Medical Policy Bulletin
Title:
Denosumab (Prolia®, Xgeva®) and related biosimilars, and Romosozumab-aqqg (Evenity®)
Policy #: MA08.052n

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

MEDICALLY NECESSARY

DENOSUMAB (PROLIA) AND RELATED BIOSIMILARS
Initial Therapy

Denosumab (Prolia) and related biosimilars, administered subcutaneously by a professional provider, are considered medically necessary and, therefore, covered for the following indications:

- Treatment of postmenopausal individuals with a documented diagnosis of osteoporosis (defined as T-score less than or equal to -2.5 for osteoporosis or documented history of an osteoporotic non-collision fracture [e.g., vertebral, hip, nonvertebral]) when **EITHER** of the criteria listed below are met:
    - The individual has multiple risk factors for fracture (e.g., endocrine disorders, gastrointestinal disorders, use of medications associated with low bone mass or bone loss [e.g., daily systemic glucocorticoids and expected to continue for at least three months])
    - The individual has or has had **ONE** of the following:
        - Documented intolerance to at least one other osteoporosis medicine (e.g., oral or injectable bisphosphonates, estrogens) due to side effects
        - Documented inadequate response from at least one other available osteoporosis medicine (e.g., oral or injectable bisphosphonates, estrogens) after a trial of 12 months
        - A severely deteriorated condition indicating that the osteoporosis is so significant that a trial of bisphosphonates is not medically warranted (e.g., very low T-score [less than -3.0], high risk for falls/history of injurious falls, very high fracture probability by fracture risk assessment tool [FRAX] [e.g., major osteoporosis fracture >30 percent, hip fracture >4.5 percent])
        - Documented moderate to severe renal insufficiency (glomerular filtration rate [GFR] 30 to 35 mL/min or less)

- Treatment of males (genotypic males) 50 years of age and older with a documented diagnosis of osteoporosis (defined as T-score less than or equal to -2.5 for osteoporosis or documented history of an osteoporotic non-collision fracture [e.g., vertebral, hip, nonvertebral]) when **EITHER** of the criteria listed below are met:
    - The individual has multiple risk factors for fracture (e.g., endocrine disorders, gastrointestinal disorders, use of medications associated with low bone mass or bone loss [e.g., daily systemic glucocorticoids and expected to continue for at least three months])
    - The individual has or has had **ONE** of the following:
        - Documented intolerance to at least one other osteoporosis medicine (e.g., oral or injectable bisphosphonates) due to side effects
        - Documented inadequate response from at least one other available osteoporosis medicine (e.g., oral or injectable bisphosphonates) after a trial of 12 months
        - A severely deteriorated condition indicating that the osteoporosis is so significant that a trial of bisphosphonates is not medically warranted (e.g., very low T-score [less than -3.0], high risk for falls/history of injurious falls, very high fracture probability by FRAX [e.g., major osteoporosis fracture >30 percent, hip fracture >4.5 percent])
        - Documented moderate to severe renal insufficiency (glomerular filtration rate [GFR] 30 to 35 mL/min or less)
- Treatment of individuals less than 50 years of age with documented diagnosis of glucocorticoid-induced osteoporosis **AND** history of an osteoporotic non-collision fracture contributing to high risk for fracture when **ALL** of the following criteria are met:
    - The individual is initiating or continuing daily systemic glucocorticoids and expected to continue for at least three months
    - The individual is not pregnant and is using effective contraception during therapy
    - The individual has or has had **ONE** of the following:
        - Documented intolerance to at least one other osteoporosis medicine (e.g., oral or injectable bisphosphonates, estrogens) due to side effects
        - Documented inadequate response from at least one other available osteoporosis medicine (e.g., oral or injectable bisphosphonates, estrogens) after a trial of 12 months
        - A severely deteriorated condition indicating that the osteoporosis is so significant that a trial of bisphosphonates is not medically warranted (e.g., very low T-score [less than -3.0], high risk for falls/history of injurious falls, very high fracture probability by FRAX [e.g., major osteoporosis fracture >30 percent, hip fracture >4.5 percent])
        - Documented moderate to severe renal insufficiency (glomerular filtration rate [GFR] 30 to 35 mL/min or less)
- Treatment of osteopenia (defined as T-score less than -1.0, but greater than -2.5), when the individual meets **EITHER** of the following criteria:
    - Receiving adjuvant aromatase inhibitor therapy for breast cancer (either invasive [with lobular, mixed, metaplastic, ductal/NST, micropapillary, pure tubular, pure mucinous, pure cribriform, encapsulated or solid papillary carcinoma, other rare forms, adenoid cystic and other salivary carcinomas, secretory carcinoma, rare low-grade forms of metaplastic carcinoma histology, ductal carcinoma in situ] or inflammatory) (assure that the individual is not pregnant and is using effective contraception during therapy)
    - Receiving androgen deprivation therapy for nonmetastatic prostate cancer
- Treatment of males (genotypic males) 50 years of age and older or postmenopausal individuals with a diagnosis of osteopenia (defined as T-score less than -1.0 but greater than -2.5) when the individual meets **BOTH** of the following criteria:
    - The individual has or has had **ONE** of the following:
        - Documented intolerance to at least one other osteoporosis medicine (e.g., oral or injectable bisphosphonates, estrogens) due to side effects
        - Documented inadequate response from at least one other available osteoporosis medicine (e.g., oral or injectable bisphosphonates, estrogens) after a trial of 12 months
        - Documented moderate to severe renal insufficiency (glomerular filtration rate [GFR] 30 to 35 mL/min or less) not receiving dialysis or diagnosed with stage 5 kidney disease
    - The individual has **ONE** of the following:
        - US-adapted World Health Organization (WHO) 10-year probability of a hip fracture based on the Fracture Risk Assessment tool (FRAX) assessment is three percent or more
        - US-adapted WHO 10-year fracture probability of any major osteoporosis-related fracture based on the FRAX assessment is 20 percent or more

Continuation Therapy

Denosumab (Prolia) and related biosimilars are considered medically necessary and, therefore, covered for continuation therapy unless the individual has a documented intolerance, contraindication, or nonresponse to the drug.

ROMOSOZUMAB-AQQG (EVENITY)
Romosozumab-aqqg (Evenity), administered subcutaneously by a professional provider, for a limited duration of 12 monthly doses is considered medically necessary and, therefore, covered for the following indication:

- Treatment of postmenopausal individuals with a documented diagnosis of osteoporosis (defined as T-score less than or equal to -2.50 for osteoporosis or documented history of an osteoporotic non-collision fracture [e.g., vertebral, hip, nonvertebral]) when **EITHER** of the criteria listed below are met:
    - The individual has multiple risk factors for fracture (e.g., endocrine disorders, gastrointestinal disorders, use of medications associated with low bone mass or bone loss [e.g., daily systemic glucocorticoids and expected to continue for at least three months])
    - The individual has or has had a documented intolerance due to side effects, or inadequate response after a trial of 12 months to at least one other osteoporosis medicine (e.g., oral or injectable bisphosphonates, estrogens, Receptor Activator of Nuclear factor Kappa-B [RANK] ligand inhibitor [e.g. denosumab {Prolia} and related biosimilars])

Romosozumab-aqqg (Evenity) is not recommended for individuals with a history of a myocardial infarction or stroke within the preceding year; (consider benefit versus risk in individuals with other cardiovascular risk factors).

