DRUG DETERMINATION POLICY

Title: DDP-33 Osteoporosis Agents

Effective Date: 11/14/2019

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:

A. Oral brand bisphosphonate agents.

   1. Diagnosis and severity (see Appendix II) (one below):

      a. Treatment and prevention of postmenopausal osteoporosis (PMO) in women.

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

      c. Treatment of glucocorticoid-induced osteoporosis (GIO) in women and men.

      d. Treatment of PMO in women with high risk of fractures (history of/or multiple risk factors for fracture).

   2. Other therapies: contraindicated, failed or had significant adverse effects.

      a. Failed two generic bisphosphonates (all below):

i. Equal to or greater than 5% decrease bone mineral density (BMD) loss on generic bisphosphonates(s).

ii. Verified adequate intake of calcium and vitamin D.

iii. Consistent medication fill history over a one year period.

3. Approval.

a. Initial: one year.

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

B. Parenteral parathyroid hormone analogs or Sclerostin Inhibitors: Forteo SC (teriparalide), Tymlos SubC (abaloparatide), Evenity (romosozumab)

1. Diagnosis and severity.

a. Second line therapy.

b. T score (see Appendix I) (one below):

i. No fracture: equal to or less than -3.5 even; or

ii. Fragility fracture: equal to or less than -2.5.

2. Other therapies: contraindicated, failed or had significant adverse effects.

a. Failed generic oral bisphosphonates and zoledronic acid (all below):

i. Equal to or greater than 5% decrease bone mineral density (BMD) on bisphosphonate(s).

ii. Verified adequate intake of calcium and vitamin D.

iii. Consistent medication fill history over a one year period.

b. Contraindications:

i. Oral bisphosphonate (one of the following): hypocalcemia, esophagus anomalies (e.g., structure, achalasia) delaying esophageal emptying, inability to stand/sit upright for 30 minutes.

ii. Zoledronic acid: hypocalcemia, creatinine clearance less than 35ml/min.

c. Dosage regimen:

i. Forteo SubQ (teriparatide): 20 mcg once daily for up to two years.

ii. Tymlos SubQ (abaloparatide): 80 mcg once daily for up to two years.

iii. Evenity SubQ (romosozumab): 210 mg (two consecutive 105mg injections) per month for one year.

3. Approval.

a. Initial:

i. Forteo SubQ (teriparatide) and Tymlos SubQ (abaloparatide): two years.

ii. Evenity SubQ (romosozumab): one year.

b. Re-approval: not indicated.

4. Exclusions.

a. Evenity SubQ (romosozumab): myocardial infarction or stroke within the previous year.

C. Other issues

1. Long-term bisphosphonate treatment in postmenopausal osteoporosis.

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

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

c. Treatment continuation after three to five years.

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

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

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

a. Bone mineral density (BMD):

i. Hip: significant increase BMD at one year.

ii. Spine/femoral neck: no significant change.

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

b. Risk of non/vertebral fracture:

i. No significant change.

ii. Moderate level of evidence.

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

4.0 Coding:

AFFECTED CODES				
Code	**Brand Name**	**Generic Name**	**Billing Units (1 Unit)**	**Prior Approval**
J3110	Forteo	teriparatide	10mcg	Y
Pending	Tymlos	abaloparatide	NA	Y
Pending	Evenity	romosozumab	NA	Y

5.0 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. Lexicomp Online®, Lexi-Drugs® , Hudson, Ohio: Lexi-Comp, Inc.; Forteo, Tymlos, Reclast , bisphosphonates.

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.

6.0 Appendices:

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 (PMO): treatment (Tx) & prevention in women • Osteoporosis in men: treat to ↑ bone mass • Glucocorticoid-induced osteoporosis (GIO):Tx in men & women	• PMO: prevention – 35mg/wkly or 5mg/daily po; treatment - 10mg/day or 70mg/wk po • Osteoporosis in men: 70mg/wk or 10mg/day po • GIO: 5-10mg/day po
Ibandronate (Boniva)	• PMO: Tx & prevention in women	• PO - 150mg/mon. • IV - 3mg/3 mon. IV
Risedronate (Actonel), Risedronate ER (Atelvia)	• PMO: Tx & prevention in women* • Osteoporosis in men: treat to ↑ bone mass • GIO: Tx in men & women	• PMO: IR - 75mg x 2 days/mon or 150mg/mon po, 35mg/wk or 5mg/day; ER - 35mg/wk po • Osteoporosis in men: 35mg/wk po • GIO: 5mg/day po
Zoledronic Acid (Reclast)	• PMO: Tx & prevention in women • Osteoporosis in men: treat to ↑ bone mass • GIO: Tx in men & women	• All Indications: 5mg/yr IV
Parathyroid Hormone Analog		
Teriparatide (Forteo)	• GIO: Tx in men & women • Osteoporosis in men: treat to ↑ bone mass • PMO: Tx. in women at high risk for fracture	• 20mcg/day SC
Abaloparatide (Tymlos)	• PMO: Tx in women at high risk for fracture	• 80mcg/day SC
Bone-modifying Agent		
Denosumab (Prolia)	• PMO: treat women at high risk for fracture • Osteoporosis in men: treat to ↑ bone mass • Breast cancer bone loss: treat to ↑ bone mass in women at high risk of fracture & using aromatase inhibitors • Prostate cancer bone loss: treat to ↑ bone mass in amen at high risk of fracture & using androgen therapy	• 60mg/6 mon SC
Sclerostin Inhibitor		
Evenity SubQ romosozumab	• PMO: Tx & prevention in women	• 210 mg (2 consecutive 105mg injections) per month for one year

