

**Regence BlueCross BlueShield of Oregon • Regence BlueShield  
Regence BlueCross BlueShield of Utah • Regence BlueShield of Idaho  
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**Medication Policy Manual**

**Policy No:** dru085

**Topic:** Forteo<sup>®</sup>, teriparatide

**Date of Origin:** June 20, 2003

**Revised/Effective Date:** July 17, 2009

**Next Review Date:** July 2010

**IMPORTANT REMINDER**

This Medical 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 medical policy is to provide a guide to coverage. Medical 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<sup>®</sup>) 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 prior to coverage. Teriparatide may be considered medically necessary in post-menopausal female patients with osteoporosis or in male patients with primary or hypogonadal osteoporosis that 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.** At least one bisphosphonate (preferred alternatives include alendronate and risedronate) is not effective after at least a 24-month treatment period based on objective documentation **except if**:

**1.** Bisphosphonates are contraindicated based on current medical literature and objective documentation describing the contraindication is provided.

**OR**

**2.** Bisphosphonates are not tolerated due to documented clinical side effects.

**II.** Administration, Quantity Limitations, and Authorization Period

**A.** Regence considers teriparatide to be a self-administered medication.

**B.** When prior authorization is approved, teriparatide may be authorized one-time 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 is considered investigational when used for all other conditions, including, but not limited to, the prevention of osteoporosis.

## **Position Statement**

### *Summary*

- Teriparatide is approved in 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. <sup>[1]</sup> Patients treated in the pivotal trial of teriparatide 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. <sup>[2]</sup>
- Data comparing teriparatide to other therapies for the treatment of osteoporosis are limited and teriparatide has not been shown to be more effective than other agents used for the treatment of osteoporosis.
- Alendronate, risedronate, raloxifene, and calcitonin have been shown to increase bone mineral density and reduce the incidence of fractures in patients with osteoporosis. <sup>[3-21]</sup> Risedronate and alendronate have been shown to be well-tolerated out to at least 5 years of therapy.
- The 2008 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. <sup>[41]</sup>
- Treatment decisions should be based on clinical information as well as intervention thresholds. <sup>[41]</sup>
- The World Health Organization (WHO) algorithm (FRAX<sup>®</sup>) 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. <sup>[41]</sup>

## Appendix 1: World Health Organization Criteria for Osteoporosis <sup>[31]</sup>

- 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.

### *Clinical Efficacy*

- Published data comparing teriparatide to other therapies for the treatment of osteoporosis are limited to one small trial comparing teriparatide (40 mcg once daily, not the FDA-approved dose) to alendronate (10 mg PO QD) in postmenopausal women (n=146) with osteoporosis. <sup>[22]</sup> Incidence of non-vertebral fracture was significantly less in patients receiving teriparatide compared to patients receiving alendronate (4.1% versus 13.7%, respectively; p=0.042); however, incidence of non-vertebral fracture was not a primary endpoint.
- It appears that continued anti-resorptive therapy is necessary to maintain gains in BMD after withdrawal of teriparatide. <sup>[23-25]</sup> Administration of alendronate following 1 year of teriparatide treatment resulted in an increase in BMD that was considerably more than has been reported with alendronate or estrogens alone. <sup>[5]</sup> Effect on fracture was not evaluated.
- Combination therapy using teriparatide and alendronate may lead to therapeutic failure. Alendronate may impair the ability of teriparatide to increase the bone mineral density at the lumbar spine and femoral neck in men. <sup>[26]</sup>
- The efficacy and safety of teriparatide in reducing the risk of osteoporotic vertebral fractures in postmenopausal women has been confirmed by large randomized controlled trials. <sup>[27-29]</sup>
- In a 6-month study of postmenopausal women with osteoporosis who were taking teriparatide, the addition of raloxifene resulted in additional increases in bone mineral density in the hip. <sup>[31]</sup> Additional studies over longer durations that include fracture endpoints are necessary to ascertain clinical benefit of combination therapy.

