Therapeutic Class Overview
Intranasal Corticosteroids

Therapeutic Class

Overview/Summary: Intranasal corticosteroids are primarily used to treat perennial and seasonal allergic rhinitis and may be useful in the treatment of some forms of nonallergic rhinitis.[1-9] Symptoms typically associated with allergic rhinitis include nasal congestion, rhinorrhea, sneezing and/or nasal itching. These symptoms result from a complex allergen driven mucosal inflammation caused by interplay between resident and infiltrating inflammatory cells and a number of vasoactive and proinflammatory mediators.[10] Intranasal corticosteroids downregulate the inflammatory response by binding to the intracellular glucocorticoid receptors of inflammatory cells and causing a conformational change, thereby controlling the rate of protein synthesis and suppressing the transcription of cytokine and chemokine genes.[11] Continuous administration of intranasal corticosteroids is more efficacious than as-needed dosing, and the onset of therapeutic effect occurs between three and twelve hours.[10] As a result of the route of administration and the relatively low systemic bioavailability of these agents, intranasal corticosteroids are generally not associated with any clinically significant systemic side effects. Drug interactions are limited when administered at recommended doses. The most common side effects include nasal irritation and mild epistaxis.[1-9] Triamcinolone (Nasacort AQ®), mometasone (Nasonex®) and fluticasone furoate (Veramyst®) are Food and Drug Administration (FDA) approved for use in children two years of age and older and fluticasone propionate (Flonase®) is FDA-approved for use in children four years of age and older. Beclomethasone (Beconase AQ®), budesonide (Rhinocort Aqua®), ciclesonide (Omnaris®), and flunisolide are FDA-approved for use in children six years of age and older. A recently approved product, beclomethasone nasal aerosol (QNASL®), is approved for used in adolescents and adults 12 year of age and older. [1-9] There are currently, three intranasal corticosteroids that are available generically: flunisolide, fluticasone propionate and triamcinolone.[13]

Table 1. Current Medications Available in Therapeutic Class[1-9]

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Beclomethasone (Beconase AQ®, QNASL®)	Treatment of seasonal and perennial allergic rhinitis, nonallergic rhinitis*, and nasal polyps*	Aerosol for nasal inhalation: 80 µg/actuation (120 actuations) Suspension for nasal inhalation: 42 µg/inhalation (180 metered doses)	-
Budesonide (Rhinocort Aqua®)	Treatment of seasonal and perennial allergic rhinitis	Suspension for nasal inhalation: 32 µg/inhalation (120 metered doses)	-
Ciclesonide (Omnaris®)	Treatment of seasonal and perennial allergic rhinitis	Suspension for nasal inhalation: 50 µg/inhalation (120 metered doses)	-
Flunisolide	Treatment of seasonal and perennial allergic rhinitis	Suspension for nasal inhalation: 25 µg/inhalation (200 metered doses) 29 µg/inhalation (200 metered doses)	✔
Fluticasone furoate (Veramyst®)	Treatment of seasonal and perennial allergic rhinitis	Suspension for nasal inhalation: 27.5 µg/inhalation (120 metered doses)	-
Fluticasone propionate (Flonase®)	Treatment of seasonal and perennial allergic rhinitis and nonallergic rhinitis	Suspension for nasal inhalation: 50 µg/inhalation (120 metered sprays)	✔

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Mometasone (Nasonex®)	Treatment of seasonal and perennial allergic rhinitis, nasal polyps and prophylaxis of seasonal allergic rhinitis	Suspension for nasal inhalation: 50 µg/inhalation (120 metered doses)	-
Triamcinolone (Nasacort AQ®)	Treatment of seasonal and perennial allergic rhinitis	Suspension for nasal inhalation: 55 µg/inhalation (120 metered doses)	✔

*Beconase AQ only

Evidence-based Medicine

- Recently published clinical trials comparing the various intranasal corticosteroids in the treatment of allergic rhinitis have not consistently demonstrated any clinically different results between agents within the class.
- Studies evaluating the safety and efficacy of beclomethasone nasal aerosol (QNASL®) have not been published outside of the prescribing information.

Key Points within the Medication Class

- According to Current Clinical Guidelines:
  - Intranasal corticosteroids are the most effective drugs for treating allergic rhinitis.[14]
  - Intranasal corticosteroids should be considered first-line therapy in patients with moderate to severe allergic rhinitis and may also be effective in some forms of nonallergic rhinitis.[10,14-16]
  - Clinical response does not seem to vary significantly between the available intranasal corticosteroids.[15]
- Other Key Facts:
  - The role of the intranasal corticosteroids in the treatment of allergic rhinitis has been well established.
  - The intranasal corticosteroids have been shown to be safe and effective in the treatment of allergic and nonallergic rhinitis though studies have not shown a significant difference between products.
  - Currently, there are three generic products available within the class- flunisolide, fluticasone propionate and triamcinolone.[13]
  - A new beclomethasone “dry” nasal aerosol product, QNASL®, is the first non-aqueous formulation available; all other agents within the class are aqueous suspensions.[13]

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Therapeutic Class Review
Intranasal Corticosteroids

Overview/Summary

Intranasal corticosteroids are primarily used to treat perennial and seasonal allergic rhinitis and may be useful in the treatment of some forms of nonallergic rhinitis.[1-9] Symptoms typically associated with allergic rhinitis include nasal congestion, rhinorrhea, sneezing and/or nasal itching. These symptoms result from a complex allergen driven mucosal inflammation caused by interplay between resident and infiltrating inflammatory cells and a number of vasoactive and proinflammatory mediators.[10] Intranasal corticosteroids downregulate the inflammatory response by binding to the intracellular glucocorticoid receptors of inflammatory cells and causing a conformational change, thereby controlling the rate of protein synthesis and suppressing the transcription of cytokine and chemokine genes.[11]

Continuous administration of intranasal corticosteroids is more efficacious than as-needed dosing, and the onset of therapeutic effect occurs between three and twelve hours.[10] As a result of both the route of administration and the relatively low systemic bioavailability of these agents, intranasal corticosteroids are generally not associated with any clinically significant systemic side effects. Moreover, drug interactions are limited when administered at recommended doses. The most common side effects include nasal irritation and mild epistaxis.[1-9]

All nine intranasal corticosteroids are approved by the Food and Drug Administration (FDA) for the treatment of perennial and seasonal allergic rhinitis. Mometasone (Nasonex®) carries an additional indication for the prophylaxis of seasonal allergic rhinitis.[8] Two currently available intranasal corticosteroids, beclomethasone (Beconase AQ®) and mometasone, are also FDA-approved for the treatment of nasal polyps.[1,8] Nasal polyposis is an inflammatory condition of the nasal and sinus mucosa and usually presents as persistent nasal obstrutction.[10] Intranasal beclomethasone is used principally to prevent recurrence of nasal polyps following surgical removal.[1]

Beclomethasone and fluticasone propionate (Flonase®) have an FDA-approved indication for the management of nonallergic rhinitis.[1,7] Examples of nonallergic rhinitis include infectious rhinitis, hormonal rhinitis and vasomotor nonallergic rhinitis with eosinophilia syndrome. Unlike allergic rhinitis, nonallergic rhinitis is characterized by periodic or perennial symptoms that are not a result of immunoglobulin E-dependent events.[12]

Flunisolide, fluticasone propionate and triamcinolone (Nasacort AQ®) are the three intranasal corticosteroids currently available in a generic nasal spray formulation.[13] A new beclomethasone product, QNASL®, was recently approved by the FDA and is the first intranasal corticosteroid product formulated as a “dry” nasal aerosol. All other products in within the class are formulated as aqueous suspensions.[14] Fluticasone furoate (Veramyst®), mometasone and triamcinolone are approved for use in children two years of age and older.[6,8-9] The intranasal corticosteroids are typically dosed once or twice daily.

According to the current clinical guidelines on the management of rhinitis, treatment should consist of patient education, allergen avoidance activities and pharmacological therapies. Patients should be educated on how to avoid known triggers, such as aeroallergens, dust mites, molds and irritants whenever possible. In addition to environmental control measures, pharmacological therapies may be used to control symptoms. Intranasal corticosteroids should be considered first-line therapy in patients with moderate to severe allergic rhinitis.[10,15-17] While differences in potencies, lipid solubility and systemic bioavailability exist between the older and newer intranasal corticosteroid products, no single agent has consistently has been demonstrated to be more effective than another.[18] Moreover, no one intranasal corticosteroid product is recommended over another as initial treatment in patients with perennial or seasonal allergic rhinitis.[15-17]

Medications

Table 1. Medications Included Within Class Review

Generic Name (Trade name)	Medication Class	Generic Availability
Beclomethasone (Beconase AQ®, QNASL®)	Intranasal corticosteroid	-
Budesonide (Rhinocort Aqua®)	Intranasal corticosteroid	-
Ciclesonide (Omnaris®)	Intranasal corticosteroid	-
Flunisolide	Intranasal corticosteroid	✔
Fluticasone furoate (Veramyst®)	Intranasal corticosteroid	-
Fluticasone propionate (Flonase®)	Intranasal corticosteroid	✔
Mometasone (Nasonex®)	Intranasal corticosteroid	-
Triamcinolone (Nasacort AQ®)	Intranasal corticosteroid	✔

Indications

Table 2. Food and Drug Administration Approved Indications[1-9,13,20]

Generic Name	Nasal Polyps	Nonallergic (Vasomotor) Rhinitis	Perennial Allergic Rhinitis	Seasonal Allergic Rhinitis	Prophylaxis of Seasonal Allergic Rhinitis
Beclomethasone	✔ *†	✔ †	✔	✔	
Budesonide			✔	✔	
Ciclesonide			✔	✔	
Flunisolide			✔	✔	
Fluticasone furoate			✔	✔	
Fluticasone propionate		✔	✔	✔	
Mometasone	✔		✔	✔ ‡	✔
Triamcinolone			✔	✔	

*For the prevention of recurrence of nasal polyps following surgical removal.
† Beconase AQ only
‡ For the treatment of symptoms and relief of nasal congestion associated with seasonal allergic rhinitis.

Pharmacokinetics

Table 3. Pharmacokinetics[1-9,13,20]

Generic Name	Bioavailability (%)	Absorption (%)	Renal Excretion (%)	Active Metabolites	Serum Half-Life (hours)
Beclomethasone	1	44	<12	Beclomethasone-17-monopropionate	2.8
Budesonide	<10	34	60	None	2 to 3
Ciclesonide	<1	Not reported	≤20	Des-ciclesonide	<7*
Flunisolide	Not reported	Not reported	50	6-beta-hydroxylated metabolite	1 to 2
Fluticasone furoate	0.5	30	<5	None	15.1†
Fluticasone propionate	<2	Not reported	<5	None	7.8†
Mometasone	<1	Not reported	Minimal	None	5.8
Triamcinolone	Low	Minimal	40	None	18 to 36

*Half-life for the desciclesonide metabolite
†After intravenous dosing.

Clinical Trials

Numerous clinical trials have demonstrated the safety and efficacy of intranasal corticosteroids in the treatment of both perennial and seasonal allergic rhinitis and non allergic rhinitis.[20-71] Daily administration

of intranasal corticosteroids improved both total nasal symptom and health related quality of life scores in patients with rhinitis and therapy was well tolerated. In addition, numerous head-to-head clinical trials have demonstrated no significant clinical differences among the currently available intranasal corticosteroids.[34-71]

Differences in sensory perceptions and patient preference of one agent over another have been noted in clinical trials. [37,45,53-54,64-65,67,70] Patients administering the agents noted differences in odor, aftertaste, and severity of irritation, though these differences do not result in improved outcomes.

Head-to-head trials evaluating the efficacy and safety of fluticasone propionate and flunisolide demonstrate that these agents are comparable to other agents within the class.[46,48-52,55-58,63,68-69,72] In one study, treatment with fluticasone propionate resulted in significantly less nasal blockage (P=0.002), nasal discharge (P=0.002) and eye watering/irritation (P=0.048) compared to treatment with beclomethasone.[55] In a second study, fluticasone propionate reduced patient-rated nasal symptom scores significantly better than beclomethasone at all time points measured (P<0.05).[56] However, additional results of these studies reinforce that all of the intranasal corticosteroids should be considered equally efficacious.

