LifeWise Assurance Company

PHARMACY / MEDICAL POLICY – 5.01.596

Pharmacologic Treatment of Osteoporosis

Effective Date:	Jun. 1, 2026	RELATED MEDICAL POLICIES:
Last Revised:	May 25, 2026	None
Replaces:	N/A	

The Site of Service Medical Necessity criteria within this policy DOES NOT apply to Alaska fully-insured members; refer to the infusion and injection drug Medical Necessity criteria only.

Site of Service *and* the infusion and injection drug Medical Necessity criteria apply to all other plan members.

Please contact Customer Service for more information.

Select a hyperlink below to be directed to that section.

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RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

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Introduction

Bone is living tissue, and the body constantly renews this living system by naturally breaking down and replacing bone. This is known as bone remodeling or bone turnover. As people age, however, bone remodeling changes. More old bone is lost than new bone is created. This can result in reduced bone mass. Osteoporosis, which means "porous bone," is a condition caused by the body's loss of too much bone. Osteoporosis leads to bones that are fragile. Thin, fragile bones are at high risk of fracture. Specific drugs can be used to try to reduce the risk of fracture due to osteoporosis. This policy describes when osteoporosis drugs may be considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for

providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Site of Service (SOS) Medical Necessity criteria applies ONLY to medical benefit reviews. SOS Medical Necessity criteria does NOT apply to Alaska fully-insured members; refer to the infusion and injection drug Medical Necessity criteria only. Please contact Customer Service for more information.

We will review specific intravenous (IV) and injectable drugs for medical necessity for all ages.

For those age 13 and older, we also will review the site of service for medical necessity. Site of service is defined as the location where the drug is administered, such as a hospital-based outpatient setting, an infusion center, a physician's office, or at home.

Drugs subject to site of service review addressed in this policy are:

- Evenity (romosozumab-aqqg)

Site of Service Administration	Medical Necessity
Medically necessary sites of service • **Physician's office** • **Infusion center** • **Home infusion**	**IV infusion and injection therapy of various medical or biologic agents will be covered in the most appropriate, safe and cost-effective site:** • These are the preferred **medically necessary** sites of service for specified drugs.
Hospital-based outpatient setting • **Outpatient hospital IV infusion department** • **Hospital-based outpatient clinical level of care**	**IV infusion and injection therapy of various medical or biologic agents will be covered in the most appropriate, safe and cost-effective site.** **This site is considered medically necessary for the first 90 days for the following:** • The initial course of infusion or injection of a pharmacologic or biologic agent

Site of Service Administration	Medical Necessity

	OR
	• Re-initiation of an agent after 6 months or longer following discontinuation of therapy*
	
	Note: *This does not include when standard dosing between infusions or injections is 6 months or longer
	
	This site is considered medically necessary when there is no outpatient infusion center within 50 miles of the individual's home and there is no contracted home infusion agency that will travel to their home, or a hospital is the only place that offers infusions or injections of this drug.
	
	This site is considered medically necessary only when the individual has a clinical condition which puts him or her at increased risk of complications for infusions or injections, including any 1 of the following:
	• Known cardiac condition (e.g., symptomatic cardiac arrhythmia) or pulmonary condition (e.g., significant respiratory disease, serious obstructive airway disease, %FVC less than or equal to 40%) that may increase the risk of an adverse reaction
	• Unstable renal function which decreases the ability to respond to fluids
	• Difficult or unstable vascular access
	• Acute mental status changes or cognitive conditions that impact the safety of infusion or injection therapy
	• A known history of severe adverse drug reactions and/or anaphylaxis to prior treatment with a related or similar drug
	
	This site is considered medically necessary when the individual has cytokine release syndrome (CRS) and all the following are met:
	• CRS is grade 3 or 4 as evidenced by ALL the following:
	  ○ Temperature at least 38 °C
	  ○ Hypotension that requires 1 or more vasopressors

Site of Service Administration	Medical Necessity
	○ Hypoxia that requires oxygen through a high-flow nasal cannula, face mask, non-rebreather mask, or Venturi mask OR positive pressure (continuous positive airway pressure [CPAP], bilevel positive airway pressure [BiPAP], intubation, or mechanical ventilation) **AND** • The individual will be admitted into an inpatient setting as soon as possible
Hospital-based outpatient setting • **Outpatient hospital IV infusion department** • **Hospital-based outpatient clinical level of care**	**These sites are considered not medically necessary for infusion and injectable therapy services of various medical and biologic agents when the site-of-service criteria in this policy are not met.**

