Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for Tymlos when it is determined to be medically necessary because the following criteria have been met.

When Policy Topic is covered

Abaloparatide (Tymlos) injection is considered medically necessary for the treatment of osteoporosis to increase bone mass when all the following criteria are met (A through E):

A. Individual is a postmenopausal female with one of the following (1 or 2):
   1. A diagnosis of osteoporosis defined as a bone mineral density (BMD) T-score in the spine, femoral neck, total hip or distal 1/3 of the radius of less than or equal to -2.5 as compared to a young-adult reference population; or
   2. A diagnosis of osteoporosis based on history of an osteoporotic low trauma fracture (fragility fracture) and considered at high risk for additional fractures; and

B. The individual meets one of the following (1 or 2):
   1. Has been refractory to a prior trial of an oral bisphosphonate; or
   2. Is intolerant of or has a contraindication to oral bisphosphonate therapy as defined by one of the following (a through e):
      a. Hypersensitivity to TWO oral bisphosphonates (one of which must be generic alendronate); or
      b. Inability to stand or sit upright for at least 30 minutes; or
      c. A pre-existing gastrointestinal disorder (for example, Barrett's esophagus, hypersecretory disorders, delayed esophageal emptying, etc.); or
      d. Uncorrected hypocalcemia; or
      e. Severe renal insufficiency as defined by creatinine clearance less than 35 mL/min for alendronate agents or creatinine clearance less than 30 mL/min for risedronate and ibandronate; and

C. The individual has been refractory to, or intolerant of, or has a contraindication to one of the following drugs (1 through 4):
   1. Prolia (denosumab); or
   2. Evista (raloxifene); or
3. Miacalcin/Fortical (calcitonin nasal spray); or
4. Reclast (zoledronic acid);

and

D. The individual is not using abaloparatide injection in combination with any of the following drugs (1 through 6):
   1. Prolia (denosumab); or
   2. Bisphosphonates; or
   3. Evista (raloxifene); or
   4. Miacalcin/Fortical (calcitonin nasal spray); or
   5. Reclast (zoledronic acid); or
   6. Forteo (teriparatide);

   and

E. The individual has utilized abaloparatide injection AND parathyroid hormone analogs (for example, teriparatide [Forteo®]) for a combined total duration of less than 24 months in the individual's lifetime.

When Policy Topic is not covered
Abaloparatide (Tymlos) injection is considered not medically necessary for any of the following (A, B, or C):

A. When abaloparatide (Tymlos) injection has been used for more than a total lifetime duration of 2 years; or

B. If a parathyroid hormone analog (for example, teriparatide [Forteo]) has been used for more than a total lifetime duration of 2 years time; or

C. If abaloparatide and a parathyroid hormone analog (for example, teriparatide [Forteo]) have been used for a combined total lifetime duration of 2 years or longer.

Note: Cumulative use of Tymlos and parathyroid hormone analogs (for example, teriparatide [Forteo]) for more than 2 years during an individual's lifetime is not recommended (FDA Black Box Warning, 2017).

Investigational:
Abaloparatide (Tymlos) is considered investigational in males and when the criteria are not met and for all other indications.

Considerations
Tymlos requires prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.
**Description of Procedure or Service**

According to the National Institute of Arthritis and Musculoskeletal and Skin Diseases (2014), more than 53 million people in the United States today either have osteoporosis or are at high risk for the disease, as a result of low bone mass. Osteoporosis is a disease in which the bones become weak and are more likely to break. The disease is 4 times more likely to occur in women than in men. It is estimated that a total of 1.5 million fractures occurring annually, (that is, 1 out of every 2 women over age 50) are due to osteoporosis. These fractures are most common at the hip, spine, and wrist and can result in serious morbidity, including death. As the U.S. population ages, the incidence of osteoporosis in the U.S. is expected to increase significantly in the future.

Abaloparatide is an analog of human parathyroid hormone related peptide, PTHrP (1-34) that selectively activates the parathyroid hormone type 1 receptor for the treatment of postmenopausal osteoporosis in a select population of women considered at high risk for fractures.

