

## Angiotensin Receptor Blockers: Impact on Costs of Care

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### **Abstract**

Direct and indirect costs related to the treatment of hypertension are estimated at nearly \$60 billion annually. Short- and long-term costs of healthcare utilization and treatment are, therefore, important considerations in selection of antihypertensive therapy. Studies of patients with hypertension and type 2 diabetes have shown that treatment with angiotensin receptor blockers (ARBs) can reduce healthcare costs as a result of a decreased incidence of end-stage renal disease and other clinical end points. ARBs also increase survival in these patients. Cost savings have also been reported in patients with heart failure as a result of reductions in office and emergency department visits, hospital admissions, and hospital stays.

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**H**ypertension affects nearly 65 million American adults.<sup>1</sup> Pharmacologic treatment of hypertension can significantly reduce mortality and morbidity.<sup>2</sup> It is estimated that antihypertensive therapy may reduce the incidence of stroke by 35% to 40%, myocardial infarction by 20% to 25%, and heart failure by more than 50%.<sup>3</sup>

Direct and indirect costs related to the treatment of hypertension are estimated at nearly \$60 billion annually.<sup>4</sup> Given these costs, healthcare delivery systems are challenged to select appropriate pharmacologic agents for the treatment of hypertension while keeping in mind both short- and long-term costs associated with healthcare utilization and treatment.

Angiotensin receptor blockers (ARBs) are highly effective and well-tolerated antihypertensive agents. Studies comparing cost effectiveness of ARBs with each other and with other drug classes are rare and are frequently based on data provided by randomized, controlled clinical trials.<sup>5</sup>

One study compared the cost effectiveness of losartan, valsartan, irbesartan, and olmesartan for treatment of hypertension.<sup>5</sup> The investigators used differences in diastolic blood pressure (BP) reductions with the comparative agents to estimate reductions in the annualized risk of cardiovascular (CV) and cerebrovascular events based on Framingham data. They then translated these annualized risks into reductions in healthcare costs associated with treating CV events in a managed care setting. Based on antihypertensive efficacy (reductions in diastolic BP), olmesartan was found to be the most cost effective in a managed care setting. Another study compared candesartan, losartan, valsartan, and irbesartan using a pharmacoeconomic model and found candesartan to be most cost effective.<sup>6</sup> However, such in-class comparisons based on outcomes from a single trial should be interpreted with some caution.<sup>7</sup> A meta-analysis of 43 trials by Conlin and associates of the ARB class as a whole showed comparable antihypertensive efficacy across agents,<sup>8</sup> which may make outcomes-based claims of cost efficacy of one ARB over another open to question.

Two studies in US and Spanish settings have compared the cost effectiveness of irbesartan with that of other standard antihypertensive therapies (excluding angiotensin-converting enzyme inhibitors [ACEIs]) in the treatment of patients with hypertension, type 2 diabetes, and microalbuminuria.<sup>9,10</sup> Both studies were based on a computer simulation model used to predict the progression to end-stage renal disease (ESRD) and death in patients with type 2 diabetes and hypertension.

In both the US and Spanish settings,

treatment with irbesartan was projected to delay the onset of ESRD, prolong life expectancy, and lower overall direct medical costs. Both studies provide supportive evidence for the early initiation of irbesartan in patients with diabetic nephropathy to increase life expectancy and cost savings as a result of a decreased incidence of ESRD.

Similar results were reported using losartan in the Reduction of End Points in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) trial.<sup>11</sup> The RENAAL investigators reported that losartan reduced the number of days with ESRD by 33.6% over 3.5 years, resulting in a savings of \$3522 per patient over 3.5 years.<sup>12</sup>

Another computer simulation model was used in an analysis of the health and economic outcomes of therapy with valsartan versus amlodipine in patients with type 2 diabetes and microalbuminuria, based on clinical end points from the Microalbuminuria Reduction with Valsartan (MARVAL) study.<sup>13,14</sup> In this budget-impact analysis, urinary albumin excretion rate data were used to project patient distributions to 7 possible health states over 8 years. Valsartan was less costly and more effective in terms of quality-adjusted survival than amlodipine.<sup>13</sup> Compared with patients treated with amlodipine, those treated with valsartan gained a mean of 7 months per patient of quality-adjusted survival (77 vs 70 months;  $P < .01$ ). Also, mean per patient medical costs were significantly lower for valsartan patients than for amlodipine patients (\$92 058 vs \$124 470;  $P < .01$ ).

