**Parathyroid Hormone Analog for Osteoporosis**

**Prior Authorization with Quantity Limit Program Summary**

This program applies to Medicaid.

Prior authorization applies to Tymlos only. Quantity limits apply to Tymlos and Forteo.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
<th>Dosage and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Forteo</strong> (teriparatide) 20 mcg / injection pen</td>
<td>Treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, teriparatide reduces the risk of vertebral and nonvertebral fractures. Increase bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy. Treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy (daily dosage equivalent to 5 mg or greater of prednisone) at high risk for fracture, defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.</td>
<td>Recommended dose is 20 mcg subcutaneously once a day. Use of the drug for more than 2 years during a patient’s lifetime is not recommended.</td>
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<tr>
<td>Tymlos (abaloparatide) 80 mcg / injection pen</td>
<td>Treatment of postmenopausal women with osteoporosis at high risk for fracture defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, abaloparatide reduces the risk of vertebral fractures and nonvertebral fractures.</td>
<td>Recommended dose is 80 mcg subcutaneously once daily; patients should receive supplemental calcium and vitamin D if dietary intake is inadequate. Because of the unknown relevance of the rodent osteosarcoma findings to humans, cumulative use of abaloparatide and parathyroid hormone analogs (e.g., teriparatide) for more than 2 years during a patient’s lifetime is not recommended.</td>
</tr>
</tbody>
</table>

**CLINICAL RATIONALE**

**Postmenopausal Osteoporosis**

The diagnosis of osteoporosis (OP) in postmenopausal women and men over the age of 50 can be established through one of the following:

- Presence of fragility fractures (hip or spine) in the absence of other metabolic bone disorders
- T-score of -2.5 or lower in the lumbar spine, femoral neck, total hip
- T-score between -1 and -2.5 and increased risk using FRAX country specific thresholds
- T-score between -1 and -2.5 with a fragility fracture of the proximal humerus, pelvis, or possibly distal forearm

<table>
<thead>
<tr>
<th>BMD-based definitions of bone density</th>
</tr>
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<tbody>
<tr>
<td>Normal</td>
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<tr>
<td>Low bone mass (osteopenia)</td>
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<tr>
<td>Osteoporosis</td>
</tr>
</tbody>
</table>

The NAMS and NOF as well as the American Association of Clinical Endocrinologists (AACE) recommend OP drug therapy in the following populations:

- All men and postmenopausal women who have had an osteoporotic vertebral or hip fracture
- All men and postmenopausal women who have BMD values consistent with OP (i.e., T-scores ≤ -2.5) at the lumbar spine, femoral neck, or total hip region.
- All men age 50 and older, and postmenopausal women who have T-scores from -1.0 to -2.5 at the femoral neck, total hip, or spine and a 10-year probability of a hip fracture ≥ 3% or a 10-year probability of a major OP-related fracture ≥ 20%.

The risk for a second fragility fracture decreases as time passes from the first fracture. The study by Johnell et al. found that for all fractures, more fractures occurred in the first year after initial fracture than in subsequent years. The number of fractures decreased progressively thereafter with time. Schousboe et al. found that prior non-spine non-hip fracture confers a modest excess risk for incident hip fracture independent of BMD after 10 years; that excess risk, however, was only about one third the excess risk during the first 5 years of follow-up.
The NAMS recommends bisphosphonates as first line therapy in the treatment of postmenopausal OP. They also recommend teriparatide “offered to women with OP who are at high risk for fracture.” Teriparatide therapy is not indicated for ≥ 24 months.5

Guidelines from the American Association of Clinical Endocrinologists (AACE)9 and the American College of Obstetricians and Gynecologists (ACOG)14 state that although evidence for the efficacy in reducing the risk of new vertebral fractures is available for all of the agents approved for the treatment of osteoporosis (alendronate, ibandronate, risedronate, zoledronic acid (5 mg/100 mL), calcitonin, denosumab (60mg/mL), raloxifene, and teriparatide), only alendronate, risedronate, zoledronic acid, denosumab, and teriparatide reduce the risk of non-vertebral fractures. Alendronate, risedronate, zoledronic acid, and denosumab have demonstrated reduction of the risk of hip fractures in prospective controlled osteoporosis trials.9,14

The AACE recommends alendronate, risedronate, zoledronic acid, or denosumab as first line agents. For patients unable to use oral therapy, teriparatide, denosumab, or zoledronic acid should be considered as initial therapy. Teriparatide, denosumab, or zoledronic acid can be considered as initial therapy for those who have the highest fracture risk (e.g., older women who have had multiple vertebral fractures or hip fractures, or who have very low T-scores). For patients at high risk of spine fracture but not at risk for hip or nonvertebral fractures, ibandronate and raloxifene may be appropriate, and raloxifene has a "side benefit" of reducing breast cancer risk. Raloxifene or ibandronate may be appropriate initial therapy in some cases where patients require drugs with spine-specific efficacy. Denosumab is the agent of choice for patients with renal insufficiency, but this agent is not recommended for dialysis patients or those with stage 5 kidney disease due to the high risk of hypocalcemia.9

