

Drug Class Review on Nasal Corticosteroids

Update #2: Preliminary Scan Report #1

July 2009

**The Agency for Healthcare Research and
Quality has not yet seen or approved this report**

The purpose of this report is to make available information regarding the comparative effectiveness and safety profiles of different drugs within pharmaceutical classes. Reports are not usage guidelines, nor should they be read as an endorsement of, or recommendation for, any particular drug, use or approach. Oregon Health & Science University does not recommend or endorse any guideline or recommendation developed by users of these reports.

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OBJECTIVE:

The purpose of this preliminary updated literature scan process is to provide the Participating Organizations with a preview of the volume and nature of new research that has emerged subsequent to the previous full review process. Provision of the new research presented in this report is meant only to assist with Participating Organizations' consideration of allocating resources toward a full update of this topic. Comprehensive review, quality assessment and synthesis of evidence from the full publications of the new research presented in this report would follow only under the condition that the Participating Organizations ruled in favor of a full update. The literature search for this report focuses only on new randomized controlled trials, and actions taken by the FDA or Health Canada since the last report. Other important studies could exist.

Date of Last Update:

Update #1 Final Report was completed in June 2008.

Date of Last Update Scans:

None

Scope and Key Questions

Report authors drafted preliminary key questions, identifying the populations, interventions, and outcomes of interest, and based on these, the eligibility criteria for studies. For the Original Report and for Update #1, these were reviewed and revised by the Washington State Preferred Drug Program (PDP). Washington State PDP was responsible for ensuring that the scope of the review reflected the populations, drugs, and outcome measures of interest to both clinicians and patients. The Washington State PDP approved the following key questions to guide this review:

1. For adults and children with seasonal or perennial (allergic and non-allergic) rhinitis, do nasal corticosteroids differ in effectiveness?
2. For adults and children with seasonal or perennial (allergic and non-allergic) rhinitis, do nasal corticosteroids differ in safety or adverse events?
3. Are there subgroups of patients based on demographics (age, racial groups, gender), other medications, or comorbidities, or in pregnancy and lactation for which one nasal corticosteroid is more effective or associated with fewer adverse events?

Inclusion Criteria

Population(s)

Adult patients and children (under age 18) in outpatient settings with the following diagnosis:

- Seasonal or perennial allergic or non-allergic rhinitis

Table 1. Interventions

Generic name	Trade name(s)	Forms
Beclomethasone	Beconase [®] , Beconase AQ [®] , Vancenase [®] , Vancenase AQ [®]	Nasal spray
Budesonide	Rhinocort [®] , Rhinocort Aqua [®]	Nasal spray
Ciclesonide	Omnaris [®]	Nasal spray
Flunisolide	Nasalide [®] , Nasarel [®]	Nasal spray
Fluticasone furoate	Veramyst [®]	Nasal spray
Fluticasone propionate ^a	Flonase [®]	Nasal spray
Mometasone	Nasonex [®]	Nasal spray
Triamcinolone	Nasacort [®] , Nasacort AQ [®]	Nasal spray

^a Unless otherwise stated, fluticasone propionate is referred to as 'fluticasone' or 'fluticasone aqueous' throughout this report; fluticasone furoate is always referred to as such.

Effectiveness outcomes

- Symptomatic relief
- Onset of action

Safety outcomes

- Overall adverse effect reports
- Withdrawals due to adverse effects
- Serious adverse events reported
- Specific adverse events (localized infection of nasal mucosa, hypersensitivity, hypercorticism, HPA suppression, growth suppression in pediatric population, headache, throat soreness, dry mouth, nasal irritation)

Study designs

1. For efficacy, controlled clinical trials and good-quality systematic reviews
2. For safety, controlled clinical trials and good-quality systematic reviews and observational studies.