Abaloparatide most closely compares with Forteo (teriparatide), which is a recombinant human parathyroid hormone that stimulates bone formation. Abaloparatide is indicated for treatment of postmenopausal women with osteoporosis who are determined to be at higher-than-average risk for non-vertebral fractures. Both Forteo and abaloparatide are for daily subcutaneous injections.

According to the American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis (updated 2016), Forteo has a 2-year lifetime maximum limitation of use (Grade A, BEL: 1), due to the lack of long-term safety data, and an FDA Black Box warning for possible risk of osteosarcoma. The FDA labeling for abaloparatide (Tymlos) injection contains this same 2 year limitation of use due to possible risk for osteosarcoma.

**Rationale**

On April 28, 2017 the U.S. Food and Drug Administration (FDA) approved abaloparatide (Tymlos) injection, which is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture. This decision was based on the studies described below. Abaloparatide is intended for daily subcutaneous injection and is supplied in a pre-assembled disposable pen for self-injection use for up to 30 days. Notably, the FDA issued a Black Box Warning for risk of osteosarcoma as follows:

- It is unknown whether TYMLOS will cause osteosarcoma in humans.
- The use of TYMLOS is not recommended in patients at increased risk of osteosarcoma including those with Paget's disease of bone or unexplained elevations of alkaline phosphatase, open epiphyses, bone metastases or skeletal malignancies, hereditary disorders predisposing to osteosarcoma, or prior external beam or implant radiation therapy involving the skeleton.
- Cumulative use of TYMLOS and parathyroid hormone analogs (e.g., teriparatide) for more than 2 years during a patient's lifetime is not recommended.

Additionally, Tymlos is not indicated for use in females of reproductive potential (FDA, 2017). For additional warnings, precautions, and possible adverse reactions, see the FDA prescribing information.

To date, clinical trials of abaloparatide have consisted of a phase II dose ranging study (Leder, 2015) and one phase III double-blinded randomized controlled trial, the Abaloparatide Comparator Trial In Vertebral Endpoints (ACTIVE), which published results in 2016. From March 2011 to October 2014, 28 sites in 10 countries recruited postmenopausal women with bone mineral density (BMD) T-scores of less than or equal to -2.5 and greater than -5.0 at the lumbar spine or femoral neck, and radiological evidence of greater than or equal to 2 mild or 1 moderate lumbar or thoracic vertebral fracture or history of low-trauma nonvertebral fracture within the past 5 years. For 18 months, blinded, daily subcutaneous injections of placebo (n=821); abaloparatide, 80 µg (n=824); or open-label teriparatide, 20 µg (n=818) were administered. The primary endpoint was the percentage of participants with new
vertebral fracture in the abaloparatide vs. placebo groups. Sample size was set to detect a 4% difference (57% risk reduction) between treatment groups. Secondary endpoints included change in BMD at total hip, femoral neck, and lumbar spine in abaloparatide-treated vs. placebo participants and time to first incident of nonvertebral fracture. Hypercalcemia was a prespecified safety endpoint in the abaloparatide-treated vs. teriparatide participants.

Results showed that, among 2463 women (mean age, 69 years [range, 49-86]), 1901 completed the study. New morphometric vertebral fractures occurred less frequently in the active treatment groups vs. placebo. The Kaplan-Meier estimated event rate for nonvertebral fracture was lower with abaloparatide vs. placebo. BMD increases were greater with abaloparatide than placebo (all p<0.001). The incidence of hypercalcemia was lower with the abaloparatide group (3.4%) vs. the teriparatide group (6.4%) (risk difference [RD], -2.96 [95% confidence interval (CI), -5.12 to -0.87]; p=0.006). The authors concluded that among postmenopausal women with osteoporosis, the use of subcutaneous abaloparatide, compared with placebo, reduced the risk of new vertebral and nonvertebral fractures over 18 months. However, further research is needed to understand the clinical importance of the difference in risk (RD), the risks and benefits of abaloparatide treatment, and the efficacy of abaloparatide vs. other osteoporosis treatment options (Miller, 2016).

References

Peer Reviewed Publications:


Government Agency, Medical Society, and Other Authoritative Publications:


Websites for Additional Information


Billing Coding/Physician Documentation Information

Tymlos is considered a specialty pharmacy benefit

Additional Policy Key Words

5.01.638

Policy Implementation/Update Information

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