

The Costs of Nonsedating Antihistamine Therapy for Allergic Rhinitis in Managed Care: An Updated Analysis

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Abstract

Objective: To update a prior study evaluating the use and costs of new-generation antihistamines for the treatment of allergic rhinitis in a managed care population.

Study Design: A retrospective database review of rhinitis-related medical and pharmacy-related claims during a treatment period of 12 months.

Methods: Patients who had been diagnosed as having allergic rhinitis and had at least 1 prescription claim were identified from a database containing patient-level medical and pharmaceutical claims. The treatment patterns for patients meeting study criteria were documented for a 12-month period to describe how nonsedating antihistamines are being used in allergic rhinitis, and to assess the associated costs of various medications. Subanalyses of patients categorized by comorbidity status were also performed.

Results: A total of 105,696 patients were included in this updated analysis, covering calendar year 1999. Nonsedating antihistamines were used by 68% of the sample, with loratadine and fexofenadine being the most commonly prescribed agents. The mean annual rhinitis-specific charge for fexofenadine-treated patients was \$409 (standard deviation [SD] 727), which was significantly lower compared with charges for loratadine-treated patients, \$424 (SD 740), $P = .0144$, or cetirizine-treated patients, \$444 (SD 625), $P < .0001$. This trend was also observed in comparisons of patient subgroups.

Conclusions: Consistent with our prior study, loratadine and cetirizine were generally associated with significantly higher treatment charges than fexofenadine. This result was observed across different stratifications of patients, including those with comorbid respiratory illness, concomitant use of nasal steroids, and asthma and/or sinusitis. These results provide further useful insights into the differential costs associated with the use of nonsedating antihistamines for allergic rhinitis treatment.

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This analysis is an update of a prior study in which the utilization and costs associated with new-generation antihistamines for the treatment of allergic rhinitis in a managed care population were evaluated during calendar years 1997 and 1998.¹ The goal of this updated analysis was to determine whether findings from the prior study continued to persist.

It is important from a societal perspective to assess changes in utilization and cost trends from one calendar year to the next. It has been shown that allergic rhinitis affects 20 million to 40 million people in the United States annually, including 10% to 30% of adults and up to 40% of children, and the costs of treating this disease are substantial.² The estimated cost of allergic rhinitis based on direct and indirect costs was \$2.7 billion in the United States for the year 1995.² More recently, a study assessing the costs of allergic rhinitis based on National Health Interview Survey data estimated the annual at-work productivity losses to be in the range of \$2.4 billion to \$4.6 billion.³

Allergic rhinitis is the fifth most common chronic illness in the United States, affecting 20% of the population.⁴ Furthermore, symptoms of allergic rhinitis, which accounts for 32 million annual visits to a healthcare practitioner, can mimic symp-

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toms of viral upper respiratory tract infections and may be misdiagnosed as such.⁴

As in the prior study, head-to-head comparisons of healthcare resource use and costs for fexofenadine, cetirizine, and loratadine under actual practice conditions during a 1-year observational period were conducted. Herein we have described the use of allergic rhinitis agents and costs associated with allergic rhinitis treatment within multiple treatment cohorts, stratified by comorbidity.

Methods

Database Description. Patient-level clinical and cost data were captured from a retrospective database analysis using a proprietary database developed by PharMetrics (Watertown, MA). PharMetrics' clinical database contains more than 100 million episode-of-care linked medical and pharmaceutical claims, constructed using state-of-the-art database technology. The PharMetrics clinical database contains patient-specific and disease-specific episodes of care, which reflect a longitudinal picture of the resources consumed by continuously enrolled member populations. The database contains patient-level medical and pharmaceutical claims representing more than 16 million managed care lives across the United States.

To create its unique episode-based database, PharMetrics uses Episode Treatment Group (ETG) analytical methodology (Symmetry Health Data Systems, Phoenix, AZ). The ETG "grouping" software allows for the merging of patient-specific diagnostic, procedure, and demographic information generated by medical claims systems with prescription drug claims. Claims are grouped into episodes based on diagnosis, with sophisticated logic to ensure correct matching of drug and medical claims, and to clinically define the appropriate initiation and termination dates of each type of episode. During the current study period (1999), the database comprised approximately 13 million patients.