Table 4. Clinical Trials

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Treatment of Allergic Rhinitis (Perennial and Seasonal)				
Chervinsky et al[20] Ciclesonide 200 µg QD vs placebo	DB, MC, PC, PG, RCT Patients 12 years of age and older with a two year history of PAR, who require continuous treatment and demonstrated skin prick test sensitivity to at least one allergen known to induce PAR	N=663 52 weeks	Primary: Treatment-emergent adverse events, 24 hour urinary free cortisol and morning cortisol levels at weeks 24 and 48 Secondary: Change from baseline in patient evaluated morning 24 hour rTNSS, PANS score at the end of treatment, combined RQLQ scores at end point	Primary: There were no clinically significant differences in the incidence of treatment-emergent adverse events with ciclesonide compared to placebo (75.1 vs 74.3%; *P* value not reported). No clinically significant differences were seen between the ciclesonide and placebo groups with regards to 24 hour urinary free cortisol and morning cortisol levels and ocular examinations. Secondary: There was a significantly greater reduction from baseline in 24 hour rTNSS in the ciclesonide group (-2.3) compared to placebo (-1.8) (*P*<0.001). No appreciable differences were found between ciclesonide and placebo groups in PANS score at the end of treatment. At the end point, ciclesonide produced a greater improvement in combined RQLQ scores compared to placebo (-1.07 vs -0.88; *P*=0.04).
Meltzer et al[21] Ciclesonide 200 µg QD vs placebo	DB, MC, PC, RCT Patients 12 years of age and older with a two year history of PAR, who required continuous or intermittent treatment and demonstrated skin prick test sensitivity to at least one allergen known to	N=676 6 weeks	Primary: Change from baseline in the average of morning and evening rTNSS Secondary: Average morning and evening patient evaluated iTNSS, PANS score at end of treatment, combined RQLQ score at the end of	Primary: Ciclesonide significantly reduced average morning and evening rTNSS compared to placebo (-2.51 vs -1.89; *P*<0.001). Secondary: Ciclesonide significantly reduced average morning and evening iTNSS through six weeks of therapy (*P*=0.001). A greater decrease from baseline was observed at the end of treatment in PANS scores for the ciclesonide group compared to the placebo group (*P*=0.051). There was a significant improvement seen in the ciclesonide group compared to placebo in combined RQLQ scores at the end of

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
	induce PAR		treatment	treatment; -1.30 vs -1.01 (*P*=0.01).
Ratner et al[22] Ciclesonide 200 µg QD vs placebo	DB, MC, PC, PG, RCT Patients 12 years of age and older with a two year history of SAR who require treatment and demonstrated skin prick test sensitivity to mountain cedar pollen	N=327 4 weeks	Primary: Change from baseline in average morning and evening rTNSS Secondary: Patient assessed iTNSS, PANS score at days 15 and 29, TMSS, combined RQLQ scores at days 15 and 29, individual nasal symptoms, time to onset of effect and adverse events	Primary: Over two weeks, ciclesonide significantly improved the average morning and evening rTNSS compared to placebo; -2.40 vs -1.50 (*P*<0.001). The change from baseline over the entire study period was significant for the ciclesonide group compared to placebo (*P*<0.001). Secondary: By two weeks, ciclesonide improved iTNSS compared to placebo (*P*<0.001). At day 15, treatment with ciclesonide provided significantly greater improvements in overall PANS and combined RQLQ scores compared to placebo (*P*≤0.002). By the end of the study statistically significant differences were not seen between the ciclesonide and placebo groups (*P* value not reported). The ciclesonide group had a greater response in reflective nonnasal symptom scores compared to placebo however this was not statistically significant (-1.73 vs -1.30; *P*=0.071). By day 15, treatment differences for nasal symptoms favoring ciclesonide were evident (*P*<0.001). Significant improvements in average morning and evening rTNSS with ciclesonide over placebo were seen by the second day of treatment (*P*<0.05). Frequency of adverse events were similar between ciclesonide and placebo treatment groups (40.2 vs 39.3%, respectively; P value not reported). The most common side effects for the ciclesonide group included nasal passage irritation (6.1%) and headache (5.5%).
Ratner et al[23] Ciclesonide 25 µg QD	DB, MC, PC, PG, Phase II, RCT	N=726 14 days	Primary: Change from baseline in sum of	Primary: Ciclesonide 100 and 200 µg/day, significantly improved the sum of morning and evening rTNSS compared to placebo. (*P*=0.04 and

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs ciclesonide 50 µg QD vs ciclesonide 100 µg QD vs ciclesonide 200 µg QD vs placebo	Adult patients 18 to 65 years of age with a two year history of SAR, experiencing nasal allergy symptoms, with a minimum score of eight in either morning or evening rTNSS for at least three days during baseline period		morning and evening rTNSS Secondary: Change from baseline in the sum of morning and evening iTNSS and use of rescue medications	*P*=0.003). The average change from baseline in rTNSS was -4.2 for placebo and -4.8, -4.8, -5.3 and -5.8 for ciclesonide 25, 50, 100 and 200 µg/day, respectively. Secondary: Both ciclesonide 100 and 200 µg/day demonstrated greater improvements in iTNSS compared to placebo (*P* value not reported). There were no appreciable differences in the use of rescue medication, chlorpheniramine, across all treatment groups.
Fokkens et al[24] Fluticasone furoate 110 µg QD vs placebo	DB, MC, PC, PG, RCT Patients 12 years of age an older with SAR (defined as onset and offset of nasal allergy symptoms during each of the past two grass pollen seasons), and either a positive skin prick test to grass pollen or a positive in vitro test for specific IgE, within 12 months prior to the study	N=285 2 weeks	Primary: Mean change from baseline over the entire treatment period in daily rTNSS Secondary: Mean change from baseline over the entire treatment period in daily rTOSS, morning predose iTNSS, overall evaluation of response to therapy, mean change from baseline in RQLQ, iTOSS, daily reflective and instantaneous	Primary: The mean change from baseline in daily rTNSS over the treatment period was greater for fluticasone furoate as compared to placebo (-4.94 and -3.18, respectively; LS mean difference, -1.757; *P*<0.001). Secondary: Fluticasone furoate was significantly more effective than placebo in improving daily rTOSS (-3.00 and -2.26, respectively; LS mean difference, -0.741; *P*<0.001) as well as in improving morning predose iTNSS (-4.50 and -2.60, respectively; LS mean difference -1.898; *P*<0.001). In terms of overall response to therapy, 67% of patients receiving fluticasone furoate reported significant or moderate improvement, compared to 39% of patients given placebo (*P*<0.001). Overall RQLQ core decreased by 2.23 points in the fluticasone furoate group and by 1.53 points in the placebo group (difference of -0.7; *P*<0.001).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
			individual symptom scores, time to onset of action	
Gradman et al[25] Fluticasone furoate 110 µg QD vs placebo	DB, NI, PC, RCT, XO Prepubertal children (6 to 11 years of age) with a diagnosis of PAR or SAR for at least one year, and either a positive skin prick test or a positive test for the specific IgE to an appropriate seasonal or perennial allergen	N=58 2 weeks	Primary: Mean growth rate in lower-leg length Secondary: Adverse events	Primary: A prespecified cutoff of no more than -0.20 mm/week was determined to be “noninferior”. The treatment difference in adjusted mean lower-leg growth rate between fluticasone furoate and placebo was -0.016 mm/week (95% CI, -0.13 to 0.10) demonstrating noninferiority. Secondary: Reported adverse events were similar between the two groups.
Kaiser et al[26] Fluticasone furoate 110 µg QD vs placebo	DB, PC, PG, RCT Patients 12 years of age and older with SAR caused by ragweed pollen, with seasonal allergy symptoms during each of the past two fall allergy seasons; positive skin prick test response to ragweed allergen within 12 months prior to start of study; only	N=299 2 weeks	Primary: Mean change from baseline over the entire treatment period in daily rTNSS Secondary: Mean change from baseline over the entire treatment period in daily rTOSS, morning predose iTNSS, overall evaluation of response to therapy, HRQL based on RQLQ	Primary: Fluticasone furoate significantly reduced nasal symptoms compared to placebo, with a treatment difference of -1.473 (*P*<0.001). Secondary: An observed difference of -0.600 (*P*=0.004) favoring fluticasone furoate over placebo was recorded for the mean change from baseline in daily rTOSS over the entire treatment period. Fluticasone furoate demonstrated a significant reduction in morning predose iTNSS of -1.375 compared with placebo (*P*<0.001). A total of 73% of patients receiving fluticasone furoate compared to 52% of placebo-treated patients reported improvement in their overall evaluation of response to therapy (*P*<0.01); significant moderate improvement was noted in 42% of fluticasone furoate-treated patients and 21% of placebo-treated patients.

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
	moderate-to-severe nasal and ocular symptoms; during 2005 fall ragweed allergy season			Fluticasone furoate-treated patients reported significant improvements in the overall RQLQ score compared to patients in the placebo group (-0.606; *P*<0.001). Adverse events occurred in 21% of patients receiving fluticasone furoate and 12% of patients that received placebo. The most common side effect was headache (>3%), which was seen more often with fluticasone furoate than placebo; epistaxis was also commonly reported.
Nathan et al[27] Fluticasone furoate 110 µg QD vs placebo	DB, MC, PC, PG, RCT Patients 12 years of age and older with a diagnosis of PAR including a positive result to a skin prick test within 12 months of study entry or at study entry	N=455 4 weeks	Primary: Change from baseline in daily rTNSS Secondary: Change from baseline in AM predose iTNSS, AM and PM rTNSS, individual nasal symptoms, ocular symptoms, itching, QOL and response to therapy	Primary: The LS mean change from baseline during the treatment period in daily rTNSS was significantly greater in fluticasone furoate-treated patients compared to patients receiving placebo (treatment difference, -0.706; *P*=0.005). Secondary: The LS mean change from baseline in AM predose iTNSS during the entire treatment period was significantly greater in the fluticasone furoate treatment group compared to placebo (treatment difference, -0.705; *P=0.*006). Patients treated with fluticasone furoate experienced a significantly greater mean reduction in morning rTNSS (*P=0.*004) and evening rTNSS (*P=0.*011compared to patients randomized to placebo. The changes from baseline in AM and PM rTNSS scores for rhinorrhea, sneezing and nasal itching were significantly greater with fluticasone furoate treatment compared to placebo (*P*≤0.05 for all). There was no difference between treatments with regard to ocular symptoms. A significantly higher percentage of patients treated with fluticasone furoate reported treatment to be effective compared to patients receiving placebo (*P*=0.005).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Meltzer et al[28] Fluticasone furoate 110 µg QD vs fluticasone furoate 55 µg QD vs placebo	DB, MD, PC, PG, RCT Patients 2 to 11 years of age with symptoms of SAR in the previous allergy season with a positive skin prick test for a specific IgE within previous 12 months	N=554 2 weeks	Primary: Change from baseline in daily rTNSS Secondary: Change from baseline in AM predose iTNSS, response to therapy, adverse events, laboratory tests, nasal examinations, vital signs and ECG	Primary: The change from baseline during the treatment period in daily rTNSS was significantly greater in the fluticasone furoate 110 µg treatment group compared to placebo (-3.16 vs -2.54; *P*=0.025). Patients receiving the 55 µg dose of fluticasone furoate experienced a numerically greater reduction in daily rTNSS compare to placebo (-2.71 vs. -2.54), although this was not statistically significant (*P*=0.553). Secondary: The least square mean change in AM predose iTNSS was significantly greater for fluticasone furoate 110 µg compared to placebo (-2.80 vs -2.13; *P*=0.015), but not for the 55 µg fluticasone furoate dose (*P* value not reported). The overall response to therapy was significantly higher for the fluticasone furoate 110 µg treatment group compared with placebo (*P*< 0.001), but not for the fluticasone furoate 55 µg treatment group compared to placebo (*P*=0.083). The types of adverse events were similar among treatment groups; however the incidence was higher with the fluticasone 110 and 55 µg doses compared to placebo (30 vs 20%; P value not reported). There were no differences in laboratory tests or vital signs between the three treatment groups. The findings from nasal examinations and ECGs were similar between the treatment groups.
Maspero et al[29] Fluticasone furoate 110 µg QD vs fluticasone furoate 55 µg QD	DB, MC, PC, PG, RCT Pediatric patients 2 to 11 years of age with a six month or longer history PAR documented by a positive skin prick	N=558 12 weeks	Primary: Mean change from baseline in daily rTNSS over four weeks Secondary: Mean change from baseline in daily	Primary: Improvements in daily rTNSS over four weeks were not statistically significant compared to placebo for the fluticasone furoate 110 µg group (-0.452; *P*=0.073). Patients treated with fluticasone furoate 55 µg had statistically significant improvements in daily rTNSS compared to placebo (-0.754; *P*=0.003). Secondary: Both fluticasone furoate 55 (-0.751) and 110 µg (-0.651) showed

