Cost Savings With Nefazodone in Treating Depression

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Pharmacoeconomic analysis of antidepressant therapy is an important tool for ensuring the most cost-cognizant approach to treat a particular mental disorder. As the number of effective antidepressant compounds continues to grow, the drug selection process must consider not only the cost of the drug itself, but also costs associated with treatment failure and management of untoward and unexpected side effects. In economic studies conducted in North America and England using a decision analysis model and a direct annual cost model, nefazodone has been shown to have an impact on costs associated with depression when compared with imipramine and fluoxetine. Nefazodone also can reduce depression-related anxiety and agitation symptoms early in treatment, and, because it improves subjective and objective sleep measures, use of concomitant anxiolytics or sedative-hypnotics with nefazodone has been shown to be less frequent and less costly than with selective serotonin reuptake inhibitors.

Analysis of the economic aspects of psychopharmacologic agents has become increasingly important in the overall approach of treating a particular mental disorder.1,2 Today, practitioners have a number of effective antidepressant agents at their disposal to treat patients suffering from depression and associated anxiety disorders. The selective serotonin reuptake inhibitors (SSRIs) have overtaken the tricyclic antidepressants (TCAs) as the most commonly used antidepressants in clinical practice.3 In addition to SSRIs, other new antidepressants, such as nefazodone, bupropion, venlafaxine, and mirtazapine, are effective for treating patients with depression. In this article, several economic analyses that have evaluated the cost impact of nefazodone versus imipramine and SSRIs for treating depression are reviewed. The potential cost savings with nefazodone as a treatment for depression, especially in patients with significant anxiety and sleep disturbance, also are analyzed.

COST-SAVINGS ANALYSES

At the time nefazodone was to be introduced in Canada in the mid-1990s, Anton and Revicki4 used a decision model approach to evaluate its cost savings. These authors estimated cost and outcomes under a variety of clinical scenarios. Health care costs were represented by estimates of direct medical costs, whereas health outcomes were defined in terms of quality-adjusted life-years (QALYs). The authors defined the QALY as a measure of “expected survival, adjusted for the impact of different clinical events on patient function and well-being.”5 This parameter measures both the change in quantity of life as reflected in decreased mortality and the change in quality of life as reflected in reduced morbidity. Quality adjustments were based on “utilities,” a measure of the preference of an individual for a health state resulting from a particular treatment.5,6

Because nefazodone was newly approved in Canada, the authors wanted to determine its relative cost savings as compared with 2 currently available antidepressants, the SSRI fluoxetine and the TCA imipramine. The authors therefore went through the following steps: they identified the decision, established a time frame for their decision, structured the decision and its consequences over time, assessed the probability of the occurrence of each consequence in the model, determined the cost associated with each treatment and the value of each possible outcome, and compared the cost savings of the medications.

The results of this study showed that the average lifetime cost associated with imipramine was $52,111; with fluoxetine, $50,678; and with nefazodone, $50,664. Consequently, nefazodone was substantially less expensive than imipramine and slightly less expensive than fluoxetine. Using the
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Various assumptions and parameters of their model, lifetime treatment with nefazodone yielded 13.90 QALYs compared with 13.79 QALYs for fluoxetine and 13.18 QALYs for imipramine. Finally, in evaluating the relative cost savings of the medications, when lifetime direct medical costs and the health consequences of treatment for the 3 antidepressants were considered, nefazodone was rated better than imipramine and fluoxetine. Revicki and colleagues published comparable findings.

Montgomery and associates conducted a similar study in England to compare the relative cost of nefazodone versus imipramine in treating depression. They used a model developed by Jonsson and Bebbington to calculate the direct annual cost of treating depression. Costs were updated to 1994 standards, and the cost of nefazodone was substituted for that of paroxetine, which was included in the original study. The authors also substituted probabilities of adverse events and relapse reported in long-term, placebo-controlled studies of nefazodone from a Bristol-Myers Squibb data set. Using updated costs and probabilities from continuation trials, the expected annual cost per successfully treated patient was £242 for nefazodone and £323 for imipramine. The expected annual cost of treatment with nefazodone was £218 and £254 with imipramine or fluoxetine. Ninety-eight percent of the 50 patients who were receiving an SSRI received concomitant medication, compared with only 26.7% of the 30 patients receiving nefazodone. Eight percent of the 30 patients receiving nefazodone. Eight percent of the 30 patients receiving nefazodone.