Note:
The anabolic effect of romosozumab-aqqg (Evenity) wanes after 12 monthly doses of therapy. Therefore, the duration of romosozumab-aqqg (Evenity) use is limited to 12 monthly doses. If osteoporosis therapy remains warranted after medical necessary romosozumab-aqqg (Evenity), continued therapy with an anti-resorptive agent (e.g., denosumab [Prolia] and related biosimilars, alendronate [Fosamax, Binosto]) should be considered.

DENOSUMAB (XGEVA) AND RELATED BIOSIMILARS
Denosumab (Xgeva) and related biosimilars, administered subcutaneously by a professional provider, are considered medically necessary and, therefore, covered for the following indications (assure that the individual is not pregnant and is using effective contraception during therapy):

- Prevention of skeletal-related events (i.e., pathologic fracture, need for radiation therapy to bone, need for surgery to bone, or spinal cord compression) in individuals with bone metastases from solid tumors. These include, but are not limited to, the following malignancy-related conditions:
    - Invasive (with lobular, mixed, metaplastic, ductal/NST, micropapillary, pure tubular, pure mucinous, pure cribriform, encapsulated or solid papillary carcinoma, other rare forms, adenoid cystic and other salivary carcinomas, secretory carcinoma, rare low-grade forms of metaplastic carcinoma histology) or inflammatory breast cancer:
        - Used with calcium and vitamin D supplementation in addition to chemotherapy or endocrine therapy for bone metastases in individuals with expected survival of three months or greater and adequate renal function
    - Non-small cell lung cancer (with squamous cell carcinoma, adenocarcinoma [with mixed subtypes], or large cell carcinoma histology):
        - Supportive therapy in individuals with bony metastases
    - Prostate cancer:
        - Individuals with bone metastases from castration-resistant prostate cancer (metastatic prostate cancer that has stopped responding to androgen deprivation therapy and continues to grow) with creatinine clearance greater than 30 mL/min (National Comprehensive Cancer Network [NCCN] preferred)
    - Thyroid cancer:
        - Individuals with bone metastases from any of the following thyroid cancer types: follicular, Hurthle cell/oncocytic, medullary, papillary carcinoma
        - Palliative care for bone metastases in individuals with anaplastic carcinoma
    - Kidney cancer (with either clear cell or non-clear cell histology):
        - As a component of best supportive care for individuals with bony metastases
- Prevention of skeletal-related events (i.e., pathologic fracture, need for radiation therapy to bone, need for surgery to bone, or spinal cord compression) in individuals with multiple myeloma
    - Used in combination with primary myeloma therapy. NCCN-preferred agent in individuals with renal insufficiency

- Treatment of adult and skeletally mature (i.e., at least one mature long bone [e.g., closed epiphyseal growth plate of the humerus]) adolescent individuals with a giant cell tumor of the bone (GCTB) in the following circumstances:
    - When the GCTB is unresectable or where surgical resection is likely to result in severe morbidity
    - Treatment as a single agent (NCCN preferred) or combined with serial embolization, (NCCN preferred) and/or radiation therapy for resectable disease with unacceptable morbidity and/or unresectable axial lesions for individuals with localized disease, metastases at presentation, or disease recurrence
    - Treatment as a single agent (NCCN preferred) for unresectable metastatic disease at presentation, unresectable metastatic recurrence, or considered prior to surgery for resectable local recurrence
- Treatment of individuals with hypercalcemia of malignancy (i.e., albumin-corrected serum calcium level greater than 12.5 mg/dL [3.1 mmol/L]) refractory to bisphosphonate therapy
- Treatment of individuals with systemic mastocytosis as a second-line therapy for osteopenia/osteoporosis in individuals with bone pain not responding to bisphosphonates or for individuals who are not candidates for bisphosphonates because of renal insufficiency.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for denosumab (Prolia, Xgeva) and related biosimilars, and romosozumab-aqqg (Evenity) are considered experimental/investigational and, therefore, not covered, unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Guidelines

There is no Medicare coverage criteria addressing this service; therefore, the Company policy is applicable.

According to the US Food and Drug Administration (FDA)-approved label, individuals with severe renal impairment (creatinine clearance less than 30 mL/min) or receiving dialysis have a significant risk of developing hypocalcemia following denosumab (Prolia, Xgeva) and related biosimilars administration.

BLACK BOX WARNINGS

Refer to the specific manufacturer's prescribing information for any applicable Black Box Warnings.

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

Denosumab (Prolia) and related biosimilars was approved by the US Food and Drug Administration (FDA) with a risk evaluation and mitigation strategy (REMS). The goal was to ensure that the benefits of the drug outweigh the risks of hypocalcemia, osteonecrosis of the jaw, atypical femoral fractures, serious infections, and dermatologic reactions.

DENOSUMAB (PROLIA, XGEVA)

Because Prolia and Xgeva and related biosimilars have the same active ingredient, and can be used for different indications, they should not be used in combination.

CALCIUM AND VITAMIN D SUPPLEMENTATION

Hypocalcemia should be corrected before initiating therapy with denosumab (Prolia, Xgeva) and related biosimilars or romosozumab-aqqg (Evenity). Supplements of calcium and vitamin D orally once daily are taken when receiving denosumab (Prolia, Xgeva) and related biosimilars or romosozumab-aqqg (Evenity) for the treatment of osteoporosis in individuals who are at high risk for fracture or for the prevention of skeletal-related events in individuals with bone metastases from solid tumors. New-onset or worsening hypocalcemia may result from use of denosumab (Prolia, Xgeva) and related biosimilars or romosozumab-aqqg (Evenity). Clinical monitoring of serum calcium and mineral levels (phosphorus and magnesium) is highly recommended, and symptoms of hypocalcemia should be monitored during therapy with denosumab (Prolia, Xgeva) and related biosimilars or romosozumab-aqqg (Evenity).

The National Osteoporosis Foundation (now called the Bone Health and Osteoporosis Foundation [BHOF]) supports the recommendation of the Institute of Medicine that men (genotypic males) ages 50-70 consume 1000 mg/day of calcium and women (genotypic females) ages 51 and older and men (genotypic males) ages 71 and older consume 1200 mg/day of calcium. In addition, the BHOF recommends an intake of 800 to 1000 IU of vitamin D per day for adults ages 50 and older.

INABILITY TO TAKE ORAL BISPHOSPHONATES FOR OSTEOPOROSIS

Individuals with any of the following conditions are considered inappropriate candidates for oral bisphosphonate therapy:

- Difficulty swallowing oral medications
- Inability to sit upright for 30 to 60 minutes
- Active esophagitis, gastritis, or gastric ulcer
- Esophageal stricture
- Esophageal motility disorder

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable Evidence of Coverage, denosumab (Prolia, Xgeva) and related biosimilars or romosozumab-aqqg (Evenity) are covered under the medical benefits of the Company’s Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

Certain drugs are available either through the member's medical benefit (Part B benefit) or through the member's pharmacy benefit (Part D benefit), depending on how the drug is prescribed, dispensed, or administered. This medical policy only addresses instances when denosumab (Prolia, Xgeva) and related biosimilars or romosozumab-aqqg (Evenity) are covered under a member's medical benefit. It does not address instances when denosumab (Prolia, Xgeva) and related biosimilars or romosozumab-aqqg (Evenity) are covered under a member’s pharmacy benefit (Part D benefit).

US FOOD AND DRUG ADMINISTRATION STATUS

Denosumab (Prolia) was approved by the US Food and Drug Administration (FDA) on June 1, 2010 for the treatment of postmenopausal individuals with osteoporosis at high risk for fracture. Supplemental approvals for denosumab (Prolia) have since been issued by the FDA. The FDA has issued subsequent approvals for related biosimilar products (e.g., denosumab-bbdz [Jubbonti]).

