# *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] 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.[2] 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.[3-12] Continuous administration of intranasal corticosteroids is more efficacious than as-needed dosing, and the onset of therapeutic effect occurs between three and twelve hours.[2] 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.[3-12] 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. Two new products, beclomethasone (QNASL®) and ciclesonide (Zetonna®), were approved in 2012 and are the only two intranasal corticosteroid products formulated as a "dry" nasal aerosol.[3-7,9-12] Both products are indicated for the treatment of nasal symptoms associated with seasonal and perennial allergic rhinitis in adults and adolescents 12 years of age and older. There are currently, three intranasal corticosteroids that are available generically: flunisolide, fluticasone propionate and triamcinolone.[14]

**Table 1. Current Medications Available in Therapeutic Class[3-12]**

| 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)<br><br>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 | Aerosol for nasal inhalation: 37 µg/actuation (60 actuations)<br><br>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)<br><br>29 µg/inhalation (200 metered doses) | a |
| Fluticasone furoate | Treatment of seasonal and perennial allergic rhinitis | Suspension for nasal inhalation: 27.5 µg/inhalation (120 metered | - |

| Generic (Trade Name) | Food and Drug Administration Approved Indications | Dosage Form/Strength | Generic Availability |
|---|---|---|---|
| (Veramyst®) | | doses) | |
| Fluticasone propionate (Flonase®) | Treatment of seasonal and perennial allergic rhinitis and nonallergic rhinitis | Suspension for nasal inhalation: 50 µg/inhalation (120 metered sprays) | a |
| 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) | a |

*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.
- To date, the newly approve intranasal corticosteroid aerosol formulations have not been evaluated against the other available intranasal corticosteroids.
- In a six-week study of patients with perennial allergic rhinitis, aerosolized beclomethasone significantly improved reflective total nasal symptom score (TNSS) compared to placebo (least squares mean change of -2.46 vs -1.63; *P*<0.001). Furthermore, beclomethasone was associated with a statistically significant improvement in quality of life scores compared to placebo (*P*=0.001).[14]
- The aerosolized ciclesonide formulation has also been show to significantly improve symptoms of allergic rhinitis compared to placebo. In a study by Ratner et al, ciclesonide administered at a daily dose of 80 µg or 160 µg reduced reflective TNSS by a 15.1% and 16.0%, respectively, compared to 3.7% in the placebo group (*P*<0.001 for both). In addition, significant improvements were observed with both doses of ciclesonide compared to placebo with regard to ocular symptom scores and quality of life (*P*<0.001 for both).[15] Similar improvements in outcomes were reported in additional studies of up to 26 weeks duration.[16-18]

**Key Points within the Medication Class**

- According to Current Clinical Guidelines:
  - Intranasal corticosteroids are the most effective drugs for treating allergic rhinitis.[2,19.20]
  - 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.[2,19.20]
  - Clinical response does not seem to vary significantly between the available intranasal corticosteroids.[2]
  - 
- 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]
  - Two new “dry” nasal aerosol products, beclomethasone (QNASL®) and ciclesonide (Zetonna®), were approved in 2012; all other agents within the class are aqueous suspensions.[13]

- No head-to-head studies are available comparing the "dry" aerosol products to each other or another intranasal corticosteroid.

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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] 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.[2] 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.[1]

All ten intranasal corticosteroids are approved by the Food and Drug Administration (FDA) for the treatment of perennial and seasonal allergic rhinitis.[3-12] Mometasone (Nasonex®) carries an additional indication for the prophylaxis of seasonal allergic rhinitis.[11] Two currently available intranasal corticosteroids, beclomethasone (Beconase AQ®) and mometasone, are also FDA-approved for the treatment of nasal polyps.[3,11] Nasal polyposis is an inflammatory condition of the nasal and sinus mucosa and usually presents as persistent nasal obstrutction.[2] 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.[13]

Flunisolide, fluticasone propionate and triamcinolone (Nasacort AQ®) are the three intranasal corticosteroids currently available in a generic nasal spray formulation.[14] Two new products, beclomethasone (QNASL®) and ciclesonide (Zetonna®), were approved in 2012 and are the only two intranasal corticosteroid products formulated as a "dry" nasal aerosol.[4,7] All other products in within the class are formulated as aqueous suspensions. Fluticasone furoate (Veramyst®), mometasone and triamcinolone are approved for use in children two years of age and older.[9,11,12] In general, the intranasal corticosteroids are typically dosed once or twice daily.[3-12]

Continuous administration of intranasal corticosteroids is more efficacious than as-needed dosing, and the onset of therapeutic effect occurs between three and twelve hours.[2] 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.[3-12,14]

