Prescribing Information.

Conexxence ▼ (Denosumab). This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Conexxence 60 mg solution for injection in pre-filled syringe. Consult the Summary of Product Characteristics (SmPC) before prescribing. Additional information is available on request. **Presentation and Active Ingredients:** Each pre-filled syringe contains 60 mg of denosumab in 1 mL. **Indications**: Treatment of osteoporosis in postmenopausal women and in men at increased risk of fractures. In postmenopausal women denosumab significantly reduces the risk of vertebral, non-vertebral and hip fractures. Treatment of bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures. Denosumab significantly reduces the risk of vertebral fractures in men with prostate cancer receiving hormone ablation. Treatment of bone loss associated with long-term systemic glucocorticoid therapy in adult patients at increased risk of fracture. **Posology:** 60 mg denosumab administered as a single subcutaneous injection once every 6 months into the thigh, abdomen or upper arm. Administration should be performed by an individual who has been adequately trained in injection techniques. Patients must be adequately supplemented with calcium and vitamin D. Patients treated with denosumab should be given the package leaflet and the patient reminder card. The optimal total duration of antiresorptive treatment for osteoporosis has not been established. The need for continued treatment should be re-evaluated periodically based on the benefits and potential risks of denosumab on an individual patient basis, particularly after 5 or more years of use. ***Elderly (age ≥ 65):*** No dose adjustment is required. ***Renal impairment:*** No dose adjustment is required 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). ***Hepatic impairment:*** The safety and efficacy of denosumab have not been studied in patients with hepatic impairment. ***Paediatric population:*** Should not be used in children aged < 18 years. Safety concerns of serious hypercalcaemia, and potential inhibition of bone growth and lack of tooth eruption. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Hypocalcaemia. **Warnings and Precautions:** The name and batch number of the administered product should be clearly recorded to improve traceability. Adequate calcium and vitamin D intake is essential for all patients. Hypocalcaemia risk must be assessed and corrected by adequate calcium and vitamin D intake before initiating therapy, with calcium levels monitored before each dose, and within two weeks after the initial dose in predisposed patients. Symptoms should prompt calcium testing, and patients should report any indicative signs. Severe symptomatic hypocalcaemia, including fatal cases, has occurred, especially in the first weeks of treatment but can occur later. Glucocorticoid use increases risk of hypocalcaemia. Patients with severe renal impairment (creatinine clearance <30 mL/min) or on dialysis are at higher risk of developing hypocalcaemia. Risks of developing hypocalcaemia and accompanying parathyroid hormone elevations increase with increasing degree of renal impairment. Ensure adequate intake of calcium and vitamin D and monitor calcium regularly. Patients on denosumab may develop skin infections (predominantly cellulitis) requiring hospitalisation; advise patients to seek prompt medical attention if cellulitis signs/symptoms. Osteonecrosis of the jaw (ONJ) has been reported rarely in patients on denosumab for osteoporosis. Delay treatment in patients with unhealed open soft tissue lesions in the mouth. Perform a dental exam with preventive dentistry and an individual benefit-risk assessment prior to denosumab treatment in patients with concomitant risk factors. Risk factors to consider include: potency of the medicine that inhibits bone resorption (higher risk with higher potency), route of administration (higher risk with parenteral administration), cumulative dose of bone resorption therapy; cancer, co-morbid conditions (e.g. anaemia, coagulopathies, infection), smoking; concomitant therapies (corticosteroids, chemotherapy, angiogenesis inhibitors, head/neck radiotherapy); poor oral hygiene, periodontal disease, poorly fitting dentures, history of dental disease, invasive dental procedures. Encourage patients to maintain good oral hygiene, receive routine dental check-ups and immediately report oral symptoms e.g. dental mobility, pain, swelling, non-healing sores, discharge during treatment. During treatment, invasive dental procedures should only be performed after careful