Denosumab (Xgeva) was approved by the FDA on November 18, 2010 for the prevention of skeletal-related events in individuals with bone metastases from solid tumors. Supplemental approvals for denosumab (Xgeva) have since been issued by the FDA. The FDA has issued subsequent approvals for related biosimilar products (e.g., denosumab-bbdz [Wyost]).

According to the US Food and Drug Administration (FDA), “a biosimilar is a biological product that has no clinically meaningful differences from the existing FDA-approved reference product. All biosimilar products meet the FDA's rigorous standards for approval for the indications described in the product labeling. Once a biosimilar has been approved by the FDA, the safety and effectiveness of these products have been established, just as they have been for the reference product." Coverage of a biosimilar product as an alternate to a reference product is not considered a form of step therapy by the Company.

Romosozumab-aqqg (Evenity) was approved by the FDA on April 9, 2019 for the treatment of postmenopausal individuals with osteoporosis at high risk for fracture with a limited duration of use to 12 monthly doses.

PEDIATRIC USE OF DENOSUMAB AND RELATED BIOSIMILARS, OR ROMOSOZUMAB-AQQG
Denosumab (Prolia) and related biosimilars: The safety and effectiveness of denosumab (Prolia) and related biosimilars in pediatric individuals have not been established. Denosumab (Prolia) and related biosimilars are not recommended in pediatric individuals.

Romosozumab-aqqg (Evenity): The safety and effectiveness of romosozumab-aqqg (Evenity) in pediatric individuals have not been established. Romosozumab-aqqg (Evenity) is not recommended in pediatric individuals.

Denosumab (Xgeva) and related biosimilars: The safety and effectiveness of denosumab (Xgeva) and related biosimilars have not been established in pediatric individuals except in skeletally mature adolescents with giant cell tumor of bone.

Description

DENOSUMAB

Denosumab is a human immunoglobulin G2 (IgG2) monoclonal antibody with affinity and specificity for human receptor activator of nuclear factor kappa-B ligand (RANKL). RANKL is a membrane protein that is essential for osteoclasts, cells that are responsible for bone resorption. Increased osteoclast activity, stimulated by RANKL, is a mediator of bone pathology in solid tumors with bone metastases. Denosumab binds to RANKL, thereby decreasing bone resorption and increasing bone mass and strength.

Hypocalcemia may be exacerbated by the use of denosumab; therefore, pre-existing hypocalcemia must be corrected prior to initiating therapy with denosumab. In individuals who are predisposed to hypocalcemia and disturbances of mineral metabolism (e.g., history of hypoparathyroidism, thyroid surgery, parathyroid surgery, excision of small intestine, severe renal impairment or dialysis, malabsorption syndromes), clinical monitoring of calcium, phosphorus, and magnesium levels is highly recommended.

Denosumab is available under two different US Food and Drug Administration (FDA)-approved trade names: Prolia and Xgeva. Denosumab is also available under the names of FDA-approved related biosimilars.

PROLIA

Osteoporosis is characterized by low bone mass, deterioration of bone tissue, disruption of bone architecture, compromised bone strength, and increased risk for fracture. According to the World Health Organization (WHO) diagnostic classification, osteoporosis is operationally defined by measurement of bone mineral density (BMD) at the hip or spine that is less than or equal to 2.5 standard deviations (SD) below the young normal mean reference population. In describing BMD, T-scores compare bone density to the optimal peak bone density for an individual's gender. A T-score is the number of units (standard deviations) above (+) or below (-) what is considered standard. A T-score is within the normal range if it is a positive number, or at least no more negative than -1.0. The more negative the number, the thinner the bones. A T-score less than -1.0 but greater than -2.5 is considered osteopenia, and a risk for developing osteoporosis. A T-score of less than -2.5 is indicative of osteoporosis. The WHO definition applies to postmenopausal individuals as well as men (genotypic males) aged 50 years or older. Half of all postmenopausal individuals will have an osteoporosis-related fracture during their lives; of those, 25 percent will develop a vertebral deformity, and 15 percent will sustain a hip fracture. According to the National Osteoporosis Foundation (now called the Bone Health and Osteoporosis Foundation [BHOF]), two million men (genotypic males) in the US have osteoporosis and another 12 million are at risk. Osteoporosis and osteoporotic fractures in men (genotypic males) remain under-diagnosed and under-treated.

Denosumab was originally approved under the trade name of Prolia in June 2010. Denosumab (Prolia) is indicated to treat postmenopausal individuals with osteoporosis who are at risk for bone fractures. In September 2011, denosumab (Prolia) was approved for treatment of bone loss in men (genotypic males) receiving androgen deprivation therapy in prostate cancer and for treatment of bone loss in women (genotypic females) receiving adjuvant aromatase inhibitor therapy for breast cancer. A new indication was approved for denosumab (Prolia) in September 2012 for the treatment to increase bone mass in men (genotypic males) with osteoporosis.

The FDA approval of denosumab (Prolia) for the treatment of osteoporosis in postmenopausal individuals who are at high risk of fracture is based on a pivotal three-year, Phase 3 study involving 7,808 postmenopausal individuals with osteoporosis who had a baseline BMD T-score between -2.5 and -4.0 at either the lumbar spine or total hip. A subcutaneous injection of denosumab (Prolia) 60 mg was administered every six months. All women (genotypic females) in the study received at least 1000 mg calcium orally once daily and at least 400 IU of vitamin D orally once daily. Denosumab (Prolia) reduced the incidence of vertebral, hip, and nonvertebral fractures. Over three years, denosumab (Prolia) significantly reduced the incidence of new vertebral fractures by 68 percent, reduced the incidence of hip fractures by 40 percent, and reduced the incidence of non-spine fractures by 20 percent.

The approval of denosumab (Prolia) for the treatment of low bone mass in women (genotypic females) at high risk for fracture who are receiving adjuvant aromatase inhibitor therapy for breast cancer is based on a two-year, randomized, double-blind, placebo-controlled, multinational study that enrolled women (genotypic females) with breast cancer. Women (genotypic females) in this study had a baseline BMD T-score between -1.0 and -2.5 and had not experienced fracture after age 25. All women (genotypic females) received at least 1000 mg calcium and 400 IU vitamin D daily. After two years denosumab (Prolia) significantly improved BMD in these individuals by 6.2 percent at the lumbar spine, 3.8 percent at the total hip, and 2.8 percent at the femoral neck.

Approval of denosumab (Prolia) for the treatment of low bone mass in men (genotypic males) at high risk for fracture who are receiving androgen-deprivation therapy (ADT) for nonmetastatic prostate cancer is based on a three-year trial that enrolled 1,468 individuals who had prostate cancer and were required to have a BMD T-score between -1.0 and -4.0, or history of osteoporotic fracture. Denosumab (Prolia) significantly increased lumbar spine BMD and significantly reduced the incidence of new vertebral fractures.

In September 2012 denosumab (Prolia) was approved by the FDA for the treatment to increase bone mass in men (genotypic males) with osteoporosis based on results from the ADAMO trial 3 (A multicenter, randomized, double-blind, placebo-controlled study to examine the efficacy and safety of DenosumAb [Prolia] 60 mg every six months vs placebo in Men with Osteoporosis). The pivotal Phase 3 study involved 242 men (genotypic males) with low BMD of T-score between -2.0 and -3.5 at the lumbar spine or femoral neck or a T-score between -1.0 and -3.5 at the lumbar spine or femoral neck with a history of prior fragility fracture. All men (genotypic males) received at least 1000 mg of calcium and at least 800 IU vitamin D daily. In the study, treatment with denosumab (Prolia) resulted in significantly greater gains at the lumbar spine when compared to placebo (5.7 percent vs. 0.9 percent). Effects of denosumab (Prolia) on BMD were independent of age, baseline testosterone levels, BMD status, and estimated fracture risk. Safety findings were consistent with those observed in other studies of Prolia in postmenopausal individuals with osteoporosis.

