Evaluating the Efficiency of Treatment in the Allergic Rhinitis Market

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ABSTRACT

BACKGROUND: In the present era of increasing health care expenditures, economic comparisons of therapeutic products play an important role in ensuring that limited health care resources are used appropriately.

OBJECTIVE: To provide a model for the comparative analysis of alternative treatments, in terms of both cost and efficacy, in allergic rhinitis that will provide decision makers in a managed care environment an additional tool to help maximize health care benefit per dollar spent. We also review current treatments in the allergic rhinitis market and their impact on cost, availability, and utilization.

SUMMARY: Efficacy estimates were derived from published reviews, meta-analyses, and guidelines, and cost data are based on average wholesale prices. Our results indicate that when cost and efficacy data are plotted on a cost-effectiveness plane, the intranasal corticosteroids appear to be the most efficient use of health care resources. Moreover, budesonide aqueous nasal spray was found to be the most efficient treatment for allergic rhinitis when compared with 3 other leading intranasal corticosteroids used at their recommended starting doses, the less-sedating/nonsedating antihistamines, and a leukotriene receptor antagonist.

CONCLUSION: Evaluating products on an efficiency frontier platform, which integrates both the effectiveness and cost of products, will allow health plan decision makers to ensure the appropriate allocation of health care resources.

KEYWORDS: Allergic rhinitis, Intranasal corticosteroids, Antihistamines, Leukotriene receptor antagonists, Cost efficiency

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Health care expenditures have increased dramatically over the last decade, leading to heavy reliance on managed care organizations (MCOs) to make decisions regarding the appropriate allocation of health care resources across an expanding number of health care conditions with an increasing number of treatment options. With prescription treatments encompassing a quickly growing portion of this overall budget, MCOs have developed a new level of scrutiny toward individual treatment regimens and have focused attention on identifying cost-effective treatments (i.e., treatments that provide maximum health benefit per dollar spent).

In an effort to ensure value-based decision making, the Academy of Managed Care Pharmacy has produced guidelines on factors for consideration in making reimbursement policy decisions. Many MCOs request information on the clinical and economic benefit of new medications before making reimbursement decisions. With continued interest in value-based decision making, pharmacoeconomic analyses are often used to help in the establishment of MCO treatment policies. Pharmacoeconomic methods provide tools to compare the value of treatment interventions, with the goal being to identify the most efficient means of expending health care resources.

Identifying efficient treatment options involves incorporating information on both the costs and effects of interventions. We briefly review cost-effectiveness analysis and highlight how it can be used to identify treatments that represent an efficient use of health care resources. We then use the allergic rhinitis (AR) market to apply these concepts to a real-world example.

The Cost-Effectiveness and Cost-Efficiency Frontier

Cost-effectiveness analysis is a form of economic evaluation that provides information on the value of an intervention or therapy in relation to its costs when compared with an alternative. The analysis is intended to compare 2 or more interventions with each other and provide information on the differences in costs and effects between the comparators. The results are summarized in a ratio that provides information on the incremental costs per unit of effect. This ratio is referred to as the incremental cost-effectiveness ratio (ICER) because it is assessing incremental differences between alternative treatments.

Results from a cost-effectiveness analysis comparing, for example, a new treatment with usual care, are often presented on a cost-effectiveness plane (Figure 1). The cost-effectiveness plane is a graphical representation of all possible results of a cost-effectiveness analysis and is divided into 4 quadrants. ICERs falling into the northwest (NW) and southeast (SE) quadrants require no decision to be made. These are quadrants where 1 of the treatments is more effective and less costly, so it dominates the other treatment. In the SE quadrant, the new treatment domi-
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We highlight many of the aforementioned issues with a hypothetical example. Figure 2 represents the average cost and effectiveness of 6 interventions. The interventions are labeled A through F and are used in the treatment of a similar condition. The average effectiveness of each treatment is plotted on the x-axis and the average cost on the y-axis. The most cost-effective intervention is treatment B because it has the line with the lowest slope (smallest ICER) from the origin to its place on the plot. No other intervention has a lower ICER; thus, a decision maker would be best served to choose this intervention compared with the other interventions. If, after choosing this intervention, the health care payer has not reached the budget constraint, then the next most efficient use of resources would be to choose treatment F because it represents the next lowest ICER as we move from treatment B to the next option. Thus, treatment B and treatment F lie on the cost-efficiency frontier and should be chosen in that order until exhausting the budget for this particular disease state.