Drug	Medical Necessity
• **Bonsity (teriparatide)** • **Forteo (teriparatide) SC**	**Bonsity (teriparatide) and Forteo (teriparatide) may be considered medically necessary for the treatment of osteoporosis when the following criteria are met:** • The individual tried and failed or had intolerance to two generic bisphosphonates (either two oral medications or one oral medication and one IV medication) unless use of bisphosphonate medications are contraindicated* **AND** • Has tried and failed or had intolerance to generic teriparatide **AND** • The dose is limited to 20 mcg per day (taken once a day) **Note:** Generic bisphosphonates include alendronate (oral), ibandronate (oral), risedronate (oral) and zoledronic acid (IV) **Note:** *In addition to contraindications in the prescribing information, oral bisphosphonates are considered contraindicated in individuals with esophageal disorders (e.g., achalasia, esophageal stricture, Barrett's

Drug	Medical Necessity
	esophagus, esophageal varices). Individuals with contraindications to oral bisphosphonates are only required to try and fail IV zoledronic acid.
Evenity (romosozumab-aqqg) SC	**Evenity (romosozumab-aqqg) is subject to review for site of service administration.** **Evenity (romosozumab-aqqg) may be considered medically necessary for the treatment of osteoporosis when the following criteria are met:** • The individual is postmenopausal female **AND** • Has tried and failed or had intolerance to two generic bisphosphonates (either two oral medications or one oral medication and one IV medication) unless use of bisphosphonate medications are contraindicated* **AND** • The dose is limited to 210 mg once every month **AND** • Total duration of therapy is 12 months or less **Note:** Generic bisphosphonates include alendronate (oral), ibandronate (oral), risedronate (oral) and zoledronic acid (IV) **Note:** *In addition to contraindications in the prescribing information, oral bisphosphonates are considered contraindicated in individuals with esophageal disorders (e.g., achalasia, esophageal stricture, Barrett's esophagus, esophageal varices). Individuals with contraindications to oral bisphosphonates are only required to try and fail IV zoledronic acid.
Calcitonin salmon nasal spray	**Calcitonin salmon nasal spray may be considered medically necessary when the following criteria are met:** • The individual is assigned female at birth **AND** • Diagnosed with postmenopausal osteoporosis **AND** • Is greater than 5 years postmenopause **AND** • Has tried and failed or had intolerance to two generic bisphosphonates (either two oral medications or one oral

Drug	Medical Necessity

	medication and one IV medication) unless use of bisphosphonate medications are contraindicated*
	AND
	• Has tried and failed or had intolerance to one of the following unless both medications are contraindicated:
	  ○ Raloxifene
	  ○ Denosumab (includes biosimilars)
	AND
	• The dose is limited to one spray (200 USP calcitonin salmon units) per day
	
	Note: Generic bisphosphonates include alendronate (oral), ibandronate (oral), risedronate (oral) and zoledronic acid (IV)
	
	Note: *In addition to contraindications in the prescribing information, oral bisphosphonates are considered contraindicated in individuals with esophageal disorders (e.g., achalasia, esophageal stricture, Barrett's esophagus, esophageal varices). Individuals with contraindications to oral bisphosphonates are only required to try and fail IV zoledronic acid.

• **Generic calcitonin salmon injection SC, IM**
• **Miacalcin (calcitonin salmon) injection SC, IM**
	Generic calcitonin salmon injection and Miacalcin (calcitonin salmon) injection may be considered medically necessary when the following criteria are met:
	• Diagnosed with postmenopausal osteoporosis and meets the following requirements:
	  ○ The individual is assigned female at birth
	  AND
	  ○ Is greater than 5 years postmenopause
	  AND
	  ○ Has tried and failed or had intolerance to two generic bisphosphonates (either two oral medications or one oral medication and one IV medication) unless use of bisphosphonate medications are contraindicated*
	  AND
	  ○ Has tried and failed or had intolerance to one of the following unless both medications are contraindicated:
	  ▪ Raloxifene
	  ▪ Denosumab (includes biosimilars)
	OR

