



Therapeutic Class ReviewSM

Osteoporosis: Bisphosphonates ibandronate (Boniva[®])

July 2005

New Product for Review:

ibandronate (Boniva[®]) [Roche and GlaxoSmithKline]

Dossier Provided by Manufacturer: Yes

Quality of Dossier: 3 (high quality)

1 - Low quality (dossier w/missing components)

2 - Medium quality (all components, except pharmacoeconomic model)

3 - High quality (all components, well done)

Executive Summary

- There is no evidence that:
 - Boniva 150 mg taken once-a-month decreases the risk of new vertebral fractures or hip fractures in postmenopausal women with osteoporosis.
 - Boniva is superior to the oral bisphosphonates (Actonel and Fosamax) on the preferred/formulary list with regard to its efficacy and safety.
- The evidence is uncertain regarding the benefit of Boniva 2.5 mg daily in reducing bone loss from the lumbar spine in postmenopausal women with osteopenia over a 2-year period when compared to placebo. [Prevention trials]
- The evidence is possibly useful (Grade B) that Boniva 2.5 mg daily may prevent new vertebral fractures in postmenopausal women with osteoporosis over a 3-year period when compared to placebo. [Treatment trial]
- Harms or potential harms from clinical trials with Boniva may include dyspepsia, diarrhea, and extremity and/or back pain and may include other risks as long-term data become available.
- Although Boniva offers the convenience of once-a-month dosing, there is no evidence that adherence to the monthly regimen is superior to a once-a-week Actonel or Fosamax regimen.

Decision

Maintain non-preferred/non-formulary status for ibandronate (Boniva) because there is no evidence that the once monthly preparation demonstrates increased clinical benefits or adherence over less costly alternatives.

I. Products

Drug Product	Date of FDA Approval	FDA Approved Indications	Dose/Route	Potential Off-Label Uses
alendronate (Fosamax®) ^{1,4}	9/1995 (daily) 10/2000 (weekly)	<ul style="list-style-type: none"> ■ Prevention of osteoporosis in postmenopausal women (PMW) ■ Treatment of osteoporosis in postmenopausal women ■ Increase bone mass in men with osteoporosis ■ Treatment of glucocorticoid-induced osteoporosis in men and women ■ Paget's disease in men and women 	5 mg p.o. daily OR 35 mg p.o. weekly 10 mg p.o. daily OR 70 mg p.o. weekly 10 mg p.o. daily OR 70 mg p.o. weekly 5 mg p.o. daily OR 10 mg p.o. daily if PMW not on estrogen 40mg p.o. daily x 6mo	osteoporosis in Crohn's disease; juvenile osteoporosis; treatment of osteoporosis secondary to organ transplantation
ibandronate (Boniva®) ^{2,4}	5/2003 (daily) 3/2005 (monthly)	<ul style="list-style-type: none"> ■ Prevention of osteoporosis in postmenopausal women (PMW) ■ Treatment of osteoporosis in postmenopausal women 	150 mg p.o. monthly 150 mg p.o. monthly	treatment of osteoporosis secondary to organ transplantation; osteoporosis in Crohn's disease; glucocorticoid-induced osteoporosis; Paget's disease; treatment of osteoporosis in men
risedronate (Actonel®) ^{3,4}	3/1998 (daily) 5/2002 (weekly)	<ul style="list-style-type: none"> ■ Prevention of osteoporosis in postmenopausal women (PMW) ■ Treatment of osteoporosis in postmenopausal women ■ Treatment and prevention of glucocorticoid-induced osteoporosis in men and women ■ Paget's disease in men and women 	5 mg p.o. daily OR 35 mg p.o. weekly 5 mg p.o. daily OR 35 mg p.o. weekly 5 mg p.o. daily 30 mg p.o. daily x 2mo	treatment of osteoporosis secondary to organ transplantation; osteoporosis in Crohn's disease; juvenile osteoporosis

*AWP (average wholesale price) based on First Data Bank as of May 2005 for one year of therapy or one treatment course, where indicated.

VIII. References

1. Fosamax® (alendronate) Product Information. Whitehouse Station, NJ: Merck & Co., Inc., 2004.
2. Boniva® (ibandronate) Product Information. Nutley, NJ: Roche Pharmaceuticals, 2005.
3. Actonel® (risedronate) Product Information. North Norwich, NY: Proctor & Gamble Pharmaceuticals, 2004.
4. Thomson Micromedex © 1974-2005. Micromedex Healthcare Series, Vol 120.
5. Chesnut CH, Skag A, Christiansen C, et al. Effects of oral ibandronate administered daily or intermittently on fracture risk in postmenopausal osteoporosis. J Bone Miner Res. 2004;19(8):1241-9.
6. Center for Drug Evaluation and Research. Approval package for application number NDA 21-455; Medical Review. Available at: http://www.fda.gov/cder/foi/nda/2003/21-455_Boniva_medr_P1.pdf. Accessed on June 6, 2005.
7. Product Dossier: Boniva® (ibandronate). Roche Pharmaceuticals; Nutley, NJ. Data reviewed 6/08/2005.
8. Tanko LB, McClung MR, Schimmer RC, et al. The efficacy of 48-week oral ibandronate treatment in postmenopausal osteoporosis when taken 30 versus 60 minutes before breakfast. Bone 2003;32(4):421-6.
9. Cooper C, Emkey RD, McDonald RH, et al. Efficacy and safety of oral weekly ibandronate in the treatment of postmenopausal osteoporosis. J Clin Endocrinol Metab. 2003;88(10):4609-15.
10. Riis BJ, Ise J, Von Stein T, et al. Ibandronate: a comparison of oral daily dosing versus intermittent dosing in postmenopausal osteoporosis. J Bone Miner Res. 2001;16(10):1871-8.

11. Black DM, Cummings SR, Karpf DB, Cauley JA, Thompson DE, Nevitt MC et al. Randomized trial of effect of alendronate on risk of fracture in women with existing vertebral fractures. *Lancet* 1996;348:1535-41.
12. McClung MR, Geusens P, Miller PD, Zippel H, Bensen WG, Roux C et al. Effect of risedronate on hip fracture risk in elderly women. *N Eng J Med* 2001;344:333-40.
13. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the prevention and treatment of postmenopausal osteoporosis: 2001 edition, with selected updates for 2003. *Endocr Pract* 2003;9(6):544-64.
14. National Osteoporosis Foundation. Physician's guide to prevention and treatment of osteoporosis. Available at: http://www.nof.org/_vti_bin/shtml.dll/physgiude/index.htm. Accessed on 6/6/2005.
15. ICSI (Institute for Clinical Improvement). Healthcare guideline: Diagnosis and Treatment of Osteoporosis. 3rd edition, July 2004. Available at: <http://www.icsi.org>. Accessed on 6/6/2005.
16. Cranney A, Adachi JD, Guyatt G, et al. Risedronate for the prevention and treatment of postmenopausal osteoporosis. *The Cochrane Database of Systematic Reviews* 2003, Issue 4. Art. No.:CD004523. DOI: 10.1002/14651858.CD004523.
17. McClung MR, Wawnich RD, Recker R, et al. Oral daily ibandronate prevents bone loss in early postmenopausal women without osteoporosis. *J Bone Miner Res.* 2004;19(1):11-8.
18. Tanko LB, Felsenberg D, Czerwinski E, et al. Oral weekly ibandronate prevents bone loss in postmenopausal women. *J Intern Med.* 2003;254(2):159-67.