Prolica® (denosumab) Injection Indications

Prolica® is indicated for:
- Prolica® is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolica® reduces the incidence of vertebral, nonvertebral, and hip fractures.
- Prolica® is indicated for treatment to increase bone mass in men with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.
- Prolica® is indicated for the treatment of glucocorticoid-induced osteoporosis in men and women at high risk of fracture who are either initiating or continuing systemic glucocorticoids in a daily dosage equivalent to 7.5 mg or greater of prednisone and expected to remain on glucocorticoids for at least 6 months. High risk of fracture is defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.
- Prolica® is indicated as a treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer. In these patients Prolica® also reduced the incidence of vertebral fractures.
- Prolica® is indicated as a treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

Important Safety Information

Contraindications
Prolica® is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating Prolica®. Prolica® is contraindicated in women who are pregnant and may cause fetal harm. In women of reproductive potential, pregnancy testing should be performed prior to initiating treatment with Prolica®. Prolica® is contraindicated in patients with a history of systemic hypersensitivity to any component of the product. Reactions have included anaphylaxis, facial swelling and urticaria.

Same Active Ingredient
Prolica® contains the same active ingredient (denosumab) found in XGEVA®. Patients receiving Prolica® should not receive XGEVA®.

Hypersensitivity
Clinically significant hypersensitivity including anaphylaxis has been reported with Prolica®. Symptoms have included hypotension, dyspnea, throat tightness, facial and upper airway edema, pruritus, and urticaria. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of Prolica®.

Hypocalcemia
Hypocalcemia may worsen with the use of Prolica®, especially in patients with severe renal impairment. In patients predisposed to hypocalcemia and disturbances of mineral metabolism, clinical monitoring of calcium and mineral levels is highly recommended within 14 days of Prolica® injection. Adequately supplement all patients with calcium and vitamin D.

Osteonecrosis of the Jaw (ONJ)
ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients receiving Prolica®. An oral exam should be performed by the prescriber prior to initiation of Prolica®. A dental examination with appropriate preventive dentistry is recommended prior to treatment in patients with risk factors for ONJ such as invasive dental procedures, diagnosis of cancer, concomitant therapies (e.g., chemotherapy, corticosteroids, angiogenesis inhibitors), poor oral hygiene, and co-morbid disorders. Good oral hygiene practices should be maintained during treatment with Prolica®. The risk of ONJ may increase with duration of exposure to Prolica®.

For patients requiring invasive dental procedures, clinical judgment should guide the management plan of each patient. Patients who are suspected of having or who develop ONJ should receive care by a dentist or an oral surgeon. Extensive dental surgery to treat ONJ may exacerbate the condition. Discontinuation of Prolica® should be considered based on individual risk/benefit assessment.

Atypical Femoral Fractures
Atypical low-energy, or low trauma fractures of the shaft have been reported in patients receiving Prolica®. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated with antiresorptive agents.

During Prolica® treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Any patient who presents with thigh or groin pain should be evaluated to rule out an incomplete femur fracture. Interruption of Prolica® therapy should be considered, pending a risk/benefit assessment, on an individual basis.

Multiple Vertebral Fractures (MVF) Following Discontinuation of Prolica® Treatment
Following discontinuation of Prolica® treatment, fracture risk increases, including the risk of multiple vertebral fractures. New vertebral fractures occurred as early as 7 months [on average 19 months] after the last dose of Prolica®. Prior vertebral fracture was a predictor of multiple vertebral fractures after Prolica® discontinuation. Evaluate an individual’s benefit/risk before initiating treatment with Prolica®. If Prolica® treatment is discontinued, consider transitioning to an alternative antiresorptive therapy.

Serious Infections
In a clinical trial (N=7808) in women with postmenopausal osteoporosis, serious infections leading to hospitalization were reported more frequently in the Prolica® group than in the placebo group. Serious skin infections, as well as infections of the abdomen, urinary tract and ear were more frequent in patients treated with Prolica®.

Endocarditis was also reported more frequently in Prolica®-treated patients. The incidence of opportunistic infections and the overall incidence of infections were similar between groups. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis. Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. In patients who develop serious infections while on Prolica®, prescribers should assess the need for continued Prolica® therapy.

Dermatologic Adverse Reactions
In the same clinical trial in women with postmenopausal osteoporosis, epidermal and dermal adverse events such as dermatitis, eczema and rashes occurred at a significantly higher rate with Prolica® compared to placebo. Most of these events were not specific to the injection site. Consider discontinuing Prolica® if severe symptoms develop.

Musculoskeletal Pain
Severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients taking Prolica®. Consider discontinuing use if severe symptoms develop.

Suppression of Bone Turnover
In clinical trials in women with postmenopausal osteoporosis, Prolica® resulted in significant suppression of bone remodeling as evidenced by markers of bone turnover and bone histomorphometry. The significance of these findings and the effect of long-term treatment are unknown. Monitor patients for these consequences, including ONJ, atypical fractures, and delayed fracture healing.

Adverse Reactions
The most common adverse reactions (> 5% and more common than placebo) in women with postmenopausal osteoporosis are back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia, and cystitis. The most common adverse reactions (> 5% and more common than placebo) in men with osteoporosis are back pain, arthralgia, and nasopharyngitis. Pancreatitis has been reported with Prolica®.

In women with postmenopausal osteoporosis, the overall incidence of new malignancies was 4.3% in the placebo group and 4.8% in the Prolica® group. In men with osteoporosis, new malignancies were reported in no patients in the placebo group and 4 (3.3%) patients in the Prolica® group. A causal relationship to drug exposure has not been established.

The most common adverse reactions (> 3% and more common than active-control group) in patients with glucocorticoid-induced osteoporosis are back pain, hypertension, bronchitis, and headache.

In postmenopausal women with osteoporosis, the overall incidence of new malignancies was 4.3% in the placebo group and 4.8% in the Prolica® group. In men with osteoporosis, new malignancies were reported in no patients in the placebo group and 4 (3.3%) patients in the Prolica® group. A causal relationship to drug exposure has not been established.

The most common adverse reactions (> 10%) after treatment with Prolica® in patients with bone loss receiving ADT for prostate cancer or adjuvant AI therapy for breast cancer are arthralgia and back pain. Pain in extremity and musculoskeletal pain have also been reported in clinical trials. Additionally, in Prolica®-treated men with nonmetastatic prostate cancer receiving ADT, a greater incidence of cataracts was observed.

Denosumab is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity.

Please see accompanying Prolica® full Prescribing Information, including Medication Guide.