09-J2000-85

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Reviewed: 01/10/24

Revised: 02/15/24

Subject: Abaloparatide (Tymlos™)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Abaloparatide (Tymlos™) is a synthetic peptide analog of parathyroid hormone-related protein (PTHrP) that selectively binds to the parathyroid hormone type 1 receptor (PTH1R). Binding to PTH1R activates signaling pathways that cause an anabolic effect on bone. This results in increases in bone mineral density (BMD) and bone mineral content that correlate with increases in bone strength.

The Food and Drug Administration (FDA) approved abaloparatide in April 2017 for the treatment of postmenopausal women with osteoporosis at high risk for fracture. High fracture risk 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. Abaloparatide is also FDA-approved to increase bone density in men with osteoporosis at high risk for fracture (defined as a history of osteoporotic fracture or multiple risk factors for fracture), or in patients who have failed or are intolerant to other available osteoporosis therapy. The cumulative use of abaloparatide and parathyroid hormone analogs such as teriparatide is not recommended for more than 2 years during a patient's lifetime due to risk of osteosarcoma. Abaloparatide caused a dose-dependent increase in the incidence of osteosarcoma in rats.

Abaloparatide was evaluated in a randomized double-blind, placebo-controlled trial in postmenopausal women for 18 months. Subjects were required to have a BMD T score between or equal to - 2.5 and -5.0 as measured at the lumbar spine or femoral neck with evidence of fracture. Women greater than 65 years of age were permitted with a T score between or equal to -3.0 and -5.0 without evidence or fracture or between or equal to -2.0 and -5.0 with fracture. The primary endpoint was the incidence of new vertebral fractures and secondary endpoints included change in BMD at the total hip, femoral neck, and lumbar spine and incident nonvertebral fractures. Abaloparatide significantly reduced the risk of new vertebral fractures as compared to placebo (0.6% vs 4.2% respectively, $p<0.001$), and also

demonstrated significant improvement in BMD at all sites as compared to placebo ($p<0.001$). Abaloparatide also reduced the incidence of nonvertebral fractures as compared to placebo ($p=0.049$).

According to evidence based guidelines (e.g., American Academy of Clinical Endocrinologists/American College of Endocrinology guidelines for treatment of postmenopausal women with osteoporosis), abaloparatide, denosumab, romosozumab, teriparatide, and zoledronic acid are appropriate initial therapy for patients at very high risk of fracture. The 2019/2020 Endocrine Society guideline recommends initial treatment with bisphosphonates (alendronate, risedronate, zoledronic acid, ibandronate) to reduce fracture risk in postmenopausal women at high risk of fractures and denosumab is an alternative initial treatment. Abaloparatide is recommended in postmenopausal women at very high risk of fracture, such as those with severe or multiple vertebral fractures for up to two years for the reduction of vertebral and nonvertebral fractures. Very high risk of fracture is further defined as those with multiple spine fractures and a BMD T-score at the hip or spine of -2.5 or below.

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

I. Initiation of abaloparatide (Tymlos™) **meets the definition of medical necessity** when **ALL** of the following criteria are met:
    1. Postmenopausal Osteoporosis
        a. Member meets **ONE** of the following:
            i. Diagnosed with osteoporosis defined as a pre-treatment bone mineral density (BMD) T-score of -2.5 or lower[a]
            ii. Member has a history of osteoporotic hip or spine fracture
            iii. Member has a BMD T-score between -1.0 and -2.5[a] and **ONE** of the following:
                1. FRAX[b] 10-year probability of major osteoporotic fracture ≥ 20%
                2. FRAX[b] 10-year probability of hip fracture ≥ 3%
                3. Fragility fracture of the proximal humerus, pelvis, or distal forearm
        b. The cumulative duration of abaloparatide (Tymlos™) and teriparatide (Forteo®) has not exceeded a total of 2 years in the member's lifetime
        c. Abaloparatide will not be used in combination with other anabolic or antiresorptive agents (e.g., bisphosphonates, denosumab, other parathyroid hormone analogs, or romosozumab)
        d. **ONE** of the following – documentation must be submitted:

i. Member has an inadequate response[c] , intolerance, or contraindication to a bisphosphonate[d]

ii. Member has an inadequate response[c] , intolerance, or contraindication to denosumab [Prolia] [d]

iii. Member has a BMD T-score of -2.5 or lower[a] **AND** a history of osteoporotic fracture

iv. Member has a history of multiple osteoporotic vertebral fractures

v. Member had osteoporotic fractures while receiving a FDA approved treatment for osteoporosis