However, the slope of the lines connecting the interventions represents the ICER, and a line from the origin to each of the treatments could be considered the ICER of the intervention compared with doing nothing. By graphing the average cost-and-effect estimates for the interventions, it is possible to identify the cost-efficiency frontier. The cost-efficiency frontier represents the combination of interventions with the most ICERs. It is identified by connecting the interventions that lie below and to the right of the frontier as needed until they have achieved the desired clinical outcome and exhausted their budget for this particular disease state.

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The example above describes a framework for comparing several interventions when deciding how to allocate health care resources. One common use of the cost-efficiency frontier is within economic evaluations that include several treatments, where the goal is to identify the most cost-effective treatment options. Another setting in which the cost-efficiency framework can be used is to summarize the costs and effects of treatments within a given health condition, from multiple sources, to identify the best use of health care resources. This is not a formal method of comparing the value of the interventions but a more qualitative method for comparing the relative cost-effectiveness of interventions. This is particularly true in conditions such as AR, where the quality and comparability of the studies on the economic outcomes of the interventions is variable. However, using the available data can still provide a qualitative comparison of treatment interventions and frequently is the only data available to managed care decision makers.

**Allergic Rhinitis as a Case Study**

### Burden of Disease

Symptoms of AR can be seasonal or perennial and include runny nose, nasal congestion, sneezing, and itching. AR may not appear to be a significant disease category in the health care industry because it is not associated with a high rate of morbidity and mortality, but the prevalence of AR has been estimated to be approximately 20 to 40 million in the U.S. population. These estimates encompass 10% to 30% of adults and 40% of children. AR is also among the top 10 diagnoses for physician office visits and is the fifth most common chronic illness reported in the United States. Direct medical costs (prescriptions and ambulatory care visits) related to the treatment of AR are on the rise ($0.8 billion in 1987, $1.2 billion in 1990, $3.4 billion in 1996, and $4.5 billion in 1997). There are also indirect costs associated with AR, which encompass missed work or school days and costs to employers, including decreases in productivity and work performance. These indirect costs were estimated to range from $2.4 billion to $4.6 billion in 1995. Not surprisingly, AR symptoms are associated with decreased health-related quality of life as well as their effects on patients’ sleeping habits, energy levels, and ability to focus. In addition to its economic burden to the MCO, AR exerts a significant burden on the patient and on society.

Despite the fact that direct costs of AR are not generally associated with hospitalizations, prescriptions and office visits impart a significant burden to the health care payer, and this disease state has received a great deal of attention in recent years by MCOs. When focusing merely on prescription utilization for the 2 most prescribed medications treating AR (antihistamines and intranasal corticosteroids [INSs]), it is clear there has been a sharp increase in expenses incurred by MCOs over the last few years. For example, per-member per-year (PMPY) costs for prescription antihistamines increased from $8.33 in 1997 to $18.98 in 2002, while PMPY costs for INSs increased from $3.59 in 1998 to $5.86 in 2002. In terms of direct sales, prescription medication costs in 1997 were $1.6 billion for antihistamines and $0.8 billion for INSs and by 2000 had increased to more than $3.5 billion for antihistamines and $1.6 billion for INSs.

In addition to the overall cost of this disease, several recent marketplace dynamics have increased the attention on expenditures for AR. Most remarkably, these include the movement of loratadine (Claritin) to over-the-counter status and a new medication class achieving an indication for AR. These recent dynamics have led many MCOs to develop new treatment guidelines for the management of AR. Here, we apply AR to the framework previously outlined and examine the efficient treatment of AR using existing data.

### Allergic Rhinitis Treatment

The components of the cost-effectiveness plane and the cost-efficiency frontier for AR are based on the relative efficacy of AR therapies and their costs. Examination of clinical study reviews, meta-analyses, and current guidelines were used as investigational sources to assess differences in product efficacy among the AR treatment classes. Cost was based on the most recent average wholesale price (AWP) for each product. This analysis focuses on 3 of the most highly prescribed classes of therapy for treating the symptoms of AR: INSs, less-sedating antihistamines (LSAs), and leukotriene receptor antagonists (LTRAs).