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs placebo	test against an appropriate perennial allergen		iTNSS, overall response to therapy, safety	significant improvements from baseline in daily iTNSS compared to placebo (*P*=0.002 and *P*=0.009). Treatment differences, determined by overall response to therapy, were not significant for patients in the fluticasone furoate 110 µg group compared to placebo (*P*=0.414) but were significant for the fluticasone furoate 55 µg group (*P*=0.024). Treatment with both doses of fluticasone furoate was well tolerated over the 12 week period. Nasal examinations were similar across all three treatment groups and ophthalmic examinations revealed no differences between groups in terms of mean change from baseline intraocular pressure in each eye. Treatment differences for mean change from baseline in 24 hour urinary cortisol excretion from placebo at either dose of fluticasone furoate were not statistically significant (*P* value not reported).
Martin et al[30] Fluticasone furoate 55 µg QD vs fluticasone furoate 110 µg QD vs fluticasone furoate 220 µg QD vs fluticasone furoate 440 µg QD	DB, PC, PG, RCT Patients 12 years of age and older with a diagnosis of SAR during the past two mountain cedar allergy seasons and a positive skin test to mountain cedar allergy	N=642 14 days	Primary: Mean change from baseline in daily rTNSS Secondary: Mean change from baseline in morning predose iTNSS, mean change from baseline in daily rTOSS and iTOSS, mean change from baseline in morning and evening rTNSS and iTNSS and overall response to therapy	Primary: Fluticasone furoate 55, 110, 220 and 440 µg QD demonstrated statistically significant improvements with respect to the mean change from baseline in daily rTNSS compared to placebo (*P*<0.001 for all measures). Secondary: Fluticasone furoate was significantly more effective than placebo for mean changes from baseline in morning predose iTNSS (*P*<0.001 each dose vs placebo), daily rTOSS (*P*≤0.013 each dose vs placebo), and iTOSS (*P*≤0.019 for fluticasone furoate 110, 220 and 440 µg/day vs placebo). Over the entire treatment period, all doses of fluticasone furoate demonstrated significantly greater efficacy compared to placebo with regards to morning and evening rTNSS and iTNSS scores (*P*<0.001 for all measures). At the end of the treatment period, patients treated with fluticasone furoate rated their overall response to therapy significantly better than

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs placebo				those treated with placebo (*P*<0.001).
Rosenblut et al[31] Fluticasone furoate 110 µg QD vs placebo	DB, MC, PC, PG, RCT Patients 12 years of age and older with a two year or longer medical history and past treatment of PAR and a positive skin-prick test to an appropriate allergen either within the last 12 months prior to or at screening	N= 806 12 months	Primary: Safety and tolerability based on adverse event data graded by severity (mild, moderate, or severe) as well as through the use of 24-hour urine samples, ECG, other laboratory measures and eye examinations Secondary: Not reported	Primary: Adverse events occurred in 77% of fluticasone furoate-treated patients and 71% of patients receiving placebo, where most were mild to moderate in intensity. The most frequently reported adverse events were headache and nasopharyngitis. Epistaxis was more frequently reported with patients given fluticasone furoate. There was no evidence of clinically relevant systemic corticosteroid exposure or impairment of HPA-axis function. Fluticasone furoate-treated patients had similar 24-hour urine cortisol results to those receiving placebo. There were no clinically meaningful differences between the groups in terms of other safety assessments, including mean changes in ophthalmic parameters. Secondary: Not reported
Vasar et al[32] Fluticasone furoate 110 µg QD vs placebo	DB, PC, PG, RCT Patients 12 years of age and older with a history of PAR for two years or longer and a positive skin-prick test to an appropriate perennial allergen	N=302 6 weeks	Primary: Mean change from baseline in rTNSS Secondary: Mean change from baseline in morning predose iTNSS, daily rTNSS, daily PNIF, and RQLQ scores, overall response to therapy and safety	Primary: The mean change from baseline in rTNSS was significantly greater in the fluticasone furoate group compared to placebo (-3.95 vs -2.69; *P*<0.001). Secondary: The mean change from baseline in morning predose iTNSS was significantly greater in fluticasone furoate patients compared to placebo (-3.82 vs -2.36; *P*<0.001). Treatment with fluticasone furoate demonstrated significantly greater efficacy compared to placebo in terms of improvements in daily iTNSS (*P*=0.004), PNIF (*P*=0.004) and overall RQLQ scores (*P*<0.001).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				Thirty seven percent of patients treated with fluticasone furoate rated their overall response to therapy as "significantly improved" compared to 14% of patients treated with placebo (*P*<0.001). Treatment was well tolerated over the six week period.
Prenner et al[33] Mometasone 2 sprays in each nostril QD vs placebo	DB, MC, PC, PG, RCT Patients 12 years of age and older with a history to SAR for two years or more, a positive skin prick test response and clinically symptomatic at screening	N=429 15 days	Primary: Change from baseline in iTOSS and iTNSS Secondary: Change from baseline in daily rTOSS and rTNSS, instantaneous nasal congestions scores, RQLQ, change from baseline in instantaneous and reflective individual symptom scores, subject and investigator evaluations of overall condition and therapeutic response	Primary: A significant reduction in iTOSS was observed in the mometasone group compared to placebo (*P*=0.026). A reduction in iTNSS was observed in the mometasone group compared to placebo (*P*<0.001). Secondary: A significant reduction in the LS mean change from baseline in rTOSS was observed in the mometasone group compared to placebo (*P*=0.005). A significant reduction in the LS mean change from baseline in rTNSS was observed in the mometasone group compared to placebo (*P*<0.001). A significant improvement in instantaneous ocular symptoms of itching/burning and watering/tearing was observed in the mometasone group compared to placebo (*P*<0.05). No significant difference was observed in the instantaneous eye redness score. A significant improvement in individual reflective ocular symptom scores was observed in the mometasone group compared to placebo (*P*<0.05). A significant improvement in all individual instantaneous and reflective nasal symptoms scores was observed in the mometasone group compared to placebo (*P*<0.05).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				Greater improvements in overall SAR condition from baseline were observed in the mometasone group compared to placebo as rated by investigators and subjects (*P*<0.001 for both). Greater improvements in the RQLQ were observed in the mometasone group compared to placebo (*P*<0.001). The mometasone group showed a significantly greater response to therapy compared to the placebo group as rated by both investigators and subjects (*P*<0.001).
Baena-Cagnani et al[34] Mometasone 1 spray in each nostril QD vs placebo	DB, MC, PC, PG, RCT Patients 3 to 11 years of age with at least a one year history of PAR requiring over-the-counter or prescription treatment and a positive skin prick test to one clinically significant perennial allergen	N=381 4 week efficacy phase followed by 6 month open-label safety period	Primary: Change from baseline to day 15 in physician assessed TNSS Secondary: Change from baseline to day 15 in subject assessed TNSS, TSS, TNNSS, individual symptom scores and condition of PAR between baseline and endpoint	Primary: Patients randomized to mometasone experienced a significantly greater reduction in physician-assessed change in TNSS at day 15 compared to patients receiving placebo (-2.8 [-39%] vs -2.2 [-32%]; *P*=0.02). The changes in TNSS were also significant in favor of mometasone at days eight and 29 (*P*≤0.02 for both). Secondary: A significantly greater improvement in subject-assessed TNSS scores at day 15 occurred with mometasone compared to placebo (-1.7 [-28%] vs -1.1 [-18%]; *P*≤0.01). Mometasone treatment was associated with lower subject-assessed TSS scores at day 15 compared to placebo -2.1 [-27%] vs -1.4 [-16%]; *P*<0.001). At day 15, subject assessed TNNSS scores were not significantly different between the treatment groups. Subject evaluations of all individual nasal symptom scores showed significantly greater improvement with mometasone compared to placebo over the first 15 days (*P*≤0.03 for all). Physician evaluation of the patients' condition favored mometasone treatment over placebo at both day 15 (*P*<0.01) and 29 (*P*=0.02).
Khanna et al[35]	SB, XO	N=114	Primary:	Primary:

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Beclomethasone, dose not specified vs budesonide, dose not specified vs fluticasone propionate, does not specified vs mometasone, dose not specified	Patients with allergic rhinitis	Duration not specified	Sensory perceptions and patient reference Secondary: Not reported	Significantly more patients preferred mometasone and reported less irritation, odor and aftertaste (*P* values not reported). Fluticasone propionate was reported by patients as having a significantly higher odor strength and amount of irritation (*P* values not reported). Eighty percent of the patients predicted better compliance with their preferred drug. Secondary: Not reported
Svendsen et al[36] Beclomethasone, dose not specified vs flunisolide, dose not specified	DB, RCT, XO Patients with perennial rhinitis	N=23 8 weeks	Primary: Rhinitis symptoms and patient preference Secondary: Not reported	Primary: There were no statistically significant differences in rhinitis symptoms or patient preference between treatments (*P* value not reported). Secondary: Not reported
Welsh et al[37] Beclomethasone 336 µg daily, administered as 2 sprays in each nostril BID vs	PC, RCT Patients 12 to 50 years of age, with at least a two year history of SAR and positive skin test to crude short	N=120 8 weeks	Primary: Symptomatic relief Secondary: Adverse events	Primary: Beclomethasone, flunisolide and cromolyn significantly reduced the use of supplemental antihistamines or decongestants and hay fever symptoms such as sneezing, nasal symptoms, eye symptoms, itchy nose, and throat symptoms compared with placebo (*P*<0.001). Beclomethasone and flunisolide significantly reduced hay fever symptoms compared to cromolyn (*P*<0.001).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
flunisolide 200 µg daily, administered as 2 sprays in each nostril BID vs cromolyn 41.6 mg daily, administered as 1 spray in each nostril QID vs placebo	ragweed extract			There were no statistically significant differences between beclomethasone and flunisolide in relief of hay fever symptoms (*P* value not reported). Secondary: There was significantly more nasal burning with flunisolide than the other treatments (*P*<0.001).
Al-Mohaimeid[38] Budesonide 200 µg BID vs beclomethasone 200 µg BID	RCT, SB Patients 18 to 70 years of age, with PAR	N=120 3 weeks	Primary: Nasal symptoms Secondary: Not reported	Primary: There were significantly fewer reports of sneezing with budesonide than beclomethasone (*P*=0.04). No statistically significant differences in symptoms of blocked nose, runny nose, itchy nose, runny eyes and sore eyes were reported (*P*>0.05). After three weeks of treatment, more patients reported being free of symptoms with budesonide compared to beclomethasone (38 vs 27%; no *P* value reported). More patients reported the treatment as noticeably, very, or totally effective with budesonide than with beclomethasone (72 vs 58%; *P* value not reported). Secondary: Not reported
McArthur[39]	DB, RCT	N=88	Primary: Nasal and non-nasal	Primary: Budesonide treatment resulted in significantly lower scores for runny