METHODS

Literature Search

To identify relevant citations, we searched MEDLINE (September 2007 through July 2009) using terms for included drugs and indications, and limits for humans, English language, and randomized controlled trials or controlled clinical trials. We also searched FDA (<http://www.fda.gov/medwatch/safety.htm>) and Health Canada (http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/index_e.html) websites for identification of new drugs, indications, and safety alerts. All citations were imported into an electronic database (EndNote v X2[®]) and duplicate citations were removed.

Study Selection

One reviewer assessed abstracts of citations identified from literature searches for inclusion, using the criteria described above.

RESULTS

Overview

Searches resulted in 44 citations. Among those, there are 14 new potentially relevant controlled clinical trials, including 1 head-to-head trial (Appendix A) and 13 placebo-controlled trials (Appendix B). The head-to-head trial represents the first direct comparison of fluticasone furoate to another nasal corticosteroid in allergic rhinitis. There are still no head-to-head trials involving ciclesonide or in patients with non-allergic rhinitis. There were no new head-to-head trials in children (2 head-to-head trials were previously included)

The Table below provides a summary of the content of the placebo-controlled trials. The majority of the new placebo-controlled trials involve fluticasone furoate, a few of which represent published versions of trials that we had previously cited based on unpublished data from the manufacturer’s dossier submission for Update #1.

Author Year	NCS	Focus/Notes
Agondi 2008	Beclomethasone	Comorbid asthma
Couroux 2009	Ciclesonide	SAR: Onset of action (TNSS), single-dose
Patel 2008	Ciclesonide	SAR: Onset of action (TNSS), single dose
Jacobs 2009	Fluticasone furoate	Non-allergic rhinitis: Study FFR30006 and FFR30007, previously cited based on unpublished data from dossier
Nathan 2008	Fluticasone furoate	PAR in adults/adolescents: Previously cited based on unpublished data from dossier
Vasar 2008	Fluticasone furoate	PAR in adults/adolescents: Previously cited based on unpublished data from dossier
Okubo 2008	Fluticasone furoate	PAR in adults: Appears new, doesn’t match duration of either trial already cited based on unpublished data from dossier
Maspero 2008	Fluticasone furoate	PAR in children: No previous trials with fluticasone furoate in children
Zieglmayer 2008	Fluticasone furoate	SAR in adults
Meltzer 2009	Fluticasone furoate	SAR in children: No previous trials with fluticasone furoate in children
Andrews 2009	Fluticasone furoate	SAR: night-time symptoms
Pedroletti 2008	Mometasone	PAR and comorbid asthma in children
Weinstein 2009	Triamcinolone	PAR in children

New Drugs

None

New Indications

In September 2008, treatments of seasonal and perennial allergic rhinitis in patients 2 to 5 years of age were added as approved indications for triamcinolone.

New Safety Alerts

No new black box warnings were found. The only new safety information was for triamcinolone. In September 2008, epistaxis and candida infection were both added to the “Warnings and Precautions” section of the product label as adverse nasal effects that were observed in clinical trials. Information about the risks of glaucoma/cataracts, immunosuppression, hypercorticism and adrenal suppression, and reduction in growth in pediatric patients associated with all corticosteroids in general was also added to the triamcinolone product label.

Appendix A.

Okubo, K., M. Nakashima, et al. (2009). "Comparison of fluticasone furoate and fluticasone propionate for the treatment of Japanese cedar pollinosis." Allergy & Asthma Proceedings **30**(1): 84-94.

