Forteo® (teriparatide) Prior Authorization Criteria

FDA APPROVED INDICATIONS AND DOSAGE

**FDA Indication:** Forteo is indicated for:
- the treatment of postmenopausal women with osteoporosis who are at high risk for fracture;
- to increase bone mass in men with primary or hypogonadal osteoporosis who are at high risk for fracture;
- the 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.

“High risk for fracture” is 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.

**Dosing:** recommended dose is 20 mcg subcutaneously once daily

**CLINICAL RATIONALE**

**Postmenopausal Osteoporosis**

The diagnosis of osteoporosis (OP) has been established by measurement of bone mineral density (BMD). BMD appears to be a predictor of fractures. BMD is expressed in absolute terms of grams of mineral per square centimeter scanned (g/cm²) and as a relationship to two norms: compared to the expected BMD for the patient’s age and sex (Z-score), or compared to “young normal” adults of the same sex (T-score). The difference between the patient’s score and the norm is expressed in standard deviations (SD) above or below the mean. Usually, 1 SD equals 10 to 15% of the BMD value in g/cm². The North American Menopause Society (NAMS), World Health Organization (WHO), International Society of Clinical Densitometry, and the National Osteoporosis Foundation (NOF) define OP in postmenopausal women or a man ≥50 years old as a BMD T-score ≤ -2.5 at the total hip, femoral hip, or lumbar spine (≥ 2 vertebral levels measured in the posterior-anterior projection not the lateral projection). In addition to diagnosis through densitometry, OP can be diagnosed clinically, regardless of the T-score. The presence of fragility fracture constitutes a clinical diagnosis of OP.

<table>
<thead>
<tr>
<th>BMD-based definitions of bone density</th>
<th>T-score range</th>
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<tbody>
<tr>
<td>Normal</td>
<td>T-score ≥ -1.0</td>
</tr>
<tr>
<td>Low bone mass (osteopenia)</td>
<td>T-score between -1.0 and -2.5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>T-score ≤ -2.5</td>
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A management strategy focused on lifestyle approaches may be all that is needed in postmenopausal women who are at low risk of OP fracture. All postmenopausal women, regardless of their BMD or clinical risk factors for OP, should be encouraged to eat a balanced diet, obtain adequate calcium and vitamin D₃, participate in appropriate exercise, avoid cigarette smoke and excessive alcohol consumption, and institute fall prevention measures.
The NAMS and NOF recommend adding OP drug therapy in the following populations:\(^5,^8\)

- All postmenopausal women who have had an osteoporotic vertebral or hip fracture
- All 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 postmenopausal women who have T-scores from -1.0 to -2.5 at the femoral neck or spine and a 10-year probability of a hip fracture \(\geq 3\%\) or a 10-year probability of a major OP-related fracture \(\geq 20\%\).

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 \(\geq 24\) months.\(^5\)

**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, and excessive alcohol intake. These factors are present in the majority of men \(\leq 65\) 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 stimulates bone formation and reverse skeletal deterioration may be necessary.\(^4\) In men, where decreased bone formation is an important etiological factor, an anabolic treatment is the treatment of choice.\(^3-^4\) Teriparatide is the only anabolic agent currently approved for treatment of OP in men.\(^3\)

**Glucocorticoid Induced Osteoporosis**

Glucocorticoids decrease bone formation by reducing the lifespan of osteoblasts and osteocytes. Bisphosphonates are effective in preventing and treating glucocorticoid induced OP (GIO) at the lumbar spine and femoral neck.\(^9\) The American College of Rheumatology recommends bisphosphonates as first line treatment for the treatment and prevention of GIO.\(^9\)