Patient Identification. Patients who had been diagnosed as having allergic

rhinitis (*International Classification of Diseases, Ninth Revision, Clinical Modification* codes: 477, 477.0, 477.8, 477.9) from January 1, 1999 to December 31, 1999, and who had submitted at least one prescription claim for a nonsedating antihistamine (cetirizine, fexofenadine, or loratadine) during the 12-month period after their initial diagnosis were identified from the database. Patients were grouped according to which nonsedating antihistamine they received, and whether or not they received concomitant intranasal corticosteroids.

For purposes of these analyses, the index claim date was defined as the earliest observed claim date for a nonsedating antihistamine. For each patient, the study period consisted of the 365-day period after the index date. Patients were required to be continuously enrolled in their health plan for the entire study period.

Stratification of Severity. Because the presence of related comorbid conditions might be an important variable in assessing treatment costs, patients were stratified according to the presence of a number of existing related comorbidities. The conditions hypothesized to be related to allergic rhinitis, and thus possibly impacting treatment or medication use, were sinusitis, upper respiratory infection, asthma, bronchitis, conjunctivitis, and otitis media. These conditions were selected after a review of the literature.⁵⁻⁹ Patients were then stratified as follows: risk category 1, 0 related comorbidities; risk category 2, 1 related comorbidity; and risk category 3, more than 1 related comorbidity. In addition to stratifying patients according to risk category, a sub-analysis of treatment charges was also conducted for patients with comorbid sinusitis and/or asthma to determine the impact of those conditions on the overall results.

Study Variables. The primary outcome of interest in this study was rhinitis-specific healthcare resource utilization by patients according to risk category. Other outcomes of interest included the total medical cost and rhinitis-specific treat-

ment charges during the postindex period. Specifically, inpatient, outpatient, ancillary, emergency department, and pharmacy-related charges were calculated. Claims analyses of these parameters allow for a consideration of costs from a payer's perspective.

A number of supporting variables were measured, including patient demographic information (ie, age, sex, region), presence of comorbid conditions (ie, upper respiratory infection, lower respiratory infection, coronary artery disease, congestive heart failure, diabetes, hypertension, depression, sinusitis, and rhinitis), and concomitant use of other rhinitis-related medications such as intranasal corticosteroids.

Analysis. All analyses were performed using SAS, Version 8.1 (SAS Institute, Cary, NC). Descriptive measures included presenting continuous variables as means with standard deviation, whereas categorical variables were presented as number and percentage of patients.

Because the cost data were not normally distributed, mean costs were modeled using the SAS Proc Genmod procedure assuming a gamma distribution. Because the gamma distribution is undefined for values of 0, an offset of 0.000001 was added to each value to prevent the exclusion of the zero values from the analyses. Pairwise comparisons of interest were made using contrast statements under Proc Genmod.

Results

A total of 105,696 patients were eligible for the study and included in the analysis. Demographic information of all eligible patients based on comorbidity status is provided in **Table 1**. The mean age of the overall sample was 36 years; 38.2% were men. Approximately 56% of patients were from the Southeast United States and 18% were from the Northeast. Approximately 35% of patients were initially diagnosed as having allergic rhinitis by their general practitioner whereas 22% were diagnosed by an allergist.

Two treatment regimens were of interest: nonsedating antihistamines used either

with or without concomitant intranasal corticosteroids. Nasal steroids used without an antihistamine were also included as a treatment cohort for comparative purposes. As shown in **Table 2**, more than 66% of all patients included in the analysis had used one of the regimens of interest. The most common regimen was monotherapy antihistamine—more specifically, monotherapy loratadine was the single most common treatment regimen (used by nearly 15% of all study patients). The second most common regimen also