vi. Member had osteoporotic fractures while on long-term therapy with a medication known to cause skeletal harm (e.g., glucocorticoids)

vii. Member has a history of osteoporotic fracture in the past 12 months

viii. Member is at high risk of falls or has a history of falls

ix. Member has a BMD T-score of -3.0 or lower [a]

x. FRAX[b] 10-year probability of major osteoporotic fracture ≥ 30%

xi. FRAX[b] 10-year probability of hip fracture ≥ 4.5%

e. Dose does not exceed 80 mcg daily

2. To increase bone density in a biological male with osteoporosis when **ALL** of the following criteria are met

a. Member is a biological male

b. Member meets **ONE** of the following:

i. Diagnosed with osteoporosis defined as a pre-treatment bone mineral density (BMD) T-score of -2.5 or lower[a]

ii. Member has a history of osteoporotic hip or spine fracture

iii. Member has a BMD T-score between -1.0 and -2.5[a] and **ONE** of the following:

1. FRAX[b] 10-year probability of major osteoporotic fracture ≥ 20%

2. FRAX[b] 10-year probability of hip fracture ≥ 3%

3. Fragility fracture of the proximal humerus, pelvis, or distal forearm

c. The dose does not exceed 80 mcg daily

d. The cumulative duration of abaloparatide (Tymlos™) and teriparatide (Forteo®) has not exceeded a total of 2 years in the member's lifetime

e. Abaloparatide will not be used in combination with other anabolic or antiresorptive agents (e.g., bisphosphonates, denosumab, other parathyroid hormone analogs, or romosozumab)

f. **EITHER** of the following:

i. Member has an inadequate response[c] to bisphosphonate therapy (oral **OR** intravenous [IV])

ii. Member has a contraindication to **BOTH** oral[d] and IV bisphosphonate therapy

3. **Glucocorticoid-induced Osteoporosis** when **ALL** of the following criteria are met:

a. History of prednisone or its equivalent at a dose of 2.5 mg/day or greater for 3 months or more

b. Member meets **ONE** of the following:

i. Diagnosed with osteoporosis defined as a pre-treatment bone mineral density (BMD) T-score of -2.5 or lower[a]

ii. Member has a history of osteoporotic hip or spine fracture

iii. Member has a BMD T-score between -1.0 and -2.5[a] and **ONE** of the following:

1. FRAX[b] 10-year probability of major osteoporotic fracture ≥ 20%

2. FRAX[b] 10-year probability of hip fracture ≥ 3%

3. Fragility fracture of the proximal humerus, pelvis, or distal forearm

c. The cumulative duration of abaloparatide (Tymlos™) and teriparatide (Forteo®) has not exceeded a total of 2 years in the member's lifetime

d. Abaloparatide will not be used in combination with other anabolic or antiresorptive agents (e.g., bisphosphonates, denosumab, other parathyroid hormone analogs, or romosozumab)

e. **ONE** of the following:

i. Member has an inadequate response[c] to bisphosphonate therapy (oral **OR** intravenous (IV))

ii. Member has a contraindication to **BOTH** oral[d] and IV bisphosphonate therapy

iii. Member has an inadequate response[c] or contraindication to denosumab [Prolia][d]

iv. Member has a history of a fragility fracture

v. Member is at high risk of falls or has a history of falls

vi. Member has a BMD T-score of -2.5 or lower[a]

vii. FRAX[b] 10-year probability of major osteoporotic fracture ≥ 20%

viii. FRAX[b] 10-year probability of hip fracture ≥ 3%

ix. High dose glucocorticoid use with prednisone equivalent of greater than or equal to 30 mg/day for 30 days or cumulative doses of greater than or equal to 5 grams per year

f. The dose does not exceed 80 mcg daily

Approval duration: 1 year (maximum lifetime duration is 2 consecutive years)

II. Continuation of abaloparatide (Tymlos™) **meets the definition of medical necessity** for the treatment of postmenopausal osteoporosis, to increase bone density in a biological male with osteoporosis, and for glucocorticoid-induced osteoporosis when **ALL** of the following criteria are met:

1. Member has demonstrated a beneficial response to therapy
2. Authorization of abaloparatide has been previously approved by Florida Blue in the past 2 years, **OR** the member currently meets all indication-specific initiation criteria
3. The cumulative duration of abaloparatide (Tymlos™) and teriparatide (Forteo®) has not exceeded a total of 2 years in the member's lifetime
4. Abaloparatide will not be used in combination with other anabolic or antiresorptive agents (e.g., bisphosphonates, denosumab, other parathyroid hormone analogs, or romosozumab)
5. The dose does not exceed 80 mcg daily

Approval duration: 1 year (maximum lifetime duration is 2 consecutive years) (all indications)

[a] Measured at the femoral neck, total hip, lumbar spine, or 33% radius

[b] FRAX® Fracture Risk Assessment Tool. https://www.sheffield.ac.uk/FRAX/index.aspx

[c] Inadequate response is defined as a new fracture in a compliant member or significant loss of bone mineral density on follow-up scans.

