[Note: This example letter is provided as a courtesy and not intended to be directive. Physicians should exercise medical judgment and discretion to appropriately diagnose and characterize the individual patient's medical condition. In addition, HCPs are responsible for ensuring the accuracy and validity of all billing and claims for appropriate reimbursement.] Please delete this paragraph prior to submitting your Letter of Medical Necessity.

[Prolia® (denosumab) Sample Letter of Medical Necessity]

[Physician Letterhead]

Patient Name: _____

Address Line 1: _____

Address Line 2: _____

Insurance Company: _____

Policy ID: _____

Policy Group: _____

Date of Birth: _____

[Date] _____

(mm/dd/yyyy)

Attn: [Medical/Pharmacy Director], [Department]

Dear [Medical/Pharmacy Director],

I am writing this letter on behalf of my patient, [Patient Name].

Prolia® (denosumab) is indicated for the treatment of osteoporosis in postmenopausal women 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.[1]

Based on the FDA-approved indication, I strongly believe that treatment with Prolia® is medically necessary.

Prolia® is medically necessary for [Patient Name] as documented by:

Based on your clinical judgment, include patient's relevant medical history, including patient's current and worst T-scores, with dates (the worst ever DXA imparts the diagnosis of osteoporosis and can carry forward for diagnosis), dates and anatomical sites of fragility fracture, FRAX® score, dates of prior osteoporosis treatments, and explanation of reasons for discontinuation, intolerance or failure and any additional information to document the disease that could be helpful.

The current treatment guidelines by the American Association of Clinical Endocrinologists (AACE) include Prolia® (denosumab) as an initial therapy option for patients at high or very high risk of fracture. High risk is defined as patients who have been diagnosed with osteoporosis but are not at very high fracture risk. Very high fracture risk is defined as ANY of the following criteria: patients with a recent fracture (e.g., within the past 12 months); fractures while on approved osteoporosis therapy; multiple fractures; fractures while on drugs causing skeletal harm; very low T-score (e.g., less than −3.0); high risk for falls or history of injurious falls; or very high fracture probability by FRAX® (fracture risk assessment tool) (e.g., major osteoporosis fracture >30%, hip fracture >4.5%) or other validated fracture risk algorithm.[2]

In summary, based on my clinical opinion, Prolia® (denosumab) is medically necessary for [Patient Name]. This is fully consistent with both the FDA-approved indication and the current standards of care.

Please call my office at [Phone Number] if I can provide you with any additional information to approve my request.

Sincerely,

[Physician's Name]

[Attach appropriate supporting documents such as excerpt(s) from patient's medical record.]

Please see Important Safety Information on next page.

These pages are for your reference only. Content on this and next page does not need to be sent to the insurance company.

IMPORTANT SAFETY INFORMATION FOR PROLIA® (DENOSUMAB) INJECTION

Contraindications: Prolia® is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating Prolia®. Prolia® 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 Prolia®. Prolia® 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: Prolia® contains the same active ingredient (denosumab) found in XGEVA®. Patients receiving Prolia® should not receive XGEVA®.

Hypersensitivity: Clinically significant hypersensitivity including anaphylaxis has been reported with Prolia®. 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 Prolia®.

Hypocalcemia: Hypocalcemia may worsen with the use of Prolia®, especially in patients with severe renal impairment. In patients predisposed to hypocalcemia and disturbances of mineral metabolism, including treatment with other calcium-lowering drugs, clinical monitoring of calcium and mineral levels is highly recommended within 14 days of Prolia® injection. Concomitant use of calcimimetic drugs may worsen hypocalcemia risk and serum calcium should be closely monitored. 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 Prolia®. An oral exam should be performed by the prescriber prior to initiation of Prolia®. 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 Prolia®. The risk of ONJ may increase with duration of exposure to Prolia®.

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 Prolia® should be considered based on individual benefit-risk assessment.

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

During Prolia® 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 Prolia® therapy should be considered, pending a risk/benefit assessment, on an individual basis.

Multiple Vertebral Fractures (MVF) Following Discontinuation of Prolia® Treatment: Following discontinuation of Prolia® 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 Prolia®. Prior vertebral fracture was a predictor of multiple vertebral fractures after Prolia® discontinuation. Evaluate an individual's benefit/risk before initiating treatment with Prolia®. If Prolia® treatment is discontinued, patients should be transitioned to an alternative antiresorptive therapy.

Serious Infections: In a clinical trial (N= 7808), serious infections leading to hospitalization were reported more frequently in the Prolia® 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 Prolia®.

Endocarditis was also reported more frequently in Prolia®-treated patients. The incidence of opportunistic infections and the overall incidence of infections were similar between the treatment 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 Prolia®, prescribers should assess the need for continued Prolia® therapy.

IMPORTANT SAFETY INFORMATION (CONT.) FOR PROLIA® (DENOSUMAB)

Dermatologic Adverse Reactions: Epidermal and dermal adverse events such as dermatitis, eczema and rashes occurred at a significantly higher rate with Prolia® compared to placebo. Most of these events were not specific to the injection site. Consider discontinuing Prolia® if severe symptoms develop.

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

Suppression of Bone Turnover: Prolia® 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 consequences, including ONJ, atypical fractures, and delayed fracture healing.

Adverse Reactions: The most common adverse reactions (>5% and more common than placebo) are back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia, and cystitis. Pancreatitis has been reported with Prolia®.

The overall incidence of new malignancies was 4.3% in the placebo group and 4.8% in the Prolia® group. A causal relationship to drug exposure has not been established. Denosumab is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity.

INDICATION

Prolia® 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, Prolia® reduces the incidence of vertebral, nonvertebral, and hip fractures.

Please see Prolia® full Prescribing Information, including Medication Guide.

References: 1. Prolia® (denosumab) prescribing information, Amgen. **2.** Camacho P, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists/American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis—2020 update. *Endocr Pract.* 2020;26(suppl 1):1-46.

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