Clinical Criteria

Subject:	Human Parathyroid Hormone Agents		
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Overview

This document addresses the use of human parathyroid hormone agents for the treatment of osteoporosis. Agents included in this clinical guideline include:

- Tymlos (abaloparatide)
- Forteo (teriparatide)
- Bonsity (teriparatide)

Tymlos (abaloparatide), Forteo (teriparatide), and Bonsity (teriparatide) are approved for the treatment of postmenopausal osteoporosis in a select population of women considered at high risk for fracture. Forteo and Bonsity are also approved for glucocorticoid-induced osteoporosis and men with hypogonadal osteoporosis at high risk for fracture. Bonsity is a follow-on to Forteo and carries the same indications. Its approval, in part, was based on safety and efficacy data from Forteo.

The American College of Endocrinology (AACE/ACE) (2020) osteoporosis treatment guidelines stratify initial treatment based on risk status. For those at high risk/no prior fractures, initial therapy options include bisphosphonates (alendronate, risedronate, or zoledronic acid) or denosumab. For those at very high risk, initial therapy options are denosumab, abaloparatide, teriparatide, romosozumab, or zoledronic acid. The Endocrine Society osteoporosis guideline update (2020) recommends initial therapy with bisphosphonates (alendronate, risedronate, zoledronic acid, or ibandronate) or alternatively denosumab for those at high risk. Teriparatide and abaloparatide are recommended for very high risk of fracture such as those with severe or multiple vertebral fractures. Due to lack of long term safety data and black box warnings, lifetime use of teriparatide or abaloparatide is limited to 2 years; and treatment should be followed with a bisphosphonate or denosumab.

Osteoporosis may be diagnosed by bone mineral density (BMD) testing indicating a T-score in the spine, femoral neck, total hip or distal 1/3 of the radius of less than or equal to -2.5 as compared to a young-adult reference population. It also may be clinically diagnosed based on a history of a fragility fracture (low trauma fracture). High risk for fracture is defined in the FDA label as history of osteoporotic fracture; or multiple risk factors for fractures; or a failure or intolerance to other osteoporosis therapies. A failure of other osteoporosis therapies, otherwise known as refractory disease, may be defined as a decline in BMD while on therapy (≥5%) or a fragility fracture while on therapy.

Tymlos (abaloparatide), Forteo (teriparatide), and Bonsity (teriparatide) have black box warnings for potential risk of osteosarcoma. In rats, an increase in the incidence of osteosarcoma (malignant bone tumor) dependent on dose and treatment duration has been identified with uncertain relevance to humans. Forteo should not be prescribed for individuals who are at increased baseline risk for osteosarcoma (including those with Paget's disease of bone or unexplained elevations of alkaline phosphatase, pediatric and young adults with open epiphyses, or prior external beam or implant radiation therapy involving the skeleton).

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Tymlos (abaloparatide)

Requests for Tymlos (abaloparatide) may be approved for the following:

I. Individual is a postmenopausal female with the following:
   A. A diagnosis of osteoporosis (defined as a bone mineral density (BMD) T-score in the spine, femoral neck, total hip or distal 1/3 of the radius of less than or equal to -2.5 as compared to a young-adult reference population OR a clinical diagnosis based on history of a low trauma fracture (fragility fracture)) at high risk for fracture;

AND

II. The individual meets one of the following:
   A. Individual is at very high risk for fracture as defined by one or more of the following (AACE/ACE 2020):
      1. Recent fracture (within the past 12 months)
      2. Fractures while on approved osteoporosis therapy
      3. Multiple fractures
      4. Fractures while on drugs causing skeletal harm (e.g. long-term glucocorticoids)
      5. Very low T-score (less than -3.0)
      6. High risk for falls or history of injurious falls
      7. Very high fracture probability by FRAX (fracture risk assessment tool) (e.g. major osteoporosis fracture >30%, hip fracture >4.5%) or other validated fracture risk algorithm;

