MVP Health Care Medical Policy

Medicare Part B: Densoumab (Prolia and Xgeva)

Type of Policy:	**Drug/Medical Therapy**
Prior Approval Date:	**N/A**
Approval Date:	**11/01/2023**
Effective Date:	**1/01/2024**

Related Policies:

Refer to the MVP Medicare website for the Medicare Part D formulary and Part D policies.

Refer to the MVP website for the Medicare Part B policies for coverage criteria of drugs covered under the medical benefit.

Overview

Considerations

Coverage guidelines for participants in the Cancer Guidance Program (CGP) where some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

Background

Osteoporosis is characterized by low bone mass, microarchitectural disruption, and increased skeletal fragility. The Word Health Organization (WHO) established diagnostic thresholds for bone mineral density (BMD) by dual-energy x-ray absorptiometry (DXA) according to the standard deviation (SD) difference between a patient's BMD and that of a young adult reference population (T-score). A T-score of -2.5 SD or below is defined as osteoporosis, provided that other causes of low BMD have been ruled out, and a T-score between -1 and -2.5 SD is defined as osteopenia. Additionally, guidelines state that osteoporosis can be diagnosed by one of the following: (1) Presence of fragility fractures in the absence of other metabolic bone disorders; (2) T-score ≤ −2.5 SD in the lumbar spine (antero-posterior), femoral neck, total hip, or one-third radius; or (3) T-score between −1.0 and −2.5 and increased fracture risk using the FRAX® (fracture risk assessment tool) country-specific thresholds. The FRAX tool is designed to assist clinicians in predicting the ten-year probability of hip fracture and 10-year probability of a major osteoporotic fracture (spine, forearm, hip or shoulder fracture) with or without the addition of femoral neck BMD. In the United States, a clinical diagnosis of osteoporosis may be made when the FRAX 10-year probability of major osteoporotic fracture (hip, clinical spine, proximal humerus, or forearm) is greater than or equal to 20 percent or the FRAX 10- year probability of hip fracture is greater than or equal to 3 percent. Denosumab binds to RANKL, a transmembrane or soluble protein essential for the formation, function, and survival of osteoclasts, the cells responsible for bone resorption, thereby modulating calcium release from bone. Denosumab prevents RANKL from activating its receptor, RANK, on the surface of osteoclasts, their precursors, and osteoclast-like giant cells. Prevention of the RANKL/RANK interaction inhibits osteoclast formation, function, and survival, thereby decreasing bone resorption and increasing bone mass and strength in both cortical and trabecular bone. Increased osteoclast activity, stimulated by RANKL, is a mediator of bone pathology in solid tumors with osseous metastases. Similarly, giant cell tumors of bone consist of stromal cells expressing RANKL and osteoclast-like giant cells expressing RANK receptor and signaling through the RANK receptor contributes to osteolysis and tumor growth. (Amgen, 2022; Amgen 2020)

Instructions for Use

This medical guideline aids in interpreting National Comprehensive Cancer Network (NCCN)® cancer guidelines. Before using this guideline, please check the member specific benefit plan documents and any applicable federal or state mandates. Optum

reserves the right to modify its Guidelines as necessary. This Guideline is provided for informational purposes and does not constitute medical advice.

This Guideline may also be applied to Medicare Advantage plans in some instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence. (Medicare IOM Pub. No. 100-16, Chapter 4, Section 90.5)

Optum Medical Benefit Guidelines are intended to be used in connection with the independent professional medical judgement of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Recommendation

Prolia (densoumab)

Prolia® is proven to increase bone mass in patients at high risk for fracture receiving androgen deprivation therapy for non-metastatic prostate cancer when all the following criteria are met:

- Initial Therapy
    - Diagnosis of non-metastatic prostate cancer; and
    - Patient is receiving androgen deprivation therapy; and
    - Prolia dosing is in accordance with the United States Food and Drug Administration approved labeling;
    - History of failure, contraindications, or intolerance to other available osteoporosis therapy (e.g., oral bisphosphonates, intravenous bisphosphonates); and
    - Authorization is for no more than 12 months.

