The Economic Impact of Payer Policies after the Rx-to-OTC Switch of Second-Generation Antihistamines*

Patrick W. Sullivan, PhD[1], Michael B. Nichol, PhD[2]

[1]Pharmaceutical Outcomes Research Program, University of Colorado School of Pharmacy, Denver, CO, USA; [2]Department of Pharmaceutical Economics and Policy, University of Southern California School of Pharmacy, Los Angeles, CA, USA

ABSTRACT

Objective: As a result of the over-the-counter (OTC) introduction of loratadine, health plans have been struggling to determine the best policy to incorporate this change within their existing drug benefit structure for second-generation antihistamines (SGA). The objective of this study was to examine the economic impact of payer policies in response to the Rx-to-OTC switch of loratadine.
Study Design: Decision analysis was used to model the budgetary impact and cost-effectiveness of four policies for SGA benefits for the managed care organization (MCO), employer, and Medicaid perspectives separately.
Patients and Methods: Outcomes included direct medical costs and lost productivity (employers only), discounted, quality-adjusted life-years (QALYs) saved because of amelioration of allergic rhinitis symptoms and avoidance of unintentional injuries associated with the use of first-generation antihistamines (FGA). Bayesian probabilistic sensitivity analysis was conducted using second-order Monte Carlo simulation.

Results: Providing limited OTC and second-tier prescription benefits would cost approximately $0.13 and $0.30 compared to third-tier prescription benefits for employers and MCOs, respectively, and would save Medicaid $.02 per member per month (PMPM). Providing limited coverage for OTC loratadine while retaining second-tier prescription benefits for SGA was the optimal policy for a willingness to pay below $26,200 per QALY for all payers.
Conclusions: Offering second-tier prescription and limited OTC benefits provides greater effectiveness and is not significantly more expensive PMPM than discontinuation. Some of the drug savings from limiting coverage of prescription SGA may be attenuated by the cost of lost productivity and direct medical expenditures due to unintentional injuries associated with increased FGA use in addition to the increased cost of therapeutic substitutes.
Keywords: budget impact analysis, cost and cost analysis, histamine H1 antagonists drugs, insurance benefits, Rx-to-OTC switch.

Background

The treatment of allergic rhinitis contributes significantly to the cost of drug benefits. Approximately 40 million Americans suffer from allergic rhinitis and the prevalence is increasing every year [1,2]. Direct expenditures for the treatment of allergic rhinoconjunctivitis are estimated to cost approximately $5.9 billion annually in the United States [3]. When the cost of lost productivity is included (esti-

mated at $4 billion), it becomes one of the most expensive health conditions treated in the United States [4,5]. In 2001, antihistamines were the eighth most expensive drug class in per member per year expenditures and have been the third fastest growing class of medications for managed care organizations (MCOs) [6]. Loratadine alone was the fourth most expensive drug per member per year for commercial health plans in 1999 [7]. Loratadine became available over-the-counter (OTC) in December 2002, and health plans have been struggling to determine the best policy to incorporate this change within their drug benefit structure for second-generation antihistamines (SGA).

A variety of policy responses exist, ranging from complete discontinuation to covering prescription SGA as OTCs. A majority of health plans have initiated policies to encourage use of OTC loratadine

Address correspondence to: Patrick Sullivan, Assistant Professor, School of Pharmacy, Pharmaceutical Outcomes Research Program, University of Colorado Health Sciences Center, 4200 East Ninth Avenue, Box C238, Denver, CO 80262, USA. E-mail: Patrick.Sullivan@UCHSC.edu
*Preliminary results of this analysis were presented at the 9th annual HMO Research Network Conference April 1–2, 2003.

by raising copayments for prescription SGA, fexofenadine, cetirizine, and desloratadine to the third-tier range ($30 to $50) [8,9].

Currently, the majority (53%) of allergic rhinitis patients are treated with first-generation antihistamines (FGA), whereas 29% are treated with SGA and 18% do nothing to treat their symptoms [10]. FGA are associated with an increased risk of unintentional injuries, deaths, and reduced productivity [4,11–19]. In health plans with very restricted drug benefits for SGA, certain price-sensitive members may substitute with FGA [20]. In this case, shifting the cost burden of prescription SGA to consumers may result in increased downstream costs due to sedation-related adverse outcomes for patients switching to FGA.

The budgetary and economic impacts of these deleterious consequences vary with the type of health plan. Limiting or eliminating prescription drug benefits for SGA may result in unintended costs to the employers who fund health plans because of reduced employee productivity, and unintentional injury if employees opt for less expensive FGA. The Medicaid population is relatively poorer and sicker and more sensitive to increases in out-of-pocket spending [21]. Hence, Medicaid's members may be more likely to switch to FGA, resulting in an increase in the cost of providing care due to sedation-related adverse events.

Given the economic pressure and inclination to restrict severely drug coverage for SGA in response to the OTC introduction of loratadine and the potential deleterious effects of FGA, it is important to provide a comprehensive economic analysis of the impact of drug benefit policies to inform decision making.

Methods

Decision Model

Decision analysis was used to model the budgetary impact and cost-effectiveness of four policies of providing prescription and OTC drug benefits for SGA in response to the OTC availability of loratadine (Fig. 1). The analysis was performed separately for three different payer perspectives: Medicaid, an employer providing health insurance for its employees, and a commercial MCO.

The time frame of the intervention was limited to 1 year, but the present value of all lifetime costs and effects attributed to the policy within the intervention year was included in the analysis. All costs are expressed in 2001 US dollars, using 3% as the discount rate. Depending on the perspective, the outcomes assessed included discounted direct and indirect costs and discounted quality-adjusted life-years (QALYs) saved because of amelioration of allergic rhinitis symptoms and avoidance of unintentional injuries.