## *Safety*

- Teriparatide 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. <sup>[1]</sup>
- Teriparatide has a black box warning stating that an increase in the incidence of osteosarcoma, dependent on dose and treatment duration, was observed in rats. <sup>[1]</sup> Additionally, the warning states that because of the uncertain relevance of the rat osteosarcoma finding to humans, teriparatide should be prescribed only to patients for whom the potential benefits are considered to outweigh the potential risk.

## **References**

1. Forteo<sup>®</sup> (teriparatide injection) package insert. Indianapolis, IN: Eli Lilly and Company; June 2008.
2. Neer RM, Arnaud CD, Zanchetta JR, et al. Effect of parathyroid hormone (I-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. *N England J Medicine* 2001;344:1434-41.
3. Actonel<sup>®</sup> (risedronate sodium tablets) package insert. Kansas City, MO: Procter & Gamble Pharmaceuticals; April 2008.
4. Evista<sup>®</sup> (raloxifene hydrochloride) package insert. Indianapolis, IN: Eli Lilly and Company; October 2008.
5. Miacalcin<sup>®</sup> (calcitonin-salmon nasal spray) package insert. East Hanover, NJ: Novartis Pharmaceuticals; June 2006.
6. Fosamax<sup>®</sup> (alendronate sodium tablets) package insert. Whitehouse Station, NJ: Merck & CO., Inc.; February 2008.
7. Liberman UA, Weiss SR, Broll J. Effect of oral alendronate on bone mineral density and the incidence of fractures in postmenopausal osteoporosis. *N England J Medicine* 1995;333:1437-43.

8. Black DM, Cummings SR, Karpf DB. Randomized trial of \_alendronate on risk of fracture in women with existing vertebral fractures. *Lancet* 1996;348:1535-41.
9. Cummings ST, Black DM, Thompson DE, et al. Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures. *JAMA* 1998; 280:2077-82.
10. Pols HAP, Felsenberg D, Hanley DA, et al. Multinational, placebo-controlled, randomized trial of the effects of alendronate on bone density and fracture risk in postmenopausal women with low bone mass: results of the FOSIT study. *Osteoporosis International* 1999;9:461-8.
11. Harris ST, Wats NB, Genant HK. Effects of risedronate treatment on vertebral and non-vertebral fractures in women with postmenopausal osteoporosis. *JAMA* 1999;282:1344-52.
12. Reginster JY, Minne HW, Sorensen OH, et al. Randomized trial of the effects of risedronate on vertebral fractures in women with established postmenopausal osteoporosis. *Osteoporosis International* 2000;11:83-91.
13. McClung MR, Geusens P, Miller PD, et al. Effect of risedronate on the risk of hip fracture in elderly women. *N England J Medicine* 2001;344:333-40.
14. Ettinger B, Black DM, Mitlak BH, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results form a 3-year randomized clinical trial. *JAMA* 1999;282:637-45.
15. Chestnut CH, Silverman SL, Andriano K, et al. A randomized trial of nasal spray salmon calcitonin in postmenopausal women with established osteoporosis: the prevent recurrence of osteoporosis fractures study. *Am J Medicine* 2000;109:267-76.
16. Watts NB, Josse RG, Hamdy RC, et al. Risedronate prevents new vertebral fractures in postmenopausal women at high risk. *J Clinical Endocrinology Metabolism* 2003;88:542-9.
17. Fogelman, Ribot C, Smith R, et al. Risedronate reverses bone loss in postmenopausal women with low bone mass: results from a multinational, double-blind, placebo-controlled trial. *J Clinical Endocrinology Metabolism* 2000;85:1895-2000.
18. Cohen S, Levy RM, Keller M, et al. Risedronate therapy prevents corticosteroid-induced bone loss. *Arthritis Rheumatology* 1999;42:2309-18.
19. Reid D, Hughs RA, Laan RFJM, et al. Efficacy and safety of daily risedronate in the treatment of corticosteroid-induced osteoporosis in men and women: a randomized trial. *JBMR* 2000;15:1006-13.