Fluticasone furoate nasal spray (FFNS) is a novel, enhanced-affinity glucocorticoid administered in a unique side-actuated device for the treatment of allergic rhinitis. No previous clinical studies have compared the efficacy of FFNS with another intranasal steroid. The purpose of this study was to compare the efficacy and safety of FFNS, 110 microg/day, once daily with fluticasone propionate nasal spray (FPNS), 200 microg/day, twice daily in patients with Japanese cedar pollinosis to support the regulatory filing in Japan. In this multicenter, randomized, placebo-controlled, double-blind, parallel-group study, patients (≥ 16 years old) were randomized to receive 2 weeks of treatment with FFNS (n = 151), FFNS placebo (n = 72), FPNS (n = 148), or FPNS placebo (n = 75). FFNS once daily was noninferior to FPNS twice daily in mean change from baseline in three total nasal symptom scores (3TNSS; sneezing, rhinorrhea, and nasal congestion; -1.23 +/- 0.140 and -1.06 +/- 0.142, respectively). Compared with placebo, FFNS was superior in reducing 3TNSS (p < 0.001). Both FFNS and FPNS showed similar mean changes from baseline in 4TNSS (3TNSS and nasal itching) and individual nasal symptom scores. The onset of action for FFNS was observed from the 1st day of treatment, whereas in the FPNS group it was observed on the 2nd day. There were similar improvements in rhinoscopy findings, activity of daily life interference, and patient-rated overall evaluation to therapy in the FFNS and FPNS groups. FFNS was well tolerated. Treatment with once-daily FFNS was effective and noninferior to twice-daily FPNS in reducing nasal symptoms. Faster onset of action for FFNS was observed.

APPENDIX B:

Agondi, R. C., M. L. Machado, et al. (2008). "Intranasal corticosteroid administration reduces nonspecific bronchial hyperresponsiveness and improves asthma symptoms." Journal of Asthma **45**(9): 754-7.

INTRODUCTION: Rhinitis and asthma are currently recognized as manifestations of a single syndrome, the chronic allergic respiratory syndrome. Nearly all individuals with asthma have rhinitis, and severe rhinitis has been associated with worse outcomes in asthma patients. Intranasal treatment has been reported to be beneficial for the lower airways. **METHODS:** This was a randomized, double-blind, placebo-controlled study. The objective was to evaluate the effects that treatment with intranasal beclomethasone dipropionate (BDP; 400 microg/d) has on nasal and bronchial symptoms, as well as on lung function test results and bronchial responsiveness to histamine in patients with allergic rhinitis and asthma. We evaluated 33 patients, divided into two groups: treatment (n = 17); and placebo (n = 16). Over the course of the 125-day study period, each patient reported daily rhinitis and asthma symptoms, as well as the need for additional medication. All patients were submitted to spirometry and histamine challenge at baseline and at each subsequent evaluation (on days 50 and 75). **RESULTS:** In comparison with the patients in the placebo group, those in the BDP treatment group presented significantly fewer nasal symptoms on day 50 and fewer asthma symptoms on day 75 (p < 0.01 for both); required rescue medications less often; and presented a significantly lower degree of bronchial responsiveness to histamine on day 75 (p < 0.01). **CONCLUSION:** In this study, intranasal BDP was effective in treating rhinitis as well as asthma. The benefits for the lower airways were observed only after prolonged treatment and might be better evaluated through nonspecific bronchial challenge.

Andrews, C. P., B. G. Martin, et al. (2009). "Fluticasone furoate nasal spray is more effective than fexofenadine for nighttime symptoms of seasonal allergy." Allergy & Asthma Proceedings **30**(2): 128-38.

Nasal symptoms of allergic rhinitis are an important cause of sleep disturbance. Reduction of nasal symptoms, particularly nasal obstruction, has been linked to improvements in self-reported sleep quality. The enhanced-affinity intranasal corticosteroid fluticasone furoate and the oral antihistamine fexofenadine were compared with respect to nighttime symptoms of seasonal allergic rhinitis. In two randomized, double-blind, double-dummy, parallel-group studies, patients received fluticasone furoate nasal spray (FFNS), 110 microg (study 1, n = 312; study 2, n = 224); fexofenadine, 180 mg (study 1, n = 311; study 2, n = 227); or placebo (study 1, n = 313; study 2, n = 229) once daily for 2 weeks. Fluticasone furoate was more effective (p < 0.001) than fexofenadine and placebo in both studies with respect to the mean changes from baseline over the treatment period in the nighttime symptoms score, nighttime reflective total nasal symptom score, predose instantaneous nasal symptom score, and morning peak nasal inspiratory flow. Fluticasone furoate was more effective than placebo (p < or = 0.001) in study 1 and more effective than both placebo and fexofenadine (p < or = 0.034) in study 2 with respect to the mean changes from baseline

in the nighttime reflective total ocular symptom score and predose instantaneous total ocular symptom score. In these double-dummy studies, fexofenadine did not separate from placebo in comparisons of the nighttime symptoms score or the nighttime nasal or ocular symptom measures. The incidence of adverse events was similar among groups. FFNS once daily was more effective than fexofenadine and placebo with respect to nighttime sleep disturbance caused by seasonal allergy symptoms.

