Cost Effectiveness Estimate of Bazedoxifene

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**Article ID:** WMC002547
**Article Type:** Original Articles
**Submitted on:** 13-Dec-2011, 05:59:08 PM GMT  **Published on:** 14-Dec-2011, 08:50:41 AM GMT
**Article URL:** http://www.webmedcentral.com/article_view/2547
**Subject Categories:** ECONOMICS OF MEDICINE
**Keywords:** Bazedoxifene, Cost effectiveness, Economics, Osteoporosis, Fracture, Women

**How to cite the article:** Iglesias A A. Cost Effectiveness Estimate of Bazedoxifene . WebmedCentral ECONOMICS OF MEDICINE 2011;2(12):WMC002547

**Source(s) of Funding:**
There isn’t any financial support.

**Competing Interests:**
The author declares no conflict of interest.
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Abstract

Background: A three-year clinical trial of bazedoxifene 20 or 40mg/day compared with raloxifene 60mg/day or placebo in postmenopausal women with osteoporosis showed that treatment with bazedoxifene significantly reduced the risk of new vertebral fracture (NVF) in this population; all subjects received oral daily calcium and vitamin D supplements. Based on this clinical trial, the aim of the present study was to assess the cost effectiveness of bazedoxifene compared with placebo or raloxifene, for the treatment of osteoporosis in postmenopausal women. Methods: The cost effectiveness was only estimated from a healthcare perspective in the 50 to 64 age group. Only drug acquisition costs and direct costs were considered. Incremental cost effectiveness ratio was calculated as cost per event avoided. Because the incidence of deep vein thrombosis events was higher with bazedoxifene and raloxifene compared with placebo, this incidence was taken in account in the decision tree. A sensitivity analysis was performed. Results: We applied a cost minimization analysis between treatment groups without differences in the primary endpoint (bazedoxifene 20mg versus 40mg and bazedoxifene 20mg versus raloxifene 60mg): the most efficient drugs were bazedoxifene 20mg and generic raloxifene 60 mg, respectively. The cost of avoiding additional NVF versus placebo (i.e. in the case of no treatment with bazedoxifene 20mg) would be 436.054,39 annual euros (256.552,60 euros per year in the case of generic raloxifene). Conclusion: Considering the defined conditions, treatment with bazedoxifene versus a placebo group would not be efficient.

Introduction

It is estimated that up to 52% of women at 70 years and older suffers from osteoporosis and it is estimated that 40% will experience a vertebral fracture before 80 years of age in Spain (1). Today we are immersed in a scenario of economic crisis and it is necessary to establish priorities in using available resources. In the field of Pharmacology, new drugs are incorporated to the therapeutic management of chronic and high prevalent diseases, as in the case of osteoporosis. Once a patient is diagnosed of osteoporosis, the goal of all treatments is preventing or, at least, reducing the incidence of fractures. Several drugs have shown that they are able to reduce the risk of vertebral fractures in placebo-controlled clinical trials. Bazedoxifene is one of the last new drugs which has been marketed. Bazedoxifene is a novel selective estrogen receptor modulator (SERM) that has shown tissue selective activities to confer favorable effects on bone metabolism without adversely affecting the uterine or breast tissues: it has been shown to prevent bone loss and decrease bone turnover in a two year randomized controlled trial in healthy postmenopausal women with normal or low bone mineral density (2). In our community, there is a reduction in raloxifene prescriptions, while it is observed an increase in the bazedoxifene prescriptions (Figure 1); for both, the highest consumption is in the 55 to 64 age group. Silverman et al (3) carried out a clinical trial in order to evaluate the safety and efficacy of bazedoxifene compared with placebo and raloxifene, in treating postmenopausal women with osteoporosis; all subjects received oral daily calcium and vitamin D supplements. The aim of the present study is to know the cost effectiveness of bazedoxifene versus raloxifene and placebo, based on the results in the Silverman et al clinical trial extrapolated to the 50 to 64 age group of women.