   OR

   ~~A.~~B. Individual ~~H~~has been refractory to a prior trial of a bisphosphonate; **OR**
   ~~B.~~C. Individual ~~i~~s intolerant to or has a contraindication to a bisphosphonate as defined by:
      1. Hypersensitivity to TWO bisphosphonates (one of which must be alendronate); **OR**
      2. Inability to stand or sit upright for at least 30 minutes; **OR**
      3. Pre-existing gastrointestinal disorders (Barrett's esophagus, hypersecretory disorders, delayed esophageal emptying, atrophic gastritis, etc.); **OR**
      4. Uncorrected hypocalcemia; **OR**
      5. Severe renal insufficiency as defined by creatinine clearance less than 35 mL/min for alendronate agents and zoledronic acid or creatinine clearance less than 30 mL/min for risedronate and ibandronate;

AND

III. Individual is not using Tymlos (abaloparatide) in combination with any of the following:
   A. Prolia (denosumab);
   B. Bisphosphonates;
   C. Evista (raloxifene);
   D. Miacalcin/Fortical (calcitonin nasal spray);
   E. Reclast (zoledronic acid);
   F. Forteo (teriparatide);
   G. Evenity (romosozumab-aqqg);

AND

IV. Individual has utilized Tymlos (abaloparatide) AND Forteo (teriparatide) for a combined total duration of less than 24 months in their lifetime.

Forteo (teriparatide); Bonsity (teriparatide)

Requests for Forteo (teriparatide) or Bonsity (teriparatide) may be approved for the following:

I. Individual has one of the following:
   A. Individual is a postmenopausal female with diagnosis of osteoporosis (defined as bone mineral density (BMD) T-score in the spine, femoral neck, total hip or distal 1/3 of the radius of less than or equal to -2.5 as compared to young-adult reference population OR a clinical diagnosis based on history of a low trauma fracture (fragility fracture)) at high risk for fracture; **OR**
   B. Individual is a male diagnosed with primary or hypogonadal osteoporosis (defined as BMD T-score in the spine, femoral neck, total hip or distal 1/3 of the radius of less than or equal to -2.5 as compared to young-adult reference population OR a clinical diagnosis based on history of a low trauma fracture (fragility fracture)) at high risk for fracture using to increase bone mass; **OR**
   C. Individual has a diagnosis of osteoporosis (defined as BMD T-score in the spine, femoral neck, total hip or distal 1/3 of the radius of less than or equal to -2.5 as compared to young-adult reference population OR a clinical diagnosis based on history of a low trauma fracture (fragility fracture)) associated with sustained systemic glucocorticoid therapy (daily dosage equivalent to 5 mg or greater of prednisone for at least 3 months) at high risk for fracture;

AND

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II. Individual meets one of the following:

A. Individual is a postmenopausal female at very high risk for fracture as defined by one or more of the following (AACE/ACE 2020):

1. Recent fracture (within the past 12 months)
2. Fractures while on approved osteoporosis therapy
3. Multiple fractures
4. Fractures while on drugs causing skeletal harm (e.g. long-term glucocorticoids)
5. Very low T-score (less than -3.0)
6. High risk for falls or history of injurious falls
7. Very high fracture probability by FRAX (fracture risk assessment tool) (e.g. major osteoporosis fracture >30%, hip fracture >4.5%) or other validated fracture risk algorithm;

OR

~~A.~~B. Individual ~~H~~has been refractory to a prior trial of a bisphosphonate; **OR**

~~B.~~C. Individual ~~i~~is intolerant to or has a contraindication to a bisphosphonate as defined by:

1. Hypersensitivity to TWO bisphosphonates (one of which must be alendronate); **OR**
2. Inability to stand or sit upright for at least 30 minutes; **OR**
3. Pre-existing gastrointestinal disorders (Barrett's esophagus, hypersecretory disorders, delayed esophageal emptying, atrophic gastritis, etc.); **OR**
4. Uncorrected hypocalcemia; **OR**
5. Severe renal insufficiency as defined by creatinine clearance less than 35 mL/min for alendronate agents and zoledronic acid or creatinine clearance less than 30 mL/min for risedronate and ibandronate;

AND

III. Individual is not using Forteo (teriparatide) in combination with any of the following:

A. Prolia (denosumab)
B. Bisphosphonates
C. Evista (raloxifene)
D. Miacalcin/Fortical (calcitonin nasal spray)
E. Reclast (zoledronic acid)
F. Tymlos (abaloparatide);
G. Evenity (romosozumab-aqqg);
H. Another teriparatide agent;

AND

IV. Individual has utilized Forteo (teriparatide) AND Bonsity (teriparatide) AND Tymlos (abaloparatide) for a combined total duration of less than 24 months in their lifetime.