**Teriparatide**

Teriparatide is a recombinant form of human parathyroid hormone (PTH) used to treat severe osteoporosis, and stimulates bone formation, rather than reducing turnover.\(^1,^3-^4\) Teriparatide’s action is similar to that of endogenous PTH, the main function of which is the regulation calcium and phosphate metabolism in the bone and kidney. Teriparatide has the same physiological actions as PTH on the bone and kidney to cause bone formation.\(^1,^3-^4\) Treatment with parathyroid hormone or teriparatide results in increased bone mineral density, improved cancellous and cortical microarchitecture, and increased bone formation rate. With teriparatide therapy, there is significantly lower matrix mineralization compared with placebo and a shift toward less mature collagen cross-links. In addition, parathyroid hormone inhibits osteoblast apoptosis, resulting in an increase in bone formation, and with enhanced deposition of new bone matrix, the osteocyte pool is replenished. These changes account for the reported increase of bone strength and the significant reduction in vertebral and nonvertebral fracture risk.\(^3\) Teriparatide in a dose of 20 \(\mu\)g daily was shown to decrease the risk of vertebral fractures by 65% and non-vertebral fractures by 53% in patients with osteoporosis, after an average of 18 months of therapy.\(^8\)

**Efficacy**

**Postmenopausal Osteoporosis\(^2\)**

A multicenter double blind placebo control study of once daily subcutaneous injection of teriparatide included 1637 postmenopausal women with OP. New vertebral fractures occurred in 14 percent of the women in the placebo group and in 5 % and 4 % respectively, of the women in the 20-\(\mu\)g and 40-\(\mu\)g parathyroid hormone groups; the respective relative risks of fracture in the 20-\(\mu\)g and 40-\(\mu\)g groups, as compared with the placebo group, were 0.35 and 0.31 (95 percent confidence intervals [CI], 0.22 to 0.55 and 0.19 to 0.50). New nonvertebral fragility fractures
occurred in 6% of the women in the placebo group and in 3% of those in each parathyroid hormone group (relative risk, 0.47 and 0.46, respectively [95% CI, 0.25 to 0.88 and 0.25 to 0.86]). As compared with placebo, the 20-µg and 40-µg doses of parathyroid hormone increased BMD by 9 and 13 more percentage points in the lumbar spine and by 3 and 6 more percentage points in the femoral neck; the 40-µg dose decreased BMD at the shaft of the radius by 2 more percentage points. Both doses increased total-body bone mineral by 2 to 4 more percentage points than did placebo.

The efficacy and safety of teriparatide in combination with alendronate or raloxifene was assessed in an open label, randomized trial. Postmenopausal women with OP on alendronate or raloxifene for at least 18 months (n=198) were enrolled. Patients were randomized to either add on teriparatide to existing therapy (add group) or discontinue previous therapy and switch to teriparatide (switch group). The primary outcome measure was the change in bone mineral density (BMD) at 18 months. BMD in the lumbar spine increased 8.4% in the add group compared to 4.8% in the switch group at 18 months (p=0.003). Total hip BMD was increased 3.2% in the add group compared to 0.9% in the switch group at 18 months (p=0.02). Increases in femoral neck BMD were not significantly different between groups at 18 months. PINP (a marker of bone turnover) increases were smaller in the add group compared to the switch group (64% vs. 401%; p<0.001) at six months.12

**Osteoporosis in Men**10

Orwoll, et al. studied the effects of teriparatide on bone density in men with OP. Four hundred thirty seven men with spine or hip BMD more than 2 standard deviations below the young adult male mean were randomized to three groups: (i) daily injections of placebo, (ii) teriparatide 20 mcg, or (iii) teriparatide 40 mcg. All subjects also received supplemental calcium and vitamin D. The study was stopped after a median duration of 11 months because of a finding of osteosarcomas in rats in routine toxicology studies. Biochemical markers of bone formation increased early in the course of therapy and were followed by increases in indices of osteoclastic activity. Spine BMD was significantly greater than in placebo subjects after 3 months of teriparatide therapy, and by the end of therapy it was increased by 5.9% (20 mcg) and 9.0% (40 mcg) above baseline. Femoral neck BMD increased 1.5% (20 mcg) and 2.9% (40 mcg), and whole body bone mineral content increased 0.6% (20 mcg) and 0.9% (40 mcg) above baseline in the teriparatide-treated subjects. There was no change in radial BMD in the teriparatide-treated groups. BMD responses to teriparatide were similar regardless of gonadal status, age, baseline BMD, body mass index, smoking, or alcohol intake. Subjects experienced expected changes in mineral metabolism. Adverse events were similar in the placebo and 20-mcg groups, but more frequent in the 40-mcg group. This study shows that teriparatide treatment results in an increase in BMD and is a potentially useful therapy for OP in men.