Policies

Many of the baseline assumptions relative to the general model have been published previously [22]. The previous model examined the cost-effectiveness of making SGA available OTC from a societal perspective, whereas this analysis examines the impact
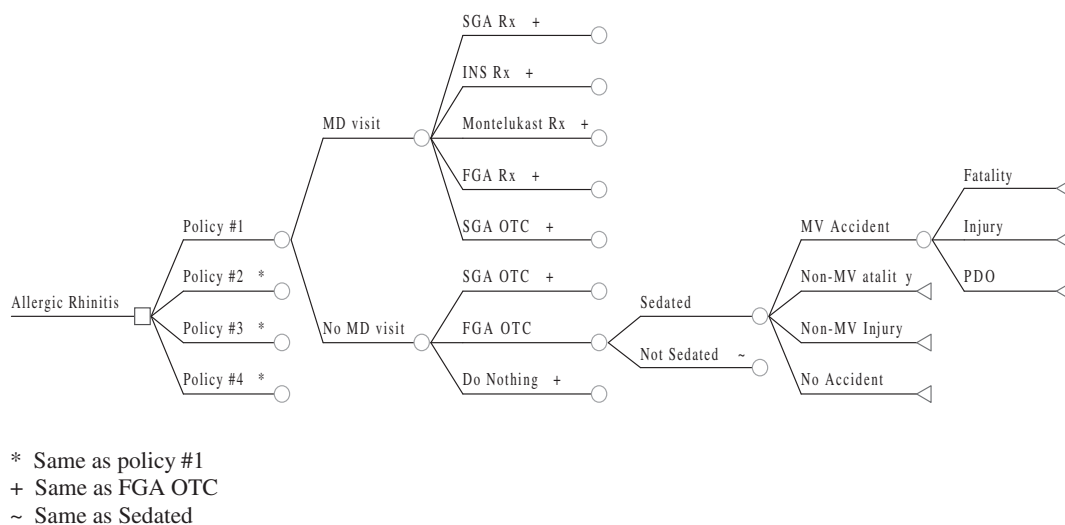

Figure 1 Decision tree of policy options for MCO given OTC availability of SGA (same decision tree for employer and MCO perspectives). FGA, first-generation antihistamines; INS, intranasal corticosteroids; MCO, managed care organization; MD, Medical Doctor; MV, motor-vehicle; OTC, over-the-counter; PDO, property damage only; SGA, second-generation antihistamines.

Table 1 Four potential drug benefit policies in response to OTC loratadine

Policy	Description
Policy 1 (OTC Second-Tier Rx)	Cover OTC loratadine and other prescription SGA at second-tier (OTC loratadine coverage requires physician prescription)
Policy 2 (Second-Tier)	Cover prescription SGA at second-tier, but not OTC loratadine
Policy 3 (Third-Tier)	Cover prescription SGA at third-tier, but not OTC loratadine
Policy 4 (No Rx)	No prescription or OTC coverage of SGA

of different policy responses from the payer perspective. Four potential drug benefit policies were modeled based on the response of health plans to the OTC availability of loratadine (Table 1) [8,9,23]. Policy 1 is to provide coverage for OTC loratadine while retaining second-tier drug benefits for other prescription SGA (OTC Second-Tier Rx). Under this policy, managed care patients need to obtain a physician prescription to qualify for OTC SGA reimbursement and must pay the same second-tier copayment as for prescription SGA. Policy 2 is to retain second-tier drug benefits for prescription SGA but not to provide coverage for OTC loratadine (Second-Tier). Policy 3 is to provide drug coverage for prescription SGA only at the highest third-tier copayment but offer no drug coverage for OTC loratadine (Third-Tier). Policy 4 is to provide no prescription or OTC drug coverage for SGA (No Rx). All policies assume that the payer does not provide coverage for OTC or prescription FGA.

The drug benefit structure and copayments used in the model were based on estimates from the literature. Before the OTC introduction of loratadine, at least one SGA was available through most health plans as a second-tier (preferred brand) product with a copayment of approximately $16 per month supply for commercial MCOs and $1 for Medicaid [6,24,25]. Hence, these are the copayments for policy 1 (OTC Second-Tier Rx) and 2 (Second-Tier). After OTC availability of loratadine, many health plans moved SGA to third-tier status. The commer-cial MCO copayment amount used in the analysis for policy 3 (Third-Tier) was $29, based on national averages for third-tier or nonpreferred brands [6]; the copayment for Medicaid remained $1 for policy 3 (Third-Tier), but benefits for prescription SGA were available by prior authorization only.

Demand Estimates

Demand estimates were projected based on current national utilization rates, market share data, and previous research [4,6,10,22]. Projected member responses to different policies for the Medicaid and commercial managed care populations were based on presumed elasticity of demand for each respective population (Table 2). Empirical evidence suggests that when coinsurance is high (i.e., the member pays a large portion of the cost of drugs), the demand for prescription drugs is lower than when coinsurance is low [26]. The demand for OTC drugs was assumed to be slightly higher than prescription drugs for similar out-of-pocket expense based on two factors: First, empiric evidence demonstrates that the improved access and ease of purchase provided by OTC availability result in a positive impact on demand independent of the change in price [27]; and second, the opportunity cost of obtaining prescription SGA is a deterrent. The opportunity cost of obtaining a prescription for SGA is approximately $55 to $75: $15 copay for the physician visit plus 2 to 3 hours of lost time at $20/hour. Hence, although policy 3 (Third-Tier)

Table 2 Percentage of allergic rhinitis patients receiving treatment by perspective and policy (projected)