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Budesonide 200 µg BID vs beclomethasone 200 µg BID	Adults with SAR	3 weeks	symptom score Secondary: Adverse events	nose, itchy nose and sneezing compared with beclomethasone at all time points (*P*<0.05), but the greatest difference occurred at the end of the treatment period. There was no statistically significant difference between treatment groups in scores for nasal blockage, runny eyes, and sore eyes (*P* value not reported). Secondary: Adverse events for both treatments were mild and transient.
Vanzieleghem et al[40] Budesonide as needed, up to 2 sprays of 50 µg/spray in each nostril QID vs beclomethasone as needed, up to 2 sprays of 50 µg/spray in each nostril QID	DB, DD, RCT Patients with SAR during the ragweed-pollen season	N=61 7 weeks	Primary: Nasal symptoms, use of chlorpheniramine as rescue medication Secondary: Adverse events	Primary: Less budesonide was administered by the subjects than beclomethasone to maintain good control of nasal symptoms (*P*=0.016). No statistically significant difference was observed between treatment groups in the amount of oral chlorpheniramine used as rescue medication (*P*=NS). Secondary: Reported adverse events with both treatments were mild and transient.
Andersson et al[41] Budesonide 200 or 400 µg QD vs fluticasone propionate 200 µg QD vs placebo	MC, PC, PG, RCT Patients with PAR	N=98 6 weeks	Primary: Rhinitis symptoms, use of terfenadine as rescue medication Secondary: Safety as assessed by rhinoscopy, urine cortisol, adverse events	Primary: There were no significant differences in nasal symptoms or eye symptoms between active treatment groups (*P* value not reported). All active treatments reduced the use of terfenadine when compared with baseline, but this was significant with budesonide only (*P*<0.05). Secondary: Reported adverse events were few and minor. No significant differences in adverse events or 24-hour cortisol levels were reported between treatment groups (*P* value not reported).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Day et al[42] Budesonide 256 µg QD vs fluticasone propionate 200 µg QD	DB, MC, PC, PG, RCT Patients 18 years of age and older with at least a one year history of PAR and positive skin test to one or more perennial allergens	N=273 6 weeks	Primary: Nasal symptoms, patients' overall evaluation of efficacy, and use of rescue medication Secondary: Adverse events	Primary: Both treatments resulted in significantly greater improvement in combined nasal symptom scores, runny nose and sneezing from baseline compared with placebo (*P*≤0.0012). Budesonide showed greater improvement in combined nasal symptom scores (*P*=0.031) and nasal blockage (*P* value not reported) than fluticasone propionate, but no statistically significant differences in runny nose or sneezing symptoms were detected (*P* value not reported). Significant improvements in nasal symptoms were seen at 36 hours with budesonide and 60 hours with fluticasone propionate (*P* value not reported). At six weeks of treatment, there were no statistically significant differences in patients' overall evaluation of efficacy (*P*=0.44) or use of antihistamines as rescue medication (no *P* values reported) between treatment groups. Secondary: The rates of reported adverse events were 46% with budesonide, 37% with fluticasone propionate, and 36% with placebo (no *P* values reported). No signs of fungal infection were detected in the study population.
Shah et al[43] Study 1: Budesonide 32 µg in each nostril for one dose vs fluticasone propionate 100 µg in each nostril for one dose	MC, RCT, SB, XO Patients 18 years of age and older, with a one year or longer history of allergic rhinitis and experiencing mild to moderate symptoms	N=181 (Study 1) N=190 (Study 2) 1 day	Primary: Sensory Perceptions Questionnaire and patients' product preference Secondary: Adverse events	Primary: In study 1, significantly fewer patients perceived the scent (*P*<0.001), taste (*P*<0.001), aftertaste (*P*<0.001), throat rundown (*P*<0.001), and nose run out (*P*<0.019) with budesonide than with fluticasone propionate. In study 2, significantly fewer patients detected an altered scent or taste with budesonide than with fluticasone propionate (*P*<0.001). There were no significant differences between budesonide and fluticasone propionate in aftertaste, throat rundown, and nose run out. More patients perceived the spray in the throat as less wet (*P*<0.004

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Study 2: budesonide 32 µg in each nostril for one dose vs fluticasone propionate 50 µg in each nostril for one dose				for study 1 and *P*<0.002 for study 2) and therefore preferred the feel of the spray in the throat (*P*<0.001 for both studies) of budesonide to that of fluticasone propionate. More patients perceived the spray in the nose as less wet (*P*<0.001 for both studies) and therefore preferred the feel of the spray in the nose (*P*<0.001 for both studies) of budesonide to fluticasone propionate. Significantly more patients perceived a less forceful spray with budesonide and therefore preferred budesonide to fluticasone propionate (*P*<0.001). Overall, significantly more patients preferred budesonide to fluticasone propionate (*P*=0.02). Secondary: Budesonide and fluticasone propionate were both well tolerated.
Stern et al[44] Budesonide 128 µg or 256 µg QD vs fluticasone propionate 200 µg QD vs placebo	MC, PC, PG, RCT Patients 18 to 72 years of age, with at least a two-year history of allergic rhinitis	N=635 4 to 6 weeks	Primary: Nasal and eye symptoms Secondary: Adverse events	Primary: Budesonide and fluticasone propionate resulted in significant improvements in individual nasal symptoms such as blocked nose, runny nose, sneezing (*P*<0.001), combined nasal symptoms (*P*<0.001), eye symptoms (*P* value not reported) and overall substantial or total control of symptoms (*P*<0.001) compared to placebo. Budesonide produced significant reduction in sneezing compared with fluticasone propionate (*P*=0.04). There were no other significant differences in individual nasal symptoms, combined nasal symptoms, eye symptoms, or overall substantial or total control of symptoms between treatment groups (*P* values not reported). Secondary: Budesonide and fluticasone propionate were well tolerated, with reported adverse events mild to moderate in severity.
Naclerio et al[45]	PG, RCT	N=20	Primary:	Primary:

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Budesonide 32 µg in each nostril QD vs mometasone 100 µg in each nostril QD	Patients >18 years of age with PAR, who were symptomatic on the majority of days of each year and had a positive skin test to dust mites	2 weeks	Symptomatic relief and quality of life as assessed by the RQLQ and nasal clearance Secondary: Not reported	The RQLQ scores showed that both budesonide and mometasone resulted in a significant improvement in quality of life compared with baseline (*P* value not reported). There were no significant differences between treatment groups for any of the individual domains in the RQLQ (*P* value not reported). Data on nasal clearance could not be interpreted by the authors. Secondary: Not reported
Aasand et al[46] Flunisolide 50 µg in each nostril BID vs beclomethasone 50 µg in each nostril QID	MC, PG, SB Patients with at least a two-year history of seasonal rhinitis	N=47 4 weeks	Primary: Nasal symptoms Secondary: Adverse events	Primary: Flunisolide and beclomethasone improved nasal rhinitis symptoms (88% of patients showed improvement with flunisolide vs 91% with beclomethasone; *P* value not reported). No statistical differences were observed between treatment groups (*P* value not reported). Secondary: The only reported adverse event with both medications was mild stinging of transient duration.
Langrick[47] Flunisolide 200 µg daily, administered as 2 sprays in each nostril BID vs beclomethasone 400 µg daily, administered as 2 sprays in each nostril BID	PG, RCT, SB Patients 18 to 60 years of age, with a history of moderate to severe hay fever	N=69 7 weeks	Primary: Signs and symptoms of hay fever, severity of symptoms, and physicians' and patients' evaluation of overall effect of treatment Secondary: Adverse events	Primary: There were no significant differences between treatment groups in severity of symptoms, overall treatment effect, or patients' self-assessment of symptoms such as sneezing, runny nose and blocked nose (*P* value not reported). Secondary: One patient in the flunisolide group reported a dry throat of moderate severity. One patient in the beclomethasone group reported a mild tickling sensation inside the nose.
McAllen et al[48]	SB, XO	N=34	Primary: Rhinitis symptoms	Primary: Treatment with flunisolide and beclomethasone significantly reduced

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Flunisolide 50 µg in each nostril BID vs beclomethasone 50 µg in each nostril QID	Patients 19 to 58 years of age who had perennial rhinitis with or without seasonal exacerbations and had moderate to severe symptoms of six months to 50 years in duration	8 weeks	Secondary: Adverse events and *Candida* growth	sneezing, stuffiness, runny nose, nose-blowing and interference with routine life when compared with baseline (*P* value not reported). There were no statistical differences between the flunisolide and beclomethasone treatment groups in nasal symptoms, physicians' and patients' preference, and interference with routine life (*P* value not reported). Secondary: Neither treatment resulted in *Candida* growth. Reported side effects were minor and were mostly nasal irritation or dryness.
Sahay et al[49] Flunisolide 50 µg in each nostril BID vs beclomethasone 50 µg in each nostril QID	OL, PG Patients with PAR, with or without SAR	N=56 4 weeks	Primary: Symptom relief Secondary: Detection of *Candida* growths and safety	Primary: Flunisolide and beclomethasone resulted in significant reductions in sneezing, stuffiness, runny nose, nose blowing, postnasal drip, epistaxis and interference by symptoms with routine life or sleep when compared to baseline (*P*<0.01 for all). There were no statistically significant differences in control of symptoms between the two treatment groups (*P* value not reported). Secondary: There were no signs of adrenal suppression or *Candida* growths in either group. There were four side effects in the flunisolide group and five in the beclomethasone group that were considered to be probably drug related (*P* value not reported).
Sipila et al[50] Flunisolide 50 µg in each nostril BID vs	OL, PG Patients with allergic rhinitis and seasonal symptoms for at least two years	N=45 4 weeks	Primary: Daily symptoms and severity of nasal symptoms Secondary: Adverse events	Primary: There were no significant differences between the treatment groups in the change from baseline in daily symptoms such as runny nose, stuffiness, sneezing, and eye symptoms (*P* value not reported). Improvement in the severity of nasal symptoms compared with baseline was similar in both treatment groups (*P* value not reported).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
beclomethasone 50 µg in each nostril QID				Secondary: The reported side effects were mild and primarily consisted of local irritation.
Meltzer et al[51] Fluticasone furoate 110 µg QD followed by fluticasone propionate 220 µg QD vs fluticasone propionate 200 µg QD followed by fluticasone furoate 110 µg QD vs fluticasone furoate placebo QD followed by fluticasone propionate placebo QD vs fluticasone propionate placebo QD followed by fluticasone furoate placebo QD	DB, PC, RCT, XO Patients 18 years of age and older with SAR and nasal symptoms during the two previous fall allergy seasons and a positive skin test result and exposure to fall allergens	N=360 21 days	Primary: Patient preference at the end of the second XO period based on scent or odor Secondary: Patient preference at the end of the second XO period based on leaking out of the nose and down the throat, ease of use, and gentleness of mist, delivery of consistent dose/use, comfort of nose tip, spray delivery method, aftertaste and TNSS	Primary: Twice as many patients preferred fluticasone furoate compared to fluticasone propionate based on scent or odor (P<0.001). Fifteen percent of patients had no preference for either product based on scent or odor. Secondary: Significantly more patients preferred fluticasone furoate compared to fluticasone propionate based on medication leaking out of the nose and down the throat, gentleness of the mist, and less aftertaste (P<0.001). No statistically significant differences were observed between products in ease of use, consistency of medication dose delivered, delivery method or device comfort. TNSS were similar between treatment groups. Fluticasone furoate and fluticasone propionate significantly reduced TNSS compared to their respective placebo ($P\leq$0.01). The proportion of patients with any adverse event was similar between treatments.
Meltzer et al[52] Fluticasone furoate 2 sprays in each nostril	DB, MC, RCT, SD, XO Patients 18 years	N=127 1 day	Primary: Overall patient preference for fluticasone furoate or	Primary: Significantly more patients favored fluticasone furoate compared to fluticasone propionate (P=0.003).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
for one dose followed by fluticasone propionate 2 sprays in each nostril for one dose vs fluticasone propionate 2 sprays in each nostril for one dose followed by fluticasone furoate 2 sprays in each nostril for one dose A ten minute washout period occurred between XO treatments.	of age and older with a diagnosis of allergic rhinitis		fluticasone propionate Secondary: Patient preference for individual sensory attributes and their ratings	Secondary: Significantly more patients favored fluticasone furoate compared to fluticasone propionate based on odor, taste, aftertaste drip down the throat and nose runoff ($P \leq 0.037$). No significant differences were observed between groups with respect to whether the medication felt soothing, caused nasal irritation or caused sneezing.
Haye et al[53] Fluticasone propionate 200 µg BID vs beclomethasone 200 µg BID	DB, MC, PG, RCT Patients 16 years of age and older with perennial rhinitis	N=251 1 year	Primary: Rhinitis symptoms Secondary: Safety	Primary: Fluticasone propionate treatment resulted in significantly less nasal blockage (P=0.002), nasal discharge (P=0.002) and eye watering/irritation (P=0.048) compared to beclomethasone. No significant differences were observed in the amount of sneezing (P=0.114) or nasal itching (P=0.052) between treatment groups. Secondary: There were no significant differences in nasal itching (P=0.052), sneezing (P value not reported), nasal examination by rhinoscopy, hematologic, biochemical, and urinary parameters, plasma cortisol level or adverse events (P values not reported) between treatment groups.
LaForce et al[54]	DB, MC, PC, PG, RCT	N=238	Primary: Nasal symptoms	Primary: Fluticasone propionate reduced patient-rated nasal symptom scores