Couroux, P., S. Kunjibettu, et al. (2009). "Onset of action of ciclesonide once daily in the treatment of seasonal allergic rhinitis." Annals of Allergy, Asthma, & Immunology **102**(1): 62-8. BACKGROUND: Ciclesonide is an intranasal corticosteroid approved for the treatment of allergic rhinitis (AR). OBJECTIVE: To evaluate the time to onset of action of ciclesonide, 200 microg/d, in patients with seasonal AR (SAR). METHODS: In a double-blind, randomized, placebo-controlled study conducted in an environmental exposure chamber, 509 adults with at least a 2-year history of SAR completed 1 to 5 priming sessions of ragweed pollen exposure (mean [SD] of 3,500 [500] grains/m³). Patients with successful priming visits (defined as patient-assessed instantaneous total nasal symptom scores [TNSSs] > or =6 and rhinorrhea or nasal congestion scores > 2) received a single dose of intranasal ciclesonide, 200 microg (n = 255), or placebo (n = 254). The difference in the change from baseline in TNSSs between the ciclesonide and placebo groups was measured hourly 1 to 12 hours after study drug administration. RESULTS: At hour 6, the mean treatment difference in TNSSs between ciclesonide and placebo was 0.53 (95% confidence interval, 0.03-1.03; P = .02). Significant treatment differences in favor of ciclesonide were also observed at 2 additional time points: hour 10 (P = .01) and hour 12 (P = .008). CONCLUSIONS: These results confirm that intranasal ciclesonide, 200 microg/d, has an onset of action of 6 hours in patients with SAR.

Jacobs, R., P. Lieberman, et al. (2009). "Weather/temperature-sensitive vasomotor rhinitis may be refractory to intranasal corticosteroid treatment." Allergy & Asthma Proceedings **30**(2): 120-7.

Vasomotor rhinitis (VMR) is a common but poorly understood disorder of which there are two major subgroups: VMR(w/t), triggered by weather/temperature and VMR(ir), triggered by airborne irritants. No specific biological pathways or specific treatments for VMR(w/t) or VMR(ir) have been identified. However, intranasal corticosteroids (INSs) are effective in treating many forms of nonallergic rhinitis that include these conditions. A recently introduced INS with established efficacy in allergic rhinitis and enhanced affinity, fluticasone furoate, may possess the potency and safety profile required to treat chronic VMR(w/t). Two replicate studies (FFR30006 and FFR30007) were conducted in six countries to evaluate the efficacy and safety of fluticasone furoate nasal spray in subjects with VMR(w/t). After a 7- to 14-day screening period, subjects (n = 699) with symptomatic VMR(w/t) received fluticasone furoate, 110 mug q.d. or placebo for 4 weeks in these two randomized, double-blind, parallel-group studies. Subjects rated their nasal symptoms (congestion, rhinorrhea, and postnasal drip) twice daily on a 4-point categorical scale and evaluated their overall response to treatment at study end. Fluticasone furoate did not significantly improve daily reflective total nasal

symptom scores, the primary end point, versus placebo ($p = 0.259$) and there was no improvement in any other measure of efficacy. The active treatment was well tolerated. Fluticasone furoate was not effective in treating subjects with a newly defined condition, weather-sensitive VMR. These unexpected results suggest that VMR(w/t) is a distinct subgroup of VMR that is refractory to treatment with INs. Additional study of other treatments for VMR(w/t) (including INs) is warranted.