Perspective Policy	Medicaid baseline percentage (range)*				Employer/MCO baseline percentage (range)*			
	1	2	3	4	1	2	3	4
MD visit	35 (19–53)	35 (19–53)	32 (30–34)	25 (20–29)	32 (31–33)	32 (31–33)	28 (27–29)	27 (26–28)
SGA Rx	50 (43–57)	82 (74–88)	53 (39–66)	0	50	82	58	0
INS Rx	0	0	05 (03–07)	10 (07–14)	0	0	05 (03–07)	10 (07–14)
Montelukast Rx	0	0	2.5 (02–04)	05 (03–07)	0	0	2.5 (02–04)	05 (03–07)
SGA OTC	32 (31–33)	0	3.3 (00–08)	04 (00–08)	32 (26–38)	0	10.5 (07–14)	61 (52–69)
FGA Rx	18 (09–27)	18 (12–25)	36 (22–50)	81 (79–87)	18 (16–20)	18 (12–26)	24 (10–42)	24 (17–32)
No MD visit	65 (47–81)	65 (47–81)	69 (66–70)	75 (71–80)	68 (67–69)	68 (67–69)	72 (71–73)	73 (72–74)
SGA OTC	20 (18–22)	20 (18–22)	14 (11–17)	14 (11–17)	47 (43–51)	47 (43–51)	47 (43–51)	47 (43–51)
FGA OTC	58 (50–64)	58 (50–65)	64 (63–65)	64 (63–65)	39 (35–43)	39 (35–43)	39 (35–43)	39 (35–43)
Do Nothing	22 (13–32)	22 (13–32)	22 (18–26)	22 (18–26)	14 (10–18)	14 (10–18)	14 (10–18)	14 (10–18)

*The 95% intervals give the credible range of values from the 97.5th and 2.5th percentiles of the 10,000 second-order Monte Carlo simulations.
Policy 1, OTC Second-Tier Rx; policy 2, Second-Tier; policy 3, Third-Tier; policy 4, No Rx.

would result in a similar out-of-pocket expense for OTC loratadine compared to prescription SGA for the non-Medicaid population, it was expected that the demand for OTC SGA would significantly increase. Demand for OTC loratadine was projected to increase for the Medicaid population because of the encumbrance of prior authorization and opportunity cost, but less significantly because of the low copayment for prescription SGA. In addition, because of the opportunity cost, it is likely that fewer patients would visit the physician to obtain treatment under policy 3 (Third-Tier) or 4 (No Rx) compared to policy 1 (OTC Second-Tier Rx) or 2 (Second-Tier) for all payers.

The Medicaid population was assumed to have a more elastic demand curve for SGA than the commercial managed care population based on previous research, demonstrating that patients with lower income reduced their consumption of drugs by approximately 12% for a $3 increase in out-of-pocket spending [21]. In addition, the commercial managed care population was assumed to have a relatively less elastic demand curve based on empiric evidence, showing that a small increase in out-of-pocket spending does not significantly impact drug utilization in this population [28]. The assumptions underpinning the shifts in demand were varied in the sensitivity analysis to incorporate the uncertainty surrounding projected demand levels.

Restrictive insurance policies may encourage patients to seek substitute therapies. In addition to other antihistamines, the most likely substitutes are intranasal corticosteroids (INS) and leukotriene receptor antagonists. We assumed that there would be an absolute increase in the use of INS and montelukast (Table 2) as a direct result of the more restrictive policies as patients seek covered treatment alternatives. Utilization of INS and montelukast before the change in drug benefit policy was considered to be the baseline. Increases in the market share of either were incorporated in the model as absolute increases above this baseline. Hence, the 0% use of INS and montelukast for MCO under policies 1 and 2 in Table 2 represents no change compared to the market share before the policy change and 5% and 10% for MCO under policies 3 and 4 represent an absolute increase of 5% and 10% above the baseline level.

Safety and Efficacy of Treatments

FGA and SGA were considered comparable in terms of safety and efficacy within their respective classes [29–37]. The two classes, when compared against each other, were assumed to be comparable in terms of efficacy but different in the incidence of sedation [29,34,38–41]. Although recent estimates suggest that the incidence of sedation is much higher [42], the model assumed that 17% of individuals taking FGA experienced sedation whereas SGA had no sedative effect (Table 3) [33,34,36–40,43–48]. The use of INS has been shown to have comparable or superior efficacy compared to antihistamines. Nevertheless, it is unclear if this potential difference in efficacy equates to higher utility estimates for INS compared to antihistamines. To date, no head-to-head studies have assessed their differential impact on utility. Hence the current analysis assumes a comparable impact on effectiveness as a result of treatment with INS, antihistamines, and montelukast.

Table 3 Utilization and sedation rates and ranges used in sensitivity analysis

Variables	Baseline value (percent)	Range (percent)*
Antihistamine use, % of year	33	25–42
Rate of sedation, FGA	17	10–25
Rate of sedation, SGA	0	0
Cost MD visit	167	138–196
Number of MD visits per year	3.5	2.7–4.4
Price prescription SGA (loratidine 10 mg #120)	261	184–339
Price FGA (chlorpheniramine 12 mg #240)	33	26–41
Price INS (#4 16 g bottles of 50 μ fluticasone)	216	
Price montelukast (10 mg #120)	288	
Price OTC SGA (loratidine 10 mg #120)	15	9–22
Cost of MV injury/fatality	6172	5228–7113
Cost of MV PDO	31	24–38
Cost of non-MV injury	3136	2357–3926
Lost productivity cost, FGA users	522	324–717
QALY decrement, untreated AR	0.19	0.12–0.27
QALY decrement, MV injury	0.36	0.29–0.43
QALY decrement, non-MV injury	0.52	0.48–0.57
Baseline QALY	22.02	20.02–23.96

*The 95% intervals give the credible range of values from the 97.5th and 2.5th percentiles of the 10,000 second-order Monte Carlo simulations.
Abbreviations: AR, allergic rhinitis; MV, motor-vehicle; PDO, property damage only.

Sedation-Associated Adverse Events

FGA use is associated with a significant increase in the risk of motor-vehicle accidents (2.5- to 40-fold), a 1.5-fold increase in the risk of occupational injuries and a 2.2-fold increase in the risk of all types of unintentional injuries compared to loratadine [11,13,49–52]. Based on this evidence, FGA use was assumed to result in a 4-fold increase in motor-vehicle accidents and a 1.5-fold increase in the risk of non-motor-vehicle unintentional injuries. Rates of unintentional injuries for the general population were based on published estimates of injury in the United States [2,53,54].

