The Cost-Effectiveness of Ibandronate in the Treatment of Postmenopausal Osteoporosis in the US

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ABSTRACT

Objectives: We determined the cost-effectiveness of monthly ibandronate compared to weekly bisphosphonate treatments for women in the US, age ≥50 years, with prevalent radiologic vertebral deformity and hip BMD T-score ≤–2.5.

Methods: A Markov model was developed to evaluate the lifetime cost-effectiveness of monthly ibandronate and weekly bisphosphonates. Vertebral, hip, and wrist fracture efficacy were assigned a bisphosphonate class effect as estimated by the literature. Persistence with weekly bisphosphonates was evaluated at rates reported from observational studies (36% at year 1, 24% for years 2 through 5). Fifty percent relative improvement in persistence (54% at year 1, 36% for years 2 through 5) among women receiving ibandronate was assumed based on previous improvements in persistence for weekly bisphosphonates. Both fracture risk and mortality were allowed to increase as patients aged. Yearly drug costs were referenced to wholesale acquisition costs for each bisphosphonate. Direct health resource costs for fracture states were estimated from published literature and discounted 3% per annum. All costs were reported in 2004 US$.

Results: More fractures were avoided (vs. no treatment) with monthly ibandronate (99.8 per 1,000 women) than with weekly bisphosphonates (62.9 per 1,000 women), resulting in lower fracture care costs per woman ($6,352 and $6,663, respectively). Five-year drug costs per patient were $1,138 with weekly bisphosphonates and $1,576 under conditions of improved persistence with monthly ibandronate. The incremental cost per quality-adjusted life year (QALY) gained (vs. no treatment) was lower with monthly ibandronate ($13,470) compared to weekly bisphosphonates ($16,742). Changing assumptions in the model to those of previously published cost-effectiveness models produced similar results, providing external validity for this model.

Conclusion: Ibandronate is a cost-effective intervention for the treatment of postmenopausal osteoporosis. Incremental persistence with bisphosphonate therapy thus improves the benefit realized in patient populations. These benefits include fewer fractures for patients without significant increases in costs to payers.

BACKGROUND

Bisphosphonates are currently the most widely used drugs for osteoporosis and have been shown to be effective in preventing osteoporotic fractures (Kanis et al., 2002). However, more than 50% of patients on weekly bisphosphonate regimens discontinue use within 1 year (Gold et al., 2006; Cramer et al., 2005). Previously, weekly dosing showed an improvement in patient persistence over daily dosing (Gold et al., 2006; Cramer et al., 2005). Ibandronate, a new monthly administered oral bisphosphonate, provides an opportunity to further improve persistence, a parameter not well modeled in previous analyses on the cost-effectiveness of osteoporosis therapy (Johnell et al., 2003; Grima et al., 2002). We developed a model to determine the cost-effectiveness of monthly ibandronate compared to weekly bisphosphonate treatments for women in the US with postmenopausal osteoporosis.

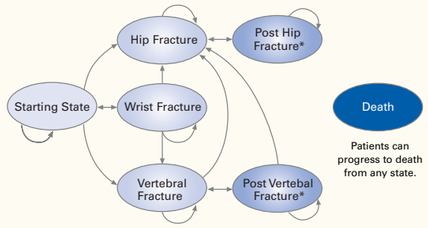
METHODS

A Markov model (Figure 1) was used to simulate a cohort of postmenopausal women aged ≥50 years with a prevalent radiologic vertebral deformity and a hip bone mineral density T-score of ≤–2.5. Model parameters and assumptions are as follows:

Parameters and Assumptions

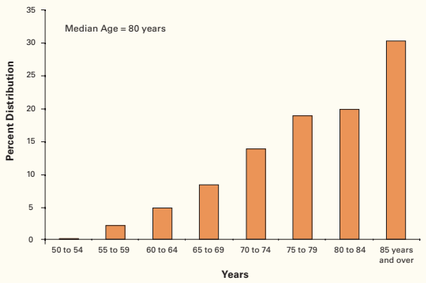
- Patients transition between the health states annually for the remainder of their lifetime.
- Age distribution of osteoporotic women (US Census Bureau, 2002), the prevalence of T-scores ≤–2.5 (Looker et al., 1997), and the prevalence of vertebral fractures among those with T-scores ≤–2.5 (O'Neill et al., 1996) were obtained from published literature. It was assumed that the postmenopausal population is represented by those aged ≥50 years (Figure 2).
- Third-party payer perspective was taken.
- Comparators included monthly ibandronate or weekly bisphosphonates versus no treatment.
- Transition probabilities were based on published literature, accounting for the impact of increasing age, prior fracture, and mortality (Black et al., 1999; Kanis et al., 2000a, 2000b; Johnell et al., 2004; Klotzbeucher et al., 2000; CDC, 2003).
- Fracture risk reduction efficacy for vertebrae (43%), hip (33%), and wrist (17%) were assigned a bisphosphonate class effect, as estimated in the literature (Kanis et al., 2002).
- Onset of efficacy was assumed to occur linearly until full fracture efficacy is achieved at 6 months.
- Maximum time on therapy was assumed to be 5 years.
- Waning fracture benefit following therapy discontinuation was modeled as a linear decline proportional to the mean length of time on therapy.
- Persistence with weekly bisphosphonates was evaluated at rates reported from observational studies (36% at year 1; 24% for years 2 through 5). A 50% relative improvement in persistence with monthly ibandronate (54% at year 1; 36% for years 2 through 5) was selected to approximately match the difference observed between weekly bisphosphonate regimens compared to daily dosing (Gold et al., 2006; Cramer et al., 2005).
- Yearly drug costs were referenced to wholesale acquisition costs for each bisphosphonate (Red Book, 2006).