Maspero, J. F., A. Rosenblut, et al. (2008). "Safety and efficacy of fluticasone furoate in pediatric patients with perennial allergic rhinitis." Otolaryngology - Head & Neck Surgery **138**(1): 30-7.

OBJECTIVE: To evaluate the safety and efficacy of once-daily (QD) fluticasone furoate (FF) nasal spray in children with perennial allergic rhinitis (PAR). STUDY DESIGN: A global, randomized, double-blind, placebo-controlled study. SUBJECTS AND METHODS: Pediatric patients (aged 2-11 years; $n = 558$) with PAR received once-daily placebo, FF 110 microg, or FF 55 microg for 12 weeks. Efficacy was evaluated by nasal symptom scores. General safety and corticosteroid-specific safety (nasal and ophthalmic examinations, and hypothalamic-pituitary-adrenal assessments) were assessed. RESULTS: No findings of clinical concern were identified from the safety assessments. For primary efficacy analysis of mean change from baseline over the first 4 weeks of treatment in daily reflective total nasal symptom score, FF 55 microg demonstrated significant improvement ($P = 0.003$) compared with placebo; however, the improvement for FF 110 microg versus placebo did not reach statistical significance ($P = 0.073$). CONCLUSION: FF QD was well tolerated and demonstrated efficacy in children aged 2 to 11 years with PAR.

Meltzer, E. O., J. Lee, et al. (2009). "Efficacy and safety of once-daily fluticasone furoate nasal spray in children with seasonal allergic rhinitis treated for 2 wk." Pediatric Allergy & Immunology **20**(3): 279-86.

The objective of this study was to evaluate the efficacy and safety of fluticasone furoate (FF) nasal spray 55 and 110 microg once daily in children with seasonal allergic rhinitis (SAR). Patients ($n = 554$) received placebo nasal spray or FF, administered using a unique side-actuated device, in a 2-wk, randomized, double-blind study. Symptoms were evaluated by patients using a 4-point categorical scale. Efficacy assessments included reflective and instantaneous total nasal symptom scores (r/iTNSS). Primary analyses were conducted in patients aged 6-11 yr in the intent-to-treat population (ITT); the 2-11 yr group provided supportive analyses. In patients aged 6-11 yr, FF 110 microg once daily significantly improved the daily rTNSS compared with placebo. FF 55 microg once daily was only numerically better for rTNSS and iTNSS. Secondary pre-dose iTNSS and overall response to therapy were significant with FF 110 microg. The significant findings for FF 110 microg were supported by analyses in the entire ITT population of 2-11 yr olds. Both doses of FF were well tolerated. These study results suggest that FF nasal spray administered once daily for 2 wk is well tolerated and effective for the treatment of SAR symptoms in children aged 2-11 yr.

Nathan, R. A., W. Berger, et al. (2008). "Effect of once-daily fluticasone furoate nasal spray on nasal symptoms in adults and adolescents with perennial allergic rhinitis." Annals of Allergy, Asthma, & Immunology **100**(5): 497-505.

BACKGROUND: Intranasal corticosteroids are recommended as first-line therapy for the treatment of allergic rhinitis. Fluticasone furoate is a novel enhanced-affinity glucocorticoid for the treatment of allergic rhinitis. **OBJECTIVE:** To compare the efficacy and safety of intranasal fluticasone furoate with those of vehicle placebo nasal spray in adult and adolescent patients with perennial allergic rhinitis (PAR). **METHODS:** After screening (7-14 days), patients 12 years and older with confirmed PAR were randomized to receive fluticasone furoate, 110 microg once daily, or placebo once daily intranasally for 4 weeks in this double-blind, multicenter study. The primary end point was mean change from baseline during the entire treatment period in daily reflective total nasal symptom score (rTNSS), recorded on diary cards by patients, using a 4-point categorical scale. **RESULTS:** The mean reduction from baseline during the treatment period in daily rTNSS was significantly greater in fluticasone furoate recipients than in placebo recipients ($P = .005$). This finding was supported by significantly greater mean reductions in morning rTNSS and evening rTNSS ($P = .004$ and $P = .011$, respectively). A significantly greater mean reduction in instantaneous morning predose TNSS with fluticasone furoate compared with placebo ($P = .006$) confirmed the efficacy of once-daily administration. Fluticasone furoate was also significantly more effective than placebo in overall response to therapy ($P = .005$). **CONCLUSIONS:** Fluticasone furoate nasal spray, 110 microg once daily, effectively relieved nasal symptoms of PAR in adults and adolescents 12 years and older.