consideration and be avoided in close proximity to denosumab administration. If patients develop ONJ, the management plan should involve close collaboration between treating physician and dentist/oral surgeon with ONJ expertise. Consider temporary interruption of treatment until condition resolves and risk factors are mitigated where possible. Osteonecrosis of the external auditory canal has been reported with denosumab. Possible risk factors include steroid use, chemotherapy, local infection or trauma. Consider possibility of osteonecrosis of the external auditory canal in patients who present with ear symptoms including chronic ear infections.. Atypical femoral fractures have been reported in patients on denosumab. Atypical femoral fractures may occur with little or no trauma in the subtrochanteric and diaphyseal regions of the femur. They have been reported in patients with certain co-morbid conditions (vitamin D deficiency, rheumatoid arthritis, hypophosphatasia) and with certain medicines (bisphosphonates, glucocorticoids, proton pump inhibitors). They have also occurred without antiresorptive therapy. Similar fractures reported with bisphosponates are often bilateral – examine the contralateral femur in denosumab patients who have sustained a femoral shaft fracture. Consider discontinuation of denosumab if suspected atypical femur fracture pending evaluation based on benefit-risk assessment. While on treatment, advise patients to report new/unusual thigh, hip or groin pain. Evaluate such patients for an incomplete femoral fracture. Long-term antiresorptive treatment may increase risks of jaw osteonecrosis and atypical femoral fractures due to significantly suppressed bone remodelling. Denosumab should not be used concurrently with other denosumab containing products for prevention of skeletal related events in adults with bone metastases from solid tumours. Do not use denosumab in paediatric patients (age < 18) due to reports of serious hypercalcaemia and acute renal injury. Each mL of solution contains 47 mg sorbitol – consider additive effect of concomitant products containing sorbitol or fructose and dietary intake. Contains 0.1 mg polysorbate 20 in each mL of solution -may cause allergic reactions. Advise doctor of any known allergies. Contains less than 1 mmol sodium (23 mg) per 60 mg, making it essentially 'sodium-free'. **Interactions:** Denosumab should not alter pharmacokinetics of medicines metabolised by CYP3A4. No clinical data available but the potential for a pharmacodynamic interaction between denosumab and hormone replacement therapy (oestrogen) is considered to be low. In postmenopausal women with osteoporosis, prior alendronate treatment did not impact denosumab's pharmacokinetics or pharmacodynamics, based on data from a transition study (alendronate to denosumab). **Pregnancy and lactation:** Not recommended for use in pregnant women and women of child-bearing potential not using contraception. Advise women not to become pregnant during and for at least 5 months after denosumab treatment.Denosumab effects are likely to be greater during the second and third trimesters of pregnancy. A decision on whether to abstain from breast-feeding or to abstain from therapy with denosumab should be made, taking into account the benefit of breast-feeding to the newborn/infant and the benefit of denosumab therapy to the woman. **Adverse Reactions:** Consult SmPC for full safety information. Very common (≥ 1/10): Pain in extremity, musculoskeletal pain. Common (≥ 1/100 to < 1/10): Urinary tract infection, upper respiratory tract infection, sciatica, constipation, abdominal discomfort, rash, alopecia, eczema. Uncommon (≥1/1000 to <1/100) serious: Cellulitis. Rare (≥1/10000 to <1/1000) serious: drug hypersensitivity, anaphylactic reaction, hypocalcaemia, osteonecrosis of jaw, atypical femoral fractures. Very rare (<1/10000) serious: hypersensitivity vasculitis. Frequency not known serious: osteonecrosis of external auditory canal. Prescribers should consult the summary of product characteristics in relation to other adverse reactions **Pack Sizes:** *One 60 mg pre-filled syringe*: ***Ireland:*** €114.13; ***United Kingdom***: £164.70**. Legal Category:** POM. **Marketing Authorisation Number:** ***Ireland*****:** EU/1/25/1954/01. ***United Kingdom***: PL 08828/0381. **Marketing Authorisation Holder:** ***Ireland***: Fresenius Kabi Deutschland GmbH, Else-Kroener-Strasse 1, 61352 Bad Homburg von der Hoehe, Germany. ***United Kingdon***: Fresenius Kabi Limited, Cestrian Court, Eastgate Way, Manor Park Runcorn, Cheshire, WA7 1NT, United Kingdom. **Date of Preparation:** January 2026. **Job Code**: IE-CON-2500002

Adverse events should be reported. Reporting forms and information can be found at: https://yellowcard.mhra.gov.uk Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL — Dublin 2, Tel: +353 1 6764971, Fax: +353-1-6764061. Website: www.hpra.ie/report-an-issue E-mail: medsafety@hpra.ie. Adverse events should also be reported to Fresenius Kabi Ltd. Cestrian Court, Eastgate Way, Manor Park, Runcorn, Cheshire, WA7 1NT Tel +44 (0)1928 533 575 via email pharmacovigilance.gb@fresenius-kabi.com