DRUG DETERMINATION POLICY

Title: DDP-33 Osteoporosis Agents

Effective Date: 10/25/23

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Health Plan covers osteoporosis agents when criteria are met. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses and mitigation of toxicity, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. Bisphosphonates: brand Reclast coverage.

A. Diagnosis and severity: see [must meet one diagnosis listed below]:

1. Treatment and prevention of postmenopausal osteoporosis in women.

2. Treatment to increase bone mass in men with osteoporosis.

3. Treatment and prevention of glucocorticoid-induced osteoporosis in women and men.

B. Other therapies: Trials of two generic oral bisphosphonates and one generic intravenous bisphosphonate are required unless all are contraindicated. Trials must result in an inadequate response after one year of consecutive use per medication or severe adverse reaction. [must meet pertinent section for contraindication or inadequate response listed below]:

C.

Drug	Contraindication*	Inadequate response
Oral bisphosphonates	• Hypocalcemia, • esophagus anomalies (e.g., structure, achalasia) delaying esophageal emptying, inability to stand/sit upright for 30 minutes.	• Equal to or greater than 5% decrease bone mineral density on other therapies; and • Verified adequate intake of calcium and vitamin D; and • Consistent medication administration based on Food and Drug Administration-approved dosage regimen and medical/pharmacy claims over a one-year period.
Zoledronic Acid	• Hypocalcemia • Creatinine clearance less than 35ml/min.	

*As listed in the package insert

D. Approval.

1. Initial: one year.

2. Re-approval: one year (increased or stable bone mineral density).

II. Bone Modifying Agent: Prolia subcutaneous (denosumab SQ).

A. Diagnosis and severity [must meet both listed below]:

1. Diagnosis: osteoporosis/bone loss.

a. Treatment of osteoporosis in postmenopausal females at high risk of fracture;

b. Treatment of osteoporosis (to increase bone mass) in males at high risk of fracture;

c. Treatment of bone loss (to increase bone mass) in males receiving androgen-deprivation therapy for nonmetastatic prostate cancer;

d. Treatment of bone loss (to increase bone mass) in females receiving aromatase inhibitor therapy for breast cancer;

e. Treatment of glucocorticoid-induced osteoporosis in patients at high risk of fracture who are initiating or continuing systemic glucocorticoids at a daily dose equivalent to ≥7.5 mg of prednisone for an anticipated duration of at least 6 months (high risk defined as osteoporotic fracture history, multiple risk factors for fracture, or failure of or intolerance to other available osteoporosis therapy).

2. Other therapies: none required.

B. Dosage regimen:

1. Prolia subcutaneous (denosumab SQ): 60mg once every six months.

C. Approval: one year (may approve up to two years if recent bone mineral density scan).

III. Parenteral parathyroid hormone analogs or Sclerostin Inhibitors: Tymlos subcutaneous (abaloparatide SQ), Evenity subcutaneous (romosozumab SQ) [must meet all listed below]:

A. No history of fragility fracture.

1. Diagnosis and severity [must meet both listed below]:

   a. Osteoporosis, postmenopausal, fracture risk reduction [must meet one listed below]

      i. Treatment of osteoporosis in males or postmenopausal female patients who are at high risk for fracture

      ii. May also be used in patients in whom other available osteoporosis therapy has failed or cannot be taken.

   b. Second line therapy.

   c. T score requirement (see Appendix I): must be equal to or less than -3 and no history of fragility fracture.

2. Other therapies: Trials of two generic oral bisphosphonates and zoledronic acid are required unless all are contraindicated. Trials must result in an inadequate response after one year of consecutive use per medication or severe adverse reaction. [must meet pertinent section for contraindication or inadequate response listed below]:

Drug	Contraindication*	Inadequate response
Oral bisphosphonates	• Hypocalcemia, • esophagus anomalies (e.g., structure, achalasia) delaying esophageal emptying, inability to stand/sit upright for 30 minutes.	• Equal to or greater than 5% decrease bone mineral density on other therapies; and • Verified adequate intake of calcium and vitamin D; and • Consistent medication administration based on Food and Drug Administration-approved dosage regimen and medical/pharmacy claims over a one-year period.
Zoledronic Acid	• Hypocalcemia • Creatinine clearance less than 35ml/min.	

*as listed in the package insert

B. History of fragility fracture.

1. Diagnosis and severity [must meet one listed below]:

   a. Treatment of osteoporosis in males or postmenopausal females who are at high risk for fracture

   b. T score: must be equal to or less than -2.5 with history of fragility fracture(s).