Methods

A bibliographic search was conducted in MEDLINE to know if any pharmacoconomic study on bazedoxifene had been made by applying the terms [bazedoxifene] and [costs] (2/7 useful references), [economic/s] (1/6 and 1/3 useful references, respectively) and [economy] (1/3 useful references). In addition, the public assessment report technologies health IPE 63/2010 of the Agencia de Evaluación de Tecnologías Sanitarias (AETS) was considered (4). Efficacy and safety data (Table 1) were obtained from the clinical trial of Silverman et al (2). The baseline characteristics of patients in the trial are available in the corresponding reference. The primary endpoint in the clinical trial was the efficacy measured as incidence of new vertebral fractures (NVF) after 36 months of treatment. Only this efficacy data was considered in our pharmacoeconomic study because there were no statistically significant differences in the incidence of non-vertebral fractures related to...
osteoporosis among treatment groups. With regard to security, we considered the incidence of deep vein thrombosis (DVT) since it is a serious adverse reaction and it was higher in groups with active treatment compared with the placebo group. In the clinical trial, there weren’t statistically significant differences in the primary endpoint (NVF) among the group treatments bazedoxifene 20 mg versus bazedoxifene 40 mg and bazedoxifene 20 mg versus raloxifene 60 mg, so we applied a minimization cost analysis in these two cases (Table 1). There were statistically significant differences in the primary endpoint between bazedoxifene versus placebo and raloxifene versus placebo groups, so we used a cost effectiveness analysis and we have developed a decision tree as shown in Figure 2. Effectiveness was defined as the absence of vertebral fracture and the absence of deep venous thrombosis. The incremental cost effectiveness ratio was expressed as cost per event avoided. Because of subgroup analyses of the incidence of NVF by baseline fracture status (i.e., with or without prevalent fracture) showed that this interaction was not statistically significant, the treatment effect was considered similar among subjects with or without prevalent fracture. Data costs were obtained from the literature (5-8) and are shown in table 1. In this study, we have considered only the costs of vertebral fractures in the 50 to 64 age group of women. The costs of calcium and vitamin D supplements have not been included because they applied equally to all trial subjects. It was considered that basal and osteoporosis monitoring visits were performed at primary care and a fracture generates a first visit at hospital level. It was included in the analysis the price of both raloxifene originator and generic (EFG) drugs. Bioavailability between them was assumed according to the Spanish legislation. The perspective of economic evaluation has been that of the health system exclusively. Horizon is in line with the three-year duration of the trial; we didn’t make projections based on the life expectancy of a population of similar characteristics and annual discount rate wasn’t applied to future effects. It wasn’t made temporary adjustments of costs (price mark raloxifene is the same in the past three years and it is assumed that there is no variation in the rest of costs in this period of time). Results were expressed in euros. A sensitivity analysis was conducted to assess the effect of: a) cost minimum (the price of generic raloxifene) and maximum (the price of bazedoxifene 40 mg/day) of drugs, b) variations in the cost of the fracture vertebral in the first year between 1500 and 3744 euros (the double cost applied to the base case), c) variations in the cost of DVT in the first year between 1500 and 5394 euros (the double cost applied to the base case), in the results of the analysis of cost effectiveness of bazedoxifene 20 mg versus placebo.

Results

Table 2 shows the results of the minimization costs analysis: the most efficient drugs were raloxifene 60 mg EFG and bazedoxifene 20 mg, when comparing bazedoxifene 20 mg versus raloxifene 60 mg and bazedoxifene 20 mg and 40 mg, respectively. The results of the cost-effectiveness analysis, from the comparison of each drug against placebo, are shown in table 2. Sensitivity analysis (Table 3) for bazedoxifene 20 mg/day versus placebo, in the three cases mentioned above, showed no changes in the sense of analysis; i.e. results were consistent with related to: a) the cost of the drug in the range from 807,17 to 2691,35 euros (three years of treatment); b) the cost of the vertebral fracture in the first year in the range of 1500 to 3744 euros; c) the cost of a DVT in the first year in the range of 1500 to 5394 euros.