Drug	Medical Necessity
	• Diagnosed with hypercalcemia defined as a documented calcium level greater than or equal to 14 mg/dL **OR** • Diagnosed with Paget's disease of bone with a documented baseline radiographic findings of osteolytic bone lesions and alternative treatments are not suitable **Note:** Generic bisphosphonates include alendronate (oral), ibandronate (oral), risedronate (oral) and zoledronic acid (IV) **Note:** *In addition to contraindications in the prescribing information, oral bisphosphonates are considered contraindicated in individuals with esophageal disorders (e.g., achalasia, esophageal stricture, Barrett's esophagus, esophageal varices). Individuals with contraindications to oral bisphosphonates are only required to try and fail IV zoledronic acid.
Generic teriparatide SC	**Generic teriparatide may be considered medically necessary for the treatment of osteoporosis when the following criteria are met:** • The individual tried and failed or had intolerance to two generic bisphosphonates (either two oral medications or one oral medication and one IV medication) unless use of bisphosphonate medications are contraindicated* **AND** • The dose is limited to 20 mcg per day (taken once a day) **Note:** Generic bisphosphonates include alendronate (oral), ibandronate (oral), risedronate (oral) and zoledronic acid (IV) **Note:** *In addition to contraindications in the prescribing information, oral bisphosphonates are considered contraindicated in individuals with esophageal disorders (e.g., achalasia, esophageal stricture, Barrett's esophagus, esophageal varices). Individuals with contraindications to oral bisphosphonates are only required to try and fail IV zoledronic acid.
Tymlos (abaloparatide) SC	**Tymlos (abaloparatide) may be considered medically necessary for the treatment of osteoporosis when the following criteria are met:** • The individual is male or postmenopausal female **AND**

Drug	Medical Necessity
	• Has tried and failed or had intolerance to two generic bisphosphonates (either two oral medications or one oral medication and one IV medication) unless use of bisphosphonate medications are contraindicated* **AND** • The dose is limited to 80 mcg per day (taken once a day) **Note:** Generic bisphosphonates include alendronate (oral), ibandronate (oral), risedronate (oral) and zoledronic acid (IV) **Note:** *In addition to contraindications in the prescribing information, oral bisphosphonates are considered contraindicated in individuals with esophageal disorders (e.g., achalasia, esophageal stricture, Barrett's esophagus, esophageal varices). Individuals with contraindications to oral bisphosphonates are only required to try and fail IV zoledronic acid.

Drug	Investigational
• **Bonsity (teriparatide)** • **Calcitonin salmon nasal spray** • **Evenity (romosozumab-aqqg)** • **Forteo (teriparatide)** • **Generic calcitonin salmon injection** • **Miacalcin (calcitonin salmon) injection** • **Generic teriparatide** • **Tymlos (abaloparatide)**	**The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.** **All other uses of Bonsity (teriparatide), calcitonin salmon nasal spray, Evenity (romosozumab-aqqg), Forteo (teriparatide), generic calcitonin salmon injection, Miacalcin (calcitonin salmon) injection, generic teriparatide, and Tymlos (abaloparatide) for conditions not outlined in this policy are considered investigational.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**All reviews for Evenity (romosozumab-aqqg) may be approved up to 12 months.** **Non-formulary exception reviews for Bonsity (teriparatide), calcitonin salmon nasal spray, Forteo (teriparatide), generic**

Length of Approval	
Approval	**Criteria**
	calcitonin salmon injection, Miacalcin (calcitonin salmon) injection, generic teriparatide, and Tymlos (abaloparatide) may be approved up to 12 months. **All other reviews for Bonsity (teriparatide), calcitonin salmon nasal spray, Forteo (teriparatide), generic calcitonin salmon injection, Miacalcin (calcitonin salmon) injection, generic teriparatide, and Tymlos (abaloparatide) may be approved up to 2 years.**
Re-authorization criteria	**Non-formulary exception reviews for calcitonin salmon nasal spray, generic calcitonin salmon injection, and Miacalcin (calcitonin salmon) injection may be approved up to 12 months in duration when there is documentation that the condition has stabilized or improved and the individual has not experienced serious or intolerable side effects.** **All other reviews for calcitonin salmon nasal spray, generic calcitonin salmon injection, and Miacalcin (calcitonin salmon) injection may be approved up to 2 years in duration when there is documentation that the condition has stabilized or improved and the individual has not experienced serious or intolerable side effects.** **Future re-authorization of Evenity (romosozumab-aqqg) beyond 12 months is considered investigational.** **Non-formulary exception reviews for Bonsity (teriparatide), generic teriparatide, Forteo (teriparatide), and Tymlos (abaloparatide) may be approved up to 12 months in duration when there is documentation the individual remains at or has returned to having a high risk for fracture.** **All other reviews for Bonsity (teriparatide), generic teriparatide, Forteo (teriparatide), and Tymlos (abaloparatide) may be approved up to 2 years in duration when there is**

Length of Approval	
Approval	**Criteria**
	documentation the individual remains at or has returned to having a high risk for fracture.