- Reauthorization/Continuation of Care Criteria

- For patients currently on Prolia® to increase bone mass in patients at high risk for fracture receiving androgen deprivation therapy for non-metastatic prostate cancer, continued use will be approved based on the following criteria:
- Patient is receiving androgen deprivation therapy; and
- Provider attests to a positive clinical response; and
- Prolia® dosing is in accordance with the United States Food and Drug Administration approved labeling; and
- Authorization is for no more than 12 months.

Prolia® is proven to treat patients at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer when all the following criteria are met:

- Initial Therapy
  - Diagnosis of breast cancer; and
  - Patient is receiving aromatase inhibitor therapy; and
  - Prolia dosing is in accordance with the United States Food and Drug Administration approved labeling;
  - History of failure, contraindications, or intolerance to other available osteoporosis therapy (e.g., oral bisphosphonates, intravenous bisphosphonates); and
  - Authorization is for no more than 12 months.

- Reauthorization/Continuation of Care Criteria
  - For patients currently on Prolia® to treat patients at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer, continued use will be approved based on the following criteria:
    - Patient is receiving aromatase inhibitor; and

        - Provider attests to a positive clinical response; and
        - Prolia® dosing is in accordance with the United States Food and Drug Administration approved labeling; and
    - Authorization is for no more than 12 months.

Xgeva (densoumab)

Xgeva is proven for the prevention of skeletal-related events in patients with multiple myeloma and with bone metastases from solid tumors when all of the following criteria are met:

- Initial Therapy
    - One of the following:
        - Diagnosis of multiple myeloma
        - Presences of metastatic disease secondary to a solid tumor (e.g., bladder, breast, kidney, lung, ovaria, thyroid, etc.)

And

    - Xgeva® dosing is in accordance with the United States Food and Drug Administration approved labeling;
    - History of failure, contraindications, or intolerance to other available osteoporosis therapy (e.g., oral bisphosphonates, intravenous bisphosphonates); and
    - Authorization is for no more than 12 months.

- Reauthorization/Continuation of Care Criteria
    - For patients currently on Xgeva® for the prevention of skeletal-related events in patients with multiple myeloma and with bone metastases from solid tumors, continued use will be approved based on the following criteria:
        - Provider attests to a positive clinical response; and

- Xgeva® dosing is in accordance with the United States Food and Drug Administration approved labeling; and
- Authorization is for no more than 12 months.

Xgeva® is proven for the treatment of giant cell tumor of the bone when all the following criteria are met:

- Initial Therapy
  - Patient is one of the following:
    - Patient is ≥ 18 years of age
    - Patient is a skeletally mature adolescent as defined by having at least 1 mature long bone (e.g., closed epiphyseal growth plat of the humerus)

And

  - Diagnosis of localized, recurrent or metastatic giant cell tumor of the bone; and
  - Disease is one of the following:
    - Unresectable
    - Surgical resection is likely to result in severe morbidity

And

  - Xgeva® dosing is in accordance with the United States Food and Drug Administration approved labeling;
  - Authorization is for no more than 12 months.

- Reauthorization/Continuation of Care Criteria
  - For patients currently on Xgeva for the treatment of giant cell tumor of the bone, continued use will be approved based on the following criteria:

- Provider attests to the positive clinical response; and
- Xgeva® dosing is in accordance with the United States Food and Drug Administration approved labeling; and
- Authorization is for no more than 12 months.

Xgeva® is proven for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy when all of the following criteria are met:

- Initial Therapy
    - Diagnosis of hypercalcemia of malignancy as defined as: albumin-corrected serum calcium level greater than 12.5 mg/dL (3.1 mmol/L); and
    - Refractory (within the last 30 days), contraindication (including renal insufficiency), or intolerance to treatment with intravenous bisphosphonates therapy (e.g., pamidronate, zoledronic acid); and
    - Xgeva® dosing is in accordance with the United States Food and Drug Administration approved labeling; and
    - Authorization is for no more than 12 months.