[d] Exception: Not required if the member previously received treatment with teriparatide (Forteo®)

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

Abaloparatide is indicated for the 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 and nonvertebral fractures. Abaloparatide is also indicated to increase bone density in men with osteoporosis at high risk for fracture (defined as a history of osteoporotic fracture or multiple risk factors for fracture), or in patients who have failed or are intolerant to other available osteoporosis therapy.

The recommended dosage of abaloparatide is 80 mcg subcutaneously once daily. The safety and efficacy of abaloparatide has not been evaluated beyond 2 years of treatment. Use for more than 2 years during a patient's lifetime is not recommended. Supplemental calcium and vitamin D is recommended if dietary intake is inadequate.

Dose Adjustments None

Drug Availability

Pre-filled pen for subcutaneous injection: 3120 mcg/1.56 mL (2000 mcg/mL). The prefilled pen delivers 30 doses, each containing 80 mcg of abaloparatide.

PRECAUTIONS:

Contraindications: Known hypersensitivity to abaloparatide.

Precautions/Warnings:

- **Osteosarcoma** – Avoid use in patients at increased risk of osteosarcoma including those with open epiphyses, metabolic bone diseases including Paget's disease, bone metastases or history of skeletal malignancies, prior external beam or implant radiation therapy involving the skeleton. or hereditary disorders predisposing to osteosarcoma.
- **Orthostatic Hypotension -** Orthostatic hypotension may occur, typically within 4 hours of injection. For the first several doses, abaloparatide should be administered where the patient can sit or lie down if necessary.
- **Hypercalcemia -** Use is not recommended in patients with pre-existing hypercalcemia or in patients who have an underlying hypercalcemic disorder, such as primary hyperparathyroidism, because of the possibility of exacerbating hypercalcemia.
- **Hypercalciuria and Urolithiasis -** If active urolithiasis or pre-existing hypercalciuria is suspected, measurement of urinary calcium excretion should be considered

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs

ICD-10 Diagnosis Codes That Support Medical Necessity

E28.310	Symptomatic premature menopause
E28.319	Asymptomatic premature menopause
E28.39	Other primary ovarian failure
E29.1	Testicular hypofunction
E34.50	Androgen insensitivity syndrome, unspecified
M80.00XA – M80.00XS M80.011A – M80.011S M80.012A – M80.012S M80.019A – M80.019S M80.021A – M80.021S M80.022A – M80.022S M80.029A – M80.029S M80.031A – M80.031S M80.032A – M80.032S M80.039A – M80.039S M80.041A – M80.041S M80.042A – M80.042S	Age-related osteoporosis with current pathological fracture

M80.049A – M80.049S M80.051A – M80.051S M80.052A – M80.052S M80.059A – M80.059S M80.061A – M80.061S M80.062A – M80.062S M80.069A – M80.069S M80.071A – M80.071S M80.072A – M80.072S M80.079A – M80.079S M80.08XA – M80.08XS M80.0AXA – M80.0AXS M80.0B1A – M80.0B1S M80.0B2A – M80.0B2S M80.0B9A – M80.0B9S	
M80.80XA – M80.80XS M80.811A – M80.811S M80.812A – M80.812S M80.819A – M80.819S M80.821A – M80.821S M80.822A – M80.822S M80.829A – M80.829S M80.831A – M80.831S M80.832A – M80.832S M80.839A – M80.839S M80.841A – M80.841S M80.842A – M80.842S M80.849A – M80.849S M80.851A – M80.851S M80.852A – M80.852S M80.859A – M80.859S M80.861A – M80.861S M80.862A – M80.862S M80.869A – M80.869S M80.871A – M80.871S M80.872A – M80.872S M80.879A – M80.879S M80.88XA – M80.88XS M80.8AXA – M80.8AXS M80.8B1A – M80.8B1S M80.8B2A – M80.8B2S M80.8B9A – M80.8B9S	Other osteoporosis with current pathological fracture
M81.0	Age-related osteoporosis without current pathological fracture
M81.8	Other osteoporosis without current pathological fracture

N95.1	Menopausal and female climacteric states
T38.0X5A – T38.0X5S	Adverse effect of glucocorticoids and synthetic analogues
Z78.0	Asymptomatic menopausal state

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the guideline creation.