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the diagnosis and medication history

Coding

Code	Description
HCPCS	
J0630	Injection, calcitonin salmon, up to 400 units (use to report: Miacalcin and generic calcitonin salmon)
J3110	Injection, teriparatide, (Bonsity, Forteo, and generic teriparatide) 10 mcg
J3111	Injection, romosozumab-aqqg (Evenity), 1 mg

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Benefit Application

Medical Benefit

Evenity (romosozumab-aqqg) is administered by a healthcare professional subcutaneously once every month and is managed through the medical benefit.

Medical / Pharmacy Benefit

Bonsity (teriparatide), generic teriparatide, and Forteo (teriparatide) are self-administered subcutaneously every day and are managed through the medical benefit and pharmacy benefit. Generic calcitonin salmon injection and Miacalcin (calcitonin salmon) injection are self-administered or administered by a healthcare provider as a subcutaneous or intramuscular injection every day and are managed through the medical benefit and pharmacy benefit.

Pharmacy Benefit

Tymlos (abaloparatide) is self-administered subcutaneously every day and is managed through the pharmacy benefit. Calcitonin salmon nasal spray is self-administered intranasally once daily and is managed through the pharmacy benefit.

Consideration of Age

For site of service for medical necessity the age described in this policy is 13 years of age or older. Site of service is defined as the location where the drug is administered, such as a hospital-based outpatient setting, an infusion center, a physician's office, or at home. The age criterion for site of service for medical necessity is based on the following: Pediatric individuals are not small adults. Pediatric individuals differ physiologically, developmentally, cognitively, and emotionally from adult individuals, and vary by age groups from infancy to teen. Children often require smaller doses than adults, lower infusion rates, appropriately sized equipment, the right venipuncture site determined by therapy and age, and behavioral management during administration of care. Specialty infusion training is therefore necessary for pediatric IV insertions and therapy. Due to pediatrics unique physiology and psychology, site of service review is limited to individuals above the age of 13.

Evidence Review

Background

Osteoporosis is a pathological condition characterized by bone fragility and increased risk of fracture. The National Osteoporosis Foundation's (NOF) estimated in 2014 that nearly half the total adult U.S. population was affected by osteoporosis and low bone mass (T-score <-1.0).

Approximately 10.2 million Americans ≥50 years of age (8.2 million women and 2.0 million men) were estimated to have osteoporosis and an additional 43.4 million (27.3 million women and 16.1 million men) to have low bone mass at the femoral neck (FN) or lumbar spine (LS) (NOF 2014). The prevalence of these conditions is expected to increase as the U.S. population ages.

The NOF also estimates approximately 2 million osteoporotic fractures occur in the U.S. each year (NOF 2014). Hip fracture is associated with the highest morbidity and mortality. Up to 24% of individuals ≥50 years of age with hip fracture die in the year following the event (NOF 2015). Each year, of nearly 300,000 hip fracture individuals, one-quarter end up in nursing homes and half never regain previous function (NOF 2015). In total, osteoporotic fractures cost individuals, families, and the American healthcare system $19 billion annually, with Medicare paying a majority of these costs (NOF 2015).

Bone is constantly remodeled (broken down and replaced). Frequently, as people age creation of new bone does not keep up with removal of the old, resulting in reduced bone mass and increased risk for fracture.

The goal of therapy for osteoporosis is to prevent fractures. There are six classes of products currently indicated for use in osteoporosis in the U.S. Approved anabolic agents include teriparatide (Forteo), a parathyroid hormone analog and abaloparatide (Tymlos), a parathyroid hormone related peptide analog. Approved anti-sclerostin humanized monoclonal antibodies include romosozumab-aqqg (Evenity). Approved antiresorptive agents include bisphosphonates (alendronate [Fosamax], risedronate [Actonel], ibandronate [Boniva], and zoledronic acid [Reclast]); raloxifene (Evista), a hormonal therapy; denosumab (Prolia, Xgeva), a RANK inhibitor; and calcitonin products.

Summary of Evidence

Teriparatide (Forteo)

The safety and efficacy of once-daily Forteo in the postmenopausal population were examined in a double-blind, multicenter, placebo-controlled clinical study of 1637 postmenopausal women with osteoporosis and reported by Neer 2001. All women received 1000 mg of calcium and at least 400 IU of vitamin D per day. Baseline and endpoint spinal radiographs were evaluated using the semi-quantitative scoring. Ninety percent of the women in the study had 1 or more radiographically diagnosed vertebral fractures at baseline. The primary efficacy endpoint was the occurrence of new radiographically diagnosed vertebral fractures defined as changes in the height of previously non-deformed vertebrae. Forteo, when taken with calcium

and vitamin D and compared with calcium and vitamin D alone, reduced the risk of 1 or more new vertebral fractures from 14.3% of women in the placebo group to 5.0% in the Forteo group. This difference was statistically significant ($p<0.001$); the absolute reduction in risk was 9.3% and the relative reduction was 65%. Forteo was effective in reducing the risk for vertebral fractures regardless of age, baseline rate of bone turnover, or baseline BMD. Additionally, postmenopausal women with osteoporosis who were treated with Forteo had statistically significant increases in BMD from baseline to endpoint at the lumbar spine, femoral neck, total hip, and total body.