**Glucocorticoid Induced Osteoporosis**11

In 2009 the FDA expanded the indications for teriparatide to include adults with a high risk for fracture related to GIO. The FDA’s decision was based on data from an 18-month randomized, double-blind, controlled clinical trial that compared teriparatide with alendronate in 428 women and men with osteoporosis (aged 22 to 89 years) who had received sustained glucocorticoid therapy. Sustained glucocorticoid therapy was defined as a mean daily dose of 5 mg or more of prednisone or its equivalent for at least 3 months. A total of 214 patients received 20 mcg of teriparatide once-daily, and 214 received 10 mg of alendronate once-daily. The primary outcome was the change in BMD at the lumbar spine. Secondary outcomes included changes in BMD at the total hip and in markers of bone turnover, the time to changes in BMD, the incidence of fractures, and safety. At the last measurement, the mean (+/- SE) BMD at the lumbar spine had increased more in the teriparatide group than in the alendronate group (7.2 +/- 0.7 % versus 3.4 +/- 0.7 %, p < 0.001). A significant difference between the groups was reached by 6 months (p < 0.001). At 12 months, BMD at the total hip had increased more in the teriparatide group. Fewer new vertebral fractures occurred in the teriparatide group than in the alendronate group.
(0.6 % versus 6.1%, p = 0.004); the incidence of non-vertebral fractures was similar in the two groups (5.6% versus 3.7%, p = 0.36).

**Safety**
In clinical trials, the frequency of at \( \geq 1 \) episode of transient hypercalcemia in the 4 to 6 hours after teriparatide administration was 11% of women and 6% of men. Antibodies to teriparatide have been noted in about 3% of women with long-term treatment; however hypersensitivity reactions or decreased efficacy has not been seen.

Teriparatide should not be used in patients at increased risk of bone cancers, such as those with:

- Paget's disease
- Hyperparathyroidism
- Open epiphyses
- A history of skeletal radiation therapy
- Unexplained increases in serum alkaline phosphatase concentration
- Pre-existing hypercalcemia or urolithiasis

Forteo's product labeling carries a Boxed Warning, which highlights the concern over the association between the drug and osteosarcomas in laboratory rats.\(^1\) Because individuals with growing bones (namely children and adolescents with open epiphyses), persons with unexplained elevations in alkaline phosphatase, patients with prior external beam or implant irradiation of the skeleton, and patients with Paget's disease of the bone have a higher risk for developing osteosarcoma, the Boxed Warning states that it is important that teriparatide not be used in these groups. Furthermore, the product labeling states that individuals with hypercalcemia, women who are pregnant or nursing, or those who have ever been diagnosed with bone cancer or other cancers that have metastasized to the bones, should not use teriparatide. According to the product labeling, because the long-term effectiveness and safety of teriparatide treatment are not known at this time, therapy for more than 2 years is not recommended.

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

**REFERENCES**


**Document History**

Original Prime Standard criteria 05/2005, UM Committee approval 05/11/2005 [PS_Forteo_PA_0505]
Annual Review Prime Standard criteria with changes approved by External UM Committee 11/2006
Initial Client Specific Review Prime Standard criteria approved by HCSC Corporate Clinical Committee 09/2008
Annual Review Prime Standard criteria, criteria maintained; approved by P&T UM Committee 02/2009
Client Specific Annual Review Prime Standard criteria, criteria maintained, approved by HCSC Corporate Clinical Committee 09/2009
Annual Review Prime Standard criteria, criteria maintained; approved by P&T UM Committee 02/2010
Mid-year Review Prime Standard criteria (removal of non-coverage of concomitant therapy) approved by P&T UM Committee 05/2010
Client Specific Annual Review Client Specific criteria, with changes, approved by HCSC Corporate Clinical Committee 09/2010
**Forteo® (teriparatide) Prior Authorization**

**OBJECTIVE**
The intent of the Forteo (teriparatide) Prior Authorization (PA) program is to ensure appropriate selection of patients for treatment according to product labeling and/or clinical studies and/or guidelines. The PA criteria for Forteo apply to both men and women. Patients considered candidates for therapy with Forteo include:

1. patients with a diagnosis of osteoporosis (T-score ≤ -2.5 standard deviations (SDs) per World Health Organization (WHO) classification system) and a preexisting vertebral or fragility fracture;
2. patients with very low bone mineral density (BMD) (T-scores ≤ -3.5 SD); and
3. patients with osteoporosis or prior low-trauma or fragility fractures who have not had an adequate response to first-line therapy.