In May 2018, denosumab (Prolia) was approved by the FDA for the treatment of glucocorticoid-induced osteoporosis in individuals at high risk for fracture who are either initiating or continuing systemic glucocorticoids in a daily dosage equivalent to greater than or equal to 7.5 mg of prednisone and expected to remain on glucocorticoids for at least six months.

The efficacy and safety of denosumab (Prolia) in the treatment of individuals with glucocorticoid-induced osteoporosis was assessed in the 12 month primary analysis of a two year, randomized, multicenter, double-blind, parallel-group, active-controlled study of 795 individuals (70 percent women [genotypic females] and 30 percent men [genotypic males]) aged 20 to 94 years (mean age of 63 years) treated with greater than or equal to 7.5 mg/day oral prednisone (or equivalent) for less than three months prior to study enrollment and planning to continue treatment for a total of at least six months (glucocorticoid-initiating subpopulation; n = 290) or greater than or equal to three months prior to study enrollment and planning to continue treatment for a total of at least six months (glucocorticoid-continuing subpopulation, n = 505). Randomization was stratified by gender within each subpopulation. Individuals received at least 1000 mg calcium and 800 IU vitamin D supplementation daily. Enrolled individuals less than 50 years of age were required to have a history of osteoporotic fracture. Enrolled individuals greater than or equal to 50 years of age who were in the glucocorticoid-continuing subpopulation were required to have a baseline BMD T-score of less than or equal to -2.0 at the lumbar spine, total hip, or femoral neck; or a BMD T-score less than or equal to -1.0 at the lumbar spine, total hip, or femoral neck and a history of osteoporotic fracture.

Results showed that compared to the active-control, treatment with denosumab (Prolia) significantly increased lumbar spine BMD at one year in the glucocorticoid-initiating subpopulation ($p<.001$). In the glucocorticoid-continuing subpopulation, treatment with denosumab (Prolia) was associated with significant increases in lumbar spine BMD compared with active-control ($p<.001$). The safety of denosumab (Prolia) was found to be consistent with previous trials (Saag et al, 2018).

XGEVA

Weakened bones due to cancer metastases can lead to fractures and compression of the spinal cord. They necessitate procedures such as surgery and radiation, which are designed to prevent or manage bone complications. The primary goal of treatment for bone metastases is to prevent the occurrence of debilitating bone complications that can affect an individual's quality of life. The major cancer types that tend to metastasize to the bone include breast, lung, prostate, thyroid, and kidney.

In January 2018, denosumab received a Supplemental Biologic License Application approval under denosumab (Xgeva) for prevention of skeletal-related events (SREs) in individuals with multiple myeloma. The efficacy was evaluated in an international, randomized double-blinded, active controlled, noninferiority trial comparing denosumab (Xgeva) with zoledronic acid in 1,718 newly diagnosed individuals with multiple myeloma. The main efficacy outcome measure was noninferiority of time to first SRE. Denosumab (Xgeva) was significantly noninferior to zoledronic acid in delaying the time to the first SRE.

In November 2010, denosumab received a Supplemental Biologic License Application approval under denosumab (Xgeva) for prevention of SREs in individuals with bone metastases from solid tumors, which are abnormal masses of tissue that usually do not contain cysts or liquid areas. In June 2013, denosumab (Xgeva) was approved for use in adults and skeletally mature adolescents for the treatment of giant cell tumor of bone (GCTB) that is unresectable or where surgical resection is likely to result in severe morbidity. In December 2014, denosumab (Xgeva) received FDA approval for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

The safety and effectiveness of denosumab (Xgeva) was confirmed in three randomized, double-blind studies of 5,723 individuals, comparing denosumab (Xgeva) with zoledronic acid (Zometa). One study involved individuals with breast cancer, the second study involved individuals with prostate cancer, and the third study involved individuals with a variety of other cancers. The studies were designed to measure the time until the occurrence of an SRE. SREs include pathological fracture, spinal cord compression due to cancer, or the need for radiation therapy or surgery to bone. In each trial, denosumab (Xgeva) was noninferior to zoledronic acid (Zometa) for the delay of time-to-first SRE in patients with bone metastasis from solid tumors. Supportive outcome measures were superiority of time-to-first SRE and superiority of time-to-first and subsequent SRE; testing for these outcome measures occurred if the main outcome measure was statistically significant.

In June 2013, denosumab (Xgeva) was granted FDA approval for treatment of GCTB, a rare and usually non-cancerous tumor usually occurring in adults between the ages of 20 and 40 years of age. Most of the time, GCTB does not spread to other areas of the body, but destroys normal bone as it grows, which causes pain, limited range of motion, and bone fractures. On rare occasion, GCTB can transform into a cancerous tumor that spreads to the lungs.

Denosumab (Xgeva) is intended for persons with GCTB who are not surgical candidates or when surgery would result in severe morbidity. The safety and effectiveness of denosumab (Xgeva) for use in GCTB is based on two open-label trials involving187 persons who had tumors that could be measured; of this group, 47 individuals experienced a reduction in the size of their tumors. In a follow-up, occurring on average 20 months later, re-growth of GCTB occurred in three individuals whose tumors had originally become smaller during the treatment phase.

The approval of denosumab (Xgeva) for individuals with hypercalcemia was based on an open-label, single-arm trial that assessed safety and effectiveness in 33 individuals with hypercalcemia of malignancy refractory to bisphosphonate therapy. In the trial refractory hypercalcemia of malignancy was defined as an albumin-corrected calcium of >12.5 mg/dL despite treatment with intravenous bisphosphonate therapy in seven to 30 days prior to denosumab (Xgeva) therapy. The median time of complete response was 23 days with a median duration of complete response of 34 days.

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company’s off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

The related biosimilars for denosumab (Prolia, Xgeva) are FDA-approved for the same indications as the originator drugs.

ROMOSOZUMAB-AQQG (EVENITY)

On April 9, 2019, romosozumab-aqqg (Evenity) was approved by the FDA for the treatment of osteoporosis in postmenopausal individuals at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk

factors for fracture; or failed or are intolerant to other available osteoporosis therapy.
Romosozumab-aqqg (Evenity) is a monoclonal antibody that binds to and inhibits sclerostin (a regulatory factor in bone metabolism), increases bone formation, and to a lesser extent, decreases bone resorption. The FDA based its approval of Romosozumab-aqqg (Evenity) on the results of two Phase 3 studies.

FRAME (FRActure study in postmenopausal woMen with osteoporosis) study is a randomized, double-blind, placebo-controlled study that evaluated 7,180 postmenopausal individuals with osteoporosis. The study evaluated the efficacy of romosozumab-aqqg (Evenity) treatment (210 mg administered monthly), compared with placebo, in reducing the incidence of new vertebral fractures through 12 months. The study also evaluated the efficacy of treating with romosozumab-aqqg (Evenity) for 12 months followed by denosumab (Prolia) for 12 months, compared with placebo followed by denosumab (Prolia), in reducing the incidence of new vertebral fractures through 24 months. The study showed that individuals randomly assigned to receive a monthly subcutaneous 210 mg dose of romosozumab (Evenity) experienced a statistically significant 73 percent reduction in the relative risk of a new vertebral (spine) fracture through 12 months, the first co-primary endpoint, compared to those receiving placebo (fracture incidence 0.5 percent versus 1.8 percent, respectively [p<0.001]). Of interest, the data showed that by six months, new vertebral fractures occurred in 14 romosozumab (Evenity) and 26 placebo individuals, and between six to 12 months, fractures occurred in two additional romosozumab (Evenity) individuals versus 33 additional placebo individuals.