- Reauthorization/Continuation of Care Criteria
    - For patients currently on Xgeva® for the treatment of hypercalcemia of malignancy, continued use will be approved based on the following criteria:
        - Provider attests to a positive clinical response; and
        - Xgeva® dosing is in accordance with the treatment of hypercalcemia of malignancy, continued use will be approved based on the following criteria:
        - Authorization is for no more than 12 months.

Xgeva® is proven for treatment of osteopenia/osteoporosis in patients with systemic mastocytosis with bone pain not responding to bisphosphonates when all the following criteria are met:

- Initial Therapy
    - Diagnosis of systemic mastocytosis; and
    - Patient has bone pain; and
    - Diagnosis of osteoporosis or osteopenia based on one of the following:
        - BMD T-score ≤ -1 based on BMD measurements from lumbar spine (at least two vertebral bodies), hip (femoral neck, total hip), or radius (one-third radius site); or
        - History of one of the following resulting from minimal trauma:
            - Vertebral compression fracture
            - Fracture of the hip
            - Fracture of the distal radius
            - Fracture of the pelvis
            - Fracture of the proximal humerus

And

- Refractory (within the past 30 days), contraindication (including renal insufficiency), or intolerance to treatment with intravenous bisphosphonate therapy (e.g., pamidronate, zoledronic acid) (for Medicare reviews, refer to the CMS section*); and
- Xgeva® dosing is in accordance with the United States Food and Drug Administration approved labeling; and
- Authorization for no more than 12 months.

- Reauthorization/Continuation of Care Criteria

- For patients currently on Xgeva for the treatment of osteopenia/osteoporosis in patients with systemic mastocytosis with bone pain not responding to bisphosphonates, continued use will be approved based on the following criteria:
    - Provider attests to a positive clinical response; and
    - Xgeva® dosing is in accordance with the United States Food and Drug Administration approved labeling; and
    - Authorization is for no more than 12 months.

Unproven/Not Medically Necessary

Denosumab is unproven and not medically necessary for the following indications:

- Combination therapy of denosumab and intravenous bisphosphonates
- Bone loss associated with hormone-ablation therapy (other than aromatase inhibitors) in breast/prostate cancer
- Cancer pain
- Central giant cell granuloma
- Hyper-parathyroidism
- Immobilization hypercalcemia
- Osteogenesis Imperfecta
- Osteopenia

Clinical Evidence

Prolia

Patients at High Risk for Fracture Receiving Androgen Deprivation Therapy for Non-Metastatic Prostate Cancer

Smith ME et al investigated the effects of denosumab in a double-blind, multicenter study, on bone mineral density and fractures in patients with non-metastatic prostate cancer who are receiving androgen-deprivation therapy.8 Patients were randomly assigned to receive denosumab at a dose of 60 mg subcutaneously every 6 months or

placebo (n = 734 per group). The primary end point was percent change in bone mineral density at the lumbar spine at 24 months. Secondary end points included percent change in bone mineral densities at the femoral neck and total hip at 24 months and at all three sites at 36 months, as well as frequency of new vertebral fractures. At 24 months, patients receiving denosumab experienced an increase in bone mineral density of the lumbar spine by 5.6% as compared with a loss of 1.0% in the placebo group ($p < 0.001$). Significant differences between the placebo and denosumab groups were seen at 1 month and continued through 36 months. Treatment was also associated with significant increases in bone mineral density at the total hip, femoral neck, and distal third of the radius. Patients who received denosumab had a decreased incidence of new vertebral fractures at 36 months (1.5%, vs. 3.9% with placebo) (relative risk, 0.38; 95% confidence interval, 0.19 to 0.78; $p = 0.006$). Similar rates of adverse events were reported in the two groups. (Smith, 2009) The authors conclude that denosumab is associated with increased bone mineral density at all sites and a reduction in the incidence of new vertebral fractures among patients receiving androgen-deprivation therapy for non-metastatic prostate cancer. (ClinicalTrials.gov number, NCT00089674)

Professional Societies

National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Several National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines®) include denosumab as a treatment for several conditions related to malignant disease. The following NCCN Guidelines® state (NCCN, 2023):

- For invasive and inflammatory breast cancer, the NCCN recommends (Category 2A) denosumab to be considered in postmenopausal (natural or induced) patients receiving adjuvant endocrine therapy along with calcium and vitamin D supplementation to maintain or improve bone mineral density and reduce risk of fractures.
- For prostate cancer, the NCCN recommends (Category 2A) denosumab for the prevention or treatment of osteoporosis during androgen deprivation therapy (ADT) for patients with high fracture risk.