Costs

Cost of treatment. Estimates of the amount paid by health plans for prescription drugs were calculated by subtracting a 30% rebate for commercial MCO and a 40% rebate for Medicaid from the retail price [55]. The percent rebate was varied in the sensitivity analysis. The cost of OTC loratadine used in the model was based on the retail price of $15.00 per month [56]. Allergic rhinitis patients in commercial MCOs utilize antihistamines for an average of 4 months per year [57]. The cost of a physician office visit for the Medicaid population was estimated to be $26 based on estimates from the State of California Medicaid program (Medi-Cal) [25]; estimates of the cost of a physician office visit for the commercial managed care population ($167) and the number of visits per year (3.5) were based on national averages [57]. It was assumed that patients required an extra physician visit to switch to INS or montelukast.

Medical expenses due to permanent injury or death resulting from unintentional motor-vehicle, home, or public accidents were included in the analysis, but were limited by the perspective of the payer [58,59]. In the year 2000, approximately 4% of motor-vehicle and 21% of non-motor-vehicle unintentional injuries and fatalities were occupation-related [54]. The medical cost of occupational injuries was typically borne by the worker's compensation insurance provider rather than by the health care insurer and was therefore excluded from the analysis.

Lost productivity. The cost of lost productivity associated with FGA-induced sedation was only included for the employer perspective. Lost productivity was quantified based on previous studies suggesting a 25% reduction in productivity for 2 weeks per year [4]. Using the national wage rate for individuals suffering from allergic rhinitis, the cost of lost productivity was estimated to be approximately $521 for each individual using FGA. We did not include the indirect cost of lost productivity for patients with untreated allergic rhinitis in the model because it was assumed to be incorporated in the utility estimates of allergic rhinitis [60].

Quality-Adjusted Life-years

Although not directly impacting the budget of health plans, the effectiveness of any treatment should be of significant concern. Health plans are willing to pay for more expensive interventions depending on the effectiveness of the intervention subject to the limitations of the payer's budget constraint. In the current analysis, the four policy options were treated as interventions; and effectiveness was measured using QALYs. To determine the discounted QALYs of untreated allergic rhinitis, the annual decrement in utility for allergic rhinitis [61] was subtracted from the age- and gender-adjusted utility of the population without allergic rhinitis [1,62]. Individuals less than 45 years of age were assumed to have a utility score of 1 because these utilities were unavailable in the Beaver Dam Health Outcomes Study. Members with untreated allergic rhinitis were assumed to have the utility of the 25th percentile of individuals suffering from allergic rhinitis whereas those treated with SGA, FGA, INS, or montelukast were assumed to have the utility of the 75th percentile [61]. Similarly, discounted QALYs for unintentional injuries resulting in permanent injury or death were calculated by subtracting the decrement caused by permanent disabling injury from the utility of individuals of similar age and gender for each year of remaining life [22].

Sensitivity analyses. In the absence of empiric data for each of the four policy options, the current model is based on several assumptions and estimates. To examine how these assumptions impact the results of the analysis, a Bayesian probabilistic sensitivity analysis was conducted using a second-order Monte Carlo simulation. This method attempts to make transparent how the uncertainty in the assumptions underlying the model impacts the results by allowing all of the input parameter values to vary simultaneously over their possible ranges. The reported ranges for costs and effects can be interpreted as including the 95% credible range of values similar to confidence intervals based on the input parameter probability distributions [63,64]. Specific probability distributions were chosen to reflect reasonable values for probabilities, incidence rates and odds ratios, costs associated

with health care use, unintentional injuries and lost productivity, market share and utilization rates, utility, and QALYs [63,65]. Probabilities, incidence rates, utilities, and market share were assumed to follow a beta distribution because they are normally distributed but restricted to take on values between 0 and 1. Mean cost was assumed to follow one of two distributions: a gamma distribution, reflecting the long right tail and restriction to positive values or when large enough to ensure positive values, a normal distribution.

Results

Budget Impact

The expected per member per month (PMPM) cost of each policy is listed in Table 4. The more generous benefits are only slightly more expensive than restricted or no-benefit-for-all health plans. The reported results are the PMPM cost of all-allergic-rhinitis-related costs by policy. To put these costs into perspective, the PMPM cost of antihistamines alone for the average health plan was $1.70 in 2001 [6].

Cost-Effectiveness

For all three payers, providing second-tier insurance benefits for OTC and prescription SGA (policy 1: OTC Second-Tier Rx) was a dominant policy (cost less and provided greater or equal effectiveness) compared to retaining prescription benefits but not providing OTC benefits (policy 2: Second-Tier—Table 4). In addition, policy 3 (Third-Tier) was eliminated through extended dominance [66]. The

elimination of policies 2 and 3 through dominance and extended dominance makes policies 1 and 4 the only viable remaining options for all payers under the base case results.

The remaining alternatives for each perspective must be judged by their respective incremental cost-effectiveness ratios subject to the payer's budget constraint. For example, policies 1 and 4 are the only remaining options after eliminating dominated strategies. If an employer is willing to pay $16,468 or less for an intervention providing one additional QALY, policy 1 is the optimal remaining strategy. Likewise, if Medicaid is willing to pay $3946 or less for an intervention providing one additional QALY, policy 1 is the optimal remaining strategy (and $26,226 for MCO). It should be noted that only policy 3 versus 4 for the employer and MCO perspectives exceeds $50,000 per QALY.

Sensitivity Analysis

The base case results are dependent on a series of assumptions and parameter values. Bayesian probabilistic sensitivity analysis allows the input parameters of the model to vary across their feasible ranges and computes the corresponding range of results. These results for the 10,000 Monte Carlo simulations are presented in Tables 2 to 4 as the 95% range of values for market share assumptions, PMPM cost, expected cost, and QALYs of each policy and perspective.

