PREVENTING BONE COMPLICATIONS*

Metastatic Castration-resistant Prostate Cancer

XGEVA® significantly delayed time to first on-study bone complication* by 18% vs zoledronic acid in patients with bone metastases from castration-resistant prostate cancer†,1

Continuous therapy every 4 weeks ensures that patients get the most out of XGEVA®2,3

*Bone complications are defined as skeletal related events, which include pathological fracture, radiation to bone, spinal cord compression or surgery to bone.[4]
†P=0.008 for superiority; P=0.0002 for noninferiority.[1]

Patients with severe renal impairment (creatinine clearance <30ml/min) or receiving dialysis are at greater risk of developing hypocalcaemia. The risk of developing hypocalcaemia and accompanying elevations in parathyroid hormone increases with increasing degree of renal impairment. Regular monitoring of calcium levels is especially important in these patients. Accompanying increases in parathyroid hormone have also been observed in patients receiving XGEVA® with severe renal impairment or receiving dialysis. Monitoring of calcium levels and adequate intake of calcium and vitamin D is especially importnat in patients with renal impairment.[4]

Study design[1]: A phase 3 study that compared denosumab with zoledronic acid for the treatment of bone metastases in castration-resistant prostate cancer patients and involved 342 centres in 39 countries. 1,904 patients were randomized to receive either a subcutaneous injection of denosumab 120 mg and an intravenous infusion of placebo every 4 weeks or an intravenous infusion of zoledronic acid 4 mg and a subcutaneous injection of placebo every 4 weeks. The primary endpoint was time to first on-study skeletal-related event (non-inferiority test). Secondary endpoint efficacy endpoint was time to first on-study SRE (superiority test).

References: 1. Fizazi K, et al. Lancet. 2011;377:813-822. **2.** Coleman R, et al. Ann Oncol. 2014;25(Suppl 3):iii124-iii137. **3.** Kettle, J.K, et al. J Oncol Pharm Pract 2018;24:343-347. **4.** XGEVA Singapore Prescribing Information.

Please review full product information before prescribing

ABBREVIATED PRODUCT INFORMATION
XGEVA SOLUTION FOR INJECTION 120 MG/VIAL
INDICATIONS: Prevention of skeletal related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in patients with multiple myeloma and in patients with bone metastases from solid tumours. Treatment of adults and skeletally mature adolescents with giant cell tumour of bone (GCTB) that is unresectable or where surgical resection is likely to result in severe morbidity.
CONTRAINDICATIONS: Hypersensitivity to denosumab or any components of XGEVA. Severe, untreated hypocalcaemia
PRECAUTIONS: Supplementation with calcium and vitamin D is required in all patients unless hypercalcaemia is present. Pre-existing hypocalcaemia must be corrected prior to initiating therapy. Hypocalcaemia can occur at any time during therapy. Monitoring of calcium levels should be conducted (i) prior to the initial dose of XGEVA, (ii) within two weeks after the initial dose, (iii) if suspected symptoms of hypocalcaemia occur. If hypocalcaemia occurs while receiving XGEVA, additional short term calcium supplementation may be necessary. Patients with severe renal impairment (creatinine clearance < 30 ml/min) or receiving dialysis are at greater risk of developing hypocalcaemia. Regular monitoring of calcium levels is especially important in these patients. ONJ has been reported commonly in patients treated with XGEVA. Caution in patients with known risk factors for osteonecrosis of the jaw (ONJ); oral and dental exam prior to therapy recommended; maintain good oral hygiene during treatment. Avoid invasive dental procedures where possible. Osteonecrosis of the external auditory canal has been reported with denosumab. Possible risk factors for osteonecrosis of the external auditory canal include steroid use and chemotherapy and/or local risk factors such as infection or trauma. Atypical femoral fracture have been reported in patients receiving denosumab. Clinically significant hypercalcaemia requiring hospitalisation and complicated by acute renal injury has been reported XGEVA-treated patients with giant cell tumour of bone weeks to months following treatment discontinuation. XGEVA is not recommended in patients with growing skeletons. Multiple vertebral fractures, not due to bone metastases, may occur following discontinuation of treatment with XGEVA, particularly in patients with risk factors such as osteoporosis or prior fractures. Patients should be advised to seek prompt medical attention if they develop signs or symptoms of cellulitis. Patients being treated with XGEVA should not be treated concomitantly with other denosumab containing medicinal products and should not be treated concomitantly with bisphosphonates. This medicinal product contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicinal product.
INTERACTIONS: No interaction studies have been performed.
PREGNANCY AND LACTATION: There are no or limited amount of data from the use of denosumab in pregnant women. XGEVA is not recommended for use in pregnant women and women of child-bearing potential not using contraception. It is unknown whether denosumab is excreted in human milk. A decision must be made on whether to abstain from breast-feeding or to abstain from therapy with XGEVA taking into account the benefit of breast-feeding to the newborn/infant and the benefit of XGEVA therapy for the woman.
ADVERSE EFFECTS: Hypocalcaemia, dyspnoea, diarrhoea, musculoskeletal pain, new primary malignancy, hypophosphataemia, tooth extraction, hyperhidrosis, alopecia, ONJ.
DOSAGE & ADMINISTRATION: *Skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumours:* Single subcutaneous injection of 120 mg once every 4 weeks. *Giant cell tumour of the bone:* Single subcutaneous injection of 120 mg once every 4 weeks, with additional 120 mg doses on days 8 and 15 of treatment of the first month of therapy. Supplementation of at least 500 mg calcium and 400 IU vitamin D is required in all patients, unless hypercalcaemia is present. No dose adjustment is required in elderly patients and patients with renal impairment. XGEVA is not recommended for use in paediatric patients other than skeletally mature adolescents (aged 13 – 17 years) with giant cell tumour of bone.

Based on approved PI dated 25 March 2021
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XGEVA®
denosumab

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