# Mometasone furoate nasal spray reduces the ocular symptoms of seasonal allergic rhinitis

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**Background: Mometasone furoate nasal spray (MFNS), a potent intranasal corticosteroid with proved efficacy in relieving nasal allergic rhinitis symptoms, has demonstrated effectiveness in improving ocular symptoms associated with seasonal allergic rhinitis (SAR) in retrospective analyses.**

**Objective: We sought to evaluate prospectively the efficacy of MFNS in reducing total ocular symptom scores (TOSSs) and individual ocular symptoms in subjects with SAR.**

**Methods: Subjects 12 years or older (n = 429) with moderate-to-severe baseline symptoms were randomized to MFNS, 200 μg once daily, or placebo in this 15-day, double-blind, parallel-group study. Subjects evaluated morning instantaneous TOSSs and daily reflective TOSSs, total nasal symptom scores (TNSSs; both instantaneous TNSSs and reflective TNSSs, respectively), and individual ocular and nasal symptoms. Mean changes from baseline averaged over days 2 to 15 (instantaneous) and days 1 to 15 (reflective) were calculated. Quality of life was assessed by using the Rhinoconjunctivitis Quality of Life Questionnaire.**

**Results: MFNS treatment yielded significant reductions from baseline versus placebo in instantaneous TOSSs (−0.34, $P = .026$, coprimary end point), instantaneous TNSSs (−0.88, $P < .001$, coprimary end point), reflective TOSSs (−0.44, $P = .005$), and reflective TNSSs (−1.06, $P < .001$). Significant decreases in all individual reflective ocular symptoms and instantaneous eye itching/burning and eye watering/tearing were observed for MFNS versus placebo ($P < .05$). Numeric improvements in instantaneous eye redness were seen but did not reach statistical significance. Improvements in Rhinoconjunctivitis Quality of Life Questionnaire total scores and individual symptom domains were achieved with MFNS treatment versus placebo ($P < .001$). MFNS was well tolerated.**

**Conclusion: This prospective study demonstrates that MFNS significantly reduces ocular symptoms in subjects with SAR.**

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***Key words:*** *Allergic rhinitis, intranasal corticosteroids, mometasone furoate nasal spray*

Both nasal and ocular allergic responses in subjects with allergic rhinitis (AR) are characterized by an IgE-mediated early-phase reaction and, in approximately 50% of patients, a late-phase reaction.[1] Mast cell degranulation, release of inflammatory mediators, and infiltration of inflammatory cells occur within the nasal mucosa and conjunctival epithelium,[2-5] resulting in nasal symptoms, such as congestion, rhinorrhea, sneezing, and nasal itching. Ocular symptoms (ie, itching, watering/tearing, and redness) occur in up to 85% of subjects with AR.[6-8] Ocular symptoms are more prevalent in subjects with seasonal allergic rhinitis (SAR) than in those with perennial AR,[7] and in a US survey of 2,500 patients with AR, more than 50% of responders characterized ocular symptoms as moderately to extremely bothersome.[9] Nasal and ocular symptoms both contribute to the negative effect that SAR can have on quality of life through interference with sleep, productivity at school/work, and daily or social activities.[7,10]

Evidence-based management guidelines recommend intranasal corticosteroids (INSs), which act on both early- and late-phase reactions of the immune response,[11] as first-line therapy for moderate-to-severe AR[8,12] and antihistamine or cromone eye drops only when ocular symptoms persist despite use of INSs or oral antihistamines.[13] Ocular antihistamines have been shown to suppress eye symptoms more effectively than INSs in allergen challenge models,[14,15] although such comparisons have not been performed under outdoor exposure conditions. In conjunctival challenge studies, ocular antihistamines with mast cell–stabilizing activity relieve eye symptoms significantly better than pure mast cell stabilizers,[16,17] whereas clinical studies show comparable or superior efficacy between the 2 classes.[18-20] Use of INSs with oral antihistamines also has been recommended based on potentially additive mechanisms of action.[21,22] However, studies and 2 meta-analyses show no advantage in nasal or ocular symptoms with combination therapy versus INS monotherapy.[23-26] One clinical

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*Abbreviations used*
AE: Adverse event
ANCOVA: Analysis of covariance
AR: Allergic rhinitis
FF: Fluticasone furoate
INS: Intranasal corticosteroid
iTNSS: Instantaneous total nasal symptom score
iTOSS: Instantaneous total ocular symptom score
LS: Least squares
MFNS: Mometasone furoate nasal spray
RQLQ: Rhinoconjunctivitis Quality of Life Questionnaire
rTNSS: Reflective total nasal symptom score
rTOSS: Reflective total ocular symptom score
SAR: Seasonal allergic rhinitis
TNSS: Total nasal symptom score
TOSS: Total ocular symptom score

study of patients with SAR found combined therapy with a nasal antihistamine spray (azelastine) and an INS significantly reduced total nasal symptoms versus use of either treatment alone.[27]

Increasing evidence is emerging from retrospective and prospective studies for the efficacy of INSs in reducing the ocular symptoms of SAR.[28-31] Overall, INSs are recommended as the most effective medication for AR, more comprehensively covering allergic symptoms,[12] with the advantages of single-agent treatment, such as better patient adherence, cost-effectiveness, and reduced risk for side effects.[5]

Mometasone furoate nasal spray (MFNS) is a potent, topically active corticosteroid and an established treatment for the nasal symptoms of AR.[32-34] Recently, MFNS has demonstrated reductions in the total ocular symptom score (TOSS) and individual ocular symptoms versus placebo in retrospective analyses of data from individual[35-37] and pooled[38,39] phase III, randomized, controlled studies of subjects with SAR in which nasal symptoms were primary end points and ocular symptoms were not entry criteria, including further subanalysis of subjects with moderate-to-severe baseline ocular symptoms.[39]

The objective of the present study was to evaluate prospectively the efficacy of once-daily MFNS versus placebo in reducing TOSSs and individual ocular symptoms in subjects with SAR while confirming the proved efficacy of the agent in reducing nasal symptoms of SAR.