Xgeva

In an ad hoc analysis of the phase 3 clinical trial of 1,776 patients with metastases from solid tumors or multiple myeloma, where it was shown that denosumab was non-inferior to zoledronic acid (ZA) in delaying or preventing SREs, Henry et al reports outcomes in the subgroup of 1,597 patients with solid tumors, excluding multiple myeloma.17 In the ad hoc analysis, denosumab significantly delayed time to first on-study SRE compared to ZA (HR, 0.81; 95% CI, 0.68–0.96) and time to first-and

subsequent SREs (RR, 0.85; 95% CI, 0.72–1.00). Denosumab also significantly delayed time to development of moderate or severe pain (HR, 0.81; 95% CI, 0.66–1.00), pain worsening (HR, 0.83; 95% CI, 0.71–0.97), and worsening pain interference in patients with no/mild baseline pain (HR, 0.77; 95% CI, 0.61–0.96). Overall survival was similar in both groups. The median KM estimate was 10.7 months for denosumab-treated patients and 10.0 months for ZA-treated patients (HR, 0.92; 95% CI, 0.81– 1.05: p = 0.215). Similarly, there was no difference between groups in time to disease progression. The median KM estimate was 5.3 (4.9, 5.7) months for denosumab-treated and 5.4 (4.8, 5.7) months for ZA-treated patients (HR, 0.96; 95% CI, 0.85–1.08: p = 0.497). The authors concluded that denosumab was more effective in delaying the incidence of SREs, however did not significantly affect the overall incidence or disease progression or overall survival.

In a double-blind, double-dummy, phase III clinical trial, Henry et al compared denosumab with zoledronic acid (ZA) for delaying or preventing skeletal-related events (SRE) in patients with advanced cancer and bone metastases (excluding breast and prostate) or myeloma (Henry, 2011). Patients were randomly assigned to receive either monthly subcutaneous denosumab 120mg (n = 886) or intravenous ZA 4mg (dose adjustment for renal impairment; n = 890). The primary end point was time to first on-study SRE (pathologic fracture, radiation or surgery to bone, or spinal cord compression). The trial demonstrated that denosumab was noninferior to ZA in delaying time to first on-study SRE (hazard ratio, 0.84; 95% CI, 0.71 to 0.98; p = 0.0007). Denosumab was not statistically superior to ZA in delaying time to first on-study SRE (p = 0.03 unadjusted; p = 0.06 adjusted for multiplicity) or time to first-and-subsequent (multiple) SRE (rate ratio, 0.90; 95% CI, 0.77 to 1.04; p = 0.14). Overall survival and disease progression were similar between groups. Hypocalcemia occurred more frequently with denosumab. Osteonecrosis of the jaw occurred at similarly low rates in both groups. Acute-phase reactions after the first dose occurred more frequently with ZA, as did renal adverse events and elevations in serum creatinine. The authors concluded that denosumab was noninferior to ZA in preventing or delaying first on-study SRE in patients with advanced cancer metastatic to bone or myeloma.

Fizazi et al evaluated the comparison of denosumab with zoledronic acid (ZA) for the prevention of skeletal-related events in men with bone metastases from castration-resistant prostate cancer (Fizazi, 2011). In a phase 3 clinical study, 1904 men with castration-resistant prostate cancer had no previous exposure to IV bisphosphonate were randomized 1:1 to either receive 120mg subcutaneous denosumab plus IV placebo (n = 950), or 4mg IV ZA plus subcutaneous placebo (n = 951) every 4 weeks. The primary endpoint was time to first on-study skeletal related event (pathological fracture, radiation therapy, surgery to bone, or spinal cord compression), and was assessed for non-inferiority. The same outcome was further assessed for superiority as a secondary endpoint. Efficacy analysis was by intention to treat. Median time to first on-study