DEFINITIONS:

Osteoporosis: reduction in the amount of bone mass, leading to fractures after minimal trauma. Osteoporosis is defined by the World Health Organization (WHO) as a bone mineral density (BMD) value for the hip, spine, or wrist of 2.5 standard deviations (SD) or more below the mean for healthy young white women, or a T-score of less than or equal to –2.5. The disease is characterized by an increased risk of fractures, which can result in pain, diminished quality of life, decreased physical mobility and independence, inability to work, and increased burden on caregivers.

Postmenopausal: occurring after menopause.

Risk Factors for Osteoporosis: For osteoporotic fractures, includes low BMD, parental history of hip fracture, low body weight, previous fracture, smoking, excess alcohol intake, glucocorticoid use, secondary osteoporosis (e.g., rheumatoid arthritis) and history of falls. These readily accessible and commonplace factors are associated with the risk of hip fracture and, in most cases, with that of vertebral and other types of fracture as well.

RELATED GUIDELINES:

Bone Mineral Density Studies, 04-70000-21
Denosumab (Prolia™, Xgeva™) Injection, 09-J1000-25
Romosozumab-aqqg (Evenity), 09-J3000-03
Teriparatide (Forteo®, Teraparatide injection), 09-J0000-47

OTHER:

None Applicable

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2023 [cited 2023-12-29]. Available from: http://www.clinicalpharmacology.com/.
2. 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. Endocr Pract. 2016; 22: Suppl 4;1-42.
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 – 2020 Update. Endocr Pract. 2020; 26: Suppl 1;1-46.
4. Cosman F, Miller PD, Williams GC et al. Eighteen months of treatment with subcutaneous abaloparatide followed by 6 months of treatment with alendronate in postmenopausal women with osteoporosis: results of the ACTIVExtend trial. Mayo Clin Proc. 2017; 92(2): 200-210.
5. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2023-12-29].
6. Eastell R, Rosen CJ, Black DM et al. Pharmacological management of osteoporosis in postmenopausal women: an Endocrine Society clinical practice guideline. 2019; 104: 1595 – 1622.
7. FRAX® Fracture Risk Assessment Tool. https://www.sheffield.ac.uk/FRAX/index.aspx.
8. Humphrey MB, Russell L, Danila M et al. 2022 American College or Rheumatology for the prevention and treatment of Glucocorticoid-induced osteoporosis. Arthritis Rheumatol. 2023 75 (12): 2088-2102.
9. Leder BZ, O'Dea L, Zanchetta JR et al. Effects of abaloparatide, a human parathyroid hormone-related peptide analog, on bone mineral density in postmenopausal women with osteoporosis. J Clin Endocrinol Metab. 2015; 100: 697-706.
10. Miller PD, Hattersley G, Riis BJ et al. Effect of abaloparatide vs placebo on new vertebral fractures in postmenopausal women with osteoporosis: a randomized clinical trial. JAMA. 2016; 316 (7): 722-733.
11. Shoback D, Rosen CJ, Black DM et al. Pharmacological management of osteoporosis in postmenopausal women: an endocrine society guideline update. J Clin Endocrinol Metab. 2020; 105: 1-8.
12. Tymlos [prescribing information]. Radius Health, Inc. Waltham, MA. June 2023.
13. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2023 [cited 2023-12-29]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 01/10/24.

GUIDELINE UPDATE INFORMATION:

09/15/17	New Medical Coverage Guideline.
11/15/17	Revision to guideline consisting of updating the Position Statement.
07/15/18	Review and revision to guideline; consisting of updating position statement.
04/15/19	Review and revision to guideline; consisting of updating references.
01/01/20	Revision to guideline consisting of updating the position statement.

04/15/20	Review and revision to guideline; consisting of updating the description, position statement and references.
10/01/20	Revision to ICD-10 coding.
02/15/21	Review and revision to guideline; consisting of updating the description, position statement and references.
02/15/22	Review and revision to guideline; consisting of updating the dosing, warnings, and references.
02/15/23	Review and revision to guideline; consisting of updating the position statement with FDA indication to increase bone density in men with osteoporosis at high risk for fracture. Updated description, dosing, coding, and references.
10/01/23	ICD-10 additions.
02/15/24	Review and revision to guideline; consisting of including glucocorticoid-induced osteoporosis and updating the references.