The safety and efficacy of once-daily Forteo in the male population with primary or hypogonadal osteoporosis were examined in a double-blind, multicenter, placebo-controlled clinical study of 437 men. All men received 1000 mg of calcium and at least 400 IU of vitamin D per day. The primary efficacy endpoint was change in lumbar spine BMD. Forteo increased lumbar spine BMD in men with primary or hypogonadal osteoporosis. Statistically significant increases were seen at 3 months and continued throughout the treatment period. Forteo was effective in increasing lumbar spine BMD regardless of age, baseline rate of bone turnover, and baseline BMD. Forteo treatment increased lumbar spine BMD from baseline in 94% of men treated. Fifty-three percent of individuals treated with Forteo achieved at least a 5% increase in spine BMD, and 14% gained 10% or more.

The safety and efficacy of once-daily Forteo in the treatment of men and women with glucocorticoid-induced osteoporosis was assessed in a randomized, double-blind, active-controlled trial of 428 individuals (19% men, 81% women) aged 22 to 89 years treated with ≥5mg/day prednisone or equivalent for a minimum of 3 months. A total of 30% of individuals had prevalent vertebral fracture(s) and 43% had prior non-vertebral fracture(s). The individuals had chronic rheumatologic, respiratory or other diseases that required sustained glucocorticoid therapy. All individuals received 1000 mg of calcium plus 800 IU of vitamin D supplementation per day. In individuals with glucocorticoid-induced osteoporosis, Forteo increased lumbar spine BMD compared with baseline at 3 months through 18 months of treatment. In individuals treated with Forteo, the mean percent change in BMD from baseline to endpoint was 7.2% at the lumbar spine, 3.6% at the total hip, and 3.7% at the femoral neck.

Abaloparatide (Tymlos)

The efficacy of Tymlos for the treatment of postmenopausal osteoporosis was evaluated in an 18-month, randomized, multicenter, double-blind, placebo-controlled clinical trial in postmenopausal women aged 49 to 86 years (mean age of 69) who were randomized to receive Tymlos 80 mcg (N = 824) or placebo (N = 821) given subcutaneously once daily. Approximately

80% of individuals were Caucasian, 16% were Asian, and 3% were Black; 24% were Hispanic. At baseline, the mean T-scores were -2.9 at the lumbar spine, -2.1 at the femoral neck, and -1.9 at the total hip. At baseline, 24% of individuals had at least one prevalent vertebral fracture and 48% had at least one prior nonvertebral fracture. Individuals took daily supplemental calcium (500 to 1000 mg) and vitamin D (400 to 800 IU).

The efficacy study was extended as an open-label study where individuals were no longer receiving Tymlos or placebo but were maintained in their original randomized treatment group and received 70 mg alendronate weekly, with calcium and vitamin D supplements for 6 months. The extended open-label study enrolled 1139 individuals, representing 92% of individuals who completed the double-blind, placebo-controlled clinical trial. This included 558 individuals who had previously received Tymlos and 581 individuals who had previously received placebo. The cumulative 25-month efficacy dataset included 18 months of exposure to Tymlos or placebo, 1 month of no treatment, followed by 6 months of alendronate therapy. The study was then continued to complete 18 months of additional alendronate exposure during which time individuals were no longer blinded to their original treatment group. The primary endpoint was the incidence of new vertebral fractures in individuals treated with Tymlos compared to placebo. Tymlos resulted in a significant reduction in the incidence of new vertebral fractures compared to placebo at 18 months (0.6% Tymlos compared to 4.2% placebo, $p < 0.0001$). The absolute risk reduction in new vertebral fractures was 3.6% at 18 months and the relative risk reduction was 86% for Tymlos compared to placebo. The incidence of new vertebral fractures at 25 months was 0.6% in individuals treated with Tymlos then alendronate, compared to 4.4% in individuals treated with placebo then alendronate ($p < 0.0001$). The relative risk reduction in new vertebral fractures at 25 months was 87% for individuals treated with Tymlos then alendronate, compared to individuals treated with placebo then alendronate, and the absolute risk reduction was 3.9%. After 24 months of open-label alendronate therapy, the vertebral fracture risk reduction achieved with Tymlos therapy was maintained. Tymlos resulted in a significant reduction in the incidence of nonvertebral fractures at the end of the 18 months of treatment plus 1 month follow-up where no drug was administered (2.7% for Tymlos-treated individuals compared to 4.7% for placebo-treated individuals). The relative risk reduction in nonvertebral fractures for Tymlos compared to placebo was 43% (logrank test $p = 0.049$) and the absolute risk reduction was 2.0%. Following 6 months of alendronate treatment, the cumulative incidence of nonvertebral fractures at 25 months was 2.7% for women in the prior Tymlos group compared to 5.6% for women in the prior placebo group. At 25 months, the relative risk reduction in nonvertebral fractures was 52% (logrank test $p = 0.017$) and the absolute risk reduction was 2.9%.