Okubo, K., M. Nakashima, et al. (2008). "Dose-ranging study of fluticasone furoate nasal spray for Japanese patients with perennial allergic rhinitis*." Current Medical Research & Opinion **24**(12): 3393-403.

BACKGROUND: This study was designed to evaluate the efficacy and safety of fluticasone furoate nasal spray (FFNS), a novel enhanced-affinity intranasal corticosteroid, in Japanese patients with perennial allergic rhinitis (PAR), and to determine the optimal dose. **METHODS:** In this phase II, multicenter, double-blind, randomized, placebo-controlled, parallel-group, dose-ranging study, 240 patients (aged ≥ 16 years) received once-daily (od) treatment for 2 weeks with either FFNS 110 microg ($n = 80$), 220 microg ($n = 81$) or placebo ($n = 79$). Patients evaluated 3 nasal symptoms using a 4-point scale. Efficacy was assessed as the mean change from baseline in total nasal symptom score (TNSS). **RESULTS:** Treatment with FFNS resulted in a significantly greater decrease over the treatment period in the mean 3TNSS (sneezing, rhinorrhea, and nasal congestion; $p < 0.001$ each dose vs. placebo), compared with placebo. More patients receiving FFNS had a markedly or moderately improved impression of treatment than placebo recipients (48% and 49% for FFNS 110 micro and 220 microg, respectively, vs. 18% for placebo; $p < 0.001$). Nasal rhinoscopy findings revealed significant improvements in mucosal swelling of the inferior turbinate (110 microg: $p = 0.004$; 220 microg: $p = 0.011$) and amount of watery rhinorrhea (110 microg: $p = 0.003$; 220 microg: $p < 0.001$), compared with placebo. Both doses of FFNS were well

tolerated. CONCLUSIONS: Both FFNS 110 microg and 220 microg od were effective in alleviating nasal symptoms in Japanese patients with PAR over the 2-week duration of this study. FFNS 110 microg od was selected as the optimal dose for further evaluation in phase III clinical trials.

Patel, P., D. Patel, et al. (2008). "Onset of action of ciclesonide once daily in the treatment of seasonal allergic rhinitis." Ear, Nose, & Throat Journal **87**(6): 340-53.

Ciclesonide is an intranasal corticosteroid approved for the treatment of allergic rhinitis. We conducted a randomized, double-blind, parallel-group, placebo-controlled study to evaluate the time to onset of action of ciclesonide 200 microg once daily in 502 adults with seasonal allergic rhinitis of at least 2 years' duration. To trigger immunologic priming, patients underwent between one and five priming sessions with exposure to 3,500 grains/m³ (+/-500) of ragweed pollen in an environmental exposure chamber. The criteria for a successful priming session were a patient-assessed instantaneous total nasal symptom score of at least 6 (of a possible 12) and a nasal congestion or rhinorrhea score of at least 2 (of a possible 3) 90 minutes after allergen exposure during at least two consecutive priming sessions. Patients were then randomly assigned to receive either a single dose of ciclesonide 200 microg (n = 251) or placebo (n = 251) administered intranasally. The difference in the change from baseline total nasal symptom scores in the two groups was assessed hourly for 12 hours after administration. Onset of action was determined to have taken place the first time that the effects of ciclesonide, as reflected in the total nasal symptom score, were significantly greater than those of placebo at a particular hourly assessment, provided that the subsequent hourly assessment also showed a statistically significant difference. The onset of action of ciclesonide occurred within 1 hour of administration (p = 0.01 vs. placebo), and the significant difference in total nasal symptom scores between ciclesonide and placebo was maintained through post-treatment hour 12 (p = 0.018).