skeletal-related event was 20.7 months (95% CI 18.8–24.9) with denosumab compared with 17.1 months (15.0–19.4) with zoledronic acid (hazard ratio 0.82, 95% CI 0.71–0.95; p = 0.0002 for non-inferiority; p = 0.008 for superiority). While there was a three-month increase in the time to first skeletal-related events observed with denosumab in men with prostate cancer, there was no clinically meaningful difference in skeletal-related events for denosumab as compared with zoledronic acid: Overall confirmed events (ZA vs. denosumab) 41% vs. 36%; radiation to bone (21% vs. 19%); pathological fracture (15% vs. 14%); spinal cord compression (4% vs. 3%); surgery to bone (< 1% vs. < 1%). The authors concluded that denosumab was better than ZA for delaying the time to first SRE, however, was not significantly better at preventing the overall incidence of SREs versus zoledronic acid.

Professional Societies

National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Several National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines®) include denosumab as a treatment for several conditions related to malignant disease. The following NCCN Guidelines® state (NCCN, 2023)

For giant cell tumor of the bone, the NCCN recommends (Category 2A) denosumab as a single agent or combined with serial embolization (preferred), and/or radiation therapy for resectable disease with unacceptable morbidity and/or unresectable axial lesions for patients with localized disease, metastases at presentation, or recurrence. Denosumab is also recommended as a single agent for unresectable metastatic disease, unresectable metastatic recurrence or considered prior to surgery for resectable local recurrence.

- For invasive or inflammatory breast cancer, the NCCN recommends (Category 1) denosumab to be used with calcium and vitamin D supplementation in addition to chemotherapy or endocrine therapy for bone metastasis in patients with expected survival ≥ 3 months with adequate renal function.
- For kidney cancer, the NCCN recommends (Category 2A) denosumab to be used as a component of best supportive care for bony metastases.
- For multiple myeloma, the NCCN recommends (Category 2A) denosumab to be used in combination with primary myeloma therapy and is the preferred agent in patients with renal insufficiency.

- For non-small cell lung cancer, the NCCN recommends (Category 2A) denosumab to be considered for supportive therapy in patients with bone metastases.
- For prostate cancer, the NCCN recommends (Category 1) denosumab as the preferred agent for the prevention of skeletal-related events in patients with castration-resistant prostate cancer who have documented bone metastases and creatinine clearance greater than 30 ml/min.
- For systemic mastocytosis, the NCCN recommends (Category 2A) denosumab as second-line therapy for osteopenia/osteoporosis in patients with bone pain not responding to bisphosphonates or for patients who are not candidates for bisphosphonates because of renal insufficiency.
- For thyroid carcinoma (anaplastic, follicular, Hürthle cell, medullary, papillary), the NCCN recommends (Category 2A) denosumab to be considered for bone metastases or palliative care for bone metastases (anaplastic).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Prolia (denosumab) is a RANK ligand inhibitor indicated for the following uses:

- 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.
- 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.
- 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.
- Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer. In these patients Prolia also reduced the incidence of vertebral fractures.
- Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

Xgeva (denosumab) is a RANK ligand inhibitor indicated for the prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors, the treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity, and for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy. (Amgen, 2020)

Medicare does not have a National Coverage Determination (NCD) specifically for denosumab (Xgeva® and Prolia®). Local Coverage Determinations (LCDs)/Local Coverage Articles (LCAs) exist; refer to the LCDs/LCAs for Bisphosphonates (Intravenous [IV] and Monoclonal Antibodies in the Treatment of Osteoporosis and their Other Indications and Drugs and Biologicals, Coverage of, for Label and Off-Label Uses.