The likelihood that any policy is cost-effective depends on the willingness to pay of the respective payer. The results of the multivariate probabilistic sensitivity analysis can be used to determine this

Table 4 Expected per member per month (PMPM) cost and cost-effectiveness results by policy and payer perspective

Variable	Medicaid (range)*	Employer (range)*	MCO (range)*
Expected PMPM cost policy 1	4.86 (4.09–5.68)	8.45 (7.19–9.74)	6.45 (5.43–7.57)
Expected PMPM cost policy 2	4.99 (4.19–5.85)	8.59 (7.31–9.93)	6.60 (5.56–7.75)
Expected PMPM cost policy 3	4.88 (4.08–5.69)	8.32 (7.04–9.68)	6.15 (5.19–7.18)
Expected PMPM cost policy 4	4.60 (3.83–5.41)	8.17 (6.92–9.47)	6.01 (5.08–7.02)
Expected cost policy 1	411 (346–480)	714 (608–823)	545 (459–640)
Expected cost policy 2	422 (354–494)	726 (618–839)	558 (470–655)
Expected cost policy 3	412 (345–481)	703 (595–818)	520 (439–607)
Expected cost policy 4	389 (324–457)	690 (585–800)	508 (429–593)
Expected QALY policy 1	21.930 (19.94–23.90)	21.957 (19.95–23.89)	21.952 (20.03–23.92)
Expected QALY policy 2	21.930 (19.94–23.90)	21.957 (19.95–23.89)	21.952 (20.03–23.92)
Expected QALY policy 3	21.928 (19.94–23.90)	21.9562 (19.95–23.89)	21.9505 (20.03–23.92)
Expected QALY policy 4	21.924 (19.94–23.90)	21.9559 (19.95–23.89)	21.9502 (20.03–23.92)
ICER policy 1 vs. 2 ($/QALY)	Dominant	Dominant	Dominant
ICER policy 1 vs. 3 ($/QALY)	Dominant	8,850	21,086
ICER policy 1 vs. 4 ($/QALY)	3,946	16,468	26,226
ICER policy 2 vs. 3 ($/QALY)	7,633	21,957	34,299
ICER policy 2 vs. 4 ($/QALY)	6,219	27,757	37,853
ICER policy 3 vs. 4 ($/QALY)	6,183	55,342	52,449

*The 95% intervals give the credible range of values from the 97.5th and 2.5th percentiles of the 10,000 second-order Monte Carlo simulations.
Policy 1, OTC Second-Tier Rx; policy 2, Second-Tier; policy 3, Third-Tier; policy 4, No Rx.
Abbreviation: ICER, incremental cost-effectiveness ratio.

likelihood over the range of possible willingness-to-pay values for each pairwise comparison of policies. Policy 1 (OTC Second-Tier Rx) is cost-effective compared to policy 4 (No Rx) in 95% of all simulations for an employer who is willing to pay $21,000 or less to gain one QALY. Hence, while the base case analysis suggests that an employer could gain one QALY for $16,468 by selecting policy 1 instead of policy 4, the sensitivity analysis results show that the employer can be 95% confident that this would cost less than $21,000 per QALY. The corresponding willingness to pay for MCO and Medicaid is $47,500 and $19,500, respectively.

Comparing each policy head-to-head as above for each payer would result in 18 different comparisons and make interpretation unwieldy. It is possible, however, to simultaneously illustrate the likelihood that each policy is cost-effective compared to all other policies using the net benefit framework [65]. This is conceptually similar to simultaneously comparing all pairwise cost-effectiveness acceptability curves. For each of the 10,000 Monte Carlo simulations, the average net benefits of the four policies were calculated for a given willingness-to-pay value [67]. The average net benefit for any given policy = expected QALYs – expected cost/willingness to pay. Hence the most cost-effective policy for a given willingness to pay would be the policy with the highest net benefit. In contrast, the average cost-effectiveness ratio for any given policy = expected cost/expected QALYs. The average cost-effectiveness ratio has no meaningful interpretation without information about the quadrant of the cost-effectiveness plane to which the cost and effectiveness pair corresponds. Furthermore, the average cost-effectiveness ratio cannot be compared between policies to determine the most cost-effective policy. There is one policy with the greatest average net benefit for each of the Monte Carlo simulation results and a given willingness-to-pay value. The proportion of times a particular policy has the greatest net benefit among the 10,000 simulations can be interpreted as the probability that the given policy is cost-effective for each value of the willingness to pay.

The likelihood that each policy is cost-effective is graphed as a function of the willingness to pay for the employer perspective in Fig. 2. For any given willingness to pay, the proportion of the 10,000 Monte Carlo simulations that result in the greatest net benefit is equivalent to the probability that the policy is cost-effective on the *y*-axis. This is why the percent cost-effective for all policies for any given willingness to pay must add up to 1. It is clear from
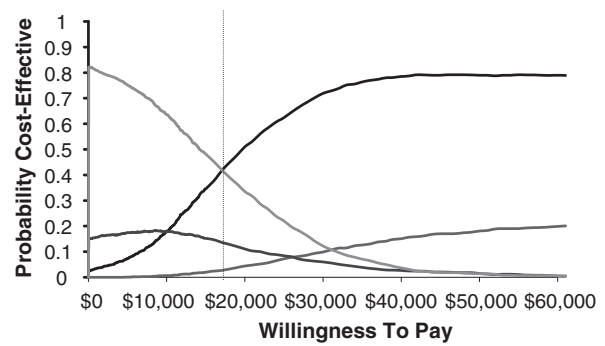

Figure 2 Cost-effectiveness acceptability curves for all policy options: employer perspective. Of the four policy options, No Rx is most likely to be cost-effective for a willingness to pay below $17,000 per QALY while OTC Second-Tier Rx is most likely to be cost-effective above $17,000.

Fig. 2 that No Rx is the most likely to be cost-effective for an employer willing to pay less than $17,000 per QALY whereas OTC Second-Tier Rx is the most likely to be cost-effective for an employer willing to pay more than $17,000. Similarly, Second-Tier is more likely to be cost-effective than No Rx and Third-Tier Rx for willingness to pay more than $31,000 per QALY. For the Medicaid perspective, No Rx is most likely to be cost-effective for a willingness to pay less than $4000 whereas OTC Second-Tier Rx is most likely to be cost-effective for a willingness to pay more than $4000 (and $26,000 for MCO).