**Atelvia only indicated for treatment of PMO*

Appendix IV: Monitoring & Patient Safety

Drug	Adverse Reactions	Monitoring	REMS
Actonel Risendro-nate	• Cardiovascular (CV): hypertension (HTN)) (11%) • Central Nervous system (CNS): headache (HA) (3-18%) • Dermatology (Derm): skin rash (8-12%) • GI: perforations/ulcers/bleeding (51%); diarrhea	• BMD: eval. q 2 yrs. • √ chronic back pain • Labs: 25(OH)D, Ca	None needed

Drug	Adverse Reactions	Monitoring	REMS
	(5-20%), nausea (4-13%), ab pain (2-12%) • Gentourinary (GU): UTI (11%) • Neurology/musculoskeletal (MSK): Arthralgia/back pain (6-33%) • Misc.: Infection (31%)		
Boniva ibandronate	• GI: dyspepsia (4-12%) • Neuro/MSK: Back pain (4-14%) • Respiratory (Resp.): URI (2-34%)		
Fosamax alendronate	• Endo/meta.: hypocalcemia (18%) • Pregnancy category C		
Reclast zoledronic acid	• CV: L ext. edema (39%), • CNS: Fatigue (39%), HA (5-19%), dizzy (18%), insomnia (16%), anxiety/depression (11-14%), agitation (13%), confusion (7-13%), hypoesthesia (12%), rigors (11%) • Derm: Alopecia (12%), dermatitis (11%) • Endocrine/metabolism:↓ hydrat. (5-14%), ↓PO/K/Mg (11-13%) • GI: N/V (14-46%), CNST (27-31%), diarrhea (17-24%), anorexia (9-22%), ab pain (14-6%), wgt ↓(16%), appetite ↓ (13%) • GU: UTI (12-14%) • Hem/Onc: anemia (22-33%), neutropenia (12%) • Neuro/MSK: Ostealgia (55%), weak (5-24%), myalgia (23%), arthralgia (5-21%), paresthenia (15%), limb/skeletal/back pain (12-15%), • Renal: ↓ renal function (8-17%); abnormal Cr.(40%) • Resp: dyspnea (22-7%), cough (12-22%) • Misc: fever (32-44%), candidiasis (12%)	• BMD: eval. q 2 yrs. • √ chronic back pain • Labs: Serum Cr (pre each dose), 25(OH)D, Ca, PO3, Mg • Fluid status: adequately hydrate pre & post dose	
Denosumab (Prolia)	• CV: HTN (11%) • Derm: dermatitis (4-11%), eczema (4-11%), • Neuro/SKM: Arthralgias (7-14%), limb pain (10-12%), back pain (8-12 %) • Other: Preg. category X, influenza (11%)	• BMD: eval. q 2 yrs. • √ chronic back pain • Labs: 25(OH)D, Ca, PO3, Mg, urinary Ca • Infections • Derm: allergic Rx. • SKM: pre oral exam	Warn re. infection, derm rxs, bone turn over ↓; Med guide dispensed
Teriparatide (Forteo)	• Endo/meta: ↑ Ca (6-11%) • Pregnancy category C	• BMD: eval. q 2 yrs. • √ Chronic back pain • Labs: 25(OH) D, urinary Ca (w prob.) • Ortho hypotension	Warn re osteo-sarcoma; Med guide dispensed
Abalopara-tide (Tymlos)	• Endo/meta: ↑ Uric acid (25%) • GU: hypercalciuria (11-20%) • Immume: antibodies49-68% • Other: erythema @ injection site, Preg cat. C		
Evenity Romosozu-mab	• Neuro/MSK: arthralgia (8-13%)	• BMD: eval q 1-3 yrs,bone turnover markerspre and q 3-6 months • CV: Signs & symptoms of Adverse CV event • Lab: calcium	

7.0 Revision History:

Original Effective Date: 07/26/2006

Next Review Date: 11/14/2020

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