Discussion

Present study doesn’t show cost saving in bazedoxifene treatment compared with placebo (all subjects were treated with calcium and vitamin D supplements) in the 50 to 64 age group of women, considering the defined conditions. It implies that bazedoxifene treatment in this population would not be efficient. In the report of the AETS (4) three bisphosphonates (alendronate, risedronate and ibandronate), raloxifene (another SERM) and strontium ranelate were studied against calcium and vitamin D supplements or placebo; bazedoxifene was not studied in this report but it seems similar in effectiveness as raloxifene as shown (3). The report demonstrates that in Spanish women at 50 years and older with osteoporosis, none of the evaluated treatments compared to calcium plus vitamin D or placebo obtained incremental cost-utility acceptable rates if treatment was started before the age of 69. They considered a partial adherence in contrast to our study: we have considered a 100% adherence because the effectiveness data were from a clinical trial in which withdrawals for adverse events were similar between bazedoxifene and placebo groups. This could mean a bias because adherence to treatment affects the interaction between cost and utility of pharmacological treatments for osteoporosis.
and it is usually lower in routine clinical practice than in clinical trials. We can therefore assume that our result could be worse if imposing a correction regarding adherence to treatment, because it would diminish the effectiveness. In the report of the AETS, the control group (calcium plus vitamin D or placebo) presents a better cost-utility rate than the other drugs when treatment was initiated in women from 50 to 72 years of age. Also, they observed that, in a scenario of partial adherence, alendronate may be considered a cost-utility option compared with the administration of calcium plus vitamin D or placebo in women aged 69 or more. Moreover, when treatment is started at an older age of 73, alendronate dominates the other considered options, including treatment with calcium plus vitamin D supplements or placebo. When adherence is optimal, quality-adjusted life-years (QALYs) cost is lower and alendronate dominates the rest of the drugs: the cost-utility incremental rate indicates that each additional QALY achieved, due to the intervention with alendronate, would cost 208.239 € per patient when treatment is initiated at aged 50. However, raloxifene doesn’t appear as a cost-utility option. Despite the limitations of the model used, alendronate (but not raloxifene and we could extrapolate this conclusion to bazedoxifene) is the option that obtains the best results in terms of cost-utility. It is not expected that the limitations of their study can alter the results in relation to the other treatments. In the study of Borgström et al (9), the base case was a 70 year-old woman with a T-score of ≥2.5 SD and a prior fragility fracture and the modeled efficacy depended on the estimated 10-year probability of a major osteoporotic fracture. They studied the cost/QALY variations between countries in Europe: the results ranged from cost saving in Sweden to 105,450 euros in Spain. These results could be explained because low-risk countries (for example, Spain) will have a lower baseline fracture risk and will experience lower anti-fracture efficacy from drugs. The large differences in QALYs gained between high- and low-risk countries could be due not only to differences in fracture risk but also for the negative effect of venous thromboembolic events (which compensates for avoided fractures to a larger extent if the baseline fracture risk is lower). For that, bazedoxifene could be a cost-effective treatment for postmenopausal osteoporosis in particular patient groups. Ström et al. (7) evaluated bazedoxifene compared to placebo, in a Swedish setting with traditional and FRAX®-based risk assessments. The objective was to compare these two methods and their Markov model included fractures and thromboembolic events. Traditional approach calculate the fracture risk taking in to account risk adjustments based on age, bone mineral density and prior vertebral fracture; the treatment effect was derived from clinical trials and the same efficacy has been assumed regardless of the fracture risk of the population. With the traditional approach, they obtained lower incremental cost effectiveness ratios at ages up to 60 years compared with the FRAX® method. In women at 70 years an older with more risk factors, the data obtained with the FRAX® method the cost per QALY gained was lower. One reason for this result could be that the fracture risk increases while increases the age, which improves the cost effectiveness estimated with the FRAX® approach. Also, in the traditional approach, all other risk factors are assumed to be at the same level as the population prevalence, whereas in the FRAX® analysis, the patients are not assumed to have any clinical prevalent risk factors (apart from low bone mineral density). They suggested that FRAX® applied in cost-effectiveness analyses is a good method because it facilitates the estimation of cost effectiveness for different types of patients with different combinations of risk factors. One more time, bazedoxifene treatment (analyzed by FRAX® approach) showed cost saving compared with no treatment in 70-year-old women with prior fracture. In an economic study based on the MORE clinical trial, Borgström et al (10) studied the benefits of raloxifene treatment (another SERM) in terms of QALYs and life-years gained. The study estimated the cost effectiveness mainly from a healthcare perspective but, also they analyzed the cost effectiveness taking a societal perspective. As in previous studies commented, QALYS costs decrease when the age of the women increase at start of treatment. So, they concluded that their model indicates that raloxifene versus placebo is cost effective for the treatment of postmenopausal women at an increased risk of vertebral fracture, from the healthcare and societal perspectives. This is a different result for raloxifene compared with the AETS document: the explanation could be, as commented previously, that low-risk countries will therefore receive lower anti-fracture efficacy from drugs. In our study, we found that the most efficient drug is bazedoxifene 20 mg and raloxifene 60 mg generic in the respective minimization cost analyses when active treatments were compared. Versus placebo, the cost of avoiding new additional vertebral fractures (that will occur without bazedoxifene 20 mg treatment), would be 436.054.39 annual euros (256.552.60 euros per year in the case of generic raloxifene) according to data of cost effectiveness in the 50 to 64 age group of women. As in other countries, in Spain it is not explicitly...
indicated a threshold of efficiency with regard to adopting new health technologies; so, it is difficult to decide whether a health technology is efficient or not. It is only evident that bazedoxifene treatment don’t show cost saving and it wouldn’t be an efficient option in the scenario studied. According to the characteristics of the pharmacoeconomic study, a pharmacological option may be appropriate in term of costs depending on other different treatments, specific population groups or particularly prevalent risk factors. For this reason, it would be necessary to conduct a study of benefits obtained with bazedoxifene 20 mg treatment measured in QALYs and years of life gained in order to estimate the cost effectiveness and cost-utility compared to placebo (i.e., treated only with calcium plus vitamin D) for the treatment of postmenopausal Spanish women aged 50-64 years with a vertebral fractures increased risk. It seems convenient to assess the effect on more specific populations with different risk levels: the degree of severity of osteoporosis, the calcium and vitamin D intake, etc. Risk levels may determine the effect of interventions evaluated. It would also be interesting to estimate productivity losses and costs related when women with osteoporosis are younger than 65 year-old.