20. Saag KG, Emkey R, Schnitzer TJ, et al. Alendronate for the prevention and treatment of glucocorticoid-induced osteoporosis. *N England J Medicine* 1998;339:292-9.
21. Orwoll E, Ettinger M, Weiss S, et al. Alendronate for the treatment of osteoporosis in men. *N Engl J Med* 2000;343:604-10.
22. Body JJ, Gaich GA, Scheele WH, et al. A randomized double-blind trial to compare the efficacy of teriparatide [recombinant human parathyroid hormone (1-34)] with alendronate in postmenopausal women with osteoporosis. *J Clinical Endocrinology Metabolism* 2002;87:4528-35.
23. Rubin MR, Bilezikian JP. New anabolic therapies in osteoporosis. *Current Opinion Rheumatology* 2002;14:433-40.
24. Rittmaster RS, Bolognese M, Ettinger MP, et al. Enhancement of bone mass in osteoporotic women with parathyroid hormone followed by alendronate. *J Clinical Endocrinology Metabolism* 2000;85:2129-34.
25. Kurland ES, Heller SL, Cosman F, et al. The post-PTH experience in men with idiopathic osteoporosis: bisphosphonates vs. non-pharmacologic therapy. American Society of Bone Mineral Metabolism 23<sup>rd</sup> Annual Meeting. 2001: Abstract.
26. Finkelstein JS, Hayes A, Hunzelman JL, Wyland JJ, Lee H, Neer RM. The effects of parathyroid hormone, alendronate, or both in men with osteoporosis. *N Engl J Med* 2003;349:1216-26.
27. Gallagher JC, Genant HK, Crans GG, Vargas SJ, Krege JH. Teriparatide reduces the fracture risk associated with increasing number and severity of osteoporotic fractures. *J Clin Endocrinol Metab* 2005;90:1583-7.
28. Crans GG, Silverman SL, Genant HK, Glass EV, Krege JH. Association of severe vertebral fractures with reduced quality of life: reduction in the incidence of severe vertebral fractures by teriparatide. *Arthritis Rheumatology* 2004;50:4028-34.
29. Oglesby AK, Minshall ME, Shen W, Xie S, Silverman SL. The impact of incident vertebral and non-vertebral fragility fractures on health-related quality of life in established postmenopausal osteoporosis: results from the teriparatide randomized, placebo-controlled trial in postmenopausal women. *J Rheumatol* 2003;30:1579-83.
30. Genant HK, Cooper C, Poor G, et al. Interim report and recommendations of the World Health Organization Task Force for Osteoporosis. *Osteoporosis Int* 2000;10:259-64.

