Parathyroid Hormone Analog for Osteoporosis Prior Authorization Through Preferred with Quantity Limit Program Summary

Program applies to FlexRx Open, FlexRx Closed, GenRx Open, GenRx Closed, Health Insurance Marketplace, FocusRx and KeyRx formularies.

This is a FlexRx standard and GenRx standard prior authorization program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

FDA APPROVED INDICATIONS AND DOSAGE\textsuperscript{1,2}

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
<th>Dosage and Administration</th>
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<tbody>
<tr>
<td>Forteo® (teriparatide) injection solution</td>
<td>Treatment of postmenopausal women with osteoporosis at high risk for fracture. &lt;br&gt; Increase bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture. &lt;br&gt; Treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy at high risk for fracture.</td>
<td>Recommended dose is 20 mcg subcutaneously once a day. &lt;br&gt; Use of the drug for more than 2 years during a patient's lifetime is not recommended.</td>
</tr>
<tr>
<td>Tymlos® (abaloparatide) injection solution</td>
<td>Treatment of postmenopausal women with osteoporosis at high risk for fracture.</td>
<td>Recommended dose is 80 mcg subcutaneously once daily; patients should receive supplemental calcium and vitamin D if dietary intake is inadequate. &lt;br&gt; Limitation of use: 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
Diagnosis of Osteoporosis
The National Osteoporosis Foundation states that the diagnosis of osteoporosis (OP) can be established by either measurement of bone mineral density (BMD) or by the occurrence of adulthood hip or vertebral fracture in the absence of major trauma (such as a motor vehicle accident or multiple story fall). For evaluation, BMD measurement should be taken by central dual-energy X-ray absorptiometry at the lumbar spine and femoral neck (hip). A BMD taken at the one-third (33%) radius site can be used for diagnosing osteoporosis when the hip and lumbar spine cannot be measured or are unusable or uninterpretable. In postmenopausal women and men age 50 and older, WHO diagnostic T-score criteria is applied to the BMD measurement. For those patients that are not postmenopausal women and not men age 50 and older, WHO BMD classification should not be applied and the diagnosis of osteoporosis should not be made on densitometric criteria alone.3

<table>
<thead>
<tr>
<th>WHO Definitions of bone density</th>
<th>T-score</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>
</tr>
</tbody>
</table>

The WHO absolute fracture risk model (Fracture Risk Algorithm, FRAX) was developed to calculate the 10-year probability of a hip fracture and the 10-year probability of a major osteoporotic fracture, taking into account femoral neck BMD and clinical risk factors.

Treatment
According to the National Osteoporosis Foundation, postmenopausal women and men age 50 and older presenting with the following should be considered for treatment:
- A hip or vertebral fracture
- T-score of -2.5 or lower at the femoral neck, total hip, or lumbar spine (or at the 33% radius site if necessary)
- Low bone mass (T-score between -1 and -2.5) and a 10-year probability of a hip fracture ≥ 3% or a 10-year probability of a major osteoporosis-related fracture ≥ 20% based on the US-adapted WHO algorithm3

The American Association of Clinical Endocrinologists (AACE)4, the Endocrine Society5, and the North American Menopause Society (NAMS)6 all agree with these treatment thresholds for postmenopausal women. The Endocrine Society also agrees with these treatment thresholds for men with increased fracture risk.7

Postmenopausal women
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.4
The Endocrine Society recommends initial treatment with bisphosphonates (e.g., alendronate, risedronate, zoledronic acid, and ibandronate) to reduce fracture risk. The Society recommends denosumab as an alternative initial treatment, with teriparatide and abaloparatide reserved for those with very high risk of fracture, and raloxifene or bazedoxifene for patients with a low risk of deep vein thrombosis and for whom bisphosphonates or denosumab are not appropriate, or with a high risk of breast cancer.\(^5\)

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.\(^8\)

- 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, \(p=0.049\). 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.

Men over the age of 50
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 \(\leq 65\) years old with osteoporosis.\(^4\)

Bisphosphonate therapy halts bone loss but does not add new bone, nor do they restore disrupted microarchitcture. 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 osteoporosis in men.\(^3\)

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) (at the time of this writing, 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), and the risk for hip fracture.\(^9\)

The ACP recommends bisphosphonates to reduce the risk for vertebral fracture in men who have clinically recognized osteoporosis.\(^10\)

**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.\(^11\)
Due to the lack of evidence on the effect on fracture risk, concomitant use of osteoporosis agents is not recommended. There are no head-to-head trials with a preplanned endpoint of reduced fractures comparing one drug with another for osteoporosis.4

Safety
Teriparatide is contraindicated in patients with hypersensitivity to teriparatide or to any of its excipients.1

Teriparatide carries the following black box warnings:1

- 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.2

Abaloparatide carries the following black box warning:2

- 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


Parathyroid Hormone Analog for Osteoporosis Prior Authorization through Preferred with Quantity Limit

TARGET PREFERRED AGENT
Tymlos® (abaloparatide)