Conclusion(s)

In the 50 to 64 age group of women, bazedoxifene treatment compared with placebo doesn’t indicate cost saving; it would not be efficient in this population.

Abbreviation(s)


Acknowledgement(s)

The author wishes to thank Ana Gómez, M Antonia Maestre and M Antonia Morey for their critical reading of the manuscript.

Reference(s)

Illustrations

Illustration 1

FIGURE 1: Raloxifene and bazedoxifene prescription percentage per year (except for 2011: from January to August)
Illustration 2

FIGURE 2: DECISION TREE.* Drug treatment could be bazedoxifene 20 or 40 mg or raloxifene 60 mg.
Illustration 3

TABLE 1: summary of values used in the cost-effectiveness model.

<table>
<thead>
<tr>
<th>Yearly drug cost: bazedoxifene or raloxifene originator</th>
<th>Yearly drug cost: raloxifene generic</th>
<th>Vertebral fracture first year</th>
<th>Vertebral fracture 2nd year and following years</th>
<th>Deep vein thrombosis (1st year)</th>
<th>Radiographs copy</th>
<th>Physician visit (general practitioner)</th>
<th>Physician visit (hospital)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cost in euros</td>
<td>5, 6</td>
<td>269,06</td>
<td>1872</td>
<td>511</td>
<td>2.697</td>
<td>20,58</td>
<td>84</td>
</tr>
<tr>
<td>reference</td>
<td>5, 6</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>8</td>
<td>8</td>
<td>8</td>
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</tbody>
</table>
Illustration 4

TABLE 2: Analysis of costs.

<table>
<thead>
<tr>
<th>MINIMIZATION COSTS ANALYSIS</th>
<th>yearly drug cost</th>
<th>yearly drug cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>bazedoxifene 20 mg</td>
<td>448,5589</td>
<td>bazedoxifene 20 mg</td>
</tr>
<tr>
<td>raloxifene 60 mg</td>
<td>448,5589</td>
<td>bazedoxifene 40 mg</td>
</tr>
<tr>
<td>raloxifene 60 mg generic</td>
<td>269,0571</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>COST -EFFECTIVENESS ANALYSIS</th>
<th>cost effectiveness</th>
<th>incremental cost</th>
<th>NVF avoided</th>
<th>cost of NVF avoided</th>
</tr>
</thead>
<tbody>
<tr>
<td>bazedoxifene 20 mg</td>
<td>1.561,62</td>
<td>86.915,37</td>
<td>15,05</td>
<td>1.308.163,17</td>
</tr>
<tr>
<td>placebo</td>
<td>220,69</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>raloxifene 60 mg *</td>
<td>1.008,22</td>
<td>51.136,66</td>
<td>15,05</td>
<td>769.657,81</td>
</tr>
<tr>
<td>placebo</td>
<td>220,69</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bazedoxifene 40 mg</td>
<td>3.008,11</td>
<td>220.303,99</td>
<td>12,08</td>
<td>2.662.153,36</td>
</tr>
<tr>
<td>placebo</td>
<td>267,31</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* cost of generic drug
Illustration 5

TABLE 3: Sensitivity analysis.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>minimum</th>
<th>C/E bazedoxifene</th>
<th>C/E placebo</th>
<th>maximum</th>
<th>C/E bazedoxifene</th>
<th>C/E placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug cost</td>
<td>807,17</td>
<td>1008,22</td>
<td>220,69</td>
<td>2691,35</td>
<td>2944,51</td>
<td>220,69</td>
</tr>
<tr>
<td>Vertebral fracture first year</td>
<td>1500</td>
<td>1552,82</td>
<td>204,79</td>
<td>3744</td>
<td>1605,86</td>
<td>300,73</td>
</tr>
<tr>
<td>Deep vein thrombosis (1st year)</td>
<td>1500</td>
<td>1556,70</td>
<td>219,50</td>
<td>5394</td>
<td>1572,70</td>
<td>223,39</td>
</tr>
</tbody>
</table>
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