Pharmacy Benefit Determination Policy

Policy Subject:	Osteoporosis Agents	**Dates:**	
Policy Number:	SHS PBD17	**Effective Date:**	July 26, 2006
Category:	Rheumatology	**Revision Date**	September 12, 2018
Policy Type:	☐ **Medical** ☒ **Pharmacy**	**Approval Date:**	October 24, 2018
Department:	Pharmacy	**Next Review Date**:	October 2019

Product (check all that apply):	**Clinical Approval By:**
☒ Group HMO/POS	**Medical Directors**
☒ Individual HMO/POS	PHP: Peter Graham, MD
☒ PPO	**Pharmacy and Therapeutics Committee**
☒ ASO	PHP: Peter Graham, MD

Policy Statement:

Physicians Health Plan, and PHP Insurance and Service Company, and Sparrow PHP will cover Osteoporosis Agents through the Pharmacy Benefit based on approval by the Clinical Pharmacist or Medical Director using the following determination guidelines

Drugs and Applicable Coding:

J-code: Forteo - J3110, Tymlos - pending

Clinical Determination Guidelines:

Document the following with chart notes

A. Diagnosis and severity (Appendix I)
   1. Treatment and prevention of postmenopausal osteoporosis (PMO) in women
   2. Treatment to increase bone mass in men with osteoporosis
   3. Treatment of glucocorticoid-induced osteoporosis (GIO) in women and men
   4. Treatment of Postmenopausal osteoporosis (PMO) in women with high risk of fractures (history of/or multiple risk factors for fracture)

B. Oral bisphosphonate agents: Branded products
   1. Other therapies:
      a. Failed generic bisphosphonates (all below)
         - ≥ 5% decrease bone mineral density (BMD) loss on generic bisphosphonate(s)
         - Verified adequate intake of calcium and vitamin D
         - Consistent medication fill history over a 1-year period
      b. Significant adverse effects experienced with generic bisphosphonate(s)
   3. Approval
      a. Initial: 1 year
      b. Re-approval: 1 year (increased or stable bone mineral density)

C. Parenteral parathyroid hormone analogs: Forteo SubQ (teriparatide), Tymos SubQ (abaloparatide)
   1. Diagnosis and severity
      a. Second line therapy
      b. T score: ≤ -3.5 even in absence of fracture, or ≤ -2.5 with fragility fracture (See Appendix III)
   2. Other therapies
      a. Failed generic oral bisphosphonates and zoledronic acid (all below):
         - ≥5% decrease bone mineral density (BMD) on bisphosphonate(s)
         - Verified adequate intake of calcium and vitamin D
         - Consistent medication fill history over a 1-year period
      b. Significant adverse effects with generic oral bisphosphonate(s) and zoledronic acid
   3. Contraindications:
      a. Oral bisphosphonate (1 of the following): Hypocalcemia, esophagus anomalies (e.g. stricture, achalasia) delaying esophageal emptying, inability to stand/sit upright for 30 minutes.
      b. Zoledronic acid: Hypocalcemia, Cr Cl < 35ml/min.
   4. Dosage regimen
      a. Forteo SubQ (teriparatide): 20mcg once daily for up to 2 years
      b. Tymlos SubQ (abaloparatide): 80mcg once daily for up to 2 years
   5. Approval
      a. Initial: 2 years
      b. Re-approval: Not indicated

D. Other
   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: 3-5 years after discontinued treatment.
      c. Treatment continuation after 3-5 years.
         - Continue: High risk of fracture with BMD t-score ≤ -2.5 and/or incidental vertebral fractures.
         - Discontinue: Low risk of fracture with BMD t-score > -2.5
   2. Combination treatment in Osteoporosis: Bisphosphonate with PTH analogues
      a. BMD:
         - Hip: significant increase BMD at 1 year.
         - Spine/femoral neck: No significant change
         - Low level of evidence (level downgraded due to high heterogeneity and low quality among studies)
      b. Risk of non/vertebral fracture:
         - No significant change
         - Moderate level of evidence
      c. Conclusion: No evidence for the superiority of combination therapy

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: Strength of Evidence for the Reduction of Risk of Fracture Types with Pharmacotherapy in women with Postmenopausal Osteoporosis

	Fracture Skeletal Site			
Agent	Vertebral	Non-veterbral	Hip	Wrist
Alendronate	●●●	●●●	●●●	●
Ibandronate	●●●	●●	●	o
Risedronate	●●●	●●●	●●●	●
Zoledronic Acid	●●●	●●●	●●●	o
Denosumab	●●●	●●●	●●●	o
Teriparatide	●●●	●●	●	o
Raloxifene	●●●	o	o	o

Strength of evidence legend: o *=insufficient strength evidence;* ● *= low strength of evidence*
●● *= moderate Strength of evidence;* ●●● *= high strength of evidence*

Appendix IV: 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 • Osteo 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 • Osteo 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

**Atelvia only indicated for treatment of PMO*

Appendix V: Monitoring & Patient Safety

Drug	Adverse Reactions	Monitoring	REMS
Actonel Risendro-nate	• CV: HTN (11%) • CNS: HA (3-18%) • Derm: Skin rash (8-12%) • GI: perforations/ulcers/bleeding (51%); diarrhea (5-20%), nausea (4-13%), ab pain (2-12%) • GU: UTI (11%) • Neuo/MSK: Arthralgia/back pain (6-33%) • Misc.: Infection (31%)	• BMD: eval. q 2 yrs. • √ chronic back pain • Labs: 25(OH)D, Ca	None needed
Boniva ibandronate	• GI: Dyspepsia (4-12%) • Neuro/MSK: Back pain (4-14%) • 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%) • Endo/meta:↓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 fx (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		

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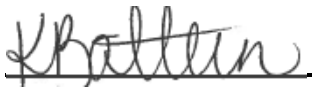
Approved By:

10/24/18

Peter Graham, MD – PHP Executive Medical Director — Date



10/24/18

Human Resources – Kurt Batteen — Date