The INSs evaluated in this report are the 4 most commonly prescribed and are the leading INSs by market share (in alphabetical order): budesonide aqueous nasal spray (BANS, Rhinocort

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**TABLE 1**

<p>| Average Wholesale Pricing for Allergic Rhinitis Products |</p>
<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult Dosage</th>
<th>Cost/Month ($)</th>
<th>Cost/Day ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>INSs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BANS</td>
<td>1 spray/nostril qd</td>
<td>35.66</td>
<td>1.19</td>
</tr>
<tr>
<td>FPNS</td>
<td>2 spray/nostril qd or 1 spray/nostril bid</td>
<td>68.26</td>
<td>2.28</td>
</tr>
<tr>
<td>MFNS</td>
<td>2 spray/nostril qd</td>
<td>68.73</td>
<td>2.29</td>
</tr>
<tr>
<td>TANS</td>
<td>2 spray/nostril qd</td>
<td>70.31</td>
<td>2.34</td>
</tr>
<tr>
<td>LSAs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cetirizine</td>
<td>5 mg or 10 mg qd</td>
<td>63.29</td>
<td>2.11</td>
</tr>
<tr>
<td>Desloratadine</td>
<td>5 mg qd</td>
<td>72.66</td>
<td>2.42</td>
</tr>
<tr>
<td>Fexofenadine</td>
<td>60 mg bid or 180 mg qd</td>
<td>73.37</td>
<td>2.45</td>
</tr>
<tr>
<td>LTRA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Montelukast</td>
<td>10 mg qd</td>
<td>93.90</td>
<td>3.13</td>
</tr>
</tbody>
</table>

Source: Cost information according to average wholesale price listings from First Data Bank as of October 15, 2003.
The Allergic Rhinitis Efficiency Frontier

![Graph](https://example.com/graph.png)

Differences in effectiveness (overall effectiveness of the products based on clinical studies, reviews, and meta-analysis; not magnitude of differences between products or an empirical value based on assessments of individual symptom scores) and costs (average wholesale price) of intranasal corticosteroids (INSs), less-sedating antihistamines (LSAs), and a leukotriene receptor antagonist are represented on the graph.

Budesonide aqueous nasal spray (BANS) appears to be the most efficient treatment (average wholesale price) of intranasal corticosteroids (INSs), less-sedating antihistamines (LSAs), and a leukotriene receptor antagonist are represented on the graph. Please note, although the effectiveness scale (x-axis) is not based on individual symptoms, Weiner et al. evaluated INSs as the most effective pharmacologic treatment for AR.24

Recent reviews and guidelines have demonstrated similar efficacy among the available INSs in the treatment of AR symptoms. This meta-analysis reviewed randomized controlled clinical trials of INSs versus LSAs and concluded that INSs were more effective than LSAs in relieving the nasal symptoms of AR. In a separate review of controlled clinical studies, Nathan,11 who evaluated the efficacy of LTRAs versus LSAs and versus INSs, found that LTRAs were “sometimes more effective than placebo, were no more effective than LSAs, and were less effective than INSs in the treatment of AR.” Therefore, based on individual research reports, reviews, and meta-analyses, recent guidelines established by the World Health Organization in collaboration with the Allergic Rhinitis and Its Impact on Asthma (ARIA) Workshop have classified INSs as the most effective pharmacologic treatment for AR.24 These guidelines are similar to those published in 1998 by the Joint Task Force on Practice Parameters in Allergy, Asthma, and Immunology that declared that INSs were the most effective medication class for controlling symptoms of AR.

Efficacy results for the INSs, LSAs, and LTRAs can be compared by placing each product on a hypothetical horizontal line separated only by the results of their reviewed efficacy measures. Because montelukast may be as effective as the LSAs in the treatment of AR symptoms, these products would appear at a similar point on the effectiveness line. In contrast, INSs are considered more clinically effective than the LTRAs and LSAs for treating AR symptoms and would therefore be grouped together farther to the right on the hypothetical horizontal effectiveness line.

**Cost**

As stated previously, the AWP for each product was obtained from the First Data Bank (as of October 15, 2003) to differentiate each product by cost per month as well as per day (Table 1). The monthly/daily cost for the INS, dosed at their recommended starting doses is as follows: BANS, $35.66/month or $1.19/day; FPNS, $68.26/month or $2.28/day; MFNS, $68.73/month or $2.29/day; and TANS, $70.31/month or $2.34/day. The monthly/daily cost of the LSAs are: cetirizine, $63.29/month or $2.11/day; desloratadine, $72.66/month or $2.42/day; and fexofenadine, $73.37/month or $2.45/day. Lastly, the monthly/daily cost of the LTRA montelukast is $93.90/month or $3.13/day.

The cost of these AR treatments could be compared by placing each product on a hypothetical vertical line, separated by its corresponding daily cost. The least costly product per day of treatment is BANS, followed by cetirizine, FPNS, TANS, MFNS, desloratadine, and fexofenadine. The most costly product per day of treatment is montelukast, and it would be placed the highest on the hypothetical vertical line.