In general, Medicare may cover outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual, Chapter 15, Section 50 – Drugs and Biologicals. (Accessed March 6, 2023)

Applicable Codes

HCPCS Code	Description
J0897	Injection, denosumab, 1 mg

Diagnosis Code	Description
Prolia®	
M81.8	Other osteoporosis without current pathological fracture
M80.811A	Other osteoporosis with current pathological fracture, right shoulder, initial encounter for fracture
M80.811D	Other osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with routine healing

M80.811G	Other osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with delayed healing
M80.811K	Other osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with nonunion
M80.811P	Other osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with malunion
M80.811S	Other osteoporosis with current pathological fracture, right shoulder, sequela
M80.8AXA	Other osteoporosis with current pathological fracture, other site, initial encounter for fracture
M80.8AXD	Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with routine healing
M80.8AXG	Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with delayed healing
M80.8AXK	Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with nonunion
M80.8AXP	Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with malunion
M80.8AXS	Other osteoporosis with current pathological fracture, other site, sequela
M80.812A	Other osteoporosis with current pathological fracture, left shoulder, initial encounter for fracture
M80.812D	Other osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with routine healing
M80.812G	Other osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with delayed healing
M80.812K	Other osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with nonunion
M80.812P	Other osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with malunion
M80.812S	Other osteoporosis with current pathological fracture, left shoulder, sequela
M80.819A	Other osteoporosis with current pathological fracture, unspecified shoulder, initial encounter for fracture
M80.819D	Other osteoporosis with current pathological fracture, unspecified shoulder, subsequent encounter for fracture with routine healing
M80.819G	Other osteoporosis with current pathological fracture, unspecified shoulder, subsequent encounter for fracture with delayed healing
M80.819K	Other osteoporosis with current pathological fracture, unspecified shoulder, subsequent encounter for fracture with nonunion
M80.819P	Other osteoporosis with current pathological fracture, unspecified shoulder, subsequent encounter for fracture with malunion
M80.819S	Other osteoporosis with current pathological fracture, unspecified shoulder,

	sequela
M80.821A	Other osteoporosis with current pathological fracture, right humerus, initial encounter for fracture
M80.821D	Other osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with routine healing
M80.821G	Other osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with delayed healing
M80.821K	Other osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with nonunion
M80.821P	Other osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with malunion
M80.821S	Other osteoporosis with current pathological fracture, right humerus, sequela
M80.822A	Other osteoporosis with current pathological fracture, left humerus, initial encounter for fracture
M80.822D	Other osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with routine healing
M80.822G	Other osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with delayed healing
M80.822K	Other osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with nonunion
M80.822P	Other osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with malunion
M80.822S	Other osteoporosis with current pathological fracture, left humerus, sequela
M80.829A	Other osteoporosis with current pathological fracture, unspecified humerus, initial encounter for fracture
M80.829D	Other osteoporosis with current pathological fracture, unspecified humerus, subsequent encounter for fracture with routine healing
M80.829G	Other osteoporosis with current pathological fracture, unspecified humerus, subsequent encounter for fracture with delayed healing
M80.829K	Other osteoporosis with current pathological fracture, unspecified humerus, subsequent encounter for fracture with nonunion
M80.829P	Other osteoporosis with current pathological fracture, unspecified humerus, subsequent encounter for fracture with malunion
M80.829S	Other osteoporosis with current pathological fracture, unspecified humerus, sequela
M80.831A	Other osteoporosis with current pathological fracture, right forearm, initial encounter for fracture
M80.831D	Other osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with routine healing
M80.831G	Other osteoporosis with current pathological fracture, right forearm, subsequent

	encounter for fracture with delayed healing
M80.831K	Other osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with nonunion
M80.831P	Other osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with malunion
M80.831S	Other osteoporosis with current pathological fracture, right forearm, sequela
M80.832A	Other osteoporosis with current pathological fracture, left forearm, initial encounter for fracture
M80.832D	Other osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with routine healing
M80.832G	Other osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with routine healing
M80.832K	Other osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with nonunion
M80.832P	Other osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with malunion
M80.832S	Other osteoporosis with current pathological fracture, left forearm, sequela
M80.839A	Other osteoporosis with current pathological fracture, unspecified forearm, initial encounter for fracture
M80.839D	Other osteoporosis with current pathological fracture, unspecified forearm, subsequent encounter for fracture with routine healing
M80.839G	Other osteoporosis with current pathological fracture, unspecified forearm, subsequent encounter for fracture with delayed healing
M80.839K	Other osteoporosis with current pathological fracture, unspecified forearm, subsequent encounter for fracture with nonunion
M80.839P	Other osteoporosis with current pathological fracture, unspecified forearm, subsequent encounter for fracture with malunion
M80.839S	Other osteoporosis with current pathological fracture, unspecified forearm, sequela
M80.841A	Other osteoporosis with current pathological fracture, right hand, initial encounter for fracture
M80.841D	Other osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with routine healing
M80.841G	Other osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with delayed healing
M80.841K	Other osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with nonunion
M80.841P	Other osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with malunion
M80.841S	Other osteoporosis with current pathological fracture, right hand, sequela