Romosozumab-aqqg (Evenity)

Evenity is the first-in-class anti-sclerostin humanized monoclonal antibody that transiently increases bone formation and reduces bone resorption to increase bone mass. Sclerostin is a protein that is mainly produced by osteocytes that produces its effects on bone by directly inhibiting Wnt pathway signaling.

The efficacy of Evenity for the treatment of postmenopausal women with osteoporosis is documented below.

- One good quality Phase 3 study (ARCH) showed Evenity 210 mg subcutaneously (SC) every 4 weeks for 1 year followed by alendronate 70 mg orally every week reduced incidence of vertebral fracture and clinical fractures (nonvertebral + symptomatic vertebral) compared to alendronate alone at Month 24 in 4093 postmenopausal women with osteoporosis (Saag 2017).
- Another good quality Phase 3 study (FRAME [NCT01575834]) showed Evenity 210 mg SC every 4 weeks for 1 year followed by denosumab 60 mg SC every 6 months reduced cumulative incidence of new vertebral fractures and clinical fractures at both Months 12 and 24 compared to placebo for 1 year followed by denosumab 60 mg SC every 6 months in 7180 postmenopausal women with osteoporosis (Cosman 2016).
- A good quality meta-analysis of randomized controlled trials shows Evenity 210 mg SC every 4 weeks ± sequential alendronate or denosumab resulted in a significantly lower risk of new vertebral fracture (RR 0.37, 95% CI 0.18-0.77, P=0.005, n=5371), nonvertebral fracture (RR 0.78, 95% CI 0.66-0.92, P<0.001, n=5635, and hip fracture (RR 0.59, 95% CI 0.44-0.79, P=0.004, n=5635) compared to controls (placebo, alendronate, and sequential placebo-denosumab) in postmenopausal women with osteoporosis (Liu 2018). The same meta-analysis also showed bone minder density at the lumbar spine, total hip, and femoral neck was significantly increased with Evenity 210 mg SC every 4 weeks vs other therapies including placebo, alendronate 70 mg orally every week, and teriparatide 20 µg SC every day.
- A moderate quality Phase 3b trial (STRUCTURE) demonstrated Evenity 210 mg SC every 4 weeks increased lumbar spine, total hip, and femoral neck bone mineral density greater than teriparatide 20 µg SC every week over one year of therapy in postmenopausal women with low bone mineral density and high risk for fracture despite ≥3 years treatment with a bisphosphonate. However, rate of fracture (a safety outcome) was similar between the two treatment groups (3% vs 4%, respectively) (Langdahl 2017).

The general safety of Evenity is primarily derived from the first 12-months data of the two Phase 3 fracture studies in postmenopausal women (ARCH and FRAME). Given a cardiovascular (CV) safety signal was identified in one of the trials (ARCH; alendronate-controlled), but not in the other (FRAME; placebo-controlled), the FDA initially issued a complete response for the agent in summer 2017 and asked for further CV outcomes data from the ongoing (at the time) Phase 3 bone mineral density trial in men (BRIDGE; placebo-controlled). Subsequent results from the BRIDGE trial then also showed a CV safety signal. After meta-analysis of related data, on January 16, 2019 the FDA Bone, Reproductive, and Urologic Drugs Advisory Committee voted 18-1 that the clinical benefit of one year of Evenity outweighed its risks in a narrower population of postmenopausal women with osteoporosis who were at high-risk for fracture (defined as history of osteoporotic fracture, multiple risk factors for fracture, or failure or intolerance to other available therapies).