Pedroletti, C., J. Lundahl, et al. (2008). "Effect of nasal steroid treatment on airway inflammation determined by exhaled nitric oxide in allergic schoolchildren with perennial rhinitis and asthma." Pediatric Allergy & Immunology **19**(3): 219-26.

Rhinitis is common in asthmatic schoolchildren who are allergic to animal dander and constantly and indirectly exposed to these allergens in their everyday environment. As a patho-physiological linkage between nasal and bronchial inflammation has been proposed to exist, the primary objective of this study was to determine whether nasal administration of mometasone furoate (MSNF) can reduce bronchial inflammation, as reflected in the level of exhaled nitric oxide (F(E)NO) in asthmatic schoolchildren with dander allergy and mild-to-moderate rhinitis. Forty such children were assigned randomly to be treated for 4 wk with MSNF or placebo, employing a double-blind procedure. F(E)NO was the primary end-point measured and secondary end-points were nasal levels of NO, the concentration of eosinophilic cationic protein (ECP) in nasal lavage, the relative numbers of eosinophils in blood, forced expiratory volume in 1 s (FEV₁), peak expiratory flow (PEF) and scoring of symptoms. There was no significant difference in the F(E)NO values of the treated and control groups at any time-point,

whereas the nasal level of ECP was lower in the treated group compared with placebo ($p = 0.05$) on both days 7 and 28, and compared with baseline for the treated group ($p = 0.06$ on day 7, $p = 0.02$ on day 28). Furthermore, the mean blood eosinophil count decreased in the treated group, which also demonstrated lower scores for nasal symptoms compared with placebo, but neither of these differences were statistically significant. FEV(1), PEF and nasal levels of NO remained unchanged in both groups. Four weeks of nasal treatment with MSNF had no effect on bronchial inflammation, as reflected by exhaled NO, whereas signs of nasal and systemic eosinophil activation were reduced. Thus, nasal administration of a steroid as a strategy to reduce asthmatic inflammation remains questionable in mild-to-moderately severe cases of perennial rhinitis and asthma.

Vasar, M., P.-A. Houle, et al. (2008). "Fluticasone furoate nasal spray: effective monotherapy for symptoms of perennial allergic rhinitis in adults/adolescents." Allergy & Asthma Proceedings **29**(3): 313-21.

Intranasal corticosteroids are widely prescribed for the treatment of perennial allergic rhinitis (PAR). The purpose of this study was to evaluate the efficacy and tolerability of intranasal fluticasone furoate, a novel enhanced-affinity glucocorticoid, in patients $> \text{ or } = 12$ years of age with PAR in a global, randomized, double-blind, placebo-controlled, 6-week study. Patients ($n = 302$) received fluticasone furoate nasal spray (FFNS) 110 microg or vehicle placebo once daily (q.d.). The primary efficacy measure was mean change from baseline over the 6-week treatment period in daily reflective total nasal symptom score (TNSS). Secondary end points included mean change from baseline in total and individual reflective nasal and ocular symptom scores and in daily peak nasal inspiratory flow (PNIF). FFNS was significantly more effective than placebo in reducing daily reflective TNSS over the treatment period (least square [LS] mean difference, -1.256 ; $p < 0.001$). Significant improvements were also established in total ocular symptom score (LS mean difference, -0.506 ; $p = 0.004$ versus placebo) and in all individual nasal ($p < 0.001$) and ocular ($p < 0.03$) symptoms assessed in a reflective manner. Improvements in daily PNIF were significantly greater with FFNS than placebo (LS mean difference, 8.376 L/minute; $p = 0.004$). FFNS was well tolerated. In this study, FFNS 110 microg q.d. was well tolerated and effective in reducing the nasal and ocular symptoms of PAR in adult and adolescent patients $> \text{ or } = 12$ years of age.