M80.842A	Other osteoporosis with current pathological fracture, left hand, initial encounter for fracture
M80.842D	Other osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with routine healing
M80.842G	Other osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with delayed healing
M80.842K	Other osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with nonunion
M80.842P	Other osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with malunion
M80.842S	Other osteoporosis with current pathological fracture, left hand, sequela
M80.849A	Other osteoporosis with current pathological fracture, unspecified hand, initial encounter for fracture
M80.849D	Other osteoporosis with current pathological fracture, unspecified hand, subsequent encounter for fracture with routine healing
M80.849G	Other osteoporosis with current pathological fracture, unspecified hand, subsequent encounter for fracture with delayed healing
M80.849K	Other osteoporosis with current pathological fracture, unspecified hand, subsequent encounter for fracture with nonunion
M80.849P	Other osteoporosis with current pathological fracture, unspecified hand, subsequent encounter for fracture with malunion
M80.849S	Other osteoporosis with current pathological fracture, unspecified hand, sequela
M80.851A	Other osteoporosis with current pathological fracture, right femur, initial encounter for fracture
M80.851D	Other osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with routine healing
M80.851G	Other osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with delayed healing
M80.851K	Other osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with nonunion
M80.851P	Other osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with malunion
M80.851S	Other osteoporosis with current pathological fracture, right femur, sequela
M80.852A	Other osteoporosis with current pathological fracture, left femur, initial encounter for fracture
M80.852D	Other osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with routine healing
M80.852G	Other osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with delayed healing
M80.852K	Other osteoporosis with current pathological fracture, left femur, subsequent

	encounter for fracture with nonunion
M80.852P	Other osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with malunion
M80.852S	Other osteoporosis with current pathological fracture, left femur, sequela
M80.859A	Other osteoporosis with current pathological fracture, unspecified femur, initial encounter for fracture
M80.859D	Other osteoporosis with current pathological fracture, unspecified femur, subsequent encounter for fracture with routine healing
M80.859G	Other osteoporosis with current pathological fracture, unspecified femur, subsequent encounter for fracture with delayed healing
M80.859K	Other osteoporosis with current pathological fracture, unspecified femur, subsequent encounter for fracture with nonunion
M80.859P	Other osteoporosis with current pathological fracture, unspecified femur, subsequent encounter for fracture with malunion
M80.859S	Other osteoporosis with current pathological fracture, unspecified femur, sequela
M80.861A	Other osteoporosis with current pathological fracture, right lower leg, initial encounter for fracture
M80.861D	Other osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with routine healing
M80.861G	Other osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with delayed healing
M80.861K	Other osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with nonunion
M80.861P	Other osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with malunion
M80.861S	Other osteoporosis with current pathological fracture, right lower leg, sequela
M80.862A	Other osteoporosis with current pathological fracture, left lower leg, initial encounter for fracture
M80.862D	Other osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with routine healing
M80.862G	Other osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with delayed healing
M80.862K	Other osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with nonunion
M80.862P	Other osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with malunion
M80.862S	Other osteoporosis with current pathological fracture, left lower leg, sequela
M80.869A	Other osteoporosis with current pathological fracture, unspecified lower leg, initial encounter for fracture
M80.869D	Other osteoporosis with current pathological fracture, unspecified lower leg,