Practice Guidelines and Position Statements

American College of Physicians Guideline

The American College of Physicians Guideline on the Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women recommended that clinicians:

- Offer pharmacologic treatment with alendronate, risedronate, zoledronic acid, or denosumab to reduce the risk for hip and vertebral fractures in women who have known osteoporosis. (Grade: strong recommendation; high-quality evidence)
- Treat osteoporotic women with pharmacologic therapy for 5 years. (Grade: weak recommendation; low-quality evidence)
- Offer pharmacologic treatment with bisphosphonates to reduce the risk for vertebral fracture in men who have clinically recognized osteoporosis. (Grade: weak recommendation; low-quality evidence)

American Association of Clinical Endocrinologists (AACE)/American College of Endocrinology (ACE) Clinical Practice Guideline

The AACE/ACE Clinical Practice Guidelines For The Diagnosis and Treatment of Postmenopausal Osteoporosis were updated in 2020. The AACE/ACE guidelines are based on diligent reviews of the clinical evidence and the 2020 updated guideline contains 52 recommendations. Recommendations on which medications should be used to treat osteoporosis include the following:

- Offer approved agents with efficacy to reduce hip, nonvertebral, and spine fractures including alendronate, denosumab, risedronate, and zoledronate are appropriate as initial therapy for most osteoporotic individuals with high fracture risk
- Abaloparatide, denosumab, romosozumab, teriparatide, and zoledronate should be considered for individuals unable to use oral therapy and as initial therapy for individuals at very high fracture risk
- Ibandronate or raloxifene may be appropriate initial therapy in some cases for individuals requiring drugs with spine-specific efficacy

Recommendations on how long individuals should be treated include the following:

- Limit treatment with abaloparatide and teriparatide to 2 years and follow abaloparatide or teriparatide therapy with a bisphosphonate or denosumab
- Limit treatment with romosozumab to 1 year and follow with a drug intended for long-term use, such as a bisphosphonate or denosumab
- For oral bisphosphonates, consider a bisphosphonate holiday after 5 years of treatment if fracture risk is no longer high (such as when the T score is greater than -2.5, or the individual has remained fracture free), but continue treatment up to an additional 5 years if fracture risk remains high
- For oral bisphosphonates, consider a bisphosphonate holiday after 6 to 10 years of stability in individuals with very high fracture risk
- For zoledronate, consider a bisphosphonate holiday after 3 years in high-risk individuals or until fracture risk is no longer high, and continue for up to 6 years in very-high risk individuals
- The ending of a bisphosphonate holiday should be based on individual patient circumstances such as an increase in fracture risk, a decrease in bone mineral density beyond the least significant change (LSC) of the dual-energy X-ray absorptiometry (DXA) machine, or an increase in bone turnover markers
- A holiday is not recommended for non-bisphosphonate antiresorptive drugs, and treatment with such agents should be continued for as long as clinically appropriate
- If denosumab therapy is discontinued, individuals should be transitioned to another antiresorptive

2020 Update

Reviewed prescribing information for all drugs in policy. Added Bonsity (teriparatide) and brand Teriparatide to the coverage criteria. Added a dose limit based on FDA-approved dosage and

administration for each drug. Added a note to each drug to clarify that oral bisphosphonates are considered contraindicated in individuals with esophageal disorders.

2021 Update

Reviewed prescribing information for all drugs listed in policy and the AACE/ACE guidelines on. No new information was identified that would result in changes to policy statements.

2022 Update

Reviewed prescribing information for all drugs listed in policy and the American Association of Clinical Endocrinologists (AACE)/American College of Endocrinology (ACE) Clinical Practice Guideline that were updated in 2020. The AACE/ACE guidelines include use of bisphosphonates for individuals that are high risk/no prior fractures and individuals that are very high risk/prior fractures. The guidelines also include use of zoledronic acid for individuals unable to use oral therapy and as initial therapy for individuals at very high fracture risk. No new information was identified that would result in changes to policy statements.

2023 Update

Reviewed prescribing information for all drugs listed in policy. Removed note about Xgeva not being targeted as Xgeva criteria will be effective from August 4, 2023, in medical policy 5.01.540 Miscellaneous Oncology Drugs.

2024 Update

Reviewed prescribing information for all drugs listed in policy. Added generic teriparatide to the coverage criteria. Updated Bonsity (teriparatide), brand Teriparatide, and Forteo (teriparatide) coverage criteria to require trial and failure with generic teriparatide.

2025 Update

Reviewed prescribing information for all drugs listed in policy. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Added site of service review for Evenity (romosozumab-aqqg). Clarified that the Site of Service Medical Necessity criteria can apply to injection drugs. Added coverage for calcitonin salmon nasal spray for the treatment of postmenopausal osteoporosis. Added coverage for generic calcitonin salmon injection and Miacalcin (calcitonin salmon) injection for the treatment of postmenopausal osteoporosis, Paget's disease of bone, and hypercalcemia. Removed brand teriparatide coverage criteria as the product has been withdrawn from the market.