ARCH (Active-contRolled FraCture Study in Postmenopausal Women with Osteoporosis at High Risk of Fracture) is a Phase 3 multicenter, international, randomized, double-blind, alendronate-controlled study of romosozumab-aqqg (Evenity) involving 4,093 postmenopausal individuals with osteoporosis at high risk for fracture based on previous fracture history. The study evaluated 12 months of subcutaneous romosozumab-aqqg (Evenity) treatment (210 mg administered monthly) followed by at least 12 months of alendronate treatment (70 mg), compared with weekly oral alendronate (70mg) treatment alone, followed by open-label alendronate in both groups. The primary end points were the cumulative incidence of new vertebral fracture at 24 months and the cumulative incidence of clinical fracture (nonvertebral and symptomatic vertebral fracture) at the time of the primary analysis (after clinical fractures had been confirmed in greater than or equal to 330 participants). Secondary end points included the incidences of nonvertebral and hip fracture at the time of the primary analysis. Serious cardiovascular adverse events, osteonecrosis of the jaw, and atypical femoral fractures were adjudicated.

Over a period of 24 months, a 48 percent lower risk of new vertebral fractures was observed in the romosozumab-to-alendronate group (6.2 percent [127 of 2,046 individuals]) than in the alendronate-to-alendronate group (11.9 percent [243 of 2,047 individuals]) (P<0.001). Clinical fractures occurred in 198 of 2,046 individuals (9.7 percent) in the romosozumab-to-alendronate group versus 266 of 2,047 individuals (13.0 percent) in the alendronate-to-alendronate group, representing a 27 percent lower risk with romosozumab-aqqg (Evenity) (P<0.001). The risk of nonvertebral fractures was lower by 19 percent in the romosozumab-to-alendronate group than in the alendronate-to-alendronate group (178 of 2,046 individuals [8.7 percent] vs. 217 of 2,047 individuals [10.6 percent]; P=0.04), and the risk of hip fracture was lower by 38 percent (41 of 2,046 individuals [2.0 percent] vs. 66 of 2,047 individuals [3.2 percent]; P=0.02). Overall adverse events and serious adverse events were balanced between the two groups. During year one, positively adjudicated serious cardiovascular adverse events were observed more often with romosozumab-aqqg (Evenity) than with alendronate (50 of 2,040 individuals [2.5 percent] vs. 38 of 2,014 individuals [1.9 percent]). During the open-label alendronate period, adjudicated events of osteonecrosis of the jaw (one event each in the romosozumab-to-alendronate and alendronate-to-alendronate groups) and atypical femoral fracture (two events and four events, respectively) were observed. The authors concluded that in postmenopausal individuals with osteoporosis who were at high risk for fracture, romosozumab-aqqg (Evenity) treatment for 12 months followed by alendronate resulted in a significantly lower risk of fracture than alendronate alone. The anabolic effect of romosozumab-aqqg (Evenity) wanes after 12 monthly doses of therapy. Therefore, the duration of romosozumab-aqqg (Evenity) use should be limited to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an anti-resorptive agent should be considered.

OFF-LABEL INDICATIONS

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)

N/A

ICD - 10 Procedure Code Number(s)

N/A

ICD - 10 Diagnosis Code Number(s)

DENOSUMAB (PROLIA) IS MEDICALLY NECESSARY WHEN REPORTED WITH THE FOLLOWING DIAGNOSIS CODES:

M80.011A	Age-related osteoporosis with current pathological fracture, right shoulder, initial encounter for fracture
M80.011D	Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with routine healing
M80.011G	Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with delayed healing
M80.011K	Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with nonunion
M80.011P	Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with malunion
M80.011S	Age-related osteoporosis with current pathological fracture, right shoulder, sequela
M80.012A	Age-related osteoporosis with current pathological fracture, left shoulder, initial encounter for fracture
M80.012D	Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with routine healing

M80.012G	Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with delayed healing
M80.012K	Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with nonunion
M80.012P	Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with malunion
M80.012S	Age-related osteoporosis with current pathological fracture, left shoulder, sequela
M80.021A	Age-related osteoporosis with current pathological fracture, right humerus, initial encounter for fracture
M80.021D	Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with routine healing
M80.021G	Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with delayed healing
M80.021K	Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with nonunion
M80.021P	Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with malunion
M80.021S	Age-related osteoporosis with current pathological fracture, right humerus, sequela
M80.022A	Age-related osteoporosis with current pathological fracture, left humerus, initial encounter for fracture
M80.022D	Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with routine healing
M80.022G	Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with delayed healing
M80.022K	Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with nonunion
M80.022P	Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with malunion
M80.022S	Age-related osteoporosis with current pathological fracture, left humerus, sequela
M80.031A	Age-related osteoporosis with current pathological fracture, right forearm, initial encounter for fracture
M80.031D	Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with routine healing
M80.031G	Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with delayed healing
M80.031K	Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with nonunion
M80.031P	Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with malunion
M80.031S	Age-related osteoporosis with current pathological fracture, right forearm, sequela
M80.032A	Age-related osteoporosis with current pathological fracture, left forearm, initial encounter for fracture
M80.032D	Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with routine healing
M80.032G	Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with delayed healing
M80.032K	Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with nonunion
M80.032P	Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with malunion
M80.032S	Age-related osteoporosis with current pathological fracture, left forearm, sequela
M80.041A	Age-related osteoporosis with current pathological fracture, right hand, initial encounter for fracture

M80.041D	Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with routine healing
M80.041G	Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with delayed healing
M80.041K	Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with nonunion
M80.041P	Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with malunion
M80.041S	Age-related osteoporosis with current pathological fracture, right hand, sequela
M80.042A	Age-related osteoporosis with current pathological fracture, left hand, initial encounter for fracture
M80.042D	Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with routine healing
M80.042G	Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with delayed healing
M80.042K	Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with nonunion
M80.042P	Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with malunion
M80.042S	Age-related osteoporosis with current pathological fracture, left hand, sequela
M80.051D	Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with routine healing
M80.051G	Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with delayed healing
M80.051K	Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with nonunion
M80.051P	Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with malunion
M80.051S	Age-related osteoporosis with current pathological fracture, right femur, sequela
M80.052A	Age-related osteoporosis with current pathological fracture, left femur, initial encounter for fracture
M80.052D	Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with routine healing
M80.052G	Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with delayed healing
M80.052K	Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with nonunion
M80.052P	Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with malunion
M80.052S	Age-related osteoporosis with current pathological fracture, left femur, sequela
M80.061A	Age-related osteoporosis with current pathological fracture, right lower leg, initial encounter for fracture
M80.061D	Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with routine healing
M80.061G	Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with delayed healing
M80.061K	Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with nonunion
M80.061P	Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with malunion
M80.061S	Age-related osteoporosis with current pathological fracture, right lower leg, sequela
M80.062A	Age-related osteoporosis with current pathological fracture, left lower leg, initial encounter for fracture