	subsequent encounter for fracture with routine healing
M80.869G	Other osteoporosis with current pathological fracture, unspecified lower leg, subsequent encounter for fracture with delayed healing
M80.869K	Other osteoporosis with current pathological fracture, unspecified lower leg, subsequent encounter for fracture with nonunion
M80.869P	Other osteoporosis with current pathological fracture, unspecified lower leg, subsequent encounter for fracture with malunion
M80.869S	Other osteoporosis with current pathological fracture, unspecified lower leg, sequela
M80.871A	Other osteoporosis with current pathological fracture, right ankle and foot, initial encounter for fracture
M80.871D	Other osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with routine healing
M80.871G	Other osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with delayed healing
M80.871K	Other osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with nonunion
M80.871P	Other osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with malunion
M80.871S	Other osteoporosis with current pathological fracture, right ankle and foot, sequela
M80.872A	Other osteoporosis with current pathological fracture, left ankle and foot, initial encounter for fracture
M80.872D	Other osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with routine healing
M80.872G	Other osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with delayed healing
M80.872K	Other osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with nonunion
M80.872P	Other osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with malunion
M80.872S	Other osteoporosis with current pathological fracture, left ankle and foot, sequela
M80.879A	Other osteoporosis with current pathological fracture, unspecified ankle and foot, initial encounter for fracture
M80.879D	Other osteoporosis with current pathological fracture, unspecified ankle and foot, subsequent encounter for fracture with routine healing
M80.879G	Other osteoporosis with current pathological fracture, unspecified ankle and foot, subsequent encounter for fracture with delayed healing
M80.879K	Other osteoporosis with current pathological fracture, unspecified ankle and foot, subsequent encounter for fracture with nonunion

M80.879P	Other osteoporosis with current pathological fracture, unspecified ankle and foot, subsequent encounter for fracture with malunion
M80.879S	Other osteoporosis with current pathological fracture, unspecified ankle and foot, sequela
M80.88XA	Other osteoporosis with current pathological fracture, vertebra(e), initial encounter for fracture
M80.88XD	Other osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with routine healing
M80.88XG	Other osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with delayed healing
M80.88XK	Other osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with nonunion
M80.88XP	Other osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with malunion
M80.88XS	Other osteoporosis with current pathological fracture, vertebra(e), sequela
Z78.310	Personal history of (healed) osteoporosis fracture

Diagnosis Code	Description
Xgeva®	
C61	Malignant neoplasm of prostrate
C79.00	Secondary malignant neoplasm of unspecified kidney and renal pelvis
C79.01	Secondary malignant neoplasm of right kidney and renal pelvis
C79.02	Secondary malignant neoplasm of left kidney and renal pelvis
C79.10	Secondary malignant neoplasm of unspecified urinary organs
C79.11	Secondary malignant neoplasm of bladder
C79.19	Secondary malignant neoplasm of other urinary organs
C79.2	Secondary malignant neoplasm of skin
C79.31	Secondary malignant neoplasm of brain
C79.32	Secondary malignant neoplasm of cerebral meninges
C79.40	Secondary malignant neoplasm of unspecified part of nervous system
C79.49	Secondary malignant neoplasm of other parts of nervous system
C79.51	Secondary malignant neoplasm of bone
C79.52	Secondary malignant neoplasm of bone marrow
C79.60	Secondary malignant neoplasm of unspecified ovary
C79.61	Secondary malignant neoplasm of right ovary

C79.62	Secondary malignant neoplasm of left ovary
C79.63	Secondary malignant neoplasm of bilateral ovaries
C79.70	Secondary malignant neoplasm of unspecified adrenal gland
C79.71	Secondary malignant neoplasm of right adrenal gland
C79.72	Secondary malignant neoplasm of left adrenal gland
C79.81	Secondary malignant neoplasm of breast
C79.82	Secondary malignant neoplasm of genital organs
C79.89	Secondary malignant neoplasm of other specified sites
C79.9	Secondary malignant neoplasm of unspecified site
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse
D47.02	Systemic mastocytosis
D48.0	Neoplasm of uncertain behavior of bone and articular cartilage
E83.52	Hypercalcemia

Exclusions

The use of <Drug> will not be covered for the following situations:

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