2. Other therapies: none.

C. Dosage regimen:

1. Tymlos subcutaneous (abaloparatide SQ): 80mcg once daily for up to two years.

2. Evenity subcutaneous (romosozumab SQ): 210mg (two consecutive 105mg injections) per month for one year.

D. Approval duration.

1. Initial:

   a. Tymlos subcutaneous (abaloparatide SQ): two years.

   b. Evenity subcutaneous (romosozumab SQ): one year.

2. Re-approval: not indicated.

E. Exclusions.

1. Evenity subcutaneous (romosozumab SQ): myocardial infarction or stroke within the previous year, uncorrected hypocalcemia.

2. Forteo subcutaneous (teriparatide SQ): Trials of all preferred formulary agents are required unless all are contraindicated. Trial must result in an inadequate response or severe adverse reaction.

IV. Other issues:

A. Bisphosphonate treatment continuation after three to five years [must meet one listed below]:

1. Continue: high risk of fracture with bone mineral density T-score below -2.5.

2. Discontinue: low risk of fracture with bone mineral density T-score at or above -2.5.

B. Combination treatment in Osteoporosis: bisphosphonate with PTH analogues.

1. Exclude: no evidence for the superiority of combination therapy.

4.0 Coding:

~~**AFFECTED**~~ **COVERED CODES – MEDICAL BENEFIT**				
HCPCS Code	**Brand Name**	**Generic Name**	**Billing Units (1 Unit)**	**Prior Approval**
J0897	Prolia	denosumab	1mg	Y

COVERED PRODCUTS – PHARMACY BENEFIT			
NDC	**Brand Name**	**Generic Name**	**Prior Approval**
All	Evenity	romosozumab	Y
All	Tymlos	abaloparatide	Y

EXCLUDED CODES AND PRODCUTS			
HCPCS Code	**Brand Name**	**Generic Name**	**Benefit Plan Reference/Reason**

EXCLUDED CODES AND PRODCUTS			
HCPCS Code	**Brand Name**	**Generic Name**	**Benefit Plan Reference/Reason**
J3310	Forteo	teriparatide	Not a preferred agent. If criteria are met for coverage of Forteo, it will be covered under the member's pharmacy benefit.
J3111	Evenity	romosozumab	Covered on the pharmacy benefit with prior approval.

5.0 Appendices:

See pages 7-11.

6.0 References, Citations & Resources:

1. An Integrated Approach: Bisphosphonate Management for the treatment of Osteoporosis. Amer J of Manag Care 2007;13:S290-S308).
2. An Update on osteoporosis. Amer J of therap. 2009;16(5):437-445.
3. Lexi comp Online®, Lexi-Drugs® , Hudson, Ohio: Lexi-Comp, Inc.; Forteo, Tymlos, Reclast,Eevenity bisphosphonates accessed August 2022.
4. Summary of AHRQ's Comparative Effectiveness Review of Treatment to Prevent Fractures in Men and Women with Low Bone Density or Osteoporosis: Update of the 2007 Report. JMCP 2012;18(4-b):S1-S15.
5. Update on long-term treatment with bisphosphonates for postmenopausal osteoporosis: A systematic review. Bone 2014;58;126-135.
6. The Efficacy of Parathyroid Hormone Analogues in Combination with Bisphosphonates for the Treatment of Osteoporosis. Medicine 2015;90(94):1-7.
7. Overview of the management of osteoporosis in postmenopausal women. http://www.uptodate.com/contents/overview-of-the-management-of-osteoporosis-in-postmenopausal-women?source=search_result&search=osteoporosis+treatment&selectedTitle=1%7E150 accessed from UpTo Date Dec 2016.
8. Romosozumab or alendronate for fracture prevention in women with Osteoporosis. N Egl J Med 2017;377:1417-27.
9. Denosumab and teriparatide transitions in postmenopausal osteoporosis (the DATA-Switch study): An extension of a randomized controlled trial. Lancet 2015:386:1147-55.
10. American Association of Clinical Endocrinologists and American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis–2020 update. *Endocr Pract*. 2020;26(suppl 1):1-46. doi:10.4158/GL-2020-0524SUPPL[PubMed 32427503]
11. National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int*. 2014;25(10):2359-2381. doi:10.1007/s00198-014-2794-2[PubMed 25182228]
12. Pharmacological management of osteoporosis in postmenopausal women: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2019;104(5):1595-1622. doi:10.1210/jc.2019-00221[PubMed 30907953]
13. North American Menopause Society. Management of osteoporosis in postmenopausal women: the 2021 position statement of The North American Menopause Society. *Menopause*. 2021;28(9):973-997. doi:10.1097/GME.0000000000001831[PubMed 34448749]