# METHODS

## Study design and subjects

This was a multicenter, phase III, randomized, double-blind, parallel-group study conducted from April through July 2007 at 25 physicians' offices in the United States in compliance with the principles of good clinical practice and other local, regional, and national regulations. The clinical protocol was reviewed and approved by a central institutional review board or independent ethics committee at each participating site. All subjects (or their legal representative) were required to provide written informed consent before study participation.

Subjects meeting eligibility criteria (Table I) entered a screening period (≥3 days, visit 1, see Fig E1 in this article's Online Repository at www.jacionline.org) and completed twice-daily diaries documenting SAR symptoms, adverse events (AEs), and use of concomitant medications. On the morning of the baseline visit (visit 2), clinically symptomatic subjects, defined by summed morning and evening symptom scores from the 3 days before baseline plus morning scores from the baseline visit (rhinorrhea, ≥14; nasal congestion, ≥14; total nasal symptom score [TNSS], ≥42; and TOSS, ≥28), were randomized sequentially in a 1:1 ratio by using a computer-generated randomization schedule to receive MFNS, 200 μg once daily (two 50-μg sprays per nostril at approximately the same time each morning), or matching vehicle placebo nasal spray for 15 days. Subjects administered the first dose of treatment at the study center (visit 2) after training in correct use of the nasal spray. Use of any other prescription or over-the-counter medications (eg, antihistamines and salines) potentially affecting ocular or nasal symptoms was not permitted during the study.

## Outcome assessments

Subjects rated the severity of their individual symptoms, including rhinorrhea, nasal congestion, nasal itching, sneezing, redness of eyes, itching/burning eyes, and tearing/watering eyes, on a 4-point scale (ie, 0, none; 1, mild; 2, moderate; and 3, severe) twice daily in subject diaries (in the morning before dosing and approximately 12 hours later [in the evening]). Instantaneous and reflective (over the previous 12 hours) scores were captured. Instantaneous TNSSs (iTNSSs) and TOSSs (iTOSSs) were derived by summing instantaneous morning individual symptom scores. Daily reflective scores (reflective TNSSs [rTNSSs] and reflective TOSSs [rTOSSs]) were obtained from averaging the reflective morning and evening individual symptom scores.

The 2 coprimary end points of the study were change from baseline in iTNSSs and iTOSSs, each averaged over days 2 to 15. Key secondary end points included change from baseline in daily rTNSSs and rTOSSs averaged over days 1 to 15 and instantaneous nasal congestion scores averaged over days 2 to 15 and change from baseline to study end point in the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) total score. Additional end points were change from baseline in instantaneous and reflective individual symptom scores and subject and investigator evaluations of overall condition (rated at the 4 study visits [see Fig E1] by using a 4-point scale, as above) and therapeutic response to study medication (assessed at visits 3 and 4 by using a 5-point scale: 1, complete relief; 2, marked relief; 3, moderate relief; 4, slight relief; and 5, no relief). The same study investigator or his or her qualified designee (subinvestigator) conducted all clinical assessments/reviews.

At visits 1 and 4, subjects aged 18 years or older completed the RQLQ before all other assessments (28 questions in 7 domains: activities, sleep, non–nose/eye symptoms, practical problems, nasal symptoms, eye symptoms, and emotions, each rated on a 7-point scale from 0 [not troubled] to 6 [extremely troubled]).[40] The total score was the mean of all 28 questions. Domain scores were the mean scores of questions within each domain. The established minimal important difference for RQLQ total score is 0.5, whereby any greater change in scores is considered a clinically significant improvement in subject quality of life.[41]

A physical examination and 12-lead electrocardiogram were completed at screening. Vital signs and AEs were recorded at visits 2, 3, and 4. Pollen counts were recorded at each study center 3 or more times per week for the study's duration.

## Statistical analysis

A sample size of 230 for each treatment arm was calculated to allow detection of a difference in iTOSSs between treatment groups of 0.55 points or more with a power of 90%, assuming a pooled SD of 1.8 points in change from baseline and a 2-sided $\alpha$ value of .05. A sample size of 230 subjects per treatment group and a difference between the MFNS and placebo groups in iTNSS of 0.8 points, assuming an SD of 2.1 points, will have a power of 98%. Assuming independent coprimary end points, the joint power for coprimary end points was estimated at approximately 88% by computing the product of the 2-power estimates.

Efficacy and safety analyses encompassed the intent-to-treat population, including all randomized subjects. Subjects with a missing evaluation at a given time point were omitted from the analysis for that specific assessment. End point values were defined as the postbaseline nonmissing observation carried forward, regardless of the visit windows. The coprimary end points were tested by using an analysis of covariance (ANCOVA) model, with treatment study center and baseline as covariates. Comparisons between the MFNS and placebo groups were made from the least-squares (LS) mean

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