**Allergic Rhinitis Cost-Efficiency Frontier**

Once the efficacy and cost of the most highly prescribed treatments for AR have been determined, their respective hypothetical line diagrams can be combined graphically to evaluate the 2 components together (Figure 3). The x-axis differentiates efficacy of...
the products while the y-axis separates cost. The 4 leading INSs (as a class) have been shown to be the most effective treatment for AR and are placed to the right on the x-axis and are separated only by their individual costs on the y-axis. The LSAs have been shown to be less effective than INSs and are therefore placed to the left of the INSs on the x-axis (less clinically effective) and are separated only by price. Because the LTRA, montelukast, has been shown to be less efficacious than INSs and no more effective than LSAs, it is also placed on the x-axis in the area of the LSAs (less clinically effective than INSs) and positioned on the y-axis according to its cost relative to the other products. This graphical representation combining the 2 measures of efficacy and cost illustrates the AR efficiency frontier.

Discussion

Health care decision makers are increasingly requiring information on both the clinical and economic outcomes associated with treatments before making reimbursement decisions. Cost-effectiveness analysis provides a tool with which to incorporate both pieces of information when assessing the value of a treatment.

When several competing alternatives exist for the treatment of a condition, it is possible to determine which of those treatments provides for the most efficient use of health care resources. This can be done by plotting the costs and effects of the intervention on a plane and determining which interventions are on the cost-efficiency frontier; this may be particularly useful when there are limited cost-effectiveness analyses comparing treatments in the condition of interest. We use the example of AR treatments to show how concepts can be used to compare, even qualitatively, the available treatments while considering both their effectiveness and costs.

The comparison of AR treatments presented here combines information on both the costs and effectiveness of treatments. As highlighted previously, INSs (e.g., BANS, FPNS, MFNS, TANS) are more effective in the treatment of AR than LSAs (cetirizine, desloratadine, fexofenadine) or the LTRA (montelukast). Additionally, the treatments can also be differentiated by their cost. Among the INSs, the cost per day varies from $1.19 for BANS to $2.34 for TANS. When this information is combined and plotted on a cost-effectiveness plane, BANS appears to represent the most efficient treatment choice for AR.

An important issue to consider is the impact of recent changes in the market dynamics of AR treatments on estimates of the most efficient use of resources. From a societal perspective, the shifting of products from prescription-only to over-the-counter would not impact identification of the most efficient treatments unless there were major changes in the cost of the products following the switch. However, many MCOs are interested in identifying efficient treatments from the perspective of the MCO. Thus, the costs to the MCO are often the only costs included in such an analysis. Consequently, the switch of a product to over-the-counter status could have an important impact on the identification of the most efficient treatment, depending on the perspective of the analysis.

For example, if the comparison is conducted from the managed care perspective and policy changes—including over-the-counter switch, prior authorization, or copayment tier movements—result in no cost per day for an over-the-counter product (i.e., it is not covered), then that product shifts downward on the y-axis of Figure 3 and will lie on the cost-efficiency frontier regardless of effectiveness. This, however, does not consider the potential for additional physician visits due to reduced effectiveness or beneficiary satisfaction, both of which could also influence decision making.

Despite a limitation of our cost-efficiency frontier analysis (qualitative versus quantitative efficacy scale), the application-based example used here is a useful approach to review treatment alternatives within a disease category. The efficacy conclusions and the effectiveness scale presented used qualitative measures, and the placement of products on the x-axis was a reflection of overall effectiveness of the 3 product classes determined from clinical reviews. These measures do not reflect the magnitude of differences between products and was not an empirical assignment dependent on assessments between individual symptom scores. Therefore, although there may be slight differences in individual LSAs,LTRAs, or INSs in treating specific symptoms of AR, the products evaluated received overall effectiveness ratings based on conclusions from reviews and meta-analyses of clinical studies.

This method allows the evaluator the freedom of lateral movement on the x-axis of our cost-efficiency frontier graph between products depending on individual preferences or feelings about a treatment for specific symptoms compared with the other products. If each clinical study used the same standardized efficacy measurement for each analyzed symptom, it would be possible to create a quantifiable effectiveness scale for the purposes described in this review.

Conclusion

Plotting the cost and effectiveness of alternative products on a cost-effectiveness plane provides for a simple graphical representation of the relative value of the products for treatment of a given disease. The simplicity of the present approach using clinical reviews and meta-analyses combined with recent cost data for each product in AR can be easily applied to any disease category in order to provide an MCO decision maker with additional information during the selection process for appropriate treatments. Importantly, one must still consider the data sources and information used in constructing the graph and the limitations of those data sources when making decisions. However, whether these representations are populated with sound quantitative information or based on qualitative comparisons, they provide decision makers with yet another tool when deciding on treatment alternatives.

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REFERENCES