Medication Policy Manual | **Policy No:** dru085

Topic: Forteo®, teriparatide | **Date of Origin:** June 20, 2003

Committee Approval: August 11, 2017 | **Next Review Date:** July 2018

Effective Date: August 11, 2017

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Teriparatide (Forteo®) is a synthetic form of parathyroid hormone (PTH), which is naturally found in the body. The synthetic hormone is to be given by subcutaneous injection for the treatment of osteoporosis.

Policy/Criteria

I. Most contracts require prior authorization approval of teriparatide (Forteo) prior to coverage. Teriparatide (Forteo) may be considered medically necessary in patients with osteoporosis who meet the following criteria under A and B:

A. Patients at high risk for fracture defined by meeting either criterion 1 or 2 below:

1. Have a bone mineral density that is 2.5 or more standard deviations below that of a "young normal" adult (T-score at or below –2.5).

OR

2. Have osteopenia (T-score between -1 and -2.5) and a history of previous fractures or glucocorticoid use for at least 3 months at a dose of 5 mg per day of prednisone (or equivalent).

AND

B. Step therapy with lower-cost alternatives has been ineffective, not tolerated or contraindicated as defined by at least one of the following:

1. At least one bisphosphonate or raloxifene is not effective after at least a 24-month treatment period based on objective documentation.

OR

2. Raloxifene and bisphosphonates (both oral **and** IV) are contraindicated based on current medical literature and objective documentation describing the contraindication is provided (including, but not limited to, creatinine clearance of less than 35 ml/min).

OR

3. Raloxifene or bisphosphonates (both oral **and** IV) are not tolerated due to documented clinical side effects.

II. Administration, Quantity Limitations, and Authorization Period

A. Regence Pharmacy Services considers teriparatide (Forteo) to be a self-administered medication.

B. When prior authorization is approved, teriparatide (Forteo) may be authorized for a maximum of 2 years of therapy.

C. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. Teriparatide (Forteo) is considered investigational when used for all other conditions, including, but not limited to,

A. The prevention of osteoporosis.

B. To promote fracture healing.

C. To promote post-fusion healing.

D. Use in combination with denosumab (Prolia®).

Position Statement

Summary

- Teriparatide (Forteo) is approved for the treatment of osteoporosis in postmenopausal women at high risk for fracture and to increase bone mass in men with primary or hypogonadal osteoporosis who are at high risk for fracture. [1] Patients treated in the pivotal trial of teriparatide (Forteo) in postmenopausal osteoporosis had a mean T-score of –2.6, a mean of 2.3 vertebral fractures, and a mean age of 69.5 years at baseline. [2]
- Data comparing teriparatide (Forteo) to other therapies for the treatment of osteoporosis are limited and teriparatide (Forteo) has not been shown to be more effective than other agents used for the treatment of osteoporosis. [3]
- Alendronate, risedronate, raloxifene, and ibandronate have been shown to increase bone mineral density and reduce the incidence of fractures in patients with osteoporosis. [3-10] Risedronate and alendronate have been shown to be well-tolerated out to at least 5 years of therapy. [3,4]
- The 2014 National Osteoporosis Foundation (NOF) Guidelines are based mainly on evidence from randomized, controlled clinical trials, and attempts to help identify who will benefit from treatment. Treatment decisions should be based on clinical information as well as intervention thresholds. [5]
- A T-score lower than -2.5 is diagnostic of osteoporosis. However a nontraumatic fracture (fragility fracture), is considered osteoporosis regardless of T-score.
- The World Health Organization (WHO) algorithm (FRAX®) was developed to calculate the 10-yr probability of a hip fracture and the 10-yr probability of any major osteoporotic fracture (defined as vertebral, hip, forearm, or humerus fracture) taking into account femoral neck BMD and the clinical risk factors. The WHO algorithm pertains only to previously untreated patients. [5]
- There are no large, randomized, double-blind, comparative trials that have demonstrated superior health outcomes (such as clinically significant fractures) with teriparatide (Forteo) as compared to bisphosphonates or other therapies for osteoporosis. [3] It is also noted that the NOF and American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) Guidelines do not specify superiority of teriparatide (Forteo) over other available therapies. [5,6]
- There is no evidence to support the use of teriparatide (Forteo) for the prevention of postmenopausal osteoporosis.
- There is insufficient evidence to support the use of teriparatide (Forteo) for bone healing.
- There is insufficient evidence to establish that the use of teriparatide (Forteo) in combination with denosumab (Prolia) is more effective than monotherapy with either agent alone.