The American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin: Osteoporosis (2012) states that teriparatide is usually reserved for cases of severe osteoporosis and for patients who have experienced fractures. Teriparatide therapy should be limited to 24 months.14

Due to the lack of evidence on the effect on fracture risk, concomitant use of osteoporosis agents is not recommended.5,9

A published study of abaloparatide provides data on an open-label teriparatide comparator arm of the trial. 2463 women were randomized to receive daily SC injections of abaloparatide, 80 μg, or matching placebo, or SC teriparatide, 20 μg. Abaloparatide and matching placebo were administered using a double-blind format, while teriparatide, because it could be administered only via its trademarked injection pen, was given open label.16

- Like abaloparatide, teriparatide resulted in similar reduction in new vertebral fractures vs. placebo (both p<0.001 vs. placebo; no statistical analysis for abaloparatide vs teriparatide).
- Incidence of nonvertebral fractures with teriparatide was not significantly different from placebo in this study (teriparatide vs. placebo: risk difference [RD]= -1.46; hazard ratio [HR]= 0.72; p=0.22). Results for abaloparatide vs. placebo was RD= -2.01, HR= 0.57, p= .049. Results for abaloparatide vs. teriparatide was RD= -0.55, HR=0.79, p= 0.44.
- Results suggested abaloparatide caused modestly higher BMD gains vs. placebo and teriparatide groups. Incidence of hypercalcemia was lower with abaloparatide vs. teriparatide, consistent with less bone resorption with abaloparatide. Differing patterns of bone formation and resorption between these agents requires further study.

Osteoporosis in Men
OP in men can be classified as primary or secondary, with primary osteoporosis often divided into idiopathic and age-related based on the age of diagnosis. Secondary osteoporosis in men is caused by glucocorticoid use, hypogonadism, or excessive alcohol intake. These factors are present in the majority of men ≤ 65 years old with OP.4
Bisphosphonate therapy halts bone loss but does not add new bone, nor do they restore disrupted microarchitecture. In severe cases of osteoporosis, putting a stop to further bone loss may not be enough to prevent further fractures. In these cases, treatments that stimulate bone formation and reverse skeletal deterioration may be necessary. In men, where decreased bone formation is an important etiological factor, an anabolic treatment is the treatment of choice. Teriparatide is the only anabolic agent currently approved for treatment of OP in men.

The Endocrine Society 2012 Clinical Practice Guideline: Osteoporosis in Men recommends the following: Men at high risk of fracture be treated with medication approved by regulatory agencies such as the U.S. FDA or the European Medicines Agency (EMA) (alendronate, risedronate, zoledronic acid, and teriparatide; also denosumab for men receiving ADT [androgen deprivation therapy] for prostate cancer) and that the selection of therapeutic agent be individualized based on factors including fracture history, severity of osteoporosis (T-scores), the risk for hip fracture.

Glucocorticoid Induced Osteoporosis
Bisphosphonates are effective in preventing and treating glucocorticoid induced OP (GIO) at the lumbar spine and femoral neck and are recommended over teriparatide. Teriparatide may be an option in those who have failed bisphosphonate therapy.

Safety
Teriparatide is contraindicated in patients with hypersensitivity to teriparatide or to any of its excipients.

Teriparatide carries the following black box warnings:

- In rats, teriparatide caused an increase in the incidence of osteosarcoma, a malignant bone tumor.
- Because of the uncertain relevance of the rat osteosarcoma finding to humans, prescribe teriparatide only for patients for whom potential benefits outweigh potential risk.
- Teriparatide should not be prescribed for patients at increased baseline risk for osteosarcoma (e.g., those with Paget’s disease of bone or unexplained elevations of alkaline phosphatase, pediatric and young adult patients with open epiphyses, or prior external beam or implant radiation therapy involving the skeleton).

Abaloparatide does not have any contraindications.

Abaloparatide carries the following black box warning:

- Abaloparatide caused a dose-dependent increase in the incidence of osteosarcoma, a malignant bone tumor, in male and female rats. It is unknown whether abaloparatide will cause osteosarcoma in humans.
- Use of abaloparatide is not recommended in patients at increased risk for osteosarcoma.
- Cumulative use of abaloparatide and parathyroid hormone analogs (e.g., teriparatide) for more than 2 years during a patient’s lifetime is not recommended.

For additional clinical information see the Prime Therapeutics Formulary Chapter 4.9A Calcium Regulators/Osteoporosis Agents.