Like diabetic nephropathy, heart failure is a major public health concern associated with substantial healthcare costs, mostly attributable to hospitalizations.<sup>15-17</sup> A subgroup analysis of the Valsartan Heart Failure Trial (Val-HeFT) was undertaken to evaluate the effects of angiotensin receptor blockade in 366 patients with heart failure not treated with ACEIs.<sup>18</sup>

In this subgroup, use of valsartan compared with placebo in addition to standard heart failure therapy was associated with relative risk reductions of 33% in all-cause mortality ( $P = .017$ ) and 53% in first hospital admission for heart failure ( $P = .0006$ ).

Valsartan also significantly reduced the total number of hospitalizations for heart failure ( $P = .01$ ). These benefits represent not only clinical efficacy, but also opportunities for important cost savings for healthcare delivery systems.

Using data related to health outcomes and resource utilization derived from Val-HeFT, a budget impact analysis was created for a hypothetical US health plan with 250 000 members. An estimated 1207 plan members were projected to have heart failure diagnoses. After deductions for medication costs, use of valsartan in this model analysis resulted in net cost savings of \$675 830 per year as a result of projected reductions in hospitalizations and shorter length of hospital stay.<sup>19</sup>

Claims-based analyses, which represent actual healthcare resource utilization, offer another perspective on cost efficiencies based on actual care, as opposed to simulated computer models or budget impact analyses based on single-trial outcomes data. A report by Thaker and colleagues presented at the 2005 American Society of Hypertension scientific meeting measured healthcare utilization and related costs incurred by hypertensive patients during the first year after initiating therapy with an ACEI versus an ARB.<sup>20</sup> In this retrospective, longitudinal pharmacy claims database analysis of approximately 11 million covered lives, economic outcome measures were used as the basis for cost comparisons. These measures included a number of CV-related office visits, hospitalizations, and emergency department visits. Overall medical and pharmacy costs were also included in the analysis. Only patients with continuous pharmacy coverage were included in the analysis of patients with a diagnosis of hypertension who initiated antihypertensive therapy between July 1, 2002, and December 31, 2002, with an ACEI or ARB. Patients were followed for 1 year from the date of the first prescription. The study cohort consisted of 26 005 patients who received ACEI therapy and 11 948 patients who received ARB therapy.

The ACEIs prescribed most frequently were lisinopril, quinapril, and ramipril, respectively; the ARBs prescribed most

frequently were valsartan, losartan, and irbesartan, respectively. The number of CV-related physician office visits per year was lower for patients initiating ARB therapy (2.02) compared with patients initiating ACEIs (2.28). The number of annual CV-related hospitalizations (0.08 vs 0.10) and annual emergency department visits (0.02 vs 0.03), respectively, was also lower. Translated into medical costs, ARB-treated patients accounted for \$2780 annually compared with \$3163 for ACEI-treated patients. Average annual pharmacy costs were somewhat lower in the ACEI group (\$893) compared with \$955 in the ARB group.

In summary, this analysis showed less overall healthcare resource utilization among patients initiating ARB therapy compared with patients initiating therapy with ACEIs.

Like outcomes-based analyses of cost efficiencies, claims-based cost analyses also have some inherent limitations. Drug-insured patients may have different healthcare-seeking patterns than uninsured patients. Additionally, many factors may have influenced agent selection and utilization, including provider specialty, copay, and formulary issues. Data on potential confounders, such as CV risk factors, efficacy, adverse events, and patient-physician relationship were not available, but these factors may have influenced utilization.

### Conclusion

Significantly more patients with hypertension should be receiving treatment. For those receiving treatment, BP is often not well controlled, leading to increased medical costs. Special attention needs to be given to patients with concomitant diseases like diabetes and CV disease. Use of ARBs within these populations has been demonstrated to have protective effects, yielding substantial cost savings according to economic analyses. Additional cost analyses of data from comparative ACEI and ARB trials in hypertension are needed, however. Both clinical and economic benefits of available agents should be taken into consideration in treatment decision making.

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