M80.062D	Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with routine healing
M80.062G	Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with delayed healing
M80.062K	Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with nonunion
M80.062P	Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with malunion
M80.062S	Age-related osteoporosis with current pathological fracture, left lower leg, sequela
M80.071A	Age-related osteoporosis with current pathological fracture, right ankle and foot, initial encounter for fractur
M80.071D	Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with routine healing
M80.071G	Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with delayed healing
M80.071K	Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with nonunion
M80.071P	Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with malunion
M80.071S	Age-related osteoporosis with current pathological fracture, right ankle and foot, sequela
M80.072A	Age-related osteoporosis with current pathological fracture, left ankle and foot, initial encounter for fracture
M80.072D	Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with routine healing
M80.072G	Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with delayed healing
M80.072K	Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with nonunion
M80.072P	Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with malunion
M80.072S	Age-related osteoporosis with current pathological fracture, left ankle and foot, sequela
M80.08XA	Age-related osteoporosis with current pathological fracture, vertebra(e), initial encounter for fracture
M80.08XD	Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with routine healing
M80.08XG	Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with delayed healing
M80.08XK	Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with nonunion
M80.08XP	Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with malunion
M80.08XS	Age-related osteoporosis with current pathological fracture, vertebra(e), sequela
M80.0AXA	Age-related osteoporosis with current pathological fracture, other site, initial encounter for fracture
M80.0AXD	Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with routine healing
M80.0AXG	Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with delayed healing
M80.0AXK	Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with nonunion
M80.0AXP	Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with malunion
M80.0AXS	Age-related osteoporosis with current pathological fracture, other site, sequela

M80.0B1A	Age-related osteoporosis with current pathological fracture, right pelvis, initial encounter for fracture
M80.0B1D	Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with routine healing
M80.0B1G	Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with delayed healing
M80.0B1K	Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with nonunion
M80.0B1P	Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with malunion
M80.0B1S	Age-related osteoporosis with current pathological fracture, right pelvis, sequela
M80.0B2A	Age-related osteoporosis with current pathological fracture, left pelvis, initial encounter for fracture
M80.0B2D	Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with routine healing
M80.0B2G	Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with delayed healing
M80.0B2K	Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with nonunion
M80.0B2P	Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with malunion
M80.0B2S	Age-related osteoporosis with current pathological fracture, left pelvis, sequela
M80.0B9A	Age-related osteoporosis with current pathological fracture, unspecified pelvis, initial encounter for fracture
M80.0B9D	Age-related osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with routine healing
M80.0B9G	Age-related osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with delayed healing
M80.0B9K	Age-related osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with nonunion
M80.0B9P	Age-related osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with malunion
M80.0B9S	Age-related osteoporosis with current pathological fracture, unspecified pelvis, 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
M80.8B1A	Other osteoporosis with current pathological fracture, right pelvis, initial encounter for fracture
M80.8B1D	Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with routine healing
M80.8B1G	Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with delayed healing
M80.8B1K	Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with nonunion
M80.8B1P	Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with malunion

M80.8B1S	Other osteoporosis with current pathological fracture, right pelvis, sequela
M80.8B2A	Other osteoporosis with current pathological fracture, left pelvis, initial encounter for fracture
M80.8B2D	Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with routine healing
M80.8B2G	Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with delayed healing
M80.8B2K	Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with nonunion
M80.8B2P	Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with malunion
M80.8B2S	Other osteoporosis with current pathological fracture, left pelvis, sequela
M80.8B9A	Other osteoporosis with current pathological fracture, unspecified pelvis, initial encounter for fracture
M80.8B9D	Other osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with routine healing
M80.8B9G	Other osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with delayed healing
M80.8B9K	Other osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with nonunion
M80.8B9P	Other osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with malunion
M80.8B9S	Other osteoporosis with current pathological fracture, unspecified pelvis, sequela
M81.0	Age-related osteoporosis without current pathological fracture
M81.8	Other osteoporosis without current pathological fracture
M85.80	Other specified disorders of bone density and structure, unspecified site
M85.811	Other specified disorders of bone density and structure, right shoulder
M85.812	Other specified disorders of bone density and structure, left shoulder
M85.821	Other specified disorders of bone density and structure, right upper arm
M85.822	Other specified disorders of bone density and structure, left upper arm
M85.831	Other specified disorders of bone density and structure, right forearm
M85.832	Other specified disorders of bone density and structure, left forearm
M85.841	Other specified disorders of bone density and structure, right hand
M85.842	Other specified disorders of bone density and structure, left hand
M85.851	Other specified disorders of bone density and structure, right thigh
M85.852	Other specified disorders of bone density and structure, left thigh
M85.861	Other specified disorders of bone density and structure, right lower leg
M85.862	Other specified disorders of bone density and structure, left lower leg
M85.871	Other specified disorders of bone density and structure, right ankle and foot
M85.872	Other specified disorders of bone density and structure, left ankle and foot
M85.88	Other specified disorders of bone density and structure, other site
M85.89	Other specified disorders of bone density and structure, multiple sites
MA80.051A	Age-related osteoporosis with current pathological fracture, right femur, initial encounter for fracture
Z87.310	Personal history of (healed) osteoporosis fracture

DENOSUMAB (XGEVA) IS MEDICALLY NECESSARY WHEN REPORTED WITH THE FOLLOWING DIAGNOSIS CODES:

C79.51	Secondary malignant neoplasm of bone
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

ROMOSOZUMAB-AQQG (EVENITY) IS MEDICALLY NECESSARY WHEN REPORTED WITH THE FOLLOWING DIAGNOSIS CODES:

M80.011A	Age-related osteoporosis with current pathological fracture, right shoulder, initial encounter for fracture
M80.011D	Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with routine healing
M80.011G	Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with delayed healing
M80.011K	Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with nonunion
M80.011P	Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with malunion
M80.011S	Age-related osteoporosis with current pathological fracture, right shoulder, sequela
M80.012A	Age-related osteoporosis with current pathological fracture, left shoulder, initial encounter for fracture
M80.012D	Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with routine healing
M80.012G	Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with delayed healing
M80.012K	Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with nonunion
M80.012P	Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with malunion
M80.012S	Age-related osteoporosis with current pathological fracture, left shoulder, sequela
M80.021A	Age-related osteoporosis with current pathological fracture, right humerus, initial encounter for fracture
M80.021D	Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with routine healing
M80.021G	Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with delayed healing
M80.021K	Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with nonunion
M80.021P	Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with malunion
M80.021S	Age-related osteoporosis with current pathological fracture, right humerus, sequela
M80.022A	Age-related osteoporosis with current pathological fracture, left humerus, initial encounter for fracture
M80.022D	Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with routine healing
M80.022G	Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with delayed healing

M80.022K	Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with nonunion
M80.022P	Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with malunion
M80.022S	Age-related osteoporosis with current pathological fracture, left humerus, sequela
M80.031A	Age-related osteoporosis with current pathological fracture, right forearm, initial encounter for fracture
M80.031D	Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with routine healing
M80.031G	Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with delayed healing
M80.031K	Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with nonunion
M80.031P	Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with malunion
M80.031S	Age-related osteoporosis with current pathological fracture, right forearm, sequela
M80.032A	Age-related osteoporosis with current pathological fracture, left forearm, initial encounter for fracture
M80.032D	Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with routine healing
M80.032G	Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with delayed healing
M80.032K	Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with nonunion
M80.032P	Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with malunion
M80.032S	Age-related osteoporosis with current pathological fracture, left forearm, sequela
M80.041A	Age-related osteoporosis with current pathological fracture, right hand, initial encounter for fracture
M80.041D	Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with routine healing
M80.041G	Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with delayed healing
M80.041K	Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with nonunion
M80.041P	Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with malunion
M80.041S	Age-related osteoporosis with current pathological fracture, right hand, sequel
M80.042A	Age-related osteoporosis with current pathological fracture, left hand, initial encounter for fracture
M80.042D	Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with routine healing
M80.042G	Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with delayed healing
M80.042K	Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with nonunion
M80.042P	Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with malunion
M80.042S	Age-related osteoporosis with current pathological fracture, left hand, sequela
M80.051A	Age-related osteoporosis with current pathological fracture, right femur, initial encounter for fracture
M80.051D	Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with routine healing