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Fluticasone propionate 100 µg BID or 200 µg QD vs beclomethasone 168 µg BID vs placebo	Patients 12 years of age and older, with at least a two-year history of SAR, who have positive skin test to at least one spring allergen and moderate to severe symptoms	4 weeks	Secondary: Adverse events	significantly more than beclomethasone (P<0.05) and placebo (P<0.01) at all time points measured. There were no statistically significant differences in clinician-rated nasal symptom scores between treatment groups (P=NS). Secondary: There were no significant differences in adverse events between treatment groups (P value not reported).
Ratner et al[55] Fluticasone propionate 200 µg QD vs beclomethasone 168 µg BID vs placebo	DB, MC, PC, PG, RCT Adult patients with at least a two-year history of SAR, who have moderate to severe symptoms and positive skin test to mountain cedar	N=313 2 weeks	Primary: Nasal symptoms, overall response to treatment, and use of rescue medication (chlorpheniramine) Secondary: Adverse events	Primary: Compared with placebo, significant improvements in nasal symptoms and overall response to treatment were seen with fluticasone propionate and beclomethasone as evaluated by the clinicians and patients (P<0.05 for all). There were no statistically significant differences between treatment groups in nasal symptoms as rated by the clinicians or the patients or overall response to treatment (P value not reported). When compared with placebo, there was a significant reduction in the use of rescue medication with fluticasone propionate and beclomethasone (P<0.05). There was no statistically significant difference between treatment groups in the amount of rescue medication used (P value not reported). Secondary: No clinically significant differences in any of the safety variables between treatment groups were reported.
Van As et al[56] Fluticasone propionate 100 µg BID or 200 µg QD	DB, MC, PC, PG, RCT Patients 12 to 71 years of age, with	N=466 6 months	Primary: Nasal symptoms and use of antihistamine as rescue medication	Primary: Fluticasone propionate and beclomethasone reduced nasal obstruction, rhinorrhea, sneezing, nasal itching and nasal eosinophilia (P value not reported).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs beclomethasone 168 µg BID vs placebo	PAR and moderate to severe symptoms, nasal eosinophils, and positive skin test to a perennial allergen		Secondary: Adverse events	There were no significant differences between active treatment groups in nasal symptoms, number of patients who used rescue medication, amount of rescue medication consumed or incidences of adverse events (*P* value not reported). Secondary: No evidence of systemic effects with drug treatment was reported.
Bachert et al[57] Fluticasone propionate 200 µg QD vs triamcinolone 220 µg QD vs placebo	DB, PC, RCT, XO Healthy volunteers 18 to 65 years of age	N=23 12 days	Primary: Suppression of the HPA axis as measured by 12 hour overnight urinary cortisol excretion and serum cortisol concentrations Secondary: Adverse events	Primary: Overnight urinary cortisol concentrations showed that there was no significant difference in HPA axis suppression with fluticasone propionate (*P*=0.609) or triamcinolone (*P*=0.194) compared to placebo. Neither fluticasone propionate (*P*=0.999) nor triamcinolone (*P*=0.521) showed a significant effect on the HPA axis activity when compared to placebo, as assessed by the mean peak serum cortisol concentrations before and after ACTH stimulation. Secondary: Both medications were well tolerated. There were no significant differences in the number of subjects who experienced adverse events between treatment groups (one with fluticasone propionate, two with triamcinolone, three with placebo; *P* value not reported).
Drouin et al[58] Mometasone 100 µg in each nostril QD vs beclomethasone 100 µg in each nostril BID vs	DB, DD, MC, PC, PG, RCT Patients 12 years of age and older, who are allergic to at least one perennial allergen, with adequate symptomatology	N=427 12 weeks	Primary: Change from baseline in total morning plus evening diary nasal symptom score over the first 15 days of treatment Secondary: Total diary nasal symptom scores	Primary: When compared to placebo, both mometasone and beclomethasone produced significantly greater improvements in the total morning plus evening diary nasal symptom scores over the first 15 days of treatment (*P*≤0.01). The difference in reduction from baseline in nasal symptom scores between mometasone and beclomethasone was not significant at any time point (*P*≥0.32). Secondary:

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
placebo			averaged over 15-day intervals beyond day 15, composite total and individual diary symptom scores, physician evaluation of response to therapy, and adverse events	Physician evaluations of nasal symptoms for mometasone and beclomethasone were not statistically different from each other at any time point (*P* value not reported). The rates of adverse events were similar for all groups (43% for mometasone, 42% for beclomethasone and 36% for placebo; *P* value not reported).
Graft et al[59] Mometasone 100 µg in each nostril QD vs beclomethasone 84 µg in each nostril BID vs placebo	DB, MC, PC, PG, RCT Patients 12 years of age and older who have at least a two-year history of moderate to severe SAR and a positive skin test response to ragweed	N=349 8 weeks	Primary: Severity score of nasal and non-nasal symptoms Secondary: Adverse events	Primary: Both treatments resulted in a significantly higher percentage of days with minimal symptoms, longer duration to the first occurrence of a non-minimal symptom day and TNSS compared with placebo (*P*≤0.01 for all). There was no statistically significant difference in the percentage of days with minimal symptoms between treatment groups (*P* value not reported). Nasal symptom scores for the treatment period prior to the allergy season onset were significantly lower with mometasone than beclomethasone (*P*=0.05). Secondary: The percentage of patients experiencing at least one adverse event that was considered possibly related to treatment was: 16% of the mometasone group, 14% of the beclomethasone group and 19% of the placebo group (*P* value not reported). The adverse events were generally mild to moderate and of short duration.
Hebert et al[60] Mometasone 100 or 200 µg QD, administered as 2 sprays of 25 or 50 µg/spray in each	DB, DD, MC, PC, PG, RCT Patients 18 years of age and older, with moderate to severe SAR for at	N=501 4 weeks	Primary: Nasal symptom score, physicians' and patients' evaluation of response to therapy, and use of loratadine	Primary: Nasal symptoms (*P*≤0.01) and use of rescue medication (*P*≤0.05) were significantly improved in all three treatment groups compared to placebo. There were no significant differences between treatment groups in nasal symptom score, physicians' evaluation of nasal symptoms,

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
nostril QD vs beclomethasone 100 µg in each nostril BID vs placebo	least two years, who have a positive skin test to at least one tree and/or grass aeroallergen		as rescue medication Secondary: Adverse events	overall condition, and response to treatment, or use of rescue medication (*P* value not reported). Secondary: The rate of adverse events were similar in all groups (25% with mometasone 100 µg, 26% with mometasone 200 µg, 30% with beclomethasone, 28% with placebo; *P* value not reported).
Mandl et al[61] Mometasone 100 µg in each nostril QD vs fluticasone propionate 100 µg in each nostril QD vs placebo	DB, DD, PC, PG, RCT Patients 12 to 77 years of age, who are allergic to at least one perennial allergen, and have moderate to severe symptomatology	N=550 12 weeks	Primary: Nasal symptom score Secondary: Physicians' evaluation of nasal symptoms and response to therapy and adverse events	Primary: Both mometasone and fluticasone propionate produced significantly greater improvements in nasal symptoms than placebo (*P*<0.01). The difference in reduction of nasal symptom score between mometasone and fluticasone propionate was not significant at any time point (-37 vs -39%, respectively; *P*≥0.43). Secondary: Physicians' evaluation of nasal symptoms and response to therapy were similar for mometasone and fluticasone propionate (*P* value not reported). The rates of adverse events were similar for all groups (33% for mometasone, 38% for fluticasone propionate and 37% for placebo; *P* value not reported).
Meltzer et al[62] Mometasone, dose not specified vs fluticasone propionate 200 µg	DB, RCT, XO Patients with allergic rhinitis	N=100 Duration not specified	Primary: Individual product sensory attributes and overall sensory preference Secondary: Not reported	Primary: Significantly more patients preferred mometasone to fluticasone propionate for its scent (*P*=0.0005), immediate taste (*P*=0.005), aftertaste (*P*=0.005) and overall (54 vs 33%; *P*=0.03). Patients rated mometasone as significantly better than fluticasone propionate in individual sensory attributes, which included fewer perceived scent/odor (*P*<0.001), taste (*P*=0.002) and aftertaste (*P*=0.007).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				Patients reported significantly larger percentage of expected compliance with mometasone than fluticasone propionate (47 vs 25%; *P*=0.03). Secondary: Not reported
Lumry et al[63] Triamcinolone 220 µg QD vs beclomethasone 168 µg BID	MC, PG, RCT, SB Patients at 18 years of age and older with at least a two-year history of SAR to ragweed pollen	N=152 3 weeks	Primary: Nasal symptoms, eye symptoms, HRQL, and patient preference for sensory attributes Secondary: Adverse events	Primary: Significant improvements from baseline in rhinitis related-nasal and eye symptoms were seen with triamcinolone and beclomethasone (*P* value not reported). There were no significant differences in nasal stuffiness, nasal discharge, nasal index, nasal itching, total eye symptoms, patients' or physicians' overall assessment of efficacy or HRQL between the treatment groups (*P* value not reported). Patients rated the taste and odor of triamcinolone as significantly better than beclomethasone (*P*≤0.05). Otherwise, there were no statistically significant differences between treatment groups in the other sensory attributes such as medication running down throat, medication running out of nose, medication induced sneezing, stinging/burning sensation, nose bleed, and blood in mucus (*P*>0.05). Secondary: The rates of reported adverse events were comparable between treatment groups (34.7% with triamcinolone vs 35.1% with beclomethasone; *P* value not reported).
Winder et al[64] Triamcinolone 220 µg QD vs beclomethasone 84 µg BID	MC, PG, RCT, SB Patients 18 to 64 years of age, with at least a two-year history of PAR who have positive skin tests to indoor allergens and nasal	N=169 4 weeks	Primary: Rhinitis symptoms and global evaluations of treatment by patients and physicians Secondary: Adverse events	Primary: No statistically significant differences were found in rhinorrhea, congestion, sneezing, sum of primary symptom scores or physicians' global evaluations between treatment groups (*P* value not reported). Patients' global evaluation of treatment with triamcinolone was significantly higher than with beclomethasone (*P*<0.05). Secondary:

