

PRIOR AUTHORIZATION POLICY

POLICY: Bone Modifiers – Tymlos® (abaloparatide injection for subcutaneous use – Radius)

APPROVAL DATE: 07/03/2019

OVERVIEW

Tymlos is a human parathyroid hormone related peptide (PTHrP[1-34]) analogue indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture.¹ Patients at high risk for fracture are defined as those with a history of osteoporotic fractures, have multiple risk factors for fracture, or have failed or are intolerant to other osteoporosis therapy. The recommended dose of Tymlos is 80 mcg subcutaneously (SC) once daily (QD).¹

Guidelines

Osteoporosis in Postmenopausal Women

In 2019 the Endocrine Society updated their clinical practice guidelines for osteoporosis in postmenopausal women.² It is recommended to treat postmenopausal women with high risk of fractures as the benefits of pharmacological therapies outweigh the risks. In women at high risk of fractures, it is recommended that initial treatment include bisphosphonates (alendronate, risedronate, zoledronic acid, and ibandronate) to reduce the risk of fractures. Concerns are present with oral bisphosphonates regarding gastrointestinal irritation. Also, there are concerns about renal toxicity, therefore, bisphosphonates should not be used in patients with a low estimated glomerular filtration rate (< 35 mL/min). An alternative initial therapy is Prolia® (denosumab injection for subcutaneous use). Forteo® (teriparatide injection for subcutaneous use) or Tymlos are recommended in postmenopausal women with osteoporosis at very high risk of fracture such as patients with severe or multiple vertebral fractures. The treatment duration should be for up to 2 years to reduce vertebral and nonvertebral fractures. Comparatively, the evidence base for those two agents and fracture reduction is more limited regarding the numbers of trials and patients involved. The finding of osteosarcoma in rats led to the Boxed Warning with both agents which limits therapy for a maximum of 24 months in a lifetime.

In 2016, the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) updated clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis (PMO).³ Osteoporosis in postmenopausal women can be defined as follows: 1) T-score -2.5 or below in the lumbar spine, femoral neck, total hip, and/or 33% (one-third) radius; 2) low trauma spine or hip fracture (regardless of bone mineral density [BMD]), osteopenia or low bone mass (T-score between -1.0 and -2.5) with a fragility fracture of proximal humerus, pelvis or possibly distal forearm; 3) osteopenia or low bone mass (T-score between -1.0 and -2.5) with fragility fracture or proximal humerus, pelvis, or possibly distal forearm; 4) low bone mass or osteopenia and high FRAX® fracture probability based on country-specific thresholds. The AACE and ACE guidelines state approved agents with efficacy to reduce hip, nonvertebral and spine fractures include alendronate, risedronate, zoledronic acid injection (Reclast®, generics), and Prolia which are appropriate as initial therapy for most patients at high-risk of fracture. Forteo, Prolia or zoledronic acid injection (Reclast) should be considered for patients unable to use oral therapy and as initial therapy for patients who are at especially high-risk of fracture. Concomitant use of agents for the prevention or treatment of postmenopausal osteoporosis is not recommended.

Safety

The prescribing information for Tymlos includes a Boxed Warning regarding an increased incidence of osteosarcoma in rats at doses 4 to 28 times the exposure in humans administered as a 80 mcg dose.¹ Due to these risks, the agent should not be given to those who have an increased baseline risk for osteosarcoma. The prescribing information for Tymlos states that cumulative use of Tymlos and parathyroid hormone analogs (e.g., Forteo) for > 2 years during a patient's lifetime is not recommended.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Tymlos. Coverage cumulative with Tymlos and Forteo is recommended for up to 2 years of a patient's lifetime. All approval(s) are provided for up to 2 years in duration unless otherwise noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Tymlos is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Osteoporosis Treatment for a Postmenopausal Patient.** Approve for up to 2 years (total) if the patient meets the following criteria (A, B, and C):
 - A) The patient meets ONE of the following conditions (i, ii, or iii):
 - i. The patient has had a T-score (current or at any time in the past) at or below -2.5 at the lumbar spine, femoral neck, total hip and/or 33% (one-third) radius (wrist); OR
 - ii. The patient has had an osteoporotic fracture or a fragility fracture; OR
 - iii. The patient has low bone mass (T-score [current or at any time in the past] between -1.0 and -2.5 at the lumbar spine, femoral neck, total hip and/or 33% [one-third] radius [wrist]) and the physician determines the patient is at high risk for fracture; AND
 - B) The patient meets ONE of the following (i, ii, iii, or iv):
 - i. The patient has tried at least one oral bisphosphonate or oral bisphosphonate-containing product and meets one of the following (a, b, or c):
 - a) The patient has had an inadequate response to oral bisphosphonate therapy after a trial duration of 12 months as determined by the prescribing physician (e.g., ongoing and significant loss of BMD, lack of BMD increase); OR
 - b) The patient has had an osteoporotic fracture or fragility fracture while receiving oral bisphosphonate therapy; OR
 - c) The patient has experienced intolerance to an oral bisphosphonate (e.g., severe gastrointestinal [GI]-related adverse effects, severe musculoskeletal-related side effects, a femoral fracture); OR
 - ii. The patient cannot take an oral bisphosphonate due to one of the following circumstances (a, b, or c):
 - a) The patient cannot swallow or has difficulty swallowing; OR
 - b) The patient cannot remain in an upright position post oral bisphosphonate administration; OR
 - c) The patient has a pre-existing gastrointestinal (GI) medical condition (e.g., patient with esophageal lesions, esophageal ulcers, or abnormalities of the esophagus that delay esophageal emptying [stricture, achalasia]); OR
 - iii. The patient has tried ibandronate injection (Boniva) or zoledronic acid injection (Reclast); OR

- iv. The patient meets one of the following conditions (a, b, or c):
 - a) Severe renal impairment (creatinine clearance < 35 mL/min); OR
 - b) Chronic kidney disease (CKD); OR
 - c) The patient has had an osteoporotic fracture or a fragility fracture; AND
- C) Use of Tymlos and/or Forteo does not exceed 2 years during a patient's lifetime. Note: Approve the duration necessary to complete a maximum of 2 years of therapy during a patient's lifetime (e.g., a patient who has already received 3 months of treatment with Tymlos or Forteo or should be approved for a duration of 21 months. This allows for completion of a maximum of 2 years of therapy).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Tymlos has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Osteoporosis Prevention.** Tymlos has not been studied in this patient population. The benefits and risks of building bone with Tymlos in a condition in which substantial bone loss has not occurred have not been investigated.¹
2. **Concurrent Use with Other Medications for Osteoporosis.** Note: Examples of other therapies are Prolia® (denosumab injection for subcutaneous use), bisphosphonates (alendronate, risedronate, ibandronate, zoledronic acid injection [Reclast]), calcitonin nasal spray, Forteo® (teriparatide injection for subcutaneous use), and Evenity® (romosozumab-aqqg injection for subcutaneous use). Calcium and Vitamin D may be given concurrently.
3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Tymlos® injection for subcutaneous use [prescribing information]. Waltham, MA: Radius Health; October 2018.
2. Eastell R, Rosen CJ, Black DM, et al. Pharmacological management of osteoporosis in postmenopausal women: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2019;104(5):1595-1622. Available at: <https://www.endocrine.org/guidelines-and-clinical-practice/clinical-practice-guidelines/osteoporosis-in-postmenopausal-women>. Accessed on July 5, 2019.
3. 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. *Endocrin Pract.* 2016;22(Suppl 4):1-42. Available at: <http://journals.aace.com/doi/pdf/10.4158/EP161435.GL>. Accessed on June 15. 2018.