Univariate Sensitivity Analysis
Although second-order probabilistic sensitivity analysis provides a thorough assessment of the impact of uncertainty in the input assumptions on the results of the model, univariate sensitivity analysis elucidates the impact of specific variables and provides additional insight into the structure of the model. Because conducting univariate sensitivity analyses for all variables and assumptions is untenable, this analysis has focused on some of the more important input variables such as the odds of motor-vehicle and non-motor-vehicle accident, the cost of lost productivity for employers only, QALY estimates, and changes in demand. The model results do not vary significantly if the odds of motor-vehicle accidents, while sedated, range from 1.0 (no effect) to 8.0 for the MCO perspective (the base case is 4.0): the incremental cost-effectiveness ratio of policy 1 versus policy 4 ranges from $27,360 per QALY (odds 1.0) to 24,671 (odds 8.0). The results are similar for the odds of non-motor-vehicle accident: odds of 1.0 have very little impact on the results, whereas odds of 8.0 make policy 1

significantly more cost-effective (the base case is 1.5). Varying the decrement in QALYs due to allergic rhinitis does not significantly impact the results unless there is no QALY decrement (a 100% reduction from the base case), in which case policy 1 is no longer cost-effective compared to policy 4. Nevertheless, assuming that there is no QALY decrement for motor-vehicle injuries or fatalities has no impact on the model results. From the employer perspective, policy 1 would remain cost-effective compared to policy 4 if the cost of lost productivity was assumed to be $0 ($26,217 per QALY). If the percent of patients who visit the physician under policy 4 is increased to 32% (27% is the base case), policy 1 becomes less cost-effective compared to policy 4 ($46,867 per QALY). In contrast, varying the percent of patients who switched to INS or montelukast due to policy 4 had no impact on the model results.

Comments

Decision analysis was used to model the impact of four policy responses to the Rx-to-OTC switch of loratadine for three different payer perspectives. In addition to the direct medical costs and effectiveness of treatment with antihistamines, the impact of unintentional injuries and lost productivity was included within the confines of the different perspectives.

Based on the assumptions in the model, the results suggest that providing second-tier prescription and limited OTC benefits for all SGA is not significantly more expensive PMPM and in some cases less expensive than limiting SGA benefits to third-tier status. To obtain improved effectiveness for members, policy 1 (OTC Second-Tier Rx) would cost approximately $0.13 and $0.30 PMPM compared to policy 3 (Third-Tier) for employers and MCOs, respectively, and would actually save Medicaid $0.02. Although the PMPM cost of antihistamines for health plans was approximately $1.70 in 2001 (before OTC loratadine), discontinuing coverage altogether does not afford this level of savings. Some of the drug savings from discontinuing coverage of SGA may be attenuated by the cost of direct medical expenditures and lost productivity associated with the increased use of FGA and resultant unintentional injuries in addition to an unanticipated increase in the cost of substitute therapies.

The differential impact of INS, montelukast, and antihistamines on effectiveness was assumed to be approximately comparable. Some studies have suggested that INS offer superior efficacy compared to antihistamines, but how this potential difference in efficacy correlates to improvements in utility is unclear. It is unlikely that the marginal improvement in effectiveness would offset the higher cost of prescription INS. (In particular because the univariate sensitivity analysis showed no impact on the model results from significant changes in the QALY associated with allergic rhinitis and the market share of INS and montelukast). Future studies are needed to address the differential impact of treatment with INS versus antihistamines on the utility of allergic rhinitis patients for use in cost-effectiveness analyses.

The intangible cost of administrative time spent by the health plan was not included. For example, the cost of patient telephone inquiries about benefit changes and the administration of prior authorization were not included. The impact of including these costs would likely make the more restrictive policies (policies 3 and 4) cost more and hence appear less cost-effective compared to policies 1 and 2.

It is important to note that the limited focus of the payer perspective ignores the enormous societal cost of FGA-induced sedation and includes only those costs directly born by the individual payers. In addition, budget impact analysis ignores the impact of policies on the effectiveness of treatment. A formal cost-effectiveness analysis is a more comprehensive measure of the impact of the different policies and provides estimates of how much a given payer would need to pay for specific improvements in effectiveness. For a willingness to pay less than $26,200 per QALY, providing limited coverage for OTC SGA while retaining second-tier prescription benefits for SGA was the best policy option for all payers. Although the majority of health plans seem poised to implement policy option 2 or 3, based on the assumptions in this model the results suggest that these two policy options are not optimal. Results from the sensitivity analysis demonstrate that policies 2 and 3 are the least likely to be cost-effective for all payers. Policy 4, however, is less costly but also less effective. If employers are willing to pay $17,000 or less for an additional QALY ($4,000 and $26,000 for Medicaid and MCO, respectively), policy 1 is the most likely to be cost-effective compared to policy 4. However, if payers are not willing to pay for improved effectiveness in treating allergic rhinitis, policy 4 is the least expensive option.

The SGA have been one of the most expensive drug classes for health plans and OTC availability of loratadine has been viewed as a convenient

opportunity to reduce this cost burden. The results of this analysis show that although there are some savings afforded by shifting the cost burden to the consumer, these savings are largely eroded when a comprehensive analysis includes changes in market share for prescription and OTC treatments for allergic rhinitis, the cost of lost productivity (for employers), and medical costs associated with unintentional injuries. In addition, providing limited OTC coverage while retaining generous second-tier prescription coverage for SGA is the optimal policy compared to limiting or discontinuing prescription benefits: it improves treatment effectiveness at very minimal cost.

Decision analysis is well suited for studies where the analysts are projecting potential impact in the absence of actual data; however, this is also a limitation of the methodology. The model simplified the complexities of the real world to provide an estimate of the potential impact of benefit policies. The projected demand estimates used in the model are obviously not definitive because there are no data available to document demand shift. Although an attempt to incorporate this uncertainty in the sensitivity analysis has been made, the results of this analysis are dependent on the assumptions underpinning the model. Nevertheless, decision makers must choose between different policy options in the absence of certainty regarding potential changes in demand. This study provides preliminary information about the impact of common policy reactions to OTC loratadine to shed light on the possible consequences of such policies. When available, actual estimates of the demand for antihistamines and therapeutic substitutes, both OTC and prescription, should be incorporated to determine more precisely the impact of different policies for different payers.