Requests for Forteo (teriparatide), Bonsity (teriparatide), and Tymlos (abaloparatide) may not be approved when the above criteria are not met and for all other indications.

Step Therapy

Note: When a human parathyroid hormone agent is deemed approvable based on the clinical criteria above, the benefit plan may have additional criteria requiring the use of a preferred[1] agent or agents.

A benefit plan may select any one or more of the following as preferred human parathyroid hormone agent(s): teriparatide (Forteo, Bonsity), abaloparatide (Tymlos).

Non-Preferred Human Parathyroid Hormone Agents for Osteoporosis Step Therapy

Currently step therapy does not apply under the medical benefit.

Requests for a non-preferred human parathyroid hormone agent for osteoporosis may be approved when the following criteria are met:

I. Individual has had a trial and inadequate response or intolerance to one preferred agent;

OR

II. The preferred agents is not FDA-approved and does not have an accepted off-label use per the off-label policy for the prescribed indication and the requested non-preferred agent does.

[1]Preferred, as used herein, refers to agents that were deemed to be clinically comparable to other agents in the same class or disease category but are preferred based upon clinical evidence and cost effectiveness.

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Quantity Limits

Miscellaneous Osteoporosis Agents Quantity Limit

Drug	Limit
Tymlos (abaloparatide) Injection 3120 mcg/1.56 mL	1 pen per 30 days
Forteo (teriparatide) Injection 600 mcg/2.4 mL	1 pen per 28 days
Bonsity (teriparatide) Injection 620 mcg/ 2.48 mL	1 pen per 28 days

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

C9399	Unclassified drugs or biologicals [when specified as abaloparatide (Tymlos)]
J3490	Unclassified drugs [when specified as abaloparatide (Tymlos)]
J3110	Injection, teriparatide, 10 mcg [Bonsity] [Forteo]

ICD-10 Diagnosis

M80.00XA-M80.88XS	Osteoporosis with current pathological fracture
M81.0-M81.8	Osteoporosis without current pathological fracture

Document History

Revised: 08/21/2020
Document History:

- 08/21/2020 – Annual Review: Update criteria to include factors for very high fracture risk in individuals who have not had a trial of a bisphosphonate. Administrative update to add drug specific quantity limit. Coding Reviewed: Added drug Forteo to J3110
- 02/21/2020 – Select Review: Add PA and QL for Bonsity (teriparatide); add Bonsity as potential preferred in step therapy; Update Tymlos and Forteo criteria to include references to Bonsity where applicable. Coding Reviewed: Added HCPCS C9399 for Tymlos, Added HCPCS J3110 for Bonsity
- 08/16/2019 – Annual Review: Update bisphosphonate trial requirement wording to account for intravenous options; add Evenity to list of agents that may not be used in combination. Coding Reviewed: Removed HCPCS J3110 Forteo.
- 11/02/2018 – Added HCPCS for Forteo: J3110.
- 08/17/2018 – Annual Review: Initial review of DRUG.00103. Add new ST for Non-Preferred Human Parathyroid Hormone Agents for Osteoporosis. Update Tymlos PA to delete embedded ST through Prolia or zoledronic acid and Forteo. Update Tymlos PA to add atrophic gastritis as an example of a pre-existing gastrointestinal disorder for consistency.

References

1. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis – 2020 Update. *Endocrine Practice*. 2020;26(1):1-46.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2020. URL: http://www.clinicalpharmacology.com. Updated periodically.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 8, 2020.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Drug Facts and Comparisons. Facts and Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; 2019. Updated periodically.
6. Eastell R, Rosen CJ, Black DM, et al. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Clinical Practice Guideline, The Journal of Clinical Endocrinology & Metabolism, Volume 104, Issue 5, May 2019, Pages 1595–1622, https://doi.org/10.1210/jc.2019-00221.

7. Shoback D, Rosen CJ, Black DM, et al. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Guideline Update, The Journal of Clinical Endocrinology & Metabolism, Volume 105, Issue 3, March 2020, Pages 587-594.
8. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2020; Updated periodically.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.