Table 1. Patient Demographics by Risk Category

Characteristic	Risk Category 1	Risk Category 2	Risk Category 3	Total
Number of patients*	37,450	36,612	31,634	105,696
Male sex (%)	39.7	37.6	37.1	38.2
Mean age, years (SD)	40.9 (18)	36.7 (19)	30.5 (20)	36.3 (19)
Age category (%)				
< 12	8.3	14.1	27.5	16.1
13-18	8.2	10.1	11.0	9.7
19-45	40.6	40.6	34.3	38.7
46-65	34.1	29.1	23.0	29.0
> 65	8.8	6.1	4.2	6.5
Geographic region (%)				
Midwest	14.1	16.1	18.9	16.2
Northeast	13.9	17.7	22.4	17.8
Southeast	63.9	56.9	46.5	56.3
West	8.1	9.3	12.2	9.7
Specialty of diagnostician (%)				
Allergy	20.6	22.4	24.0	22.3
Dermatology	0.03	0.00	0.00	0.01
Ear, nose, throat	9.6	9.3	6.9	8.7
General/family practice	37.3	35.9	32.3	35.3
Internal medicine	18.5	15.1	12.4	15.5
Pediatrics	7.6	10.7	16.9	11.5
Pulmonary	0.6	0.8	0.9	0.8

Risk categories were created based on the presence of comorbid asthma, bronchitis, conjunctivitis, otitis media, sinusitis, and upper respiratory tract infection. Risk category 1, 0 related comorbidities; risk category 2, 1 related comorbidity; risk category 3, more than 1 related comorbidity.

*Patients identified from the database as having allergic rhinitis.

SD = standard deviation.

included loratadine in combination with a nasal steroid, used by about 16% of all patients. Although monotherapy antihistamines were the most common regimen overall, the use of combination therapy rose with increasing risk category—in risk category 1, 26% of patients received combination antihistamine/nasal steroid therapy, compared with 33% in risk category 3.

Table 3 provides an overview of the most commonly observed comorbid conditions according to patients' risk category. As expected, the rate of comorbid conditions increased in prevalence by risk category—upper respiratory infection increased from 28% of patients in risk category 2 to 64% of patients in risk category 3. Similarly, sinusitis increased from 36% to 65%, asthma increased from 16% to

42%, and otitis media increased from 5% to 24% in these cohorts. Conditions not included in the disease model, however, also increased in prevalence over the comorbidity strata: depression was present in 6% of patients in risk category 1 and in nearly 9% of patients in risk category 3.

As shown in Table 4, rhinitis-specific treatment charges grew with increasing risk category, from \$454 for patients with no comorbidities to \$651 for patients with 2 or more comorbid conditions. As these are rhinitis-specific charges, this result suggests that the presence of other respiratory conditions may lead to increases in rhinitis treatment charges. Specifically, inpatient charges increased from \$10.39 (SD 350) per patient in patients with no comorbidities to \$16.77 per patient

Table 2. Treatment Cohorts by Risk Category

Treatment	Risk Category 1 (n = 37,450)*	Risk Category 2 (n = 36,612)*	Risk Category 3 (n = 31,634)*	Total (N = 105,696)*
No antihistamine/nasal steroid therapy	12,069 (32.2)	12,481 (34.1)	11,047 (34.9)	35,597 (33.7)
Monotherapy				
Fexofenadine	2768 (7.4)	2204 (6.0)	1422 (4.5)	6394 (6.0)
Loratadine	6484 (17.3)	5125 (14.0)	3843 (12.1)	15,452 (14.6)
Cetirizine	1524 (4.1)	1451 (4.0)	1422 (4.5)	4397 (4.2)
Nasal steroids	4732 (12.6)	4365 (11.9)	3592 (11.4)	12,689 (12.0)
Total	15,508 (41.4)	13,145 (35.9)	10,279 (32.5)	38,932 (36.8)
Combination therapy				
Fexofenadine + nasal steroids	2944 (7.9)	3205 (8.8)	2860 (9.0)	9009 (8.5)
Loratadine + nasal steroids	5451 (14.6)	6063 (16.6)	5564 (17.6)	17,078 (16.2)
Cetirizine + nasal steroids	1478 (3.9)	1718 (4.7)	1884 (6.0)	5080 (4.8)
Total	9873 (26.4)	10,986 (30.0)	10,308 (32.6)	31,167 (29.5)

Values presented as n (%). Risk categories were created based on the presence of comorbid asthma, bronchitis, conjunctivitis, otitis media, sinusitis, and upper respiratory tract infection. Risk category 1, 0 related comorbidities; risk category 2, 1 related comorbidity; risk category 3, more than 1 related comorbidity.

*Patients identified from the database as having allergic rhinitis.

Table 3. Comorbid Conditions by Risk Category

Comorbid Condition (%)	Risk Category 1 (n = 37,450)*	Risk Category 2 (n = 36,612)*	Risk Category 3 (n = 31,634)*	Total (N = 105,696)*
Upper respiratory infection	0.0	27.9	64.5	29.0
Lower respiratory infection	2.4	4.0	8.2	4.7
Coronary artery disease	0.5	0.4	0.4	0.4
Congestive heart failure	0.8	0.8	0.9	0.8
Diabetes	4.7	4.2	4.2	4.3
Hypertension	15.7	14.0	12.6	14.2
Depression	6.2	7.4	8.8	7.4
Sinusitis	0.0	36.4	64.8	32.0
Asthma	0.0	16.3	42.5	18.4
Emphysema	0.2	0.3	0.5	0.3
Chronic obstructive pulmonary disease	1.1	4.8	16.3	6.9
Bronchitis	0.0	11.2	38.2	15.3
Conjunctivitis	0.0	3.4	10.1	4.2
Otitis media	0.0	4.9	24.0	8.9

Risk categories were created based on the presence of comorbid asthma, bronchitis, conjunctivitis, otitis media, sinusitis, and upper respiratory tract infection. Risk category 1, 0 related comorbidities; risk category 2, 1 related comorbidity; risk category 3, more than 1 related comorbidity.

*Patients identified from the database as having allergic rhinitis.

Table 4. Mean Rhinitis-Specific Treatment Charges by Risk Category

Department	Risk Category 1 (n = 37,450)*	Risk Category 2 (n = 36,612)*	Risk Category 3 (n = 31,634)*	Total (N = 105,696)*
Inpatient	\$10.39 (350)	\$17.36 (692)	\$16.77 (314)	\$14.71 (489)
Outpatient	\$299.22 (496)	\$364.58 (577)	\$422.77 (645)	\$358.84 (574)
Ancillary	\$4.46 (49)	\$5.26 (49)	\$6.82 (74)	\$5.44 (58)
Emergency department	\$0.19 (5)	\$0.29 (6)	\$0.44 (9)	\$0.30 (7)
Pharmacy	\$140.08 (206)	\$175.01 (237)	\$204.04 (260)	\$171.32 (235)
Total	\$454.33 (682)	\$562.50 (967)	\$650.84 (818)	\$550.61 (834)

Charges given in mean US dollars (SD). Risk categories were created based on the presence of comorbid asthma, bronchitis, conjunctivitis, otitis media, sinusitis, and upper respiratory tract infection. Risk category 1, 0 related comorbidities; risk category 2, 1 related comorbidity; risk category 3, more than 1 related comorbidity.

*Patients identified from the database as having allergic rhinitis.

SD = standard deviation.

(SD 314) in patients with 2 or more comorbidities; outpatient charges increased from \$299.22 (SD 496) to \$422.77 (SD 645); and pharmacy-related charges increased from \$140.08 (SD 206) to \$204.04 (SD 260), respectively.

Table 5 provides comparisons of rhinitis-related treatment charges among the 3 nonsedating antihistamines, stratified by risk category. Loratadine, the most commonly used drug, tended to be associated with the highest treatment charges. Loratadine monotherapy averaged \$424 (SD 740) per patient in rhinitis-specific treatment charges, which was significantly higher than the mean amount charged per patient in the fexofenadine monotherapy cohort (\$409, SD 727, $P = .0144$). Similar trends were observed when the data were examined according to risk cat-

egory, although the comparison was statistically significant only for risk category 1, and for patients also using nasal steroids, suggesting the strength of these findings—patients treated with fexofenadine generally had lower treatment charges than patients receiving loratadine.

Similar results were observed when comparing the fexofenadine to the cetirizine cohorts. Mean rhinitis-specific treatment charges were significantly higher in the cetirizine monotherapy cohort (\$444, SD 625, $P < .0001$) compared with those in the fexofenadine monotherapy group. Patients treated with cetirizine plus a nasal steroid also had significantly higher treatment charges, overall and for risk categories 1 and 2, than patients treated with fexofenadine plus a nasal steroid.

Table 5. Comparison of Mean Rhinitis-Specific Charges Across Treatment Cohort Stratified by Risk Category

Treatment	Risk Category 1	Risk Category 2	Risk Category 3	Total
Monotherapy				
Fexofenadine	\$332.18* (427)	\$439.16 (1027)	\$512.12 (603)	\$409.08 ^{†‡} (727)
Loratadine	\$363.82 (529)	\$446.52 (1019)	\$495.06 (577)	\$423.89 (740)
Cetirizine	\$399.34 (527)	\$461.33 (591)	\$475.12 (741)	\$444.30 (625)
Nasal steroids	\$341.72 (528)	\$441.28 (654)	\$507.60 (665)	\$422.93 (617)
Combination therapy				
Fexofenadine + nasal steroids	\$549.60 [§] (641)	\$687.99 [¶] (700)	\$808.92 (789)	\$681.15 ^{§*} (719)
Loratadine + nasal steroids	\$608.88 (723)	\$749.02 (1541)	\$842.83 (826)	\$734.85 (1114)
Cetirizine + nasal steroids	\$621.27 (674)	\$757.57 (742)	\$832.98 (1016)	\$745.88 (842)

Charges given in mean US dollars (SD). Risk categories were created based on the presence of comorbid asthma, bronchitis, conjunctivitis, otitis media, sinusitis, and upper respiratory tract infection. Risk category 1, 0 related comorbidities; risk category 2, 1 related comorbidity; risk category 3, more than 1 related comorbidity.

Test for significance comparing treatment cohorts (monotherapy or combination) within risk category (eg, fexofenadine monotherapy versus loratadine monotherapy in risk category 1).

* $P < .0001$, fexofenadine versus loratadine and fexofenadine versus cetirizine.

† $P = .0144$, fexofenadine versus loratadine.

‡ $P < .0001$, fexofenadine versus cetirizine.

§ $P < .0001$, fexofenadine + nasal steroid versus loratadine + nasal steroid.

|| $P = .0001$, fexofenadine + nasal steroid versus cetirizine + nasal steroid.

¶ $P = .0008$, fexofenadine + nasal steroid versus cetirizine + nasal steroid.

* $P < .0001$, fexofenadine + nasal steroid versus cetirizine + nasal steroid.

SD = standard deviation.

Further analysis of departmental charges indicated that the primary difference between the fexofenadine and loratadine cohort existed in pharmacy-related charges: fexofenadine patients had lower pharmacy-related charges than loratadine patients (fexofenadine monotherapy = \$160; loratadine monotherapy = \$199). The primary differences between the fexofenadine and cetirizine cohorts were in outpatient (fexofenadine monotherapy = \$229; cetirizine monotherapy = \$259) and pharmacy-related (cetirizine monotherapy = \$177) charges.

Table 6 presents drug cohort comparisons by asthma and sinusitis status. Fexofenadine, either as monotherapy or in combination with nasal steroids, was associated with significantly lower treatment charges than cetirizine in patients with comorbid sinusitis. Among these patients receiving fexofenadine, mean costs were \$492 (SD 592), compared with mean costs of \$541 (SD 806) for cetirizine patients, $P < .0041$. In this same population

of patients, those receiving fexofenadine plus a nasal steroid incurred treatment charges of \$798 (SD 769), whereas patients receiving cetirizine plus a nasal steroid had treatment charges of \$878 (SD 1025), $P < .0001$.

In contrast to the comparisons between fexofenadine and cetirizine, fexofenadine consistently had lower treatment charges than loratadine, regardless of comorbidity status or whether it was used as monotherapy or in combination with nasal steroids, with the exception of patients with both comorbid asthma and sinusitis using fexofenadine or loratadine as monotherapy. Statistically significantly lower treatment costs were observed in the comparison of fexofenadine plus nasal steroid with loratadine plus nasal steroid cohorts among patients with comorbid asthma ($P = .0022$) or among patients with comorbid sinusitis ($P = .0022$).

Finally, **Table 7** presents a comparison of specific antibiotic usage by treatment

Table 6. Comparison of Mean Rhinitis-Specific Charges Across Treatment Cohort—Impact of Comorbid Asthma or Sinusitis

Treatment	Rhinitis + Asthma	Rhinitis + Sinusitis	Rhinitis + Asthma + Sinusitis
Monotherapy			
Fexofenadine	\$619.06* (653)	\$492.22* (592)	\$680.51* (666)
Loratadine	\$633.02 (721)	\$506.47 (551)	\$668.88 (617)
Cetirizine	\$622.70 (628)	\$540.75 (806)	\$675.93 (621)
Nasal steroids	\$601.65 (764)	\$498.30 (638)	\$666.55 (729)
Combination therapy			
Fexofenadine + nasal steroids	\$907.10** (878)	\$798.04** (769)	\$1022.98§ (961)
Loratadine + nasal steroids	\$983.15 (1963)	\$844.12 (849)	\$1050.46 (940)
Cetirizine + nasal steroids	\$967.20 (1174)	\$878.19 (1025)	\$1110.63 (1521)

Charges given in mean US dollars (SD).

Test for significance comparing treatment cohorts (monotherapy or combination) within risk category (eg, fexofenadine monotherapy vs loratadine monotherapy in risk category 1).

* $P < .0041$, fexofenadine versus cetirizine.

† $P = .0022$, fexofenadine + nasal steroid versus loratadine + nasal steroid.

‡ $P < .0001$, fexofenadine + nasal steroid versus cetirizine + nasal steroid.

§ $P < .0001$, fexofenadine + nasal steroid versus cetirizine + nasal steroid.

SD = standard deviation.

cohort. The specific antibiotics of interest included azithromycin, clarithromycin, levofloxacin, and other fluoroquinolones. Azithromycin was the most prescribed antibiotic across all of the treatment cohorts. In comparing use of these antibiotics by treatment cohort, no differences in antibiotic usage were observed for fexofenadine versus loratadine, either as monotherapy or in association with a nasal steroid. However, when comparing fexofenadine with cetirizine, significantly lower use of azithromycin was observed with the monotherapy cohorts, 20.66% versus 24.27%, respectively, $P = .03504$, and when used in conjunction with nasal steroids, 24.31% versus 29.33%, respectively, $P = .00069$. In addition, when examining by overall unique patient use of antibiotics, a significantly lower percentage of fexofenadine plus nasal steroid patients required specific antibiotic treatment compared with patients taking cetirizine plus nasal steroid, 40.66% versus 45.12%, respectively, $P = .0007$.

Discussion

The primary objectives of this updated analysis were to examine the utilization and costs associated with loratadine, fexofenadine, and cetirizine rhinitis treatment and to provide support for the findings from the prior study. Consistent with the original analysis, this updated analysis indicated that fexofenadine was associated with statistically significantly lower mean annual treatment charges compared with loratadine or cetirizine. These results were consistent whether these agents were used as monotherapy or in combination with nasal steroids and across varying comorbidity strata. This consistency in relative results lends further credence to the validity of the observed findings.

However, it should be noted that although changes in the relative results did not differ between this analysis and the original analysis, there were differences in the absolute data. These differences are likely in part a result of

Table 7. Comparison of Use of Specific Antibiotics by Treatment Cohort

	Fexofenadine + Nasal Steroids	Fexofenadine	Loratadine + Nasal Steroids	Loratadine	Cetirizine + Nasal Steroids	Cetirizine	Nasal Steroids Only
Total number of patients	9009	6394	17,078	15,452	5080	4397	12,689
Number (%) of unique patients requiring treatment with one of the antibiotics of interest	3663 (40.66)*	2122 (33.19)	7077 (41.44)	5069 (32.80)	2292 (45.12)	1592 (36.21)	4562 (35.95)
Clarithromycin, n (%)	1021 (11.33)	489 (7.65)	1912 (11.20)	1151 (7.45)	632 (12.44)	350 (7.96)	1133 (8.93)
Levofloxacin, n (%)	569 (6.32)	242 (3.78)	974 (5.70)	542 (3.51)	321 (6.32)	172 (3.91)	621 (4.89)
Azithromycin, n (%)	2190 (24.31) [†]	1321 (20.66) [‡]	4433 (25.96)	3243 (20.99)	1490 (29.33)	1067 (24.27)	2683 (21.14)
Other fluoroquinolones, n (%)	1028 (11.41)	596 (9.32)	1761 (10.31)	1220 (7.90)	560 (11.02)	354 (8.05)	1271 (10.02)

* $P = .0007$, fexofenadine + nasal steroid versus cetirizine + nasal steroid.