M80.051G	Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with delayed healing
M80.051K	Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with nonunion
M80.051P	Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with malunion
M80.051S	Age-related osteoporosis with current pathological fracture, right femur, sequela
M80.052A	Age-related osteoporosis with current pathological fracture, left femur, initial encounter for fracture
M80.052D	Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with routine healing
M80.052G	Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with delayed healing
M80.052K	Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with nonunion
M80.052P	Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with malunion
M80.052S	Age-related osteoporosis with current pathological fracture, left femur, sequela
M80.061A	Age-related osteoporosis with current pathological fracture, right lower leg, initial encounter for fracture
M80.061D	Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with routine healing
M80.061G	Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with delayed healing
M80.061K	Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with nonunion
M80.061P	Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with malunion
M80.061S	Age-related osteoporosis with current pathological fracture, right lower leg, sequela
M80.062A	Age-related osteoporosis with current pathological fracture, left lower leg, initial encounter for fracture
M80.062D	Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with routine healing
M80.062G	Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with delayed healing
M80.062K	Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with nonunion
M80.062P	Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with malunion
M80.062S	Age-related osteoporosis with current pathological fracture, left lower leg, sequela
M80.071A	Age-related osteoporosis with current pathological fracture, right ankle and foot, initial encounter for fracture
M80.071D	Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with routine healing
M80.071G	Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with delayed healing
M80.071K	Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with nonunion
M80.071P	Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with malunion
M80.071S	Age-related osteoporosis with current pathological fracture, right ankle and foot, sequela
M80.072A	Age-related osteoporosis with current pathological fracture, left ankle and foot, initial encounter for fracture

M80.072D	Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with routine healing
M80.072G	Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with delayed healing
M80.072K	Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with nonunion
M80.072P	Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with malunion
M80.072S	Age-related osteoporosis with current pathological fracture, left ankle and foot, sequela
M80.08XA	Age-related osteoporosis with current pathological fracture, vertebra(e), initial encounter for fracture
M80.08XD	Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with routine healing
M80.08XG	Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with delayed healing
M80.08XK	Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with nonunion
M80.08XP	Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with malunion
M80.08XS	Age-related osteoporosis with current pathological fracture, vertebra(e), sequela
M80.0AXA	Age-related osteoporosis with current pathological fracture, other site, initial encounter for fracture
M80.0AXD	Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with routine healing
M80.0AXG	Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with delayed healing
M80.0AXK	Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with nonunion
M80.0AXP	Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with malunion
M80.0AXS	Age-related osteoporosis with current pathological fracture, other site, sequela
M80.0B1A	Age-related osteoporosis with current pathological fracture, right pelvis, initial encounter for fracture
M80.0B1D	Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with routine healing
M80.0B1G	Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with delayed healing
M80.0B1K	Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with nonunion
M80.0B1P	Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with malunion
M80.0B1S	Age-related osteoporosis with current pathological fracture, right pelvis, sequela
M80.0B2A	Age-related osteoporosis with current pathological fracture, left pelvis, initial encounter for fracture
M80.0B2D	Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with routine healing
M80.0B2G	Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with delayed healing
M80.0B2K	Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with nonunion
M80.0B2P	Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with malunion
M80.0B2S	Age-related osteoporosis with current pathological fracture, left pelvis, sequela

M80.0B9A	Age-related osteoporosis with current pathological fracture, unspecified pelvis, initial encounter for fracture
M80.0B9D	Age-related osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with routine healing
M80.0B9G	Age-related osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with delayed healing
M80.0B9K	Age-related osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with nonunion
M80.0B9P	Age-related osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with malunion
M80.0B9S	Age-related osteoporosis with current pathological fracture, unspecified pelvis, 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
M80.8B1A	Other osteoporosis with current pathological fracture, right pelvis, initial encounter for fracture
M80.8B1D	Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with routine healing
M80.8B1G	Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with delayed healing
M80.8B1K	Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with nonunion
M80.8B1P	Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with malunion
M80.8B1S	Other osteoporosis with current pathological fracture, right pelvis, sequela
M80.8B2A	Other osteoporosis with current pathological fracture, left pelvis, initial encounter for fracture
M80.8B2D	Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with routine healing
M80.8B2G	Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with delayed healing
M80.8B2K	Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with nonunion
M80.8B2P	Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with malunion
M80.8B2S	Other osteoporosis with current pathological fracture, left pelvis, sequela
M80.8B9A	Other osteoporosis with current pathological fracture, unspecified pelvis, initial encounter for fracture
M80.8B9D	Other osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with routine healing
M80.8B9G	Other osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with delayed healing
M80.8B9K	Other osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with nonunion
M80.8B9P	Other osteoporosis with current pathological fracture, unspecified pelvis, subsequent encounter for fracture with malunion

M80.8B9S	Other osteoporosis with current pathological fracture, unspecified pelvis, sequela
M81.0	Age-related osteoporosis without current pathological fracture

HCPCS Level II Code Number(s)

THE FOLLOWING CODE REPRESENTS DENOSUMAB (PROLIA® OR XGEVA®):

J0897	Injection, denosumab, 1 mg
Q5136	Injection, denosumab-bbdz (jubbonti/wyost), biosimiliar, 1 mg

THE FOLLOWING CODE REPRESENTS ROMOSOZUMAB-AQQG (EVENITY®):

J3111	Injection, romosozumab-aqqg, 1 mg

Revenue Code Number(s)

N/A

Policy History

Revisions From MA08.052n:

03/28/2025	This version of the policy will become effective 03/28/2025. Language related to denosumab biosimilars was added to the policy. Continuation therapy language for denosumab (Prolia) was added to the policy. The following unspecified laterality ICD-10 codes were removed from the policy: From denosumab (Prolia) and denosumab-bbdz (Jubbonti) M80.021A, M80.021D, M80.021G, M80.021K, M80.021P, M80.021S, M80.032A, M80.032D, M80.032G, M80.032K, M80.032P, M80.032S From romosozumab-aqqg (Evenity): M80.0B9A, M80.0B9D, M80.0B9G, M80.0B9K, M80.0B9P, M80.0B9S, M80.8B9A, M80.8B9D, M80.8B9G, M80.8B9K, M80.8B9P, M80.8B9S

Revisions From MA08.052m

12/16/2024	This version of the policy will become effective 12/16/2024. Inclusion of a policy in a Code Update memo does not imply that a full review of the policy was completed at this time. The following HCPCS code has been **added** to this policy: Q5136 Injection, denosumab-bbdz (jubbonti/wyost), biosimilar, 1 mg

Revisions From MA08.052l

01/02/2024	This version of the policy will become effective 01/02/2024. The intent of this policy remains unchanged.

