PROLIA® (denosumab) Brief Prescribing Information

Please refer to the Summary of Product Characteristics (SmPC) before prescribing Prolia**. Pharmaceutical Form:** Pre-filled syringe with automatic needle guard containing 60 mg of denosumab in 1 ml solution for injection for single use only. Contains sorbitol. **Indication:** 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. **Dosage and Administration**: 60 mg Prolia administered as a subcutaneous injection once every 6 months. Patients must be supplemented with calcium and vitamin D. No dose adjustment required in elderly and in patients with renal impairment. No data is available in patients with long-term systemic glucocorticoid therapy and severe renal impairment (GFR < 30 ml/min). Not recommended in paediatric patients under 18 years of age. Give Prolia patients the package leaflet and patient reminder card. Re-evaluate the need for continued treatment periodically based on the benefits and potential risks of denosumab on an individual patient basis, particularly after 5 or more years of use. **Contraindications:** Hypocalcaemia or hypersensitivity to the active substance or to any of the product excipients. **Special Warnings and Precautions: Traceability:** Clearly record the name and batch number of administered product to improve traceability of biological products. ***Hypocalcaemia:*** Identify patients at risk for hypocalcaemia. Hypocalcaemia must be corrected by adequate intake of calcium and vitamin D before initiation of therapy. Clinical monitoring of calcium levels is recommended before each dose and, in patients predisposed to hypocalcaemia, within 2 weeks after the initial dose. Measure calcium levels if suspected symptoms of hypocalcaemia occur. Encourage patients to report symptoms of hypocalcaemia. Concomitant glucocorticoid treatment is an additional risk factor. ***Renal Impairment*****:** Patients with severe renal impairment (creatinine clearance < 30ml/min) or receiving dialysis are at greater risk of developing hypocalcaemia. Regular monitoring of calcium levels in these patients is especially important. ***Skin infections:*** Patients receiving Prolia may develop skin infections (predominantly cellulitis) requiring hospitalisation and if symptoms develop then they should contact a health care professional immediately. ***Osteonecrosis of the jaw (ONJ):*** ONJ has been reported rarely with Prolia 60 mg every 6 months. Delay treatment in patients with unhealed open soft tissue lesions in the mouth. A dental examination with preventative dentistry and an individual benefit:risk assessment is recommended prior to treatment with Prolia in patients with concomitant risk factors. Refer to the SmPC for risk factors for ONJ. Patients should be encouraged to maintain good oral hygiene, receive routine dental check-ups and immediately report oral symptoms during treatment with Prolia. While on treatment, invasive dental procedures should be performed only after careful consideration and avoided in close proximity to Prolia administration. The management plan of patients who develop ONJ should be set up in close collaboration between the treating physician and a dentist or oral surgeon with expertise in ONJ. ***Osteonecrosis of the external auditory canal:*** Osteonecrosis of the external auditory canal has been reported with Prolia. Refer to the SmPC for risk factors. ***Atypical femoral fracture (AFF):*** AFF has been reported in patients receiving Prolia. Discontinuation of Prolia therapy in patients suspected to have AFF should be considered pending evaluation of the patient based on an individual benefit risk assessment. ***Long-term antiresorptive treatment:*** Long-term antiresorptive treatment may contribute to an increased risk for adverse outcomes such as ONJ and AFF due to significant suppression of bone remodelling. ***Concomitant medication:*** Patients being treated with Prolia should not be treated concomitantly with other denosumab containing medicinal products. ***Warnings for Excipients:*** Prolia contains 47 mg sorbitol in each mL of solution. Consider the additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose). **Interactions:** Prolia did not affect the pharmacokinetics of midazolam, which is metabolized by cytochrome P450 3A4 (CYP3A4). There are no clinical data on the co-administration of denosumab and hormone replacement therapy (HRT), however the potential for pharmacodynamic interactions would be considered low. Pharmacokinetics and pharmacodynamics of Prolia were not altered by previous alendronate therapy. **Fertility, pregnancy and lactation:** There are no or limited data on the use of Prolia in pregnant women and it is not recommended for use in these patients or in women of child-bearing potential not using contraception. It is unknown whether denosumab is excreted in human milk. A risk/benefit decision should be made in patients who are breast feeding. No data are available on the effect of Prolia on human fertility. Please consult SmPC for more detail. **Undesirable Effects:** The following adverse reactions have been reported: Very common (≥ 1/10) pain in extremity, musculoskeletal pain (including severe cases). Common (≥ 1/100 to < 1/10) urinary tract infection, upper respiratory tract infection, sciatica, constipation, abdominal discomfort, rash, alopecia and eczema. Uncommon (≥ 1/1000 to < 1/100): Diverticulitis, cellulitis, ear infection and lichenoid drug eruptions. Rare (≥ 1/10,000 to < 1/1,000): Osteonecrosis of the jaw, hypocalcaemia (including severe symptomatic hypocalcaemia and fatal cases), atypical femoral fractures and hypersensitivity (including rash, urticaria, facial swelling, erythema and anaphylactic reactions). Very rare (< 1/10,000): Hypersensitivity vasculitis. Please consult the Summary of Product Characteristics for a full description of undesirable effects. **Pharmaceutical Precautions:** Prolia must not be mixed with other medicinal products. Store at 2°C to 8°C (in a refrigerator). Prolia may be exposed to room temperature (up to 25°C) for a maximum single period of up to 30 days in its original container. Once removed from the refrigerator Prolia must be used within this 30 day period. Do not freeze. Keep in outer carton to protect from light. **Legal Category:** POM. **Presentation, Basic Costs and Marketing Authorisation Number Great Britain (GB):** Prolia 60 mg: Pack of 1 pre-filled syringe with automatic needle guard: £183.00; PLGB 13832/0042. **Marketing Authorisation Holder GB:** Amgen Limited, 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK. **Presentation, Basic Costs and Marketing Authorisation Number Northern Ireland (XI):** Prolia 60 mg: Pack of 1 pre-filled syringe with automatic needle guard: £183.00; EU/1/10/618/003. **Marketing Authorisation Holder XI:** Amgen Europe B.V., Minervum 7061, NL-4817 ZK Breda, The Netherlands. Further information is available from Amgen Limited, 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK. Prolia is a registered trademark of Amgen Inc. **Date of PI preparation:** October 2021 (Ref: GB-PRO-0721-00042)

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/. Adverse events should also be reported to Amgen Limited on +44 (0) 1223 436441