2026 Update

Reviewed prescribing information for all drugs listed in policy. Policy statements unchanged.

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23. Calcitonin salmon nasal spray. Prescribing information. Apotex Corp., Weston, FL. Revised December 2023.
24. Evenity (romosozumab-aqqg). Prescribing information. Amgen Inc., Thousand Oaks, CA. Revised January 2026.
25. Forteo (teriparatide). Prescribing information. Eli Lilly and Company. Indianapolis, IN. Revised June 2025.
26. Miacalcin (calcitonin-salmon). Prescribing information. Mylan Institutional LLC, Morgantown, WV. Revised August 2021.
27. Tymlos (abaloparatide). Prescribing information. Radius Health Inc.; Boston, MA. Revised March 2025.

History

Date	Comments
05/01/19	New policy, approved April 9, 2019, effective August 2, 2019. Add to Prescription Drug section. Forteo (teriparatide), Tymlos (abaloparatide), and Prolia (denosumab) may be considered medically necessary when criteria are met, considered investigational when criteria are not met.
06/01/19	Interim Review, approved May 14, 2019. Added criteria for Evenity (romosozumab-aqqg). Updated criteria for Tymlos (abaloparatide). Added HCPCS code J3590.
10/01/19	Interim Review, approved September 19, 2019. Updated criteria for Prolia (denosumab). Added HCPCS code J3111 (new code effective 10/1/19). Removed HCPCS code J3590.
08/01/20	Annual Review, approved July 23, 2020. Added Bonsity (teriparatide) and brand Teriparatide to the coverage criteria. Added a dose limit based on FDA-approved dosage and administration for each drug. Added a note to each drug to clarify that oral bisphosphonates are considered contraindicated in patients with esophageal disorders.
05/01/21	Interim Review, approved April 22, 2021. Updated Prolia (denosumab) initial and re-authorization duration to 2 years. Removed 2-year treatment duration limit from coverage criteria and re-authorization criteria for Bonsity (teriparatide), brand Teriparatide, Forteo (teriparatide), and Tymlos (abaloparatide) based on revised prescribing information for use beyond 2 years in patients at high risk of fracture.
01/01/22	Annual Review, approved December 2, 2021. No changes to policy statements.
01/01/23	Annual Review, approved December 23, 2022. No changes to policy statements. Changed the wording from "patient" to "individual" throughout the policy for standardization.
03/01/23	Interim Review, approved February 20, 2023. Added coverage to Tymlos (abaloparatide) for the treatment of men with osteoporosis.
05/01/23	Coding update. Removed prior authorization statement from HCPC code J0897. Xgeva now requires prior authorization.
05/09/23	Coding update. Re-added prior authorization statement for HCPC code J0897. Xgeva does not require prior authorization.
08/01/23	Annual Review, approved July 10, 2023. Removed note about Xgeva not being targeted as Xgeva criteria will be effective from August 4, 2023, in medical policy 5.01.540 Miscellaneous Oncology Drugs. Removed reference re: prior auth for HCPCS code J0897. This information is not a part of the policy directive.
02/01/24	Annual Review, approved January 9, 2024. Added generic teriparatide to the coverage criteria. Updated Bonsity (teriparatide), brand Teriparatide, and Forteo (teriparatide) coverage criteria to require trial and failure with generic teriparatide. Added HCPCS code J3110 for Forteo.

Date	Comments
03/01/25	Annual Review, approved February 24, 2025. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.
07/01/25	Interim Review, approved June 10, 2025. Added coverage for calcitonin salmon nasal spray for the treatment of postmenopausal osteoporosis. The following changes are effective October 3, 2025, following a 90-day provider notification. Added coverage for generic calcitonin salmon injection and Miacalcin (calcitonin salmon) injection for the treatment of postmenopausal osteoporosis, Paget's disease of bone, and hypercalcemia. Added HCPC code J0630 for Miacalcin and generic calcitonin salmon to match criteria update. Added site of service review for Evenity (romosozumab-aqqg). Clarified that the Site of Service Medical Necessity criteria can apply to injection drugs.
11/01/25	Interim Review, approved October 13, 2025. Moved Prolia (denosumab) from policy 5.01.596 Pharmacologic Treatment of Osteoporosis to 5.01.658 Denosumab Products. Moved HCPCS Code J0897 to policy 5.01.658.
12/01/25	Interim Review, approved November 24, 2025. Removed brand teriparatide coverage criteria as the product has been withdrawn from the market.
06/01/26	Annual Review, approved May 25, 2026. Policy statements unchanged.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2026 Premera All Rights Reserved.

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