Revisions From MA08.052k:

10/01/2023	This version of the policy will become effective 10/01/2023. Inclusion of a policy in a Code Update memo does not imply that a full review of the policy was completed at this time. The following ICD-10 codes have been **added** to this policy:

	M80.0B1A, M80.0B1D, M80.0B1G, M80.0B1K, M80.0B1P, M80.0B1S, M80.0B2A, M80.0B2D, MA80.0B2G, M80.0B2K, MA80.0B2P, M80.0B2S, M80.0B9A, M80.09D, M80.0B9G, M80.0B9K, M80.0B9P, M80.0B9S, M80.8B1A, M80.8B1D, M80.8B1G, M80.8B1K, M80.8B1P, M80.8B1S, M80.8B2A, M80.8B2D, M80.8B2G, M80.8B2K, M80.8B2P, M80.8B2S, M80.8B9A, M80.8B9D, M80.8B9G, M80.8B9K, M80.8B9P, M80.8B9S

Revisions from MA08.052j

05/09/2022	This version of the policy will become effective 05/09/2022. Medically necessary criteria for denosumab (Prolia and Xgeva) have been **revised** in accordance with US Food and Drug Administration (FDA) labeling (Prolia 05/12/2021, Xgeva 06/09/2020) and the National Comprehensive Cancer Network (NCCN) compendium (accessed 12/15/2021): • Criteria related to breast cancer were further deliniated to include both invasive (along with histology types) and inflammatory types. • Histology types were added to criteria for non-small cell lung cancer and kidney cancer The following was **added** in accordance with FDA labeling and drug manufacturer information: • Administration of drugs by a professional provider • REMS program for denosumab (Prolia) The following codes representing **unspecified** anatomical sites have been **removed** from the policy: DENOSUMAB (PROLIA, XGEVA): M80.00XA, M80.00XD, M80.00XG, M80.00XK, M80.00XP, M80.00XS, M80.019A, M80.019D, M80.019G, M80.019K, M80.019P, M80.019S, M80.029A, M80.029D, M80.029G, M80.029K, M80.029P, M80.029S, M80.039A, M80.039D, M80.039G, M80.039K, M80.039P, M80.039S, M80.049A, M80.049D, M80.049G, M80.049K, M80.049P, M80.049S, M80.059A, M80.059D, M80.059G, M80.059K, M80.059P, M80.059S, M80.069A, M80.069D, M80.069G, M80.069K, M80.069P, M80.069S, M80.079A, M80.079D, M80.079G, M80.079K, M80.079P, M80.079S, M85.819, M85.829, M85.839, M85.849, M85.859, M85.869, M85.879 ROMOSOZUMAB-AQQG (EVENITY): M80.00XA, M80.00XD, M80.00XG, M80.00XK, M80.00XP, M80.00XS, M80.019A, M80.019D, M80.019G, M80.019K, M80.019P, M80.019S, M80.029A, M80.029D, M80.029G, M80.029K, M80.029P, M80.029S, M80.039A, M80.039D, M80.039G, M80.039K, M80.039P, M80.039S, M80.049A, M80.049D, M80.049G, M80.049K, M80.049P, M80.049S, M80.059A, M80.059D, M80.059G, M80.059K, M80.059P, M80.059S, M80.069A, M80.069D, M80.069G, M80.069K, M80.069P, M80.069S, M80.079A, M80.079D, M80.079G, M80.079K, M80.079P, M80.079S

Revisions from MA08.052i:

05/10/2021	This version of the policy will become effective 05/10/2021. Medically necessary criteria for denosumab (Xgeva) have been **revised** in accordance with the National Comprehensive Cancer Network (NCCN) compendium: • Treatment as a single agent (NCCN preferred) or combined with interferon alfa/peginterferon, serial embolization, or radiation therapy for resectable disease with unacceptable morbidity and/or unresectable axial lesions for individuals with localized disease, metastases at presentation, or disease recurrence • Treatment as a single agent for unresectable metastatic disease at presentation, unresectable metastatic recurrence, or considered prior to surgery for resectable local recurrence (NCCN preferred)

Revisions from MA08.052h

10/01/2020	This version of the policy will become effective 10/01/2020. The following **ICD-10** codes have been **added** to this policy for **ROMOSOZUMAB-AQQG**

	(EVENITY™) and **DENOSUMAB (PROLIA®)** : M80.0AXA Age-related osteoporosis with current pathological fracture, other site, initial encounter for fracture M80.0AXD Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with routine healing M80.0AXG Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with delayed healing M80.0AXK Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with nonunion M80.0AXP Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with malunion M80.0AXS Age-related osteoporosis with current pathological fracture, other site, 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

Revisions from MA08.052g

10/01/2019	This version of the policy will become effective 10/01/2019. The following NOC codes have been **removed** from this policy and is replaced by the following HCPCS code: **REMOVED:** J3590 Unclassified biologics C9399 Unclassified drugs or biologicals **REPLACED WITH:** J3111 Injection, romosozumab-aqqg, 1 mg

Revisions from MA08.052f

07/15/2019	This version of the policy will become effective 07/15/2019 .

	This policy has been updated to communicate the Company's coverage criteria for Romosozumab-aqqg (Evinity™). The following ICD-10 CM code has been **added** to this policy: M81.0 Age-related osteoporosis without current pathological fracture The following HCPCS codes have been **added** to this policy: C9399 Unclassified drugs or biologicals J3590 Unclassified biologics

Revisions from MA08.052e

04/08/2019	This version of the policy will become effective 04/08/2019. This policy was updated to include the following: • Xgeva medically necessary criteria language revised from management of skeletal-related events to prevention of skeletal-related events in accordance with current FDA labeling. • Removal of Policy Guidelines statement for limitation of use regarding denosumab (Xgeva®) not indicated for the prevention of skeletal-related events in patients with multiple myeloma. • Addition of definitions for skeletal-related events; skeletally mature; and hypercalcemia of malignancy to policy criteria • Addition of denosumab (Prolia®) to policy criteria for the treatment of glucocorticoid-induced osteoporosis in individuals below age of 50 years of age with a history of an osteoporotic fracture • The following ICD-10 CM codes have been **added** to this policy: C90.00 Multiple myeloma not having achieved remission (medically necessary) C90.02 Multiple myeloma in relapse (medically necessary) M81.8 Other osteoporosis without current pathological fracture

Revisions from MA08.052d

12/31/2018	The policy criteria was updated to include the following new indications: Prolia • Osteopenia Xgeva • Anaplastic carcinoma of the thyroid • Multiple Myeloma • Systemic Mastocytosis The following diagnosis code was added to the policy: D47.02

Revisions from MA08.052c

11/22/2017	This policy has been reissued in accordance with the Company's annual review process.
03/14/2017	This policy has been updated to be consistent with the US Food and Drug Administration (FDA) labeling and Compendia. Osteopenia not associated with breast cancer or prostate cancer treatment was removed from the policy. Documented renal insufficiency was added to the the policy criteria for osteoporosis.

Revisions from MA08.052b

08/10/2016	This policy has been updated to be consistent with the US Food and Drug Administration (FDA) labeling and Compendia. The policy criteria for Prolia® was updated to include additional criteria for individuals with osteopenia. The following ICD-10 codes were added to the policy: M80.00XA M80.00XD M80.00XG M80.00XK M80.00XP M80.00XS M80.019A M80.019D M80.019G M80.019K M80.019P M80.019S M80.029A M80.029D M80.029G M80.029K M80.029P M80.029S M80.039A M80.039D M80.039G M80.039K M80.039P M80.039S M80.049A M80.049D

	M80.049G M80.049K M80.049P M80.049S M80.059A M80.059D M80.059G M80.059K M80.059P M80.059S M80.069A M80.069D M80.069G M80.069K M80.069P M80.069S M80.079A M80.079D M80.079G M80.079K M80.079P M80.079S M85.80 M85.811 M85.812 M85.819 M85.821 M85.822 M85.829 M85.831 M85.832 M85.839 M85.841 M85.842 M85.849 M85.851 M85.852 M85.859 M85.861 M85.862 M85.869 M85.871 M85.872 M85.879 M85.88 M85.89 The following ICD-10 codes were removed from the policy: M85.9 M89.9 M94.9 C79.52

Revisions from MA08.052a

07/01/2015	This policy was updated to be consistent with US Food and Drug Administration (FDA) Labeling and Drug Compendia. Denosumab (Xgeva®) has a new indication for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

MA08.052

01/01/2015	This is a new policy.

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