

Denosumab

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Pharma today

Overview: Denosumab is a bone-modifying agent belonging to the class of “Monoclonal Antibodies”. It first approved by the US FDA in June 2010 for treatment of osteoporosis in postmenopausal women at high risk for fracture, and in November 2010 for treatment for the prevention of skeletal-related events in patients with bone metastases from solid tumors. Several biosimilar have also been introduced in recent years.

Mechanism of Action: Denosumab, a fully human monoclonal anti-RANKL antibody, binds to RANKL, blocks the interaction between RANKL (Receptor activator of nuclear factor-kappa B ligand) and RANK (a receptor located on osteoclast surfaces), and prevents osteoclast formation, leading to decreased bone resorption and increased bone mass in osteoporosis.

Indications, Dose and Administration:

Indications	Dose & administration
Treatment of osteoporosis in postmenopausal females at high risk of fracture and glucocorticoid induced osteoporosis(off label use).	SUBQ: 60 mg once every 6 months
Treatment of bone loss (to increase bone mass) in females receiving aromatase inhibitor therapy for breast cancer and males receiving androgen-deprivation therapy for non metastatic prostate cancer.	SUBQ: 60 mg once every 6 months
Treatment of giant cell tumor of bone in adults and skeletally mature adolescents.	SUBQ: 120 mg once every 4 weeks; during the first month, administer an additional 120 mg on days 8 and 15.
Prevention of skeletal-related events in patients with myeloma and bone metastases from solid tumors.	SUBQ: 120 mg once every 4 weeks

Administer via SUBQ(subcutaneous) injection in the upper arm, upper thigh, or abdomen; should only be administered by a health care professional.

Dosage Adjustment

Altered Kidney function & Liver function: No dosage adjustment necessary (Hypocalcemia should be watched for patients with severe renal dysfunction).

Pregnancy and Breastfeeding Considerations: The use of denosumab is contraindicated during pregnancy; breastfeeding is not recommended.

Clinical pharmacy considerations for Denosumab

- Ensure adequate calcium(1000mg/day) and vitamin D (≥ 400 units/day) intake to prevent hypocalcemia.
- Prevent therapeutic duplication with biosimilar (e.g., Denosumab –bbdz, Denosumab –qbde).
- Ensure administration via subcutaneous route only. Prior to administration, bring the prefilled syringe or vial to room temperature in its original container (allow to stand for 15 to 30 minute); do not warm it by any other method.
- Assess medication history to prevent drug interactions - cytotoxic agents/Immunosuppressant + Denosumab (results in an increased immunosuppressive effect leading to a higher chance of infection).
- Educate patient on not discontinuing/interrupting without subsequent antiresorptive therapy (e.g. With bisphosphonates) to prevent drug rebound effect and no drug holidays are recommended.