7.0 Revision History:

Original Effective Date: 07/26/2006

Next Review Date: 11/01/2024

Revision Date	Reason for Revision
8/19	Moved to new format; reformatted beginning, completed billing table, clarified t scores, replaced abbreviations, added Evenity, added Safety & monitoring table
8/20	Annual review, added Evenity contraindication, revised other therapies language, added Prolia to B. other therapies, formatting changes, changed section A. just to brand Reclast, revised other issues and added an appendix, modified treatment of high-risk patients with fragility fracture. Added references
2/21	Off cycle review, added criteria for Prolia, listed Forteo as excluded, abbreviations replaced, formatting done
7/21	Off cycle review, clarified T-score for non-fragility fracture patients, formatting, replaced abbreviations
9/21	Code added for Evenity
10/22	Reformat other therapies; clarify Parenteral parathyroid hormone analogs or Sclerostin Inhibitor indication, added references; added Prolia codes
8/23	Annual review. Adjusted formatting. Updated other therapies language; clarify bisphosphonate, Prolia, parenteral parathyroid hormone analogs and Sclerostin Inhibitors:diagnosis and severity.

Appendix I: Osteoporosis Diagnosis Categories

Category	T Score
Normal	≥ -1
Osteopenia	≤ -1 but ≥ -2.5
Osteoporosis	≤ -2.5
Severe Osteoporosis	≤ -2.5 with history of ≤ -1 fracture

Appendix II: Risk Factors for Osteoporosis and Related Fractures

Type	Factor
Medical Risk	• Fracture: previous hip fracture after age 50 yrs. • BMD: low BMD • Frame: small body frame
Demographics	• Gender: female • Family history • Ethnicity: white, Asian, Hispanic
Lifestyle	• Physical: inadequate physical activity, falling, immobilization • Dietary: low calcium intake, vitamin D insufficiency, high caffeine intake • Substance use: alcohol (≥ 3 drinks/day), smoking (active or passive)
Endocrine disorders	• Hypothyroidism • Estrogen deficiency

Appendix III: Osteoporosis Agents

Agent	Osteoporotic Indication	Available Dosage Forms/Dosing
Bisphosphonates		
Alendronate (Fosamax)	• Postmenopausal Osteoporosis: treatment and prevention in women • Osteoporosis in Men: treat to increase bone mass • Glucocorticoid-Induced Osteoporosis: treatment in men and women	• Postmenopausal Osteoporosis: prevention – 35mg/weekly or 5mg/daily by mouth; treatment - 10mg/day or 70mg/week by mouth • Osteoporosis in Men: 70mg/week or 10mg/day by mouth • Glucocorticoid-Induced Osteoporosis: 5-10mg/day by mouth
Ibandronate (Boniva)	• Postmenopausal Osteoporosis: treatment and prevention in women	• PO - 150mg/month • IV - 3mg every3 months IV
Risedronate (Actonel), Risedronate ER (Atelvia)	• Postmenopausal Osteoporosis: treatment and prevention in women* • Osteoporosis in Men: treat to increase bone mass • Glucocorticoid-Induced Osteoporosis: treatment in men and women	• Postmenopausal Osteoporosis: IR - 75mg x 2 days/month or 150mg/month by mouth, 35mg/week or 5mg/day; ER - 35mg/weekly mouth • Osteoporosis in Men: 35mg/week by mouth • Glucocorticoid-Induced Osteoporosis: 5mg/day by mouth
Zoledronic Acid (Reclast)	• Postmenopausal Osteoporosis: treatment and prevention in women • Osteoporosis in Men: treat to increase bone mass • Glucocorticoid-Induced Osteoporosis: treatment in men and women	• All Indications: 5mg/year IV
Parathyroid Hormone Analog		
Teriparatide (Forteo)	• Glucocorticoid-Induced Osteoporosis: treatment in men and women • Osteoporosis in Men: treat to increase bone mass • Postmenopausal Osteoporosis: treatment. in women at high risk for fracture	• 20mcg/day SQ
Abaloparatide (Tymlos)	• Postmenopausal Osteoporosis: treatment in women at high risk for fracture	• 80mcg/day SQ
Bone-modifying Agent		
Denosumab (Prolia)	• Postmenopausal Osteoporosis: treat women at high risk for fracture • Osteoporosis in Men: treat to increase bone mass • Breast Cancer Bone Loss: treat to increase bone mass in women at high risk of fracture and using aromatase inhibitors • Prostate Cancer Bone Loss: treat to increase bone mass in men at high risk of fracture and using androgen therapy	• 60mg/6 mon SQ
Sclerostin Inhibitor		
Evenity SubQ romosozumab	• Postmenopausal Osteoporosis: treatment and prevention in women	• 210mg (2 consecutive 105mg injections) per month for one year

**Atelvia only indicated for treatment of PMO*

Appendix IV: Other issues in Osteoporosis Treatment

Long-term bisphosphonate treatment in postmenopausal osteoporosis.