31. Deal C, Omizo M, Schwartz EN, Eriksen EF, Cantor P, Wang J, et al. Combination teriparatide and raloxifene therapy for postmenopausal osteoporosis: results from a 6-month double-blind, placebo-controlled trial. *J Bone Miner Res* 2005;20:1905-1911.
32. Ste-Marie LG, Schwartz SL, Hossain A, Desai D, Gaich GA. Effect of teriparatide [rhPTH(1-34)] on BMD when given to postmenopausal women receiving hormone replacement therapy. *J Bone Miner Res*. 2006;21:283-91.
33. Finkelstein JS, Leder BZ, Burnett SM, Wyland JJ, Lee H, de la Paz AV, Gibson K, Neer RM. Effects of teriparatide, alendronate, or both on bone turnover in osteoporotic men. *J Clin Endocrinol Metab*. 2006 Aug;91(8):2882-7. Epub 2006 May 9.
34. Delmas PD, Licata AA, Reginster JY, Crans GG, Chen P, Misurski DA, Wagman RB, Mitlak BH. Fracture risk reduction during treatment with teriparatide is independent of pretreatment bone turnover. *Bone*. 2006 Aug;39(2):237-43. Epub 2006 Mar 24.
35. Miller PD, Schwartz EN, Chen P, Misurski DA, Krege JH. Teriparatide in postmenopausal women with osteoporosis and mild or moderate renal impairment. *Osteoporos Int*. 2007 Jan;18(1):59-68. Epub 2006 Sep 30.
36. Ma YL, Zeng Q, Donley DW, Ste-Marie LG, Gallagher JC, Dalsky GP, Marcus R, Eriksen EF. Teriparatide increases bone formation in modeling and remodeling osteons and enhances IGF-II immunoreactivity in postmenopausal women with osteoporosis. *J Bone Miner Res*. 2006 Jun;21(6):855-64.
37. Chen P, Miller PD, Delmas PD, Misurski DA, Krege JH. Change in lumbar spine BMD and vertebral fracture risk reduction in teriparatide-treated postmenopausal women with osteoporosis. *J Bone Miner Res*. 2006 Nov;21(11):1785-90.
38. Kung AW, Pasion EG, Sofiyan M, Lau EM, Tay BK, Lam KS, Wilawan K, Ongphiphadhanakul B, Thiebaud D. A comparison of teriparatide and calcitonin therapy in postmenopausal Asian women with osteoporosis: a 6-month study. *Curr Med Res Opin*. 2006 May;22(5):929-37.
39. Gallagher JC, Rosen CJ, Chen P, Misurski DA, Marcus R. Response rate of bone mineral density to teriparatide in postmenopausal women with osteoporosis. *Bone*. 2006 Dec;39(6):1268-75. Epub 2006 Aug 1.
40. Boonen S, Marin F, Mellstrom D, Xie L, Desai D, Krege JH, Rosen CJ. Safety and efficacy of teriparatide in elderly women with established osteoporosis: bone anabolic therapy from a geriatric perspective. *J Am Geriatr Soc*. 2006 May;54(5):782-9.
41. Clinician's Guide To Prevention And Treatment Of Osteoporosis. National Osteoporosis Foundation, 2008. Available at: [http://www.nof.org/professionals/Clinicians\\_Guide.htm](http://www.nof.org/professionals/Clinicians_Guide.htm). Accessed March 12, 2008.

42. Saag KG, Shane E, Boonen S, Marin F, Donley DW, Taylor KA, et al. Teriparatide or alendronate in glucocorticoid-induced osteoporosis. *N Engl J Med* 2007;357:2028-39.
43. MacLean C, Alexander A, Carter J, Chen S, Desai SB, Grossman J, Maglione M, McMahon M, McNamara M, Mojica W, Newberry S, Ranganath V, Suttorp M, Timmer M, Tringale C, Valentine D, Zhou A. Comparative Effectiveness of Treatments To Prevent Fractures in Men and Women With Low Bone Density or Osteoporosis. Comparative Effectiveness Review No. 12. (Prepared by Southern California/RAND Evidence-based Practice Center under Contract No. 290-02-0003). Rockville, MD: Agency for Healthcare Research and Quality. December 2007. Available at: [www.effectivehealthcare.ahrq.gov/reports/final.cfm](http://www.effectivehealthcare.ahrq.gov/reports/final.cfm).
44. Osteoporosis Overview. National Institutes of Health Osteoporosis and Related Bone Diseases ~ National Resource Center. Updated December 2007. Available at [http://www.niams.nih.gov/Health\\_Info/Bone/](http://www.niams.nih.gov/Health_Info/Bone/) accessed March 12, 2008.

Cross References
Actonel <sup>®</sup> , risedronate dru155
Boniva <sup>®</sup> , ibandronate injection dru156
Boniva <sup>®</sup> , ibandronate oral dru157
Reclast <sup>®</sup> , zoledronic acid dru158
Bone Density Studies rad2, TRG Medical Policy Manual, TRGMPPM - Radiology

Codes	Number	Description
HCPCS	J3110	Injection, teriparatide, 10mcg