Clinical Efficacy

- The efficacy and safety of teriparatide (Forteo) in reducing the risk of osteoporotic fractures in postmenopausal women has been confirmed by large randomized controlled trials. [7-9]
- Teriparatide (Forteo) has been shown to reduce the risk of vertebral and non-vertebral fractures; however, it is unknown if teriparatide (Forteo) protects against hip fracture. Teriparatide (Forteo) increases bone mineral density (BMD) in the spine, but has little effect on BMD in the hip or forearm. [6]
- There have been no head-to-head trials with fracture as a primary outcome comparing teriparatide (Forteo) to other therapies for the treatment of osteoporosis.
- When treatment with teriparatide (Forteo) is discontinued, bone density declines quickly the following year, although fracture reduction may persist for one to two years. It appears that continued antiresorptive therapy is necessary to maintain gains in BMD after withdrawal of teriparatide (Forteo). [10-12] Administration of alendronate following one year of teriparatide (Forteo) treatment has been shown to prevent this loss and in some cases will be associated with a further increase in BMD. Effect on fracture has not been evaluated. [13]
- Combination therapy using teriparatide (Forteo) and alendronate has not been shown to be more effective than monotherapy with either agent. [14]

INVESTIGATIONAL USES

- There is no evidence to support the use of teriparatide (Forteo) for the <u>prevention</u> of postmenopausal osteoporosis.
- There is insufficient evidence to establish that the use of teriparatide (Forteo) in combination with denosumab is more effective than monotherapy with either agent. The evidence for combination use is limited to one small trial in post-menopausal women (n=94). Although the combination resulted in a larger increase in BMD than either agent alone, there are no fracture data available. Combination therapy substantially raises the cost and probably increases the potential for side effects. Until the effect of combination therapy on fracture is better understood, the AACE/ACE does not recommend concomitant use of these agents. [6,15]
- Although there is promising animal data and a few published case reports, teriparatide has not been proven in published clinical trials to be effective or safe for fracture healing (these types of high-quality studies are “randomized,” “double-blinded,” and “controlled” and involve large treatment groups).

Safety [1]

- Teriparatide (Forteo) clinical trials were discontinued early (after mean treatment duration of 19 months) in order to evaluate osteosarcoma that developed in an animal safety study. There are no ongoing extension trials and the package labeling states that the use of the drug for more than 2 years is not recommended.

- Teriparatide (Forteo) has a box warning stating that an increase in the incidence of osteosarcoma, dependent on dose and treatment duration, was observed in rats. Teriparatide (Forteo) should not be prescribed to patients at increased risk for osteosarcoma including those with Paget's disease of bone, children or young adults, patients with previous radiation therapy, and patients with bone metastases or skeletal malignancies.
- A Risk Evaluation and Mitigation Strategy (REMS) consisting of a medication guide and communication plan is in place to mitigate the potential risk of osteosarcoma associated with teriparatide (Forteo). Providers and patients are alerted and warned about the potential risk, and providers are informed of the two-year maximum lifetime duration of treatment and proper patient selection. There is also a voluntary teriparatide (Forteo) Patient Registry. [16]

Appendix 1: World Health Organization Criteria for Osteoporosis [14]

a. Normal: Bone mineral density (BMD) within 1 standard deviation (SD) of a "young normal" adult (T-score above –1).

b. Osteopenia: BMD is between 1 and 2.5 SD below that of a "young normal" adult (T-score between –1 and –2.5).

c. Osteoporosis: BMD is 2.5 SD or more below that of a "young normal" adult (T-score at or below –2.5). Women in this group who have already experienced one or more fractures are deemed to have severe or "established" osteoporosis.

Appendix 2: 2010 National Osteoporosis Foundation Recommendations for Who should be considered for treatment [11]

Postmenopausal women and men age 50 and older presenting with the following should be considered for treatment:

- A hip or vertebral (clinical or morphometric) fracture
- T-score ≤ -2.5 at the femoral neck or spine after appropriate evaluation to exclude secondary causes
- Low bone mass (T-score between -1.0 and -2.5 at the femoral neck or spine) 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 algorithm

Cross References
risedronate-containing medications (generic, Actonel®, Atelvia™, generic risedronate delayed-release), Medication Policy Manual, Policy No dru155
Prolia®, denosumab , Medication Policy Manual, Policy No dru223
Xgeva™, denosumab, Medication Policy Manual, Policy No dru393
Bone Density Studies rad2, Medical Policy Manual, TRGMPM – Radiology

Codes	Number	Description
HCPCS	J3110	Injection, teriparatide, 10mcg
HCPCS	J0897	Injection, denosumab 1 mg
HCPCS	J3488	Injection, zoledronic acid (Reclast), 1 mg (Reclast 5 MG/100ML SOLN)

References

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16. RISK EVALUATION AND MITIGATION STRATEGY (REMS): NDA 21-318 FORTEO® (teriparatide) (rDNA origin) Injection. [cited 2/9/2017]; Available from: http://www.accessdata.fda.gov/drugsatfda_docs/rems/Forteo_2013-08-30_Full.pdf

Revision History

Revision Date	Revision Summary
8/11/2017	Added raloxifene as an option for step therapy
3/10/2017	Clarified step therapy includes both IV and oral bisphosphonates
6/10/2016	No changes