 2023 update. CMAJ 2023 October 10;195:E1333-48.