Because the safety and efficacy of Forteo beyond two years of treatment have not been evaluated, the PA criteria for Forteo will approve use initially for 2 years with no renewal. The PA criteria will not approve combination therapy with Forteo and a bisphosphonate or Forteo plus a SERM. Because concomitant use of Forteo and Prolia® (denosumab) has not been studied, this combination will also not be approved.

**TARGET DRUG**
Forteo (teriparatide)

**PRIOR AUTHORIZATION CRITERIA FOR APPROVAL**
Forteo will be approved when ALL of the following are met:

1. ONE of the following:
   a. The patient has a diagnosis of osteoporosis defined as a T-score that is ≤ -2.5 or lower (≥ 2.5 SD below the mean BMD value for a young adult) AND ONE of the following:
      i. The patient has a very low BMD defined as a T-score of ≤ -3.5 or lower OR
      ii. The patient has a history of prevalent 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] OR
      iii. The patient has had a trial and failure of a first-line agent (bisphosphonate or SERM for women, bisphosphonate for men) OR
      iv. The patient has a contraindication to SERM and bisphosphonate (bisphosphonate only if male)
   b. The patient has a history of prevalent vertebral fracture(s) or low trauma or fragility fracture(s) (without a diagnosis of osteoporosis) AND ONE of the following:
      i. The patient has had a trial and failure of a first-line agent (bisphosphonate or SERM for women, bisphosphonate for men) OR
      ii. The patient has a contraindication to SERM and bisphosphonate (bisphosphonate only if male)

2. The patient is not receiving concomitant bisphosphonate, SERM, or Prolia (denosumab) therapy

3. The total duration of treatment with Forteo has not exceeded 2 years

**Length of approval:** up to a total of 2 years of treatment
Forteo® (teriparatide) Prior Authorization

ELECTRONIC EDIT
The overall process for a prior authorization will not allow the targeted drugs to adjudicate through the claims system. When a patient requests a targeted drug the system will reject the claim with the message indicating that prior authorization is necessary.

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forteo (teriparatide)</td>
<td>30044070002020</td>
<td>M, N, O, or Y</td>
</tr>
</tbody>
</table>

**PRIOR AUTHORIZATION CRITERIA QUESTION SET**

**Initial and Renewal Evaluation**

1. Does the patient have a diagnosis of osteoporosis as defined by a T-score at or below -2.5 SD?
   If yes, continue to 3. If no, continue to 2.

2. Has the patient experienced previous fragility or low trauma fracture (e.g., prior fracture from minor trauma or falling from standing height or less)?
   If yes, continue to 5. If no, deny.

3. Does the patient have a T-score at or below -3.5 SD?
   If yes, continue to 7. If no, continue to 4.

4. Does the patient have a T-score between -2.5 and -3.5 SD and a previous fragility or low-trauma fracture?
   If yes, continue to 7. If no, continue to 5.

5. Has the patient tried and failed a selective estrogen receptor modulator (SERM) or bisphosphonate agent?
   If yes, continue to 7. If no, continue to 6.

6. Does the patient have a contraindication to SERM and bisphosphonate (for male patients: contraindication to a bisphosphonate only)?
   If yes, continue to 7. If no, deny.

7. If previously prescribed, will any bisphosphonate or SERM be discontinued before initiation of Forteo?
   If yes, continue to 8. If no, deny.
   (If no previous bisphosphonate or SERM therapy, continue to 8).

8. Is the patient currently being treated with Prolia (denosumab)?
   If yes, continue to 9. If no, continue to 10.

9. Will the Prolia be discontinued before initiation of Forteo?
   If yes, continue to 10. If no, deny.

10. Has the patient been previously treated with Forteo?
    If yes, continue to 11.
    If no, approve for 2 years.

11. Has the previous course of Forteo treatment been 2 years or greater?
    If yes, deny. If no, approve for the remainder of 2 years.