REFERENCES
4. Gagnon C, Li V, Ebeling PR. Osteoporosis in men: its pathophysiology and the role of


Parathyroid Hormone Analog for Osteoporosis Prior Authorization with Quantity Limit

OBJECTIVE
The intent of the Parathyroid Hormone Analog for Osteoporosis Prior Authorization (PA) with Quantity Limit (QL) program is to ensure appropriate selection of patients for treatment according to product labeling and/or clinical studies and/or guidelines and according to dosing recommended in product labeling. Patients considered candidates for therapy include:

1) patients with prior vertebral or low-trauma or fragility fractures in the past five years;
2) patients with a diagnosis of osteoporosis (T-score ≤ -2.5 standard deviations (SDs) per World Health Organization (WHO) classification system) who have already tried a bisphophonate, or a selective estrogen receptor modulator (SERM) for those whom it is appropriate, or cannot take those medications

Target agents will not be approved for patients in whom it would be contraindicated or for patients who are at an increased baseline risk for osteosarcoma. Because use beyond 2 years is not recommended, the PA criteria will approve for a total of 2 years of cumulative therapy between the target agents. Because concomitant use of target agents and other osteoporosis agents including bisphosphonates, SERM, Prolia® (denosumab), and other parathyroid hormone analogs is not supported, these combinations will not be approved.

TARGET AGENTS
Forteo (teriparatide)
Tymlos (abaloparatide)

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Forteo will be approved when ALL of the following are met:
1. The patient has a diagnosis of osteoporosis defined as ONE of the following:
   a. The patient has a history of vertebral fracture(s), or low trauma or fragility fracture(s) [e.g., prior fracture from minor trauma such as falling from standing height or less] within the past 5 years
   OR
   b. The patient has a T-score that is -2.5 or lower AND ONE of the following:
      i. The patient has tried and had an inadequate response to a bisphosphonate
      OR
      ii. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a bisphosphonate
      OR
      iii. BOTH of the following:
         1. ONE of the following:
            a. The patient is female
            OR
            b. The prescriber has provided documentation that a SERM is medically appropriate for the patient’s gender
         AND
         2. ONE of the following:
            a. The patient has tried and had an inadequate response to a SERM
            OR
            b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a SERM

      AND

      2. The patient does NOT have any FDA labeled contraindication(s) to the requested agent
AND
3. The patient does NOT have an increased baseline risk for osteosarcoma
AND
4. ONE of the following:
   a. The patient is not receiving a concomitant bisphosphonate, SERM, Xgeva (denosumab), Prolia (denosumab), or another parathyroid hormone analog [Tymlos (abaloparatide)] therapy in the past 90 days
   OR
   b. The prescriber indicates that the patient will discontinue the current bisphosphonate, SERM, Xgeva (denosumab), Prolia (denosumab), or parathyroid hormone analog [Tymlos (abaloparatide)] therapy before starting the requested agent
AND
5. The dose requested is within the FDA approved labeling [Forteo (teriparatide) – 20 mcg subcutaneously once daily]
AND
6. The total duration of treatment with Forteo (teriparatide) and Tymlos (abaloparatide) has not exceeded 2 years in lifetime

Length of approval: up to a total of 2 years of treatment in lifetime between Forteo (teriparatide) and Tymlos (abaloparatide). Only one parathyroid hormone analog will be approved for use at a time.

Tymlos will be approved when ALL of the following are met:
1. The patient is postmenopausal with a diagnosis of osteoporosis defined by ONE of the following:
   a. The patient has a history of vertebral fracture(s), or low trauma or fragility fracture(s) [e.g., prior fracture from minor trauma such as falling from standing height or less] within the past 5 years
   OR
   b. The patient has a T-score that is –2.5 or lower AND ONE of the following:
      i. The patient has tried and had an inadequate response to a bisphosphonate
      OR
      ii. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a bisphosphonate
      OR
      iii. BOTH of the following:
         1. ONE of the following:
            a. The patient is female
            OR
            b. The prescriber has provided documentation that a SERM is medically appropriate for the patient’s gender
         AND
         2. ONE of the following:
            a. The patient has tried and had an inadequate response to a SERM
            OR
            b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a SERM
AND
2. The patient does NOT have any FDA labeled contraindication(s) to the requested agent
3. The patient does NOT have an increased baseline risk for osteosarcoma
   AND
4. ONE of the following:
   a. The patient is not receiving a concomitant bisphosphonate, SERM, Xgeva (denosumab), Prolia (denosumab), or another parathyroid hormone analog [Forteo (teriparatide)] therapy in the past 90 days
   OR
   b. The prescriber indicates that the patient will discontinue the current bisphosphonate, SERM, Xgeva (denosumab), Prolia (denosumab), or parathyroid hormone analog [Forteo (teriparatide)] therapy before starting the requested agent
   AND
5. The dose requested is within the FDA approved labeling [Tymlos (abaloparatide) – 80 mcg subcutaneously once daily]
   AND
6. The total duration of treatment with Forteo (teriparatide) and Tymlos (abaloparatide) has not exceeded 2 years in lifetime

**Length of approval:** up to a total of 2 years of treatment in lifetime between Forteo (teriparatide) and Tymlos (abaloparatide). Only one parathyroid hormone analog will be approved for use at a time.