1. Adverse effects: no unexpected adverse effects were identified in long-term studies and tolerability profiles remain favorable.

2. Residual fracture benefits: three to five years after discontinues treatment.

3. Treatment continuation after three to five years.

    a. Continue: high risk of fracture with BMD t-score less than -2.5.

    b. Discontinue: low risk of fracture with BMD t-score equal to or greater than -2.5.

Combination treatment in Osteoporosis: bisphosphonate with parathyroid hormone analogues.

1. Bone mineral density:

    a. Hip: significant increase bone mineral density at one year.

    b. Spine/femoral neck: no significant change.

    c. Low level of evidence (level downgraded due to high heterogeneity and low quality among studies).

2. Risk of non/vertebral fracture:

    a. No significant change.

    b. Moderate level of evidence.

3. Conclusion: no evidence for the superiority of combination therapy.

Appendix V: Monitoring & Patient Safety

Drug	Adverse Reactions	Monitoring	REMS
Reclast zoledronic acid	• Cardiovascular: edema (39%), • Central Nervous System: fatigue (39%), headache (5-19%), dizziness (18%), insomnia (16%), anxiety/depression (11-14%), agitation (13%), confusion (7-13%), hypoesthesia (12%), rigors (11%) • Dermatology: alopecia (12%), dermatitis (11%) • Endocrine/Metabolism:↓ hydration. (5-14%), decreased phosphate/potassium/magnesium (11-13%) • Gastrointestinal: nausea/vomiting(14-46%), constipation (27-31%), diarrhea (17-24%), anorexia (9-22%), abdominal pain (14-6%), weight decrease (16%), appetite decrease (13%) • Genitourinary: urinary tract infection (12-14%) • Hematology/Oncology: anemia (22-33%), neutropenia (12%) • Neurology/Musculoskeletal: ostealgia (55%), weakness (5-24%), myalgia (23%), arthralgia (5-21%), paresthesia (15%), limb/skeletal/back pain (12-15%) • Renal: decreased renal function (8-17%); abnormal Creatinine. (40%) • Respiratory: dyspnea (22-7%), cough (12-22%) • Miscellaneous: fever (32-44%), candidiasis (12%)	• Bone Mineral Density: evaluate every 2 years. • Check chronic back pain • Labs: serum creatinine (pre each dose), vitamin D, calcium, phosphate, magnesium • Fluid Status: adequately hydrate pre and post dose	None needed
Denosumab (Prolia)	• Cardiovascular: hypertension (11%) • Dermatology: dermatitis (4-11%), eczema (4-11%), • Neurology/Musculoskeletal: arthralgia (7-14%), limb pain (10-12%), back pain (8-12 %) • Other: pregnancy category X, influenza (11%)	• Bone Mineral Density: evaluate every 2 years. • Check chronic back pain • Labs: vitamin D, calcium, phosphate, magnesium, urinary calcium • Infections • Dermatology: allergic reaction. • Musculoskeletal:	Warn regarding. infection, dermatological reaction prescription, bone turnover reduction; Med guide dispensed
Teriparatide (Forteo)	• Endocrine/Metabolic: increased calcium (6-11%) • Pregnancy Category C	• Bone Mineral Density: evaluate 2 years. • Check chronic back pain • Labs: vitamin D, urinary calcium • Orthostatic hypotension	Warn regarding osteosarcoma; Med guide dispensed
Abaloparatide (Tymlos)	• Endocrine/Metabolism: increased uric acid (25%) • Genitourinary: hypercalciuria (11-20%) • Immune: antibodies 49-68% • Other: erythema at injection site, pregnancy category C		

Drug	Adverse Reactions	Monitoring	REMS
Evenity Romosozu-mab	• Neurology/Musculoskeletal: arthralgia (8-13%)	• Bone Mineral Density: evaluate every 1-3 years, bone turnover markers pre and every 3-6 months • Cardiovascular: signs and symptoms of adverse cardiovascular event • Labs: calcium	