References

1 Meltzer EO. The prevalence and medical and economic impact of allergic rhinitis in the United States. J Allergy Clin Immunol 1997;99:S805–28.

2 United States Bureau of the Census. Statistical Abstract of the United States, 2000. Washington (DC): US Department of Commerce Economics and Statistics Administration Bureau of the Census, 2001.

3 Ray NF, Baraniuk JN, Thamer M, et al. Direct expenditures for the treatment of allergic rhinoconjunctivitis in 1996, including the contributions of related airway illnesses. J Allergy Clin Immuno 1999;103:401–7.

4 Crystal-Peters J, Crown WH, Goetzel RZ, Schutt DC. The cost of productivity losses associated with allergic rhinitis. Am J Manag Care 2000;6: 373–8.

5 Goetzel RZ, Ozminkowski RJ, Meneades L, et al. Pharmaceuticals—cost or investment? An employer's perspective. J Occup Environ Med 2000;42:338–51.

6 Teitelbaum F, Martinez R, Parker A, et al. 2001 Drug Trend Report. Express Scripts, 2002.

7 Emron. Novartis Pharmacy Benefit Report. Totowa: IMS Health, 2001.

8 Saranow J, Marcus AD. As claritin sells over the counter, prices for competitors climb. The Wall Street Journal Online, 2002. [Internet]. Available from: http://online.wsj.com/article_email/0,SB1039461036674072113,00.html.

9 Gellene D, White RD. WellPoint to favor nonprescription form of claritin. Los Angeles Times, March 9, 2002.

10 Roper Starch. Self-Care in the New Millennium. Consumer Healthcare Products Association. Appendix, p. 43.

11 Finkle WD, Adams JL, Greenland S, Melmon KL. Increased risk of serious injury following an initial prescription for diphenhydramine. Ann Allergy Asthma Immunol 2002;89:244–50.

12 Gaillard AW, Gruisen A, de Jong R. The influence of antihistamines on human performance. Eur J Clin Pharmacol 1988;35:249–53.

13 Gilmore TM, Alexander BH, Mueller BA, Rivara FP. Occupational injuries and medication use. Am J Ind Med 1996;30:234–9.

14 Cockburn IM, Bailit HL, Berndt ER, Finkelstein SN. Loss of work productivity due to illness and medical treatment. J Occup Environ Med 1999; 41:948–53.

15 Adelsberg BR. Sedation and performance issues in the treatment of allergic conditions. Arch Intern Med 1997;157:494–500.

16 Witek TJ, Canestrari DA, Miller RD, et al. Characterization of daytime sleepiness and psychomotor performance following H1 receptor antagonists. Ann Allergy Asthma Immunol 1995;74:419–26.

17 Kay GG, Quig ME. Impact of sedating antihistamines on safety and productivity. Allergy Asthma Proc 2001;22:281–3.

18 Estelle F, Simons R. H1-receptor antagonists: safety issues. Ann Allergy Asthma Immunol 1999;83:481–8.

19 Vuurman EF, van Veggel LM, Uiterwijk MM, et al. Seasonal allergic rhinitis and antihistamine effects on children's learning. Ann Allergy 1993;71:121–6.

20 American Academy of Allergy Asthma and Immunology, American College of Allergy Asthma and Immunology, Joint Council of Allergy Asthma and Immunology. Insurance Coverage for H1-Antihis-

tamines: Implications for Quality Healthcare and Public Safety, 2002.

21 Fairman KA, Motheral BR, Teitelbaum F. Effects of Employee Salary and Chronic Disease on Response to a Drug Copayment Increase. Office of Research and Development, Express Scripts, 2001.

22 Sullivan PW, Follin SL, Nichol MB. Transitioning the second-generation antihistamines to over-the-counter status: a cost-effectiveness analysis. Med Care 2003;41:1382–95.

23 Drug Store News. Third Party Payers Move to Incentivize OTC Claritin Use. [Internet]. [Accessed 2002 Oct 1]. Available from: http://www.drug-storenews.com/otc/index.htm?ID=1787.

24 New York Health Plan Association. Cost of Certain Antihistamines to New York's Insured Population, 2001.

25 Belshe KS, K J, Hiehle G, et al. California's Medical Assistance Program, Annual Statistical Report, Calendar Year 1997. Sacramento: California Department of Health Services, 1998.

26 Leibowitz A, Manning WG, Newhouse JP. The demand for prescription drugs as a function of cost-sharing. Soc Sci Med 1985;21:1063–9.

27 Keeler TE, Hu T, Keith A, et al. The benefits of switching smoking cessation drugs to over-the-counter status. Health Econ 2002;11:389–402.

28 Motheral BR, Henderson R. The effect of a copay increase on pharmaceutical utilization, expenditures, and treatment continuation. Am J Manag Care 1999;5:1383–94.

29 Dykewicz MS, Fineman S, Skoner DP, et al. Diagnosis and management of rhinitis: complete guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology. American Academy of Allergy, Asthma, and Immunology. Ann Allergy Asthma Immunol 1998;81:478–518.

30 Thomas JS, Heurich AE, Ralph JW, et al. Double-blind, controlled study of clemastine fumarate, chlorpheniramine and placebo in patients with seasonal allergic rhinitis. Ann Allergy 1977;38:169–74.

31 Todd G, Hopkins P, Maclay WP. Double-blind trials of clemastine ("Tavegil") in allergic rhinitis. Curr Med Res Opin 1975;3:126–31.

32 Sheriff JM, Wallace MG. A comparative study of clemastine ("Tavegil") and chlorpheniramine maleate in the treatment of hay fever. Curr Med Res Opin 1976;4:245–9.

33 Harvey RP, Comer C, Sanders B, et al. Model for outcomes assessment of antihistamine use for seasonal allergic rhinitis. J Allergy Clin Immunol 1996;97:1233–41.

