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Teriparatide

Updated: March 31, 2016.

OVERVIEW

Introduction

Teriparatide is a recombinant human parathyroid hormone analogue that is used to treat osteoporosis in women or men with a high risk for bone fracture. Teriparatide therapy has not been associated with serum aminotransferase elevations during therapy and has not been implicated in instances of clinically apparent liver injury.

Background

Teriparatide (ter" i par' a tide) is a recombinant analogue of human parathyroid hormone, consisting of the first 34 amino acids of the complete 84 amino acid peptide hormone. Parathyroid hormone (PTH) has a multitude of activities, causing increase in calcium absorption from the gastrointestinal tract and increase in bone growth. Treatment with the 34 amino acid PTH analogue teriparatide (rhPTH[1-34]) has been shown to increase bone mineral density scores as assessed by DEXA scan in patients with osteoporosis, and long term therapy has been associated with a lower rate of bone fractures. Teriparatide was approved for use in the United States in 2002, and current indications are for postmenopausal women with osteoporosis at increased risk for bone fractures, for men with reduced bone mineral density due to hypogonadism, and for men or women with osteoporosis due to corticosteroid therapy. Teriparatide is available in a multi-dose pen device with 28 doses [20 µg each] for daily administration under the trade name Forteo. The recommended dose regimen is 20 µg subcutaneously once daily. Therapy for more than 2 years is not recommended. Side effects of teriparatide are uncommon, but can include injection site reactions, rash, diarrhea, nausea and vomiting and headache. Rare side effects may include local injection reactions, hypercalcemia and osteosarcoma (an association found in rats, but unproven in humans).

Hepatotoxicity

In large clinical trials, teriparatide was not associated with changes in serum aminotransferase levels during therapy, and no cases of clinically apparent liver injury were reported. Despite availability of teriparatide for many years, there have been no published reports of clinically apparent acute liver injury attributed to its use. Thus, significant liver injury from teriparatide must be very rare, if it occurs at all.

Likelihood score: E (unlikely cause of clinically apparent liver injury).

Mechanism of Injury

Teriparatide is a recombinant polypeptide that matches the first 34 amino acids of human parathyroid hormone and, as such, is unlikely to be hepatotoxic. Polypeptide hormones are typically metabolized by the cells on or in which they act. While recombinant proteins can be metabolized by the liver, the metabolism leads largely to small peptides and amino acids which may be reused to synthesize proteins and are unlikely to be toxic or immunogenic.

Drug Class: Osteoporosis Agents, Hormonal Agents

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Teriparatide – Forteo®

DRUG CLASS

Osteoporosis Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Teriparatide	52232-67-4	C181-H291-N55-O51-S2	Not Available

ANNOTATED BIBLIOGRAPHY

References updated: 31 March 2016

Zimmerman HJ. Drugs used to treat rheumatic and musculospastic disease. In, Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999, pp. 517-54.

(Expert review of hepatotoxicity published in 1999, well before the availability of teriparatide).

Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2011.

(Textbook on drug induced liver injury; does not discuss agents for osteoporosis).

Friedman PA. Agents affecting mineral ion homeostasis and bone turnover. In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 1275-1306.

(Textbook of pharmacology and therapeutics).

Finkelstein JS, Klibanski A, Arnold AL, Toth TL, Hornstein MD, Neer RM. Prevention of estrogen deficiency-related bone loss with human parathyroid hormone-(1-34): a randomized controlled trial. JAMA 1998; 280: 1067-73. PubMed PMID: 9757854.

(Among 43 women with endometriosis receiving a gonadotrophin releasing factor [GnRH] analogue alone or in combination with teriparatide, bone mineral density decreased in those receiving GnRH alone, but increased in those given the combination; no mention of ALT elevations or hepatotoxicity).

Neer RM, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, Reginster JY, Hodsman AB, et al. Effect of parathyroid hormone(1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. N Engl J Med 2001 344: 1434-41. PubMed PMID: 11346808.

(Among 1637 women with postmenopausal osteoporosis and vertebral fractures treated with teriparatide [20 or 40 µg daily] or placebo, new vertebral fractures were less with therapy [4%-5%] than placebo [14%]; side effects more common with teriparatide included headache, nausea, dizziness, leg cramps and mild hypercalcemia; there were no cases of osteosarcoma and no mention of ALT elevations or hepatotoxicity).

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. PubMed PMID: 14500805.

(Among 83 men with osteoporosis treated with alendronate, teriparatide or both, increases in bone mineral density were greatest with teriparatide alone and side effects were similar, although headache, dizziness, joint pains and Alk P elevations were more frequent with teriparatide therapy; no mention of ALT elevations or hepatotoxicity).

Saag KG, Shane E, Boonen S, Marín F, Donley DW, Taylor KA, Dalsky GP, et al. Teriparatide or alendronate in glucocorticoid-induced osteoporosis. N Engl J Med 2007; 357: 2028-39. PubMed PMID: 18003959.

(Among 428 patients with osteoporosis attributed to corticosteroids who were treated with teriparatide or alendronate, bone density improved more with teriparatide and vertebral fractures were less often; nausea, insomnia and pharyngitis were more common with teriparatide; no mention of ALT elevations or hepatotoxicity).

Finkelstein JS, Wyland JJ, Leder BZ, Burnett-Bowie SM, Lee H, Jüppner H, Neer RM. Effects of teriparatide retreatment in osteoporotic men and women. J Clin Endocrinol Metab 2009; 94: 2495-501. PubMed PMID: 19401368.

(Retreatment of 21 patients with teriparatide after stopping for one year restored the losses in bone density associated with stopping treatment, but did not cause further improvement).

Drugs for postmenopausal osteoporosis. Med Lett Drugs Ther 2014; 56 (1452): 91-6. PubMed PMID: 25247344.

(Review of therapies for osteoporosis inlcuding parathyroid hormone which acts by stimulating bone formation rather than inhibiting bone turnover; adverse events of teriparatide can include nausea, headache, dizziness and muscle cramps; therapy has not been associated with an increased rate of osteosarcoma).

Black DM, Rosen CJ. Clinical Practice. Postmenopausal Osteoporosis. N Engl J Med 2016; 374: 254-62. PubMed PMID: 26789873.

(Review of the management of postmenopausal osteoporosis including use of teriparatide).