TARGET NON-PREFERRED AGENT
Forteo® (teriparatide)

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
<th>Quantity Limit</th>
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<tbody>
<tr>
<td>Forteo® (teriparatide)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>250 mcg/mL injection</td>
<td>30044070002020</td>
<td>M, N, O, or Y</td>
<td>2.4 mL / 28 days</td>
</tr>
<tr>
<td>Tymlos™ (abaloparatide)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2000 mcg/mL injection</td>
<td>3004400500D230</td>
<td>M, N, O, or Y</td>
<td>1.56 mL / 30 days</td>
</tr>
</tbody>
</table>

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Preferred Agent (Tymlos) will be approved when ALL of the following are met:

1. ONE of the following:
   a. ONE of the following:
      i. The patient is currently being treated with the requested agent
      OR
      ii. The prescriber states that the patient is currently being treated with the requested agent AND is at risk if therapy is changed
      OR
      iii. The patient has a diagnosis of osteoporosis AND BOTH of the following:
          A. ONE of the following:
              a. The patient is a postmenopausal female
              OR
              b. The prescriber has provided information that the requested agent is medically appropriate for the patient’s gender
          AND
          B. 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. BOTH of the following:
                 i. The patient has a T-score that is –2.5 or lower
                 AND
                 ii. ONE of the following:
                    1. The patient has tried and had an inadequate response to an oral or IV bisphosphonate
                    OR
                    2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL bisphosphonates
          AND
          2. The patient does NOT have an increased baseline risk for osteosarcoma
          AND
          3. ONE of the following:
             a. The patient is not currently being treated with or has been treated with a concomitant bisphosphonate, SERM, Xgeva (denosumab), Prolia (denosumab),
other parathyroid hormone analog [Forteo (teriparatide)] or Evenity (romosozumab-aqqg) therapy in the past 90 days

OR

b. The prescriber indicates that the patient will discontinue the current bisphosphonate, SERM, Xgeva (denosumab), Prolia (denosumab), other parathyroid hormone analog [Forteo (teriparatide)] or Evenity (romosozumab-aqqg) therapy before starting the requested agent

AND

4. The patient does NOT have any FDA labeled contraindications to the requested agent

AND

5. The dose requested is within the FDA approved labeling [Tymlos (abaloparatide) – 80 mcg subcutaneously once daily; 1.56 mLs/30 days]

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.

Non-Preferred Agent (Forteo) will be approved when ALL of the following are met:

1. ONE of the following:
   a. The patient is currently being treated with the requested agent
   OR
   b. The prescriber states that the patient is currently being treated with the requested agent AND is at risk if therapy is changed
   OR
   c. The patient has a diagnosis of osteoporosis AND BOTH of the following:
      i. 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:
            1. The patient has tried and had an inadequate response to an oral or IV bisphosphonate
            OR
            2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL bisphosphonates
      AND
      ii. ONE of the following:
         A. The patient is a postmenopausal female AND ONE of the following:
            1. The patient’s medication history includes a preferred agent (Tymlos) in the past 90 days
            OR
            2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the preferred agent (Tymlos) that is not expected to occur with the requested agent
         OR
         B. The patient is male
         OR
C. The prescriber has provided information that the requested agent is medically appropriate for the patient’s gender

OR

d. The patient has a diagnosis of glucocorticoid-induced osteoporosis AND ALL of the following:
   i. The patient is either initiating or currently taking glucocorticoids in a daily dosage equivalent to 5 mg or higher of prednisone
      AND
   ii. The patient’s expected current course of therapy of glucocorticoids is for a period of at least 6 months
      AND
   iii. 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. BOTH of the following:
         1. The patient has a T-score that is ≤-2.5 or lower
         AND
         2. ONE of the following:
            i. The patient has tried and had an inadequate response to an oral or IV bisphosphonate
            OR
            ii. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL bisphosphonates

2. The patient does NOT have an increased baseline risk for osteosarcoma

AND

3. ONE of the following:
   a. The patient is not currently being treated with or has been treated with a concomitant bisphosphonate, SERM, Xgeva (denosumab), Prolia (denosumab), other parathyroid hormone analog [Forteo (teriparatide)] or Evenity (romosozumab-aqqg) therapy in the past 90 days
      OR
   b. The prescriber indicates that the patient will discontinue the current bisphosphonate, SERM, Xgeva (denosumab), Prolia (denosumab), other parathyroid hormone analog [Forteo (teriparatide)] or Evenity (romosozumab-aqqg) therapy before starting the requested agent

AND

4. The patient does NOT have any FDA labeled contraindications to the requested agent

AND

5. The dose requested is within the FDA approved labeling [Forteo (teriparatide) – 20 mcg subcutaneously once daily; 2.4 mLs/28 days]

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.
Step Therapy Supplement

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, FocusRx and KeyRx formularies.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT

OBJECTIVE

The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL

The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   a. A statement by the prescriber that the patient is currently taking the requested agent
   AND
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
   AND
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

OR

2. The patient’s medication history include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days
   OR
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event

OR

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria