

Assessment of Intranasal Corticosteroid Use in Allergic Rhinitis: Benefits, Costs, and Patient Preferences

Leon Dupclay, Jr, PharmD, PhD; Joseph Doyle, RPh, MBA

Abstract

Current medical guidelines for allergic rhinitis, a highly prevalent disorder, recommend an intranasal corticosteroid as a safe and effective pharmacotherapeutic option. The 6 intranasal corticosteroids available in the United States have approximately equivalent efficacy, although their formulations differ and patients express preferences for specific products. While they are all generally safe at recommended doses, patient preference may increase willingness to adhere to a treatment regimen, a major goal when long-term therapy is required. Another important factor involves the direct costs of treatment associated with each intranasal corticosteroid. This review presents comparative economic data from a retrospective study using a large managed care database as well as data from controlled clinical studies comparing patient preferences for specific attributes of 4 intranasal corticosteroids. When possible, comparative data from clinical trials that assess patient preference, potential treatment adherence, and costs, as well as their interrelationships, should be considered when evaluating intranasal corticosteroid use in the managed care setting.

(Am J Manag Care 2002;8:S335-S340)

In today's cost-conscious healthcare environment, physicians and clinical pharmacists, especially those working in managed care, must weigh economic evidence as well as clinical evidence when making therapeutic choices for their patients.¹ Allergic rhinitis (AR) is the most common atopic disorder in the United States.² Economic estimates of the burden of illness to the patient, the patient's family, and society are significant in terms of healthcare costs, lost productivity, and

impaired quality of life.³ Direct expenditures for AR treatment are in the billions of dollars, and indirect costs associated with the disease are even higher.⁴ Clearly, AR and its cost-effective management are of considerable importance to patients, healthcare providers, and managed care organizations.

The primary and least expensive treatment for AR is allergen avoidance. However, it is often impractical or impossible to achieve due to unavoidable environmental factors. When pharmacotherapy is indicated, treatment is directed at the inflammatory processes underlying the disease. Intranasal corticosteroids are the gold standard of therapy for symptoms of AR.³ These anti-inflammatory medications have prolonged local action, few side effects, and few, if any, systemic effects. In addition, they effectively relieve symptoms of allergic and nonallergic rhinitis. Currently, 6 intranasal corticosteroids are available in the United States. Although the 6 medications have not been directly compared in a single trial, results from several comparison trials suggest that all of the intranasal corticosteroids have approximately equivalent efficacy.⁵ When used at recommended doses, they are generally safe; however, differences among drugs with respect to adrenal effects have been reported.⁶ What may differentiate intranasal corticosteroid sprays are their relative cost-effectiveness and the sensory attributes (eg, odor, taste) of their formulations. Patients express preferences when given a chance to compare characteristics of their nasal sprays.⁷ The importance of patient satis-

fection with treatment should not be underestimated; to be effective, an intranasal corticosteroid must be used regularly, and lack of adherence to the therapeutic regimen can thwart even the best management efforts.

This paper reviews the costs associated with AR, the utility of intranasal corticosteroids for AR treatment, and comparative economic and patient preference data from controlled clinical studies.

...ECONOMIC IMPACT OF ALLERGIC RHINITIS...

The economic repercussions of AR are likely to be underestimated because the majority of people with AR symptoms diagnose and treat themselves. More than 85% of patients with AR reportedly do not seek medical attention for their condition.⁴ Direct medical expenditures for those who do seek treatment include the costs of office visits, emergency department visits, hospitalization, and drug therapy.^{8,9} A cost-of-illness study conducted

by Malone et al showed that in 1996, 23.7 million cases of AR were reported in the United States and the overall direct costs of treatment exceeded \$3 billion.⁴

Patient self-care is not without cost; indeed, the indirect costs to patients and the healthcare system associated with untreated or inadequately treated AR may exceed the direct costs of treatment.¹⁰⁻¹² The indirect costs of AR may include days missed from work or school; costs to employers and society associated with decreases or losses in productivity and performance; and decrements in health-related quality of life, including a diminished capacity for activities of daily living. Not only do persistent rhinitis symptoms interfere with productivity at work and school, but self-medicating with sedating over-the-counter medications can lead to further performance impairment.^{8,10,13,14} In 1998, absenteeism and reduced productivity because of allergies cost US companies more than \$250 million.^{15,16}

The most significant source of indirect costs is the expense of treating comorbidities triggered or exacerbated by AR.¹⁷⁻²⁰ People with allergic rhinitis have a 3-fold increased risk of asthma compared with healthy individuals.²¹ The costs of treating potential complications of AR, including asthma, sinusitis, and otitis media, were approximately \$4 billion in 1996.⁴ A summary of the clinical and economic impact of AR is provided in the **Table**.^{4,12,15,16,22,23}

Not surprisingly, indirect costs are lowest when AR is adequately treated and highest when the disease is inadequately treated. Thus, the effectiveness of patient care strongly influences the economic burden of AR.

...CLINICAL FINDINGS IN ALLERGIC RHINITIS...

AR may be seasonal, caused by allergens released from grass, tree, or weed pollens; or perennial, caused by animal dander, dust mites, or molds. Airborne allergens are the primary trigger for the allergic response. Many of them cannot be avoided. The allergic response is charac-

Table. Clinical and Economic Impact of Allergic Rhinitis

<p>Clinical Impact</p> <ul style="list-style-type: none"> ■ In 1996, 23.7 million cases of allergic rhinitis were reported in the United States, with 15.9 million of these cases occurring in patients younger than 45 years of age.²² ■ The number of reported cases of allergic rhinitis represents only approximately 13% of the total number of existing cases.⁴ <p>Direct and Indirect Costs</p> <ul style="list-style-type: none"> ■ In 1996, the overall direct costs of treating allergic rhinitis exceeded \$3 billion; an additional \$4 billion was spent to treat related comorbidities triggered or exacerbated by the disease.¹² ■ In 1997, allergic rhinitis was the reason for more than 7.8 million office visits to primary care physicians.^{22,23} ■ In 1997, more than 40 million office visits were made to primary care physicians for related comorbidities of allergic rhinitis (asthma, sinusitis, and suppurative otitis media).²³ ■ In 1998, increased absenteeism and reduced productivity because of allergies cost US companies more than \$250 million.^{15,16} ■ In 1999, costs for prescription antihistamines and intranasal corticosteroid sprays exceeding \$3 billion and \$1 billion, respectively.¹²

terized by the accumulation of inflammatory cells, such as eosinophils, basophils, lymphocytes, monocytes, and neutrophils, in the nasal mucosa.²⁴ Consequent fluid exudation leads to nasal congestion, which is arguably the most debilitating symptom of AR. Obstruction of the nasal and sinus passages and/or the eustachian tubes can lead to infections, otitis media, sinusitis, and nasal polypoidosis.^{13,17,18} Other symptoms of AR include sneezing, rhinorrhea, nasal itching, itchy and watery eyes, conjunctivitis, postnasal drip, and a dry, irritated throat.²⁵

Although immunotherapy offers the possibility of a cure, it is reserved for certain patients, such as those with discrete, identified allergies who are willing and able to comply with the required prolonged course of therapy. For the majority of patients with AR, pharmacotherapy is indicated for symptom relief, and in most cases, includes an intranasal corticosteroid to combat the inflammatory processes underlying the disease.

...PHARMACOTHERAPY WITH INTRANASAL CORTICOSTEROIDS...

Six intranasal corticosteroid preparations are available in the United States: beclomethasone dipropionate, budesonide, fluticasone propionate, mometasone furoate, flunisolide, and triamcinolone acetonide. Their respective safety and efficacy profiles in AR have been established in clinical trials and do not vary markedly among agents.⁵ Their mechanisms of action involve reduction of fluid exudation and reducing the number of circulating inflammatory cells, including lymphocytes, basophils, mast cells, macrophages, eosinophils, and neutrophils.²⁴ By acting directly on inflammation, they relieve nasal congestion, reduce membrane permeability, inhibit both early- and late-phase reactions to allergens, minimize nasal secretions and rhinorrhea, and modulate sensitivity to nasal irritants.^{8,24,26}

Dosage and Administration

Intranasal corticosteroids are most

effective when started several days before allergen exposure and should be used on a regular, rather than an as-needed, basis.³ Clinical practice guidelines recommend tapering the intranasal corticosteroid dose to the lowest level necessary to maintain relief once nasal symptoms are under control.⁸ Treatment is usually begun about 2 weeks before the beginning of the allergy season. After the season ends, the spray may be prescribed for an additional 2 weeks to control any residual mucosal hyperreactivity.^{8,26}

Adverse Effects

Intranasal corticosteroids are usually well tolerated, with only minor variations in safety profiles among drugs within the class.^{5,27-30} In most cases, adverse effects are not severe enough to warrant discontinuation of therapy. Potential adverse effects include local irritation and epistaxis. Nasal septal perforation has occurred in rare cases and may result from repeated placement of the spray nozzle against the nasal septum.³¹ A primary advantage of topical delivery of corticosteroids is that they act locally rather than systemically, thereby minimizing or eliminating systemic side effects.²⁶

Measures of hypothalamic-pituitary-adrenal (HPA)-axis function have been used to determine the potential systemic effects of the intranasal corticosteroids. To date, no reports of adrenal crisis or chronic adrenal failure have been made in association with this class of products.^{5,32} In a study of 6- to 12-year-old children with AR, treatment with triamcinolone acetonide at doses of 220 and 440 mg/day for 6 weeks had no significant effect on HPA-axis function after corticotropin stimulation.³³ In children, the greatest concern regarding intranasal corticosteroid use is the potential to have an adverse effect on growth. Indeed, beclomethasone nasal spray has shown some negative effects on growth in 1 study, and is not recommended for children.³⁴ However, this is not a class effect, as other intranasal corticosteroids do not appear to affect growth.^{30,35}

...COSTS OF INTRANASAL
CORTICOSTEROIDS IN
MANAGED CARE SETTINGS...

Although clinical and economic outcomes assessments have some commonalities, they have important differences. Clinical decisions are usually made from the perspective of what is best for the individual patient. In contrast, economic assessments are often conducted with a broader perspective; that is, evaluating all costs and benefits attributable to the intervention, as demonstrated in large numbers of patients, such as a managed care setting.¹ Liao et al conducted a retrospective economic study in which health insurance claims from 37 managed care organizations in the United States were evaluated for medical and pharmacy costs related to intranasal corticosteroid use for treatment of AR.³⁶ A total of 35 149 patients with AR who were 18 years of age and older were treated in 1999 or 2000 with an aqueous formulation of an intranasal corticosteroid. The most frequently prescribed agents were budesonide, fluticasone, mometasone, and triamcinolone acetonide. In this analysis, patients who had AR treated with triamcinolone acetonide incurred significantly lower mean annual treatment charges, classified as medical plus pharmacy charges, as well as significantly lower mean annual pharmacy charges than patients receiving 1 of the 3 other aqueous corticosteroid intranasal sprays. Differences in mean annual treatment charges between triamcinolone acetonide (mean annual treatment charges, \$667.69) and the other nasal sprays were highly significant: mometasone (mean annual treatment charges, \$727.01, $P < .0001$), fluticasone (mean annual treatment charges, \$763.51, $P < .0001$), and budesonide (mean annual treatment charges, \$713.60, $P < .015$).³⁶ Results of this type of study, using insurance claims data from a large number of patients enrolled in managed care organizations, provide insight into actual clinical trends.

Cost-effectiveness analyses can be used to quantify the costs and clinical consequences of medical interventions.

Although clinical efficacy assessments were not part of Liao's retrospective study, as mentioned, multiple studies have shown the equivalent efficacy of available intranasal corticosteroids.^{5,29,37} Given this, it is not unreasonable to conjecture that triamcinolone acetonide would be a more cost-effective option than aqueous fluticasone, mometasone, or budesonide.

More than cost, what may differentiate intranasal corticosteroids to a greater extent than any other characteristic are their formulations. Patients can distinguish among the sensory attributes of intranasal corticosteroids, and, when able to directly compare products, they express preferences for sprays with no odor or taste.⁷ If the intranasal corticosteroid is objectionable, patients may not be compliant or persistent with the prescribed treatment regimen.

...PATIENT PREFERENCE AND
TREATMENT ADHERENCE...

Patients experience the sensory attributes of the intranasal corticosteroid formulation every time they administer the drug. Patient preferences for such attributes should not be underestimated. In order to be effective, the patient must use the intranasal corticosteroid as prescribed, in some cases for weeks or months. Some sprays are comfortable to use and well tolerated by patients, while others may have an objectionable odor or irritate the nasal mucosa or throat. If the corticosteroid nasal spray irritates the mucosa and has an unpleasant odor, the patient may not use it, or will only use it when desperate for relief. Without adherence to the daily therapeutic regimen, the drug may fail to provide the optimal benefit.⁸ As noted, inadequate treatment of AR can lead to exacerbation of other serious conditions, such as asthma and sinusitis.^{13,17} Therefore, patient acceptability should be an important consideration when making therapeutic choices.

Comparative Trials

In 2 studies comparing triamcinolone

with fluticasone and mometasone^{7,38} or triamcinolone with beclomethasone and fluticasone,³⁸ patients preferred the product attributes of triamcinolone acetate aqueous nasal spray significantly more than the other intranasal corticosteroids because it was associated with milder taste/no taste, less aftertaste, less odor/no odor, preferred odor, greater moistness of the nose and throat, and less irritation. Additionally, in the first study, a multicenter, randomized, double-blind, crossover study of 95 adult patients with AR, significantly more patients reported they would most prefer to receive a prescription for triamcinolone acetate aqueous nasal spray compared with fluticasone propionate or mometasone furoate ($P < .001$).⁷ When questioned about potential compliance with therapy, 67% of patients indicated they would definitely adhere to aqueous triamcinolone acetate if it were prescribed for them, compared with 55% for fluticasone and 50% for mometasone.⁷

...CONCLUSION...

Inadequately treated AR can result in increased direct costs of resource utilization, such as more office visits. Similarly, it can lead to increases in indirect costs related to absenteeism, productivity losses, and declines in quality of life. A review of insurance claims data from more than 35 000 patients taking various intranasal corticosteroids demonstrated significant differences in the costs associated with use of specific medications within this class. In addition to cost, results of patient preference comparisons differentiate these medications. Patients' attitudes toward features such as taste, odor, irritation, and moistness may influence adherence to therapy. A lack of adherence may result in suboptimal control of AR, potentially leading to increases in both indirect costs and direct costs to managed care.

Cost and patient acceptability are particularly important when treating AR in a managed care setting. Additional cost-effectiveness studies comparing intranasal corticosteroids, including the effects on

indirect costs, are needed to better understand economic outcomes associated with the use of these medications.

...REFERENCES...

1. Sullivan SD, Weiss KB. Health economics of asthma and rhinitis. II. Assessing the value of interventions. *J Allergy Clin Immunol*. 2001;107:203-210.
2. Storms W, Meltzer EO, Nathan RA, Selner JC. The economic impact of allergic rhinitis. *J Allergy Clin Immunol*. 1997;99(6):S820-S824.
3. Lemanske RF. A review of the current guidelines for allergic rhinitis and asthma. *J Allergy Clin Immunol*. 1998;101(2):S392-S396.
4. Malone DC, Lawson KA, Smith DH, et al. A cost of illness study of allergic rhinitis in the United States. *J Allergy Clin Immunol*. 1997;99:22-27.
5. Corren J. Intranasal corticosteroids for allergic rhinitis: how do different agents compare? *J Allergy Clin Immunol*. 1999;104:S144-S149.
6. Wihl JA, Andersson KE, Johansson SA. Systemic effects of two nasally administered glucocorticosteroids. *Allergy*. 1997;52(6):620-626.
7. Bachert C, El-Akkad T. Patient preference and sensory comparison of three nasal corticosteroids for the treatment of allergic rhinitis. *Ann Allergy Asthma Immunol*. In press.
8. American Academy of Allergy, Asthma and Immunology. *Allergic Disorders: Promoting Best Practices—The Allergy Report*. 2000. Available at: <http://TheAllergyReport.com/main.html>. Accessed March 30, 2001.
9. 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 Immunol*. 1999;103:401-407.
10. Stephenson J. No cures, but the remedies are improving. *Business Health*. 2000;4:19-25.
11. Crystal-Peters J, Crown WH, Goetzel RZ, Schutt DC. The cost of productivity losses associated with allergic rhinitis. *Am J Managed Care*. 2000;6:373-378.
12. Nash DB, Sullivan SD, Mackowiak J. Optimizing quality of care and cost effectiveness in treating allergic rhinitis in a managed care setting. *Am J Managed Care*. 2000;6(suppl):S3-S20.
13. Meltzer, EO, Grant JA. Impact of cetirizine on the burden of allergic rhinitis. *Ann Allergy Asthma Immunol*. 1999;83:455-463.
14. Thompson AK, Juniper E, Meltzer EO. Quality of life in patients with allergic rhinitis. *Ann Allergy Asthma Immunol*. 2000;85:338-348.
15. American Academy of Allergy, Asthma, and Immunology. *Fast Facts: Statistics on Asthma & Allergic Diseases, 1999*. Updated October 1999. Available at: <http://www.aaaai.org/public/fastfacts/statistics.stm>. Accessed May 15, 2001.
16. Hewitt Associates LLC. Allergy costs may cause watery eyes for employers. *Managing Health and Business Productivity*. Available at: http://www.was.hewitt.com/hewitt/business/healthmgt/subhealth/hlbus_allergies.htm. Accessed June 3, 2002.
17. Settignano RA. Complications of allergic rhinitis.

- Allergy Asthma Proc. 1999;20:209-213.
- 18. Spector SL.** Overview of the comorbid associations of allergic rhinitis. *J Allergy Clin Immunol.* 1997;99:S773-S780.
- 19. Fireman P.** Treatment of allergic rhinitis: effect on occupation productivity and work force costs. *Allergy Asthma Proc.* 1997;18:63-67.
- 20. Fireman P.** Rhinitis and asthma connection: management of coexisting upper airway allergic diseases and asthma. *Allergy Asthma Proc.* 2000; 21:45-54.
- 21. Settiple RG, Hagy GW, Settiple GA.** Long-term risk factors for developing asthma and allergic rhinitis: a 23-year follow-up of college students. *Allergy Asthma Proc.* 1984;15:21-25.
- 22. Centers for Disease Control and Prevention. Allergic Rhinitis: Prevalence.** Vital and Health Statistics Series 10, No. 200. May 17, 2002. Available at: http://www.cdc.gov/nchs/data/10_200_1.pdfm. Accessed June 3, 2002.
- 23. American Academy of Family Physicians.** Facts About Family Practice—1999. Available at: [http://www.aafp.org/facts/Tables 17, 18, 22](http://www.aafp.org/facts/Tables_17,_18,_22). Accessed August 14, 2002.
- 24. Meltzer EO.** The pharmacological basis for the treatment of perennial allergic rhinitis and non-allergic rhinitis with topical corticosteroids. *Allergy.* 1997;52(suppl 36):33-40.
- 25. 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. Executive summary. *Ann Allergy Asthma Immunol.* 1998;81:478-518.
- 26. Rachelefsky GS.** Pharmacologic management of allergic rhinitis. *J Allergy Clin Immunol.* 1998;101(2): S367-369.
- 27. Adamopoulos G, Manolopoulos L, Giotakis I.** A comparison of the efficacy and patient acceptability of budesonide and beclomethasone dipropionate aqueous nasal sprays in patients with perennial rhinitis. *Clin Otolaryngol.* 1995;20:340-344.
- 28. Day J, Carrillo T.** Comparison of the efficacy of budesonide and fluticasone propionate aqueous nasal spray for once daily treatment of perennial rhinitis. *J Allergy Clin Immunol.* 1998;102:902-908.
- 29. Mandl M, Nolop K, Lutsky BN.** Comparison of once daily mometasone furoate (Nasonex) and fluticasone propionate aqueous nasal sprays for the treatment of perennial rhinitis. 194-079 Study Group. *Ann Allergy Asthma Immunol.* 1997;79:370-378.
- 30. Skoner DP, Angelini BJ, Gentile DA, et al.** The effects of intranasal triamcinolone acetonide and intranasal fluticasone propionate on short-term bone growth and HPA axis in children with allergic rhinitis. *Ann Allergy Asthma Immunol.* In press.
- 31. Blaiss M.** How to determine the cost-effectiveness of available allergic rhinitis treatments. *Drug Benefit Trends.* 1998;10:32-36.
- 32. Wilson AM, McFarlane LC, Lipworth BJ.** Effects of repeated once daily dosing of three intranasal corticosteroids on basal and dynamic measures of hypothalamic-pituitary-adrenal-axis activity. *J Allergy Clin Immunol.* 1998;101:470-474.
- 33. Nayak AS, Ellis MH, Gross GN, et al.** The effects of triamcinolone acetonide aqueous nasal spray on adrenocortical function in children with allergic rhinitis. *J Allergy Clin Immunol.* 1998;101:157-162.
- 34. Skoner D, Rachelefsky GS, Meltzer EO, et al.** Detection of growth suppression in children during treatment with intranasal beclomethasone dipropionate. *Pediatrics.* 2000;105:E23.
- 35. Schenkel EJ, Skoner DP, Bronsky EA, et al.** Absence of growth retardation in children with perennial allergic rhinitis after one year of treatment with mometasone furoate aqueous nasal spray. *Pediatrics.* 2000;105:E22.
- 36. Liao E, Griffis D, Huse DM.** Cost of treating allergic rhinitis and sinusitis with intranasal corticosteroids in a managed care population. *JMCM.* 2002;6:6-12.
- 37. Gross G, Jacobs RL, Woodworth TH, Georges GC, Lim JC.** Comparative efficacy, safety, and effect on quality of life of triamcinolone acetonide and fluticasone propionate aqueous nasal sprays in patients with fall seasonal allergic rhinitis. *Ann Allergy Asthma Immunol.* 2002;89:56-62.
- 38. Gerson I, Green L, Fishken D.** Patient preference