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
	eosinophilia or basophilia			There were no statistically significant differences between treatments in burning/stinging, nasal dryness, nasal bleeding, bloody mucus, nasal congestion, throat discomfort and bad taste (*P*=NS). There was significantly more medication-induced sneezing with triamcinolone compared to beclomethasone (*P*=0.024). There was significantly more medication runoff from the nose and throat with beclomethasone than triamcinolone (*P*<0.05).
Bachert et al[65] Triamcinolone 110 µg in each nostril QD vs fluticasone propionate 100 µg in each nostril QD vs mometasone 100 µg in each nostril QD	DB, MC, RCT, XO Patients 18 years of age or older with at least a two-year history of allergic rhinitis	N=95 1 day	Primary: Sensory perceptions, patient preferences, and likelihood of compliance Secondary: Not reported	Primary: Overall, more patients preferred triamcinolone to fluticasone propionate (*P*≤0.05) and mometasone (*P*≤0.001). Patients preferred the odor, sensation of greater moisture, less aftertaste, and less irritation of triamcinolone to that of fluticasone propionate and mometasone (*P*<0.05 for all). Triamcinolone was preferred more than mometasone for the taste, comfort and less irritation (*P*<0.05 for all). Fluticasone propionate was also preferred more than mometasone in terms of taste, comfort and amount of irritation (*P*≤0.05). There were no significant differences between fluticasone propionate and mometasone in aftertaste and amount of irritation (*P* value not reported). Patients reported a higher likelihood of compliance with triamcinolone (67.4%) than with fluticasone propionate (54.7%) and mometasone (49.5%); *P* value not reported. Secondary: Not reported
Gross et al[66] Triamcinolone 110 µg	AC, PG, RCT, SB Patients 12 to 70	N=352 3 weeks	Primary: Nasal symptoms, effects on HRQL as	Primary: No statistically significant differences were reported between the treatment groups in daily TNSS (*P*=0.332), individual symptom

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
in each nostril QD vs fluticasone propionate 100 µg in each nostril QD	years of age, with fall SAR and positive skin test to ragweed		measured by RQLQ, adverse events Secondary: Not reported	scores (*P* value not reported), treatment-related side effects (*P* value not reported), overall HRQL scores (*P*=0.4) or overall RQLQ scores (*P* value not reported). Secondary: Not reported
Small et al[67] Triamcinolone 110 µg in each nostril QD vs fluticasone propionate 100 µg in each nostril QD	MC, PG, RCT, SB Patients 12 to 70 years of age with spring pollen allergic rhinitis for at least two years, who had at least two nasal symptoms (rhinorrhea, congestion, sneezing, and itching) at baseline, and who had a Rhinitis Index Score of at least 24 out of 48	N=233 21 days	Primary: Rhinitis Index Score and individual symptom score Secondary: Physicians' and patients' global evaluations, patients' acceptance of the study medications, and safety	Primary: There were no significant differences between treatment groups in the change from baseline in Rhinitis Index Score (*P*=0.23) or individual symptoms, such as congestion (*P*=0.58), rhinorrhea (*P*=0.08), sneezing (*P*=0.51) and nasal itching (*P*=0.64). Secondary: There were no statistically significant differences between treatment groups in physicians' and patients' global evaluations (*P* value not reported). Fluticasone propionate was rated as significantly more intolerable than triamcinolone with respect to medication "running down the throat" and "medication running out of nose" (*P*<0.01). Triamcinolone was rated as significantly more intolerable than fluticasone propionate with respect to "medication causing dry nostril" and "medication causing stuffed-up nose" (*P*<0.01). Adverse events were experienced by 26% of the patients receiving triamcinolone and 22% of the patients receiving fluticasone propionate (*P* value not reported).
Berger et al[68] Triamcinolone 110 µg in each nostril QD vs fluticasone propionate	AC, MC, PG, SB Patients 12 to 70 years of age with seasonal allergic rhinitis for at least two years and a positive	N=295 21 days	Primary: Mean TNSS Secondary: Mean individual symptom scores, dropout rate due to insufficient	Primary: Both triamcinolone and fluticasone propionate were effective at significantly reducing TNSS scores from baseline (P<0.05). After 21 days, there was no difference between treatments in regard to change in TNSS scores (95% CI, 0.7391 to 0.3693). Secondary: Both treatments were equally effective at reducing symptom scores

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
100 µg in each nostril QD	epicutaneous or intradermal test to one or more tests of grass pollen, tree pollen, and/or outdoor molds present in their environment		therapeutic effect, RQLQ scores and SAQ scores	from baseline including nasal discharge (*P*=0.9539), nasal stuffiness (*P*=0.7666), sneezing (*P*=0.5559) and nasal itching (*P*=0.7858). Zero patients discontinued study the study medications due to lack of therapeutic effect. There were no significant differences in mean overall RQLQ scores (*P*=0.54) or in individual domain scores between treatments. All changes were statistically significant compared to baseline scores (*P*<0.001). On the SAQ, patients reported significantly less odor with triamcinolone compared to fluticasone propionate (12.3 vs 40.7; *P*<0.0001).
Stokes et al[69] Triamcinolone 220 µg one time vs fluticasone propionate 200 µg one time vs mometasone 200 µg one time	DB, MC, RCT, XO Patients 18 to 70 years of age, with at least a two-year history of allergic rhinitis, who were symptomatic at baseline	N=215 1 day	Primary: Patients' sensory perception measured by the NSEQ, patients' preference measured by the ONSEQ, patients' self reported expected compliance score using the four-point Likert scale Secondary: Not reported	Primary: The NSEQ scores for triamcinolone were significantly higher than fluticasone propionate and mometasone (78.6 vs 72.3 and 69.3, respectively, *P*<0.001 for all). Based on the ONSEQ scores, significantly more patients preferred triamcinolone (50% for triamcinolone vs 25% for fluticasone propionate and 25% mometasone; *P*<0.001 for all). A larger percentage of the patients reported a Likert score of one or "definitely complying" with triamcinolone (62.5% for triamcinolone, 49.0% for fluticasone, 51.0% for mometasone; *P*<0.01 for all). Secondary: Not reported
Garris et al[70] Fluticasone furoate, dose not specified vs	RETRO Patients four years of age or older with at least one pharmacy claim for a branded	N=793,349 10 months	Primary: Time to concomitant use of a prescription non-sedating antihistamine, montelukast, or ocular medications	Primary: A higher proportion of patients in the fluticasone furoate cohort did not have concomitant prescription medication use during follow-up compared to the other cohorts. Patients in the fluticasone furoate cohort had, on average, a 21% lower risk of having a concomitant prescription for allergic rhinitis

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
budesonide, dose not specified vs mometasone, dose not specified vs triamcinolone, dose not specified	intranasal corticosteroid between April 2007 and July 2007		Secondary: Cost	compared to the other cohorts (*P*<0.05). The risk reduction was the greatest for concomitant use of a non-sedating antihistamine followed by ocular medications (25 and 16% respectively, *P*<0.05). No significant difference was observed between the fluticasone furoate cohort, the combination cohort of any other branded corticosteroid, mometasone or triamcinolone in the time to use of montelukast. Secondary: The unadjusted average 60-day overall cost/patient for concomitant prescription allergic rhinitis medications was lower for the fluticasone furoate cohort compared to the other cohorts (*P*<0.001).
Treatment of Nonallergic Rhinitis				
Scadding et al[71] Fluticasone propionate 200 µg QD or BID vs beclomethasone 200 µg BID vs placebo	DB, MC, PC, PG, RCT Patients with allergic and nonallergic perennial rhinitis	N=not specified 12 weeks	Primary: Nasal symptoms Secondary: Adverse events	Primary: There were no significant differences between active treatment groups in regard to nasal symptoms (*P* value not reported). Secondary: Few adverse events and no treatment-related abnormalities in laboratory measurements were reported.

Drug regimen abbreviations: BID=twice daily, QD=once daily, QID=four times daily
Study abbreviations: AC=active-controlled, CI=confidence interval, DB=double-blind, DD=double-dummy, MC=multi-center, NI=noninferiority, NS=nonsignificant, OL=open-label, PC=placebo-controlled, PG=parallel-group, RCT=randomized controlled trial, RETRO=retrospective, SB=single-blinded, SD=single dose, XO=cross-over
Miscellaneous abbreviations: ACTH=adrenocorticotropic hormone, ECG=electrocardiogram, HRQL=health related quality of life, HPA=hypothalamic-pituitary-adrenal, IgE=immunoglobulin E, iTNSS=instantaneous total nasal symptom score, iTOSS=instantaneous total ocular symptom score, LS=least square, NSEQ=nasal spray evaluation questionnaire, ONSEQ=overall nasal spray evaluation questionnaire, PANS=physician assessed overall nasal signs and symptoms, PAR=perennial allergic rhinitis, PNIF=peak nasal inspiratory flow, RQLQ=rhinoconjunctivitis quality of life questionnaire, rTNSS=reflective total nasal symptom score, rTOSS=reflective total ocular nasal symptom score, SAR=seasonal allergic rhinitis, TNSS=total nasal symptom score

Special Populations

Table 5. Special Populations[1-9]

Generic Name	Population and Precaution				
	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
Beclomethasone	No dosage adjustment required in the elderly population. Approved for use in children six years of age and older.	No dosage adjustment required.	No dosage adjustment required.	C	Unknown
Budesonide	No dosage adjustment required in the elderly population. Approved for use in children six years of age and older.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	B	Yes
Ciclesonide	No dosage adjustment required in the elderly population. Approved for use in children six years of age and older.	Not studied in renal dysfunction.	No dosage adjustment required.	C	Unknown
Flunisolide	No dosage adjustment required in the elderly population. Approved for use in children six years of age and older.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	C	Unknown
Fluticasone furoate	No dosage adjustment required in the elderly population. Approved for use in children two years of age and older.	No dosage adjustment required.	No dosage adjustment required. Monitoring is recommended with severe hepatic dysfunction.	C	Unknown
Fluticasone propionate	No dosage adjustment required in the elderly population. Approved for use in children four years of age and older.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	C	Unknown

Generic Name	Population and Precaution				
	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
Mometasone	No dosage adjustment required in the elderly population. Approved for use in children two years of age and older.	Not studied in renal dysfunction.	No dosage adjustment required.	C	Unknown
Triamcinolone	No dosage adjustment required in the elderly population. Approved for use in children two years of age and older.	No dosage adjustment required.	No dosage adjustment required.	C	Unknown

Adverse Drug Events

The most common adverse events reported with the use of intranasal corticosteroids include headache, pharyngitis, epistaxis, cough, nasal irritation and pharyngolaryngeal pain. Reports of nasal septal perforation associated with the use of intranasal corticosteroids are rare.