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.[2,15,16] 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.[17] Moreover, no one intranasal corticosteroid product is recommended over another as initial treatment in patients with perennial or seasonal allergic rhinitis.[15,16]

## 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®, Zetonna®) | Intranasal corticosteroid | - |
| Flunisolide | Intranasal corticosteroid | a |
| Fluticasone furoate (Veramyst®) | Intranasal corticosteroid | - |
| Fluticasone propionate (Flonase®) | Intranasal corticosteroid | a |
| Mometasone (Nasonex®) | Intranasal corticosteroid | - |
| Triamcinolone (Nasacort AQ®) | Intranasal corticosteroid | a |

## Indications

**Table 2. Food and Drug Administration Approved Indications[3-12,14]**

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

*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.
§ Ciclesonide nasal suspension is indicated in children six years of age and older. Ciclesonide nasal aerosol is indicated in adults and adolescents 12 years of age and older.

## Pharmacokinetics

**Table 3. Pharmacokinetics[3-12,14]**

| 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

The clinical trials demonstrating the safety and efficacy of the intranasal corticosteroids in the respective Food and Drug Administration-approved indications are described in Table 4.[18-76]

Daily administration of intranasal corticosteroids is associated with statistically significant improvements in allergy-related total nasal symptom scores (TNSS), health related quality of life scores and minimal adverse events. Furthermore, numerous head-to-head clinical trials comparing the available intranasal corticosteroids have generally demonstrated no significant clinical differences among the currently available intranasal corticosteroids with regard to efficacy.[41-55,57-76] Some studies have reported differences in sensory perceptions and patient preference with one agent compared to another.[42,50,59,60,70,71,73,76] Patients administering the agents noted differences in odor, aftertaste, and severity of irritation, though these differences were not associated with differences in efficacy between the agents.

Head-to-head trials evaluating the efficacy and safety of beclomethasone, fluticasone propionate and flunisolide demonstrate that these agents are comparable to other agents within the class.[51,53-55,57,58,61-64,69,74,75,77] However, additional results of these studies reinforce that all of the intranasal corticosteroids should be considered equally efficacious.

To date, the newly approved intranasal corticosteroid aerosol formulations have been demonstrated to be significantly more effective compared to placebo. In a six-week study of patients with perennial allergic rhinitis, aerosolized beclomethasone significantly improved reflective TNSS compared to the placebo (LS mean change of -2.46 vs -1.63; $P<0.001$). Furthermore, beclomethasone was associated with a statistically significant improvement in quality of life scores compared to placebo ($P=0.001$).[18] The aerosolized ciclesonide formulation has also been shown to significantly improve symptoms of allergic rhinitis compared to placebo. In a study by Ratner et al, ciclesonide administered at a daily dose of 80 µg or 160 µg reduced reflective TNSS by a 15.1% and 16.0%, respectively, compared to a 3.7% in the placebo group ($P<0.001$ for both). In addition, significant improvements were observed with both doses of ciclesonide compared to placebo with regard to ocular symptoms scores and quality of life ($P<0.001$ for both).[22] Similar improvements in outcomes were reported in additional studies of up to 26 weeks duration.[23-26]