34 Horak F, Bruttmann G, Pedrali P, et al. A multi-centric study of loratadine, terfenadine and placebo in patients with seasonal allergic rhinitis. Arzneimittelforschung 1988;38:124–8.

35 Del Carpio J, Kabbash L, Turenne Y, et al. Efficacy and safety of loratadine (10 mg once daily), ter-

fenadine (60 mg twice daily), and placebo in the treatment of seasonal allergic rhinitis. J Allergy Clin Immunol 1989;84:741–6.

36 Bruttmann G, Charpin D, Germouty J, et al. Evaluation of the efficacy and safety of loratadine in perennial allergic rhinitis. J Allergy Clin Immunol 1989;83:411–6.

37 Day JH, Briscoe MP, Clark RH, et al. Onset of action and efficacy of terfenadine, astemizole, cetirizine, and loratadine for the relief of symptoms of allergic rhinitis. Ann Allergy Asthma Immunol 1997;79:163–72.

38 Kemp JP, Buckley CE, Gershwin ME, et al. Multicenter, double-blind, placebo-controlled trial of terfenadine in seasonal allergic rhinitis and conjunctivitis. Ann Allergy 1985;54:502–9.

39 Dockhorn RJ, Bergner A, Connell JT, et al. Safety and efficacy of loratadine (Sch-29851): a new non-sedating antihistamine in seasonal allergic rhinitis. Ann Allergy 1987;58:407–11.

40 Lockey RF, Fox RW. Loratadine (SCH 29851) 10 mg OD versus clemastine 1 mg BID in the treatment of perennial allergic rhinitis. Immunol Allergy Pract 1989;11:10–6.

41 Buckley CE, Buchman E, Falliers CJ, et al. Terfenadine treatment of fall hay fever. Ann Allergy 1988;60:123–8.

42 American College of Allergy Asthma and Immunology. Allergy Survey Fact Sheet. RoperASW, 2002.

43 Druce HM, Thoden WR, Mure P, et al. Brompheniramine, loratadine, and placebo in allergic rhinitis: a placebo-controlled comparative clinical trial. J Clin Pharmacol 1998;38:382–9.

44 Alexander M, Small P, Thomson D. Efficacy and tolerability of cetirizine, loratadine and placebo in the treatment of seasonal allergic rhinitis (SAR): a Canadian multicentre study (abstract). J Allergy Clin Immunol 1994;93:163.

45 Brandon ML, Weiner M. Clinical investigation of terfenadine, a non-sedating antihistamine. Ann Allergy 1980;44:71–5.

46 Melillo G, D'Amato G, Zanussi C, et al. A multicentre controlled trial of terfenadine, dexchlorpheniramine, and placebo in allergic rhinitis. Arzneimittelforschung 1982;32:1202–3.

47 Brostoff J, Lockhart JD. Controlled trial of terfenadine and chlorpheniramine maleate in perennial rhinitis. Postgrad Med J 1982;58:422–3.

48 Backhouse CI, Brewster BS, Lockhart JD, et al. Terfenadine in allergic rhinitis. A comparative trial of a new antihistamine versus chlorpheniramine and placebo. Practitioner 1982;226:347–51.

49 Weiler JM, Bloomfield JR, Woodworth GG, et al. Effects of fexofenadine, diphenhydramine, and alcohol on driving performance. A randomized, placebo-controlled trial in the Iowa driving simulator. Ann Intern Med 2000;132:354–63.

50 O'Hanlon JF, Ramaekers JG. Antihistamine effects on actual driving performance in a standard test: a summary of Dutch experience, 1989–94. Allergy 1995;50:234–42.

51 Vinson DC, Mabe N, Leonard LL, et al. Alcohol and injury. A case-crossover study. Arch Fam Med 1995;4:505–11.

52 Simpson H. Polydrug effects and traffic safety. J Alcohol Drugs Driving 1985;1:17–44.

53 National Highway Traffic Safety Administration. Traffic Safety Facts 2000. Washington (DC): US Department of Transportation, 2001.

54 National Safety Council. Injury Facts. Itasca (IL): National Safety Council, 2000.

55 Drugstore.com. [Internet]. [Accessed 2002 Mar 18]. Available from: http://www.drugstore.com.

56 http://www.walgreens.com. [Internet]. [Accessed 2003 May 8]. Available from: http://www.walgreens.com.

57 Managed Care Measures LLC. Respiratory Benchmarks, 2000.

58 National Safety Council. Estimating the Costs of Unintentional Injuries, 2000. Itasca (IL): National Safety Council, 2001.

59 Blincoe L, Seay A, Zaloshnja E, et al. The Economic Impact of Motor Vehicle Crashes, 2000. Washington (DC): National Highway Traffic Safety Administration, US Department of Transportation, 2002.

60 Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. Cost-Effectiveness in Health and Medicine. New York: Oxford University Press, 1996.

61 Gold MR, Franks P, McCoy KI, Fryback DG. Toward consistency in cost-utility analyses: using national measures to create condition-specific values. Med Care 1998;36:778–92.

62 Fryback DG, Dasbach EJ, Klein R, et al. The Beaver Dam Health Outcomes Study: initial catalog of health-state quality factors. Med Decis Making 1993;13:89–102.

63 Fryback DG, Stout NK, Rosenberg MA. An elementary introduction to bayesian computing using WinBUGS. Int J Technol Assess 2001;17:98–113.

64 Briggs AH. Handling uncertainty in cost-effectiveness models. Pharmacoeconomics 2000; 17:479–500.

65 Briggs AH, Goeree R, Blackhouse G, O'Brien BJ. Probabilistic analysis of cost-effectiveness models: choosing between treatment strategies for gastroesophageal reflux disease. Med Decis Making 2002;22:290–308.

66 Cantor SB. Cost-effectiveness analysis, extended dominance, and ethics: a quantitative assessment. Med Decis Making 1994;14:259–65.

67 Stinnett AA, Mullahy J. Net health benefits: a new framework for the analysis of uncertainty in cost-effectiveness analysis. Med Decis Making 1998;18 (2 Suppl.):S68–80.