Table 6. Adverse Drug Events[1-9,13,20]

Adverse Events	Beclomethasone	Budesonide	Ciclesonide	Flunisolide	Fluticasone Furoate	Fluticasone Propionate	Mometasone	Triamcinolone
Cardiovascular								
Chest pain	-	-	-	-	-	-	2 to <5	-
Palpitations	-	✔	-	-	-	-	-	-
Central Nervous System								
Dizziness	-	-	✔	-	-	1 to 3	-	✔
Headache	<5	-	6.0 to 6.6	≤5	8 to 9	6.6 to 16.1	26	5.5
Insomnia	-	-	-	-	-	-	-	✔
Lightheadedness	<5	-	-	-	-	-	-	-
Gastrointestinal								
Abdominal pain	-	-	-	-	-	1 to 3	-	4.7
Diarrhea	-	-	-	-	-	1 to 3	2 to <5	3
Dyspepsia	-	-	-	-	-	-	2 to <5	3.4
Nausea	<5	-	-	≤5	-	2.6 to 4.8	2 to <5	✔
Vomiting	-	-	-	≤5	-	2.6 to 4.8	5	-
Hypersensitivity reactions								
Anaphylaxis	✔	✔	-	-	✔	✔	✔	-
Angioedema	✔	✔	-	-	✔	✔	✔	-
Bronchospasm	✔	2	-	-	-	✔	-	-
Dermatitis	-	✔	-	-	-	-	-	-
Dyspnea	-	-	-	-	-	✔	-	✔
Edema of face/tongue	-	-	-	-	-	✔	-	-
Pruritus	-	✔	-	-	-	✔	-	✔
Rash	✔	✔	-	-	✔	✔	-	2.5
Wheezing	✔	✔	-	-	-	✔	2 to <5	-
Urticaria	✔	✔	-	-	✔	✔	-	-
Respiratory								
Asthma symptoms	-	-	-	-	-	3.3 to 7.2	2 to <5	2.5
Bronchitis	-	-	≥3	-	-	1 to 3	2 to <5	3.4
Cough	-	2	≥3	>1	3 to 4	3.6 to 3.8	7	2.1 to 8.4
Epistaxis	<3	8	4.9	3 to 9	4 to 6	6.0 to 6.9	1 to 13	2.7 to 5.1
Mild nasopharyngeal irritation	24	-	-	-	-	-	-	-

Adverse Events	Beclomethasone	Budesonide	Ciclesonide	Flunisolide	Fluticasone Furoate	Fluticasone Propionate	Mometasone	Triamcinolone
Nasal burning/stinging	-	-	-	13 to 45	-	2.4 to 3.2	✔	-
Nasal discomfort	5.2*							
Nasal dryness	✔	-	-	>1	-	-	-	-
Nasal irritation	✔	2	≥3	≤5	-	-	2 to <5	✔
Nasal mucosal ulceration	✔	-	✔	≤1	1	✔	✔	-
Nasal septal perforation	✔	✔	-	✔	-	✔	✔	✔
Nasal stuffiness/ congestion	<3	-	✔	≤5	-	-	-	✔
Nasopharyngitis	-	-	3.7 to 6.6	-	-	-	-	5.1
Pharyngitis	-	4	3.4	>1	2 to 4	6 to 7.8	12	5.1 to 7.8
Rhinitis	-	-	-	-	-	-	2 to <5	-
Rhinorrhea	<3	-	-	-	-	1 to 3	-	2.1
Sinusitis	-	-	≥3	≤1	-	-	5	-
Sneezing	4	-	-	≤5	-	-	-	-
Throat discomfort (burning, itching, swelling, pain)	-	✔	-	≤5	-	✔	-	-
Throat dryness/irritation	✔	✔	-	-	-	✔	-	-
Upper respiratory tract infection	-	-	-	-	-	-	5 to 7	-
Special senses								
Aftertaste	-	-	-	8 to 17	-	-	-	-
Blurred vision	-	-	-	-	-	✔	-	-
Cataracts	✔	✔	✔	-	✔	✔	✔	✔
Conjunctivitis	-	-	-	-	-	✔	2 to <5	-
Dry/irritated eyes	-	-	-	-	-	✔	-	-
Earache	-	-	2.2	-	-	-	2 to <5	-
Glaucoma	✔	✔	✔	-	✔	✔	✔	✔
Hoarseness	-	-	-	≤1	-	✔	-	-
Increased intraocular pressure	✔	✔	-	-	-	✔	-	✔
Loss of taste/smell	✔	✔	-	✔	-	✔	-	-
Otitis media	-	-	-	-	-	-	2 to <5	-
Unpleasant taste/smell	✔	-	-	-	-	-	✔	✔
Watery eyes	<3	-	-	≤5	-	-	-	-
Miscellaneous								
Aches and pains	-	-	-	-	-	1 to 3	-	-
Arthralgia	-	-	-	-	-	-	2 to <5	-
Back pain	-	-	≥3	-	1	-	-	-
Dysmenorrhea	-	-	-	-	-	-	5	-

Adverse Events	Beclomethasone	Budesonide	Ciclesonide	Flunisolide	Fluticasone Furoate	Fluticasone Propionate	Mometasone	Triamcinolone
Excoriation	-	-	-	-	-	-	-	2.5
Fatigue	-	-	-	-	-	-	-	✔
Fever	-	-	-	-	4 to 5	1 to 3	-	-
Flu-like symptoms	-	-	-	-	-	1 to 3	2 to <5	-
Growth suppression	✔	✔	✔	✔	✔	✔	✔	✔
Immunosuppression	-	✔	✔	-	✔	-	✔	✔
Impaired wound healing	-	✔	✔	-	✔	-	✔	✔
Infection	✔	✔	✔	✔	✔	✔	✔	✔
Influenza	-	-	≥3	-	-	-	-	8.9
Myalgia	-	-	-	-	-	-	2 to <5	-
Skin trauma	-	-	-	-	-	-	2 to <5	-
Tooth disorder	-	-	-	-	-	-	-	3.4
Urinary tract infection	-	-	≥3	-	-	-	-	-
Viral infection	-	-	-	-	-	-	14	-
Voice changes	-	-	-	-	-	✔	-	-

✔ Percent not specified.
- Event not reported.

Contraindications/Precautions[1-9]

The use of intranasal corticosteroids in patients with a known hypersensitivity to any component of the preparation is contraindicated.

Several local nasal effects are associated with the use of intranasal corticosteroids, such as epistaxis, nasal ulceration, *Candida* infection and nasal septal perforation. In addition, because of the inhibitory effect on wound healing, intranasal corticosteroids should be avoided in patients who have experienced recent nasal ulcers, nasal surgery or nasal trauma until healing has occurred.

The development of glaucoma and/or cataracts may also result from the use of intranasal corticosteroids. Close monitoring is warranted in patients who experience a change in vision or who have a known history of increased intraocular pressure, glaucoma or cataracts.

Due to the potential for worsening of infection, corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculosis infections of the respiratory tract, untreated local or systemic fungal or bacterial infections, systemic viral or parasitic infections or ocular herpes simplex. Patients administering immunosuppressant doses of corticosteroids should avoid exposure to chickenpox and measles. Hypercorticism and adrenal insufficiency may appear in patients who administer higher than recommended doses of intranasal corticosteroids. If such changes occur, the dose of intranasal corticosteroid should be discontinued slowly, consistent with accepted procedure for discontinuing oral corticosteroid therapy. Also, if systemic corticosteroids are replaced with topical corticosteroids, signs of adrenal insufficiency and symptoms of corticosteroid withdrawal (i.e. joint and/or muscle pain, lassitude and depression) may develop.

In addition, corticosteroids may cause a reduction in growth velocity when administered to pediatric patients. Growth should be routinely monitored in pediatric patients administering intranasal corticosteroids and the lowest dosage that effectively controls symptoms should be used.

Drug Interactions

Drug interactions associated with the use of intranasal corticosteroids are limited due to both the route of administration and the relatively low systemic bioavailability of the agents. There are no clinically significant drug interactions reported with beclomethasone, flunisolide, and triamcinolone. Since budesonide, ciclesonide, fluticasone furoate, fluticasone propionate, and mometasone are primarily metabolized in the liver by the cytochrome P450 3A4 (CYP3A4) isoenzymes systems, there are potential drug interactions with drugs that inhibit CYP3A4.

Table 7. Drug Interactions[1-9,13,20]

Generic Name	Interacting Medication or Disease	Potential Result
Budesonide ciclesonide, fluticasone furoate, fluticasone propionate, mometasone	Ketoconazole	Concurrent administration with ketoconazole, a potent inhibitor of CYP3A4, may increase the plasma concentration of budesonide, ciclesonide, fluticasone furoate, fluticasone propionate and mometasone.
Fluticasone furoate, fluticasone propionate	Ritonavir	Fluticasone is metabolized by CYP3A4. Concurrent administration with ritonavir, a potent CYP3A4 inhibitor, may increase the plasma concentration of fluticasone.

Dosage and Administration

Table 8. Dosing and Administration[1-9]

Generic Name	Adult Dose	Pediatric Dose	Availability
Beclomethasone	Nasal polyps, nonallergic (vasomotor) rhinitis: Suspension:1 to 2 inhalations in	Nasal polyps, nonallergic (vasomotor) rhinitis, perennial allergic rhinitis,	Aerosol for nasal inhalation: 80 µg/actuation

Generic Name	Adult Dose	Pediatric Dose	Availability
	each nostril BID Perennial allergic rhinitis, seasonal allergic rhinitis: Aerosol: 2 inhalations in each nostril QD, Suspension: 1 to 2 inhalations in each nostril BID	seasonal allergic rhinitis in children 6 to 12 years old: Suspension: Initial, 1 inhalation in each nostril BID; maximum, 2 inhalations in each nostril BID	(120 actuations) Suspension for nasal inhalation: 42 µg/inhalation (180 metered doses)
Budesonide	Perennial allergic rhinitis, seasonal allergic rhinitis: Suspension:1 inhalation in each nostril QD; maximum, 4 inhalations in each nostril QD	Perennial allergic rhinitis, seasonal allergic rhinitis in children 6 to 12 years old: Suspension: 1 inhalation in each nostril QD; maximum, 2 inhalations in each nostril QD	Suspension for nasal inhalation: 32 µg/inhalation (120 metered doses)
Ciclesonide	Perennial allergic rhinitis, seasonal allergic rhinitis: Suspension: 2 inhalations in each nostril QD	Perennial allergic rhinitis in children ≥12 years old: Suspension: 2 inhalations in each nostril QD Seasonal allergic rhinitis in children ≥6 years old: Suspension: 2 inhalations in each nostril QD	Suspension for nasal inhalation: 50 µg/inhalation (120 metered doses)
Flunisolide	Perennial allergic rhinitis, seasonal allergic rhinitis: Suspension: 2 inhalations in each nostril BID; maximum, 8 inhalations in each nostril daily	Perennial allergic rhinitis, seasonal allergic rhinitis in children 6 to 14 years old: Suspension: 1 inhalation in each nostril TID or 2 inhalations in each nostril BID; maximum, 4 inhalations in each nostril daily	Suspension for nasal inhalation: 25 µg/inhalation (200 metered doses) 29 µg/inhalation (200 metered doses)
Fluticasone furoate	Perennial allergic rhinitis, seasonal allergic rhinitis: Suspension: 2 inhalations in each nostril QD; maintenance, 1 inhalation in each nostril QD	Perennial allergic rhinitis, seasonal allergic rhinitis in children 2 to 11 years old: Suspension: 1 inhalation in each nostril QD; maximum, 2 inhalations in each nostril QD	Suspension for nasal inhalation: 27.5 µg/inhalation (120 metered doses)
Fluticasone propionate	Nonallergic (vasomotor) rhinitis, perennial allergic rhinitis, seasonal rhinitis: Suspension: 2 inhalations in each nostril QD or 1 inhalation in each nostril BID; maintenance, 1 inhalation in each nostril QD	Nonallergic (vasomotor) rhinitis, perennial allergic rhinitis, seasonal rhinitis in children ≥4 years old: Suspension: 1 inhalation in each nostril QD; maximum, 2 inhalations in each nostril QD	Suspension for nasal inhalation: 50 µg/inhalation (120 metered sprays)
Mometasone	Nasal congestion associated with seasonal allergic rhinitis: Suspension: 1 inhalation in each nostril QD	Nasal congestion associated with seasonal allergic rhinitis in children 2 to 11 years old:	Suspension for nasal inhalation: 50 µg/inhalation (120 metered

Generic Name	Adult Dose	Pediatric Dose	Availability
	Nasal polyps in adults ≥18 years old: Suspension: 2 inhalations in each nostril QD to BID Perennial allergic rhinitis, seasonal allergic rhinitis: Suspension: 2 inhalations in each nostril QD Prophylaxis of seasonal allergic rhinitis in individuals >12 years old: Suspension: 2 inhalations in each nostril QD	Suspension: 1 inhalation in each nostril QD Perennial allergic rhinitis, seasonal allergic rhinitis in children 2 to 11 years old: Suspension: 1 inhalation in each nostril QD	doses)
Triamcinolone	Perennial allergic rhinitis, seasonal allergic rhinitis: Suspension: 2 inhalations in each nostril QD; maintenance, 1 inhalation in each nostril QD	Perennial allergic rhinitis, seasonal allergic rhinitis in children 2 to 5 years old: Suspension: 1 inhalation in each nostril QD Perennial allergic rhinitis, seasonal allergic rhinitis in children 6 to 12 years old: Suspension: 1 or 2 inhalations in each nostril QD; maintenance, 1 inhalation in each nostril QD	Suspension for nasal inhalation: 55 µg/inhalation (120 metered doses)