Figure 1. Model Structure



* For simplification, we assume that once patients experience a hip fracture or vertebral fracture they can experience no further wrist fractures. Patients in the post-hip-fracture state can experience further vertebral fractures through a state prevalence estimate.

Figure 2. Age Distribution of Bisphosphonate-Treated Patients in the Economic Model



- Direct health resource care costs (Eddy et al., 1998) and utilities (Brazier et al., 2002; Tosteson et al., 2001) for fracture states were estimated from published literature and discounted 3% per annum.
- A sensitivity analysis was performed around the expected improvement in persistence for monthly ibandronate.

RESULTS

Modeled results in terms of fractures avoided, per-patient costs, and cost-effectiveness are presented in Table 1 and Figure 3.

Table 1. Estimated Fractures Avoided per 1,000 Patients and Average Costs per Patient

Outcome	Monthly Ibandronate	Weekly Bisphosphonates
Number of fractures avoided per 1,000 patients		
Hip	20.7	13.7
Vertebral	77.1	47.6
Wrist	2.0	1.6
Total	99.8	62.9
Average costs per patient treated (US$)		
Drug	$ 1,576	$ 1,138
Fracture Care	$ 6,352	$ 6,663
Total	$ 7,927	$ 7,801

Note: With no treatment, 160 hip fractures, 455 vertebral fractures, and 53 wrist fractures are incurred per 1,000 patients.

- A 50% relative improvement in persistence yields approximately 59% more fractures avoided.
- Increased persistence does result in increased drug costs. However, fewer fractures estimated with monthly ibandronate results in a reduction in fracture care costs compared to weekly bisphosphonates.
- A 50% improvement in persistence lowers incremental cost-effectiveness ratios (ICERs) by 20% to 23%.

Sensitivity Analysis

A sensitivity analysis was performed for monthly ibandronate around the increased amount of persistence expected due to the monthly formulation of ibandronate (Figure 4).

- Small improvements in persistence produce clinical benefits in terms of decreased number of fractures.

Comparison to Other Models

By changing model parameters and assumptions to resemble those of a previous osteoporosis economic model (Grima et al., 2002), ICERs for QALYs gained were similar between the two models for weekly bisphosphonates vs. no treatment (published model = $16,158 vs. our model = $18,534).

Figure 3. Incremental Cost-Effectiveness Ratios for Selected Endpoints

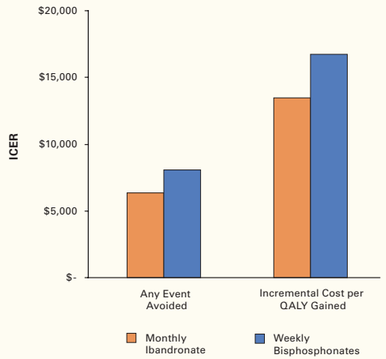
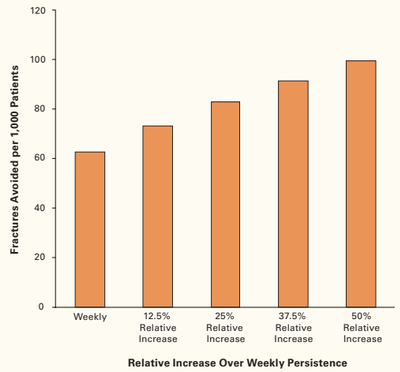


Figure 4. Sensitivity Analysis of Estimated Fractures Avoided per 1,000 Patients for Increased Persistence with Monthly Ibandronate



CONCLUSIONS

- Treating postmenopausal, osteoporotic women with monthly ibandronate is cost-effective.
- Model results consider direct costs only. The addition of societal costs is likely to further improve the cost-effectiveness of all bisphosphonate treatments.
- Greater fracture reduction is seen when persistence is improved.

REFERENCES

Black DM et al. *J Bone Miner Res* 1999; 14:821–8.

Brazier JE et al. *Osteoporos Int* 2002; 13:768–76.

Centers for Disease Control and Prevention. 2003. US National Vital Statistics Reports.

Cramer JA et al. *Curr Med Res Opin* 2005; 21:1453–60.

Eddy DM et al. *Osteoporos Int* 1998; Suppl 4.

Gold DT et al. Consistent Improvement in Bisphosphonate Persistence with Less Frequent Dosing: Review Comparing Results of Three Database Studies. International Society for Clinical Densitometry Annual Meeting, 2006.

Grima DT et al. *P&T* 2002; 27:448–55.

Johnell O et al. *Osteoporos Int* 2004; 15:38–42.

Johnell O et al. *Pharmacoeconomics* 2003; 21:305–14.

Kanis JA et al. *Health Technol Assess* 2002; 6(29).

Kanis JA et al. *Osteoporos Int* 2000a; 11:669–74.

Kanis JA et al. *Osteoporos Int* 2000b; 12:356–61.

Klotzbeucher CM et al. *J Bone Miner Res* 2000; 15:38–42.

Looker AC et al. *J Bone Miner Res* 1997; 12:1761–8.

O'Neill TW et al. *J Bone Miner Res* 1996; 11:1010–8.

Tosteson ANA et al. *Osteoporos Int* 2001; 12:1042–9.

Red Book for Windows 2006. Version 61127(39).

US Census Bureau. 2002. 2002 US Census.

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