



DESCRIPTION

D-Mab™ contains Denosumab, a human monoclonal IgG2 antibody produced by recombinant DNA technology in Chinese hamster ovary cells. It binds with high affinity and specificity to RANKL (Receptor Activator of Nuclear Factor Kappa-B Ligand), a protein essential for osteoclast formation, function, and survival. By blocking the interaction between RANKL and its receptor RANK on osteoclasts and their precursors, **D-Mab™** inhibits osteoclast-mediated bone resorption, thereby increasing bone mass and strength in both cortical and trabecular bone.

INDICATIONS

D-Mab™ is indicated for:

- Treatment of postmenopausal women with osteoporosis at high risk for fracture.
- Increase of bone mass in men with osteoporosis at high risk for fracture.
- Treatment of glucocorticoid-induced osteoporosis in men and women at high risk for fracture.
- Increase of bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer.
- Increase of bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

DOSAGE AND ADMINISTRATION

The recommended dose of **D-Mab™** is 60 mg, administered as a single subcutaneous injection once every 6 months by a healthcare provider in the upper arm, upper thigh, or abdomen. Patients should be instructed to take daily calcium (1000 mg) and vitamin D (at least 400 IU) supplements.

If a dose is missed, it should be administered as soon as possible, with subsequent doses scheduled every 6 months from the last injection date.

In patients with advanced chronic kidney disease, evaluation for chronic kidney disease mineral and bone disorder (CKD-MBD) is required before initiation.

CONTRAINDICATIONS

Denosumab is contraindicated in patients with:

- Hypocalcemia (pre-existing hypocalcemia must be corrected prior to therapy).
- Pregnancy (may cause fetal harm).
- Known hypersensitivity to Denosumab or any component of the product.

SIDE EFFECTS

- Postmenopausal osteoporosis: Most common adverse reactions are back pain, pain in extremity, hypercholesterolemia, musculoskeletal pain, and cystitis. Pancreatitis has been reported in clinical trials.
- Male osteoporosis: Most common adverse reactions are back pain, arthralgia, and nasopharyngitis.
- Glucocorticoid-induced osteoporosis: Most common adverse reactions are back pain, hypertension, bronchitis, and headache.
- Bone loss due to hormone ablation for cancer: Most common adverse reactions are arthralgia and back pain. Pain in extremity and musculoskeletal pain have also been reported in clinical trials.

PRECAUTION AND WARNING

Hypocalcemia: Pre-existing hypocalcemia must be corrected before Denosumab is initiated. It may be worsened, especially in patients with renal impairment. All patients must be adequately supplemented with calcium and vitamin D, and the concomitant use of calcimimetic drugs may also worsen hypocalcemia risk. The presence of chronic kidney disease mineral-bone disorder must be evaluated, and serum calcium must be monitored.

Same Active Ingredient: Denosumab should not be administered concomitantly with other Denosumab-containing products.

Osteonecrosis of the Jaw: Osteonecrosis of the jaw (ONJ) has been reported in patients receiving Denosumab. Symptoms must be monitored.

Atypical Femoral Fractures: Atypical femoral fractures have been reported in patients receiving Denosumab. Patients presenting with thigh or groin pain must be evaluated to rule out a femoral fracture.

Multiple Vertebral Fractures: Multiple vertebral fractures have been reported following Denosumab discontinuation. Patients should be transitioned to another antiresorptive agent if Denosumab therapy is discontinued.

Serious Infections: Serious infections, including those of the skin, may occur and can lead to hospitalization. Patients must be advised to seek prompt medical attention if signs or symptoms of infection, such as cellulitis, develop.

Dermatologic Reactions: Dermatitis, rashes, and eczema have been reported in patients receiving Denosumab. Discontinuation of therapy should be considered if severe symptoms develop.

Severe Bone, Joint, and Muscle Pain: Severe bone, joint, or muscle pain may occur during treatment. Use should be discontinued if severe symptoms develop.

Suppression of Bone Turnover: Significant suppression of bone turnover has been demonstrated. Consequences of bone over-suppression must be monitored.

USE IN PREGNANCY AND LACTATION

Denosumab is contraindicated in pregnancy due to potential fetal harm, including fetal loss, stillbirth, and bone abnormalities. Females of reproductive potential should use effective contraception during therapy and for at least 5 months after the last dose. There are no data on the presence of Denosumab in human milk; breastfeeding is not recommended during treatment.

PEDIATRIC USE

Denosumab is not approved for use in pediatric patients. Safety and effectiveness have not been established. Hypercalcemia has been reported in pediatric patients with osteogenesis imperfecta treated with Denosumab products, and treatment may impair long-bone growth and tooth eruption in young children.

DRUG INTERACTION

No clinically significant pharmacokinetic interactions have been observed with etanercept or midazolam (a CYP3A4 substrate). However, concomitant use of calcimimetic drugs may increase the risk of hypocalcemia. Denosumab should not be used with other Denosumab-containing products.

OVERDOSE

No experience with overdose was obtained in clinical studies. In clinical studies, Denosumab was administered at doses up to 180 mg every 4 weeks (cumulative doses up to 1,080 mg over 6 months), and no additional adverse reactions were observed.

PHARMACEUTICAL PRECAUTION

D-Mab™ must be stored refrigerated at 2 °C to 8 °C temperature. Do not freeze. Once removed from refrigeration, it must be kept at or below 25 °C (77 °F) and used within 30 days. Keep away from light and wet place, kept out of reach of children. Do not shake. Any unused product must be discarded after the expiry date.

PACKAGING:

D-Mab™ 60 mg SC Injection: Each box contains 1 pre-filled syringe. Each pre-filled syringe contains 1 mL sterile solution of Denosumab INN 60 mg.

SK+F

Manufactured by
ESKAYEF PHARMACEUTICALS LIMITED
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TM TRADEMARK
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