BID=twice daily, QD=once daily, TID=three times daily

Clinical Guidelines

Table 9. Clinical Guidelines

Clinical Guideline	Recommendations
Allergic Rhinitis and its Impact on Asthma and the Global Allergy and Asthma European Network: **Guideline Revisions (2010)**[15]	Diagnosis • The diagnosis of allergic rhinitis is based upon the concordance between typical history of allergic symptoms and diagnostic response. • Typical symptoms of allergic rhinitis include rhinorrhea, sneezing, nasal obstruction and pruritus. • Diagnostic tests are based on the demonstration of allergen-specific immunoglobulin E (IgE) in the skin or blood. • Many asymptomatic patients can have positive skin tests or detectable serum levels of IgE. Treatment • The treatment of allergic rhinitis should consider the severity and duration of the disease, the patient's preference, as well as the efficacy, availability and cost of the medication. • A stepwise approach depending on the severity and duration of rhinitis is proposed. • Not all patients with moderate/severe allergic rhinitis are controlled despite optimal pharmacotherapy. • Intranasal glucocorticoids are recommended over oral H1-antihistamines

Clinical Guideline	Recommendations
	for the treatment of allergic rhinitis in adults and children. They are the most effective drugs for treating allergic rhinitis. In many patients with strong preferences for the oral route, an alternative choice may be reasonable. • Second-generation oral or intranasal H1-antihistamines are recommended for the treatment of allergic rhinitis and conjunctivitis in adults and children. • First generation oral H1-antihistamines are not recommended when second-generation ones are available, due to safety concerns. • Intranasal H1-antihistamines are recommended for the treatment of adults and children with seasonal allergic rhinitis, but data regarding their relative safety and efficacy is limited. Therefore, their use in persistent allergic rhinitis is not recommended. • Intramuscular glucocorticoids and long-term use of oral glucocorticoids are not recommended due to safety concerns. • Topical chromones are recommended in the treatment of allergic rhinitis but they are only modestly effective. • Montelukast is recommended for adults and children with seasonal allergic rhinitis, and in pre-school children with persistent allergic rhinitis. Montelukast has limited efficacy in adults with persistent allergic rhinitis. • Intranasal ipratropium is recommended for the treatment of rhinorrhea associated with allergic rhinitis. • Intranasal decongestants may be used for a short period (<5 days) for patients with severe nasal obstruction. Nasal decongestants should not be used in pre-school aged children. • Combination oral decongestants and oral H1-antihistamines may be used for the treatment of allergic rhinitis in adults, but should not be administered regularly due to adverse effects. • For patients experiencing ocular symptoms associated with allergic rhinitis intraocular antihistamines or chromones may be considered.
Joint Task Force on Practice Parameters for Allergy and Immunology: **The Diagnosis and Management of Rhinitis: An Updated Practice Parameter (2008)**[10]	<u>Diagnosis</u> • An effective evaluation of a patient with rhinitis includes a determination of the pattern, chronicity, and seasonality of nasal and related symptoms; response to medications; presence of coexisting conditions; occupational exposure; and a detailed environmental history and identification of precipitating factors. • A physical examination with emphasis on the upper respiratory tract should be performed in patients with a history of rhinitis. • Skin testing is the preferred test for the diagnosis of IgE-mediated sensitivity and is indicated to provide evidence of allergic basis for the causes of the patient's symptoms. • Nasal smears for eosinophils are not necessary for routine use in diagnosing allergic rhinitis but may be useful when the diagnosis of allergic rhinitis is in question. • The measurement of total IgE should not be routinely performed. • Cytotoxic tests, provocation-neutralization, electrodermal testing, applied kinesiology, iridology, and hair analysis are not recommended diagnostic procedures. <u>Treatment</u> • The management and monitoring of rhinitis should be individualized and based on symptoms, physical examination findings, comorbidities, patient age and patient preferences.

Clinical Guideline	Recommendations
	• Environmental control measures include avoidance of known allergic triggers when possible. • The available second-generation oral antihistamines, which are generally preferred over first-generation antihistamines, appear to be equally effective in the treatment of allergic rhinitis. • Concerning the second generation antihistamines, fexofenadine, loratadine, and desloratadine do not cause sedation at recommended doses; loratadine and desloratadine may cause sedation at doses exceeding the recommended dose; cetirizine and intranasal azelastine may cause sedation at recommended doses. • Intranasal antihistamines are efficacious and equal to or "superior" to oral second-generation antihistamines for treatment of seasonal allergic rhinitis. • Intranasal antihistamines may be considered for use as first-line treatment for allergic and nonallergic rhinitis. • Leukotriene receptor antagonists alone or in combination with antihistamines are effective in the treatment of allergic rhinitis. • Topical decongestants are not recommended for regular daily use but can be considered for short-term management of nasal congestion. • Intranasal corticosteroids are the most effective medication class for controlling symptoms of allergic rhinitis and all are considered equally efficacious. • Intranasal corticosteroids can provide significant relief of symptoms when used on a regular basis as well as an as-needed basis. • Intranasal corticosteroids may be useful in the treatment of some forms of nonallergic rhinitis. • A short course of oral corticosteroids may be appropriate for very severe or intractable nasal symptoms or significant nasal polyposis. • Intranasal cromolyn sodium may be effective for the prevention and treatment of allergic rhinitis. • Intranasal anticholinergics may be effective in reducing rhinorrhea and are more effective when used in combination with intranasal corticosteroids. • Allergen immunotherapy is effective and should be considered for patients with allergic rhinitis who have demonstrable evidence of specific IgE antibodies to clinically relevant allergens. • Surgery may be indicated in the management rhinitis.
Institute for Clinical Systems Improvement: **Diagnosis and Treatment of Respiratory Illness in Children and Adults (2011)**[16]	Diagnosis • Patients can present with any of the following symptoms: congestion, rhinorrhea, pruritus, sneezing, posterior nasal discharge, and sinus pressure/pain. • A past medical history of facial trauma or surgery, asthma, rhinitis, atopic dermatitis, or thyroid disease may be suggestive of a rhinitis. In addition, a family history of atopy or other allergy associated conditions make allergic rhinitis more likely. • The most common physical findings suggestive of rhinitis tend to be swollen nasal turbinates, rhinorrhea and pruritus however allergic conjunctivitis may also be present. • Symptoms suggestive of allergic etiology include sneezing, itching of the nose, palate or eyes, and clear rhinorrhea. Nasal congestion is the most significant complaint in patients with perennial rhinitis. • Diagnostic testing should be considered if the results would change management.

Clinical Guideline	Recommendations
	• Skin tests and radioallergosorbent tests identify the presence of IgE antibody to a specific allergen and are used to differentiate allergic from nonallergic rhinitis and to identify specific allergens causing allergic rhinitis. • A nasal smear for eosinophils is a good predictor of a patient's response to treatment topical nasal corticosteroids. • Peripheral blood eosinophil count, total serum IgE level, Rinkel method of skin titration and sublingual provocation testing are not recommended. Treatment • If a clinical diagnosis is obvious, symptomatic treatment, which consists of education on avoidance and medication therapy, should be initiated. • Avoidance of triggers is recommended. • Intranasal corticosteroids are the most effective single agents for controlling the spectrum of allergic rhinitis symptoms and should be considered first-line therapy in patients with moderate to severe symptoms. • Regular daily use of intranasal corticosteroids is required to achieve optimal results. • It may be best to start treatment one week prior to the start of the allergy season for prophylaxis. • Clinical response does not seem to vary significantly between the available intranasal corticosteroids. • Systemic corticosteroids should be reserved for refractory or severe cases of rhinitis. Injectable steroids are not generally recommended. • Antihistamines are effective at controlling all symptoms associated with allergic rhinitis except nasal congestion. • Antihistamines are somewhat less effective than intranasal corticosteroids but they can be used on a daily or as needed basis. • Second-generation antihistamines are recommended because they are less sedating and cause less central nervous system impairment. • Leukotriene inhibitors may be as effective as second-generation antihistamines for the treatment of allergic rhinitis and less effective than intranasal corticosteroids. • Oral decongestants are effective in reducing nasal congestion. Oral decongestants can be a useful addition to antihistamines. • Topical decongestants, which have the potential to induce rebound congestion after three days, are effective for the short-term relief of nasal congestion. • Cromolyn is less effective than intranasal corticosteroids and is most effective when used prior to the onset of allergic symptoms. • Cromolyn is a good alternative for patients who are not candidates for corticosteroids. • Intranasal anticholinergics are effective in relieving anterior rhinorrhea in allergic and nonallergic rhinitis. • Reserve immunotherapy for patients with significant allergic rhinitis in which avoidance activities and pharmacotherapy are insufficient to control symptoms. • If adequate relief is achieved appropriate follow-up should include further education on avoidance activities and medications. • If patients anticipate unavoidable exposure to known allergens they should begin the use of medications prior to exposure. • If adequate relief is not achieved within two to four weeks consider a trial

Clinical Guideline	Recommendations
	of another medication, allergen skin testing by a qualified physician, a complete nasal examination, or a diagnosis of nonallergic rhinitis. • Treatment options for nonallergic rhinitis include intranasal corticosteroids, oral decongestants and antihistamines, topical antihistamines, and nasal strips.
American Academy of Family Physician: **Treatment of Allergic Rhinitis (2010)**[17]	• Treatment should be based on the patient's age and severity of symptoms. • Intranasal corticosteroids are the most effective treatment and should be first-line therapy for mild to moderate disease. • Moderate to severe disease not responsive to intranasal corticosteroids should be treated with second-line therapies, including antihistamines, decongestants, cromolyn, leukotriene receptor antagonists, and nonpharmacologic therapies (e.g., nasal irrigation). • Immunotherapy should be considered in patients with inadequate response to usual treatments. • Omalizumab has been shown to be effective in reducing nasal symptoms and improving quality of life scores in patients with allergic rhinitis. However, its high cost (average wholesale price of $679 to $3,395/month) and lack of Food and Drug Administration approval for home administration are the main limitations to its use.

Conclusions

Intranasal corticosteroids are used for the management of allergic rhinitis, some forms of nonallergic rhinitis and nasal polyps. They are generally well tolerated and are associated with limited drug interactions due to their localized administration and limited systemic absorption. In addition, like other corticosteroids, intranasal corticosteroids carry warnings regarding the use in patients with active infection and the development of signs of adrenal insufficiency with the administration of higher than recommended doses.

Intranasal corticosteroids are considered first-line agents for the treatment of allergic rhinitis; especially for patients with moderate to severe symptoms. Consensus guidelines do not recommend the use of one intranasal corticosteroid product over another. [10,15-17] All available intranasal corticosteroids have demonstrated safety and efficacy for their respective indications.[20-71] These agents have been shown to be effective in reducing rhinitis-related nasal symptoms such as congestion, rhinorrhea, sneezing, nasal itch, and postnasal drip. The differences in tolerability and sensory perceptions noted in clinical trials were minor and did not translate to improved outcomes. Head-to-head trials have not consistently demonstrated clinically significant differences between products.[44,46-50,53-56, 61,66-67,71]

Triamcinolone (Nasacort AQ®), mometasone (Nasonex®) and fluticasone furoate (Veramyst®) are Food and Drug Administration (FDA)-approved for use in children two years of age and older and fluticasone propionate (Flonase®) is FDA-approved for use in children four years of age and older. Beclomethasone (Beconase AQ®), budesonide (Rhinocort Aqua®), ciclesonide (Omnaris®), and flunisolide are approved for use in children six years of age and older.[1-9] A recently approved product, beclomethasone nasal aerosol (QNASL®), is approved for used in adolescents and adults 12 years of age and older. There are currently, three intranasal corticosteroids that are available generically: flunisolide, fluticasone propionate and triamcinolone.[13]

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