Table 1. Summary of Objective Electroencephalographic
Sleep Measures With Nefazodone and Fluoxetine in Depressed Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nefazodone</th>
<th>Fluoxetine</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of awakenings</td>
<td>↓</td>
<td>↑</td>
<td>≤.01</td>
</tr>
<tr>
<td>% Awake time</td>
<td>↓</td>
<td>↑</td>
<td>≤.01</td>
</tr>
<tr>
<td>Sleep efficiency</td>
<td>↓</td>
<td>↓</td>
<td>≤.01</td>
</tr>
<tr>
<td>Sleep latency</td>
<td>↔</td>
<td>↔</td>
<td>NS</td>
</tr>
</tbody>
</table>

aData from references 12–14. Abbreviation: NS = not significant.
Symbols: ↓ = decrease, ↑ = increase, ↔ = no change.
bDifference between drugs in change from baseline.
Includes awake and movement time by electroencephalogram.

Clinical, as many psychiatrists have observed, as depression-related anxiety symptoms increase, the frequency and severity of depression-related sleep disturbance also increase. As the frequency and severity of sleep disturbances increase, the frequency of physicians' prescribing anxiolytics or sedative-hypnotics also increases. One group of investigators sought to retrospectively determine the prevalence of concomitant medication use in 80 elderly depressed patients who were diagnosed with depression and either agitation or anxiety. Patients were receiving an SSRI (fluoxetine, paroxetine, or sertraline) or nefazodone. Ninety-eight percent of the 50 patients who were receiving an SSRI received concomitant medication, compared with only 26.7% of the 30 patients receiving nefazodone. Eight percent of the
SSRI-treated patients reported continued anxiety and 6% reported sleep disturbances. None of the nefazodone-treated patients reported either anxiety symptoms or sleep difficulties.

A larger systematic review involved a random sample of California Medicaid (MediCal) patients from January 1, 1995, through May 31, 1995, to determine both the percentage of patients on treatment with various antidepressant agents receiving an antianxiety or sedative-hypnotic agent and the cost associated with concomitant use within the first 30 days of antidepressant treatment. Nefazodone-treated patients had the smallest percentage of patients taking either a sedative-hypnotic or an anxiolytic (Figure 3). Higher rates were noted in patients taking SSRIs and venlafaxine. When the cost of concomitant medications was calculated, nefazodone was a less expensive treatment alternative (Figure 4).

**NEFAZODONE IN CHRONIC DEPRESSION**

The relative cost savings of nefazodone, the cognitive behavioral-analysis system of psychotherapy (CBASP), and their combination in chronically depressed individuals has also been evaluated. In one study, the direct treatment cost per patient was $770 for nefazodone, $1800 for CBASP, and $3400 for their combination. Thus, direct treatment costs were lowest for nefazodone monotherapy, and treatments utilizing nefazodone, alone or in combination with CBASP, were the most cost saving.
SUMMARY

In studies conducted in Canada, England, and the United States, nefazodone has been shown to be a cost-saving treatment for depression when compared with imipramine and fluoxetine on the basis of a decision analysis model and a direct annual cost model. In addition, nefazodone reduces depression-related anxiety and agitation symptoms early in treatment, even before therapeutic doses are achieved. Because it also improves subjective and objective sleep measures, the use of concomitant anxiolytics or sedative-hypnotics with nefazodone has been shown to be less frequent and less costly than with SSRIs.

Drug names: bupropion (Wellbutrin and others), fluoxetine (Prozac and others), mirtazapine (Remeron), nefazodone (Serzone), paroxetine (Paxil), sertraline (Zoloft), venlafaxine (Effexor).

REFERENCES


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