[†] $P = .00069$, fexofenadine + nasal steroid versus cetirizine + nasal steroid.

[‡] $P = .03504$, fexofenadine versus cetirizine.

variations in the patient populations of the original and updated analyses.

The mean age of patients in this updated analysis was 36.3 years, whereas in the original analysis, the mean age was 33.99 years. In addition, the geographic distribution of patients in the updated analysis was primarily in the Southeast and Northeast United States (56.3% and 17.8%, respectively). In contrast, most patients in the original analysis were from the Southeast and Midwest (52.5% and 27.7%, respectively). The number of patients taking no antihistamine or nasal steroid therapies was much higher in the updated analysis, compared with the first analysis, 33.7% versus 9.3%, respectively. Finally, the incidence of comorbidities in the patient populations for the 2 analyses also differed. Fewer patients in the updated analysis had upper respiratory tract infection (29.0% versus 32.2%, respectively) or otitis media (8.9% versus 11.5%, respectively) comorbidities, compared with the first analysis, whereas more patients in the updated analysis had lower respiratory tract infections (4.7% versus 3.3%, respectively), conjunctivitis (4.2% versus 0.4%, respectively), and bronchitis (15.3% versus 0.7%, respectively). It is possible that these patient population differences are related to inherent differences in the 1999 (updated analysis) allergy season, compared with the 1997 to 1998 (original analysis) allergy seasons, for example, variations in daily pollen counts, duration of allergy season, and timing of rainfall affecting daily pollen count.

The mean annual per-patient rhinitis-related total treatment charge in this updated analysis was \$551, which was 18% higher than the mean per-patient treatment charge in the original analysis. Similarly, mean annual treatment charges (overall) by drug cohort and by drug cohort and comorbid asthma or sinusitis in this updated analysis was also higher compared with the first analysis, ranging from 13% to 32% higher and 7% to 27% higher, respectively. It is possible that the differences in the patient population between the 2 analyses as described above contributed to these observed variations

in mean treatment charges, as well as higher medical and prescription charges in 1999 compared with 1997 to 1998.

The findings of this study are of importance to clinicians, healthcare providers, and public and private health insurers. The results are applicable to real-world practice, because the perspective adapted for the purpose of the analysis was of a third-party payer, thus including only the direct costs of allergic rhinitis treatment.

Limitations of this study must be recognized. The study compared 3 treatments within the 12-month period after the initial prescription. Therefore, the observed differences in resource utilization cannot be easily generalizable beyond the 12 months after the initiation of therapy. Also, data on prior history of rhinitis and related utilization and cost were not available for all patients, hence it was not possible to determine how the treatment groups may have differed in these respects. Finally, the administrative data used for the analysis were claims data from a managed care population, and thus, the findings may not be extractable to other populations or settings.

Patients were classified according to initial assignment regardless of subsequent switches or augmentations. This intent-to-treat design focused on all consequences of initial treatment selection; switches or augmentations were regarded as common and important consequences of initial treatment selection.

These data focused specifically on demographic and economic parameters associated with the use of these agents in a population of patients diagnosed as having allergic rhinitis. Clinical outcomes associated with use of any particular agent were not considered. Thus, these results should be interpreted relative to existing available data regarding the safety and efficacy of these agents in the treatment of allergic rhinitis.

Conclusion

This updated analysis represents a follow-up to one of the first head-to-head comparisons of nonsedating antihistamines with respect to the impact on direct

medical costs of treating allergic rhinitis. In this analysis, loratadine, which was the most commonly used agent by the patients studied, was associated with significantly higher treatment charges than fexofenadine, the second most commonly used agent, across different stratifications of patients, including quantification of comorbid respiratory illness, concomitant use of nasal steroids, and presence of asthma and/or sinusitis. Similar observations were noted when comparing cetirizine with fexofenadine. These results were also observed in the original analysis, suggesting the strength of these findings.

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