Weinstein, S., P. Qaqundah, et al. (2009). "Efficacy and safety of triamcinolone acetonide aqueous nasal spray in children aged 2 to 5 years with perennial allergic rhinitis: a randomized, double-blind, placebo-controlled study with an open-label extension." Annals of Allergy, Asthma, & Immunology **102**(4): 339-47.

BACKGROUND: Intranasal corticosteroids (INSs) are the most effective treatment for allergic rhinitis (AR). However, available INS safety and efficacy data in children younger than 6 years are limited. **OBJECTIVE:** To report the first well-controlled study assessing the safety and efficacy of an INS in children aged 2 to 5 years with perennial AR.

METHODS: In a 4-week, multicenter, double-blind, parallel-group study, patients were randomized to receive triamcinolone acetonide aqueous nasal spray (TAA AQ), 110

microg once daily, or placebo. A subset of children continued into a 6-month, open-label phase. Efficacy end points included total nasal symptom scores. Safety measures included reports of adverse events, morning serum cortisol levels before and after cosyntropin infusion, and growth as measured using office stadiometry. RESULTS: A total of 474 patients were randomized to receive TAA AQ (n = 236) or placebo (n = 238); 436 entered the open-label extension phase. Adjusted mean (SE) changes from baseline during the double-blind period in instantaneous and reflective total nasal symptom scores were -2.28 (0.16) and -2.31 (0.15), respectively, in the TAA AQ group (P = .09) vs -1.92 (0.16) and -1.87 (0.15) in the placebo group (P = .03). Adverse event rates were comparable between treatment groups. There was no significant change from baseline in serum cortisol levels after cosyntropin infusion at study end. The distribution of children by stature-for-age percentile remained stable during the study. CONCLUSIONS: Use of TAA AQ, 110 microg once daily, for up to 6 months offers a favorable efficacy to safety ratio in children aged 2 to 5 years with perennial AR.

Zieglmayer, P., R. Zieglmayer, et al. (2008). "Fluticasone furoate versus placebo in symptoms of grass-pollen allergic rhinitis induced by exposure in the Vienna Challenge Chamber." Current Medical Research & Opinion **24**(6): 1833-40.

OBJECTIVE: The Vienna Challenge Chamber (VCC) offers a controlled and controllable paradigm in which to reproducibly evaluate the efficacy of anti-allergic treatment. The aim of this study was to assess the efficacy of the novel intranasal corticosteroid fluticasone furoate (FF) in the VCC. METHODS: The single-centre, randomised, double-blind, placebo-controlled, two-period crossover study was conducted in 59 adult males with grass pollen allergic rhinitis (AR). Patients received either Fluticasone furoate 200 mcg once-daily, or placebo intranasally for 8 days. AR symptoms were induced during 4-hour allergen challenges with grass pollen in the VCC at the end of each 8-day treatment period. A first challenge was conducted at 1-5 hours post-dose, followed by a second challenge at 22-26 hours post-dose. The primary endpoint was total nasal symptom score (TNSS; sum of itch, sneeze, rhinorrhoea, obstruction symptoms assessed on a categorical scale of 0-3) weighted mean over 2-5 hours post-dose. Secondary endpoints included: TNSS weighted mean over 23-26 hours post-dose and global symptom score, eye symptom score, nasal secretions and nasal airflow weighted means over 2-5 and 23-26 hours post-dose. RESULTS: Fluticasone furoate showed consistent attenuation of AR symptoms in both the early and late challenges. Compared with placebo, weighted mean of TNSS was reduced on average by 4.14 point-scores at 2-5 hours post-dose and 3.63 point scores at 23-26 hours post-dose. These positive effects were also seen across all secondary endpoints. CONCLUSION: An 8-day treatment course of intranasal FF 200 mcg given once-daily statistically significantly reduced symptoms of AR including associated eye symptoms. Statistical significance was declared where the relevant two-sided 95% confidence interval did not contain zero. This positive effect was sustained over 24 hours suggesting that fluticasone furoate could be efficacious as a once daily steroid.