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.

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

**FDA APPROVED INDICATIONS AND DOSAGE**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
<th>Dosage and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Forteo</strong></td>
<td>Treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, multiple risk</td>
<td>Recommended dose is 20 mcg subcutaneously once a day. Use of the drug for more than 2 years</td>
</tr>
<tr>
<td>teriparatide</td>
<td>factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with</td>
<td>during a patient's lifetime is not recommended.</td>
</tr>
<tr>
<td>20 mcg / injection pen</td>
<td>osteoporosis, teriparatide reduces the risk of vertebral and nonvertebral fractures.</td>
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<td></td>
<td>Increase bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture,</td>
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<td></td>
<td>multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.</td>
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<td></td>
<td>Treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy (daily dosage equivalent to 5 mg or</td>
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<td>greater of prednisone) at high risk for fracture, defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients</td>
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<td></td>
<td>who have failed or are intolerant to other available osteoporosis therapy.</td>
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<tr>
<td><strong>Tymlos</strong></td>
<td>Treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, multiple risk</td>
<td>Recommended dose is 80 mcg subcutaneously once daily;</td>
</tr>
<tr>
<td>abaloparatide</td>
<td>factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.</td>
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<tr>
<td>80 mcg / injection pen</td>
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</tbody>
</table>
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.

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.

**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>
<th>T-score ≥ -1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>T-score between -1.0 and -2.5</td>
</tr>
<tr>
<td>Low bone mass (osteopenia)</td>
<td>T-score ≤ -2.5</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 can 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=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.

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 stimulates 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**


Parathyroid Hormone Analog for Osteoporosis Prior Authorization through Preferred 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 bisphosphonate, or a selective estrogen receptor modulator (SERM) for those whom it is appropriate, or cannot take those medications.

The program also encourages the use of the preferred agent where appropriate per labeling. In addition, the program will allow for the use of the non-preferred agent if the patient has had a trial of the preferred agent, or the patient has an intolerance, contraindication, or hypersensitivity to the preferred agent that is not expected to occur with the requested agent. The program will allow for continuation of therapy if the patient does not have contraindications to the requested agent, does not have increased baseline risk for osteosarcoma, is not on concomitant osteoporosis therapy, is requesting dosing within FDA approved labeling, and has received less than 2 years of total duration of therapy with either abaloparatide or teriparatide.

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 PREFERRED AGENT
Tymlos (abaloparatide)

TARGET NON-PREFERRED AGENT
Forteo (teriparatide)

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Preferred Agent (Tymlos) will be approved when ALL of the following are met:

1. ONE of the following:
   a. The patient is currently using the requested agent
   OR
   b. The patient is postmenopausal with a diagnosis of osteoporosis defined by ONE of the following:
      i. 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
      ii. 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 a bisphosphonate
         OR
         2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a bisphosphonate
         OR
3. BOTH of the following:
   a. ONE of the following:
      i. The patient is female
      OR
      ii. The prescriber has provided documentation that a SERM is medically appropriate for the patient’s gender
   AND
   b. ONE of the following:
      i. The patient has tried and had an inadequate response to a SERM
      OR
      ii. 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 [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.

Non-Preferred Agent (Forteo) will be approved when ALL of the following are met:
1. ONE of the following:
   a. The patient is currently taking the requested agent
   OR
   b. ALL of the following:
      i. ONE of the following:
         1. The patient’s medication history includes a preferred agent (Tymlos) in the past 90 days
         OR
         b. 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
      2. The patient is not postmenopausal
   AND
The patient has a diagnosis of osteoporosis defined as ONE of the following:

1. 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**
2. The patient has a T-score that is −2.5 or lower **AND** ONE of the following:
   a. The patient has tried and had an inadequate response to a bisphosphonate **OR**
   b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a bisphosphonate **OR**
   c. BOTH of the following:
      i. **ONE** of the following:
         1. The patient is female **OR**
         2. The prescriber has provided documentation that a SERM is medically appropriate for the patient’s gender
      AND
      ii. **ONE** of the following:
         1. The patient has tried and had an inadequate response to a SERM **OR**
         2. 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.
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