**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)** | | | | |
| Meltzer et al[18]<br><br>Beclomethasone 320 µg QD (QNASL®)<br><br>vs<br><br>placebo | DB, MC, PC, PC, RCT<br><br>Patients ≥12 years of age with a ≥2 year history of PAR, a positive skin test to at least one perennial allergen and an average rTNSS of ≥6/12 and an average minimum reflective nasal congestion score of 2/3 | N=474<br><br>6 weeks | Primary:<br>Change from baseline in rTNSS<br><br>Secondary:<br>Change from baseline in iTNSS, individual symptom scores, PNSS, RQLQ and safety | Primary:<br>After six weeks of treatment, subjects treated with beclomethasone reported significantly greater improvement from baseline in rTNSS compared to those treated with placebo. (LS mean change of -2.46 vs -1.63; *P*<0.001).<br><br>Secondary:<br>A significantly greater improvement in iTNSS was achieved over six weeks in the beclomethasone treatment group compared to the placebo group (LS mean change of -2.14 vs -1.36; *P*<0.001).<br><br>As demonstrated with overall nasal symptom improvement, beclomethasone significantly improved reflective and instantaneous individual nasal symptom scores for all four of the components of the TNSS compared with placebo (*P*<0.05 for all).<br><br>The change from baseline in PNSS was significantly greater with beclomethasone compared to placebo over six weeks (*P*<0.001). Furthermore, patients treated with beclomethasone achieved significant improvements in all individual symptoms of the PNSS compared to those treated with placebo (*P*≤0.001 for all).<br><br>Beclomethasone treatment significantly improved RQLQ scores compared to placebo (*P*=0.001).<br><br>There were no differences between beclomethasone and placebo with regard to the incidence, type and severity of adverse events. Nasal discomfort was frequently reported with both beclomethasone and placebo treatment (5.9 and 5.0%, respectively). |
| Chervinsky et al[19]<br><br>Ciclesonide 200 µg QD | DB, MC, PC, PG, RCT<br><br>Patients ≥12 years of age with a ≥2 | N=663<br><br>52 weeks | Primary:<br>Treatment-emergent adverse events, 24 hour urinary free cortisol and morning | Primary:<br>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). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| vs<br><br>placebo | year history of PAR, who require continuous treatment and demonstrated skin prick test sensitivity to at least one allergen known to induce PAR | | cortisol levels at weeks 24 and 48<br><br>Secondary:<br>Change from baseline in patient evaluated morning 24 hour rTNSS,<br>PANS score at the end of treatment,<br>combined RQLQ scores at end point | 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.<br><br>Secondary:<br>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).<br><br>No appreciable differences were found between ciclesonide and placebo groups in PANS score at the end of treatment.<br><br>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[20]<br><br>Ciclesonide 200 µg QD<br><br>vs<br><br>placebo | DB, MC, PC, RCT<br><br>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 induce PAR | N=676<br><br>6 weeks | Primary:<br>Change from baseline in the average of morning and evening rTNSS<br><br>Secondary:<br>Average morning and evening patient evaluated iTNSS,<br>PANS score at end of treatment,<br>combined RQLQ score at the end of treatment | Primary:<br>Ciclesonide significantly reduced average morning and evening rTNSS compared to placebo (-2.51 vs -1.89; *P*<0.001).<br><br>Secondary:<br>Ciclesonide significantly reduced average morning and evening iTNSS through six weeks of therapy (*P*=0.001).<br><br>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).<br><br>There was a significant improvement seen in the ciclesonide group compared to placebo in combined RQLQ scores at the end of treatment; -1.30 vs -1.01 (*P*=0.01). |
| Ratner et al[22 21]<br><br>Ciclesonide 200 µg QD<br><br>vs | DB, MC, PC, PG, RCT<br><br>Patients 12 years of age and older with a two year | N=327<br><br>4 weeks | Primary:<br>Change from baseline in average morning and evening rTNSS | Primary:<br>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). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| placebo | history of SAR who require treatment and demonstrated skin prick test sensitivity to mountain cedar pollen | | Secondary:<br>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 | Secondary:<br>By two weeks, ciclesonide improved iTNSS compared to placebo (*P*<0.001).<br><br>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).<br><br>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).<br><br>By day 15, treatment differences for nasal symptoms favoring ciclesonide were evident (*P*<0.001).<br><br>Significant improvements in average morning and evening rTNSS with ciclesonide over placebo were seen by the second day of treatment (*P*<0.05).<br><br>The frequency of adverse events was similar between the 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[22]<br><br>Ciclesonide 80 µg QD (Zetonna®)<br><br>vs<br><br>ciclesonide 160 µg QD (Zetonna®) | DB, MC, PC, PG, RCT<br><br>Patients ≥12 years of age with SAR to mountain cedar pollen for ≥2 years and a sensitivity to mountain cedar pollen through a | N=777<br><br>2 weeks | Primary:<br>Change from baseline in rTNSS<br><br>Secondary:<br>Change from baseline in iTNSS, rTOSS, iTOSS, individual symptom scores, RQLQ and | Primary:<br>The 80 µg and 160 µg treatment groups experienced a 15.1% and 16.0% reduction in rTNSS, respectively, compared to a 3.7% reduction for the placebo group (*P*<0.001 for both).<br><br>Patients randomized to receive 80 µg or 160 µg of ciclesonide experienced a 14.3% and 15.4% reduction, respectively, in iTNSS score, compared to placebo (3.9%; *P*<0.001).<br><br>Both the 80 µg and 160 µg doses of ciclesonide were associated with |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| vs<br><br>placebo | standard skin prick test | | safety | statistically significant improvements in rTOSS compared to placebo (15.7 and 15.0 vs 6.8%, respectively; *P*<0.01).<br><br>An improvement in iTOSS from baseline was also achieved with both 80 µg (*P*=0.008) and 160 µg (*P*=0.002) of ciclesonide compared to placebo.<br><br>Furthermore, individual morning and evening reflective and instantaneous nasal symptom scores of nasal congestion, runny nose, sneezing, and nasal itching were significantly improved with 80 µg and 160 µg doses of ciclesonide compared to placebo (*P*<0.001 for all).<br><br>Overall, both doses of ciclesonide were associated with statistically significant improvements in RQLQ scores from baseline compared to patients receiving placebo (*P*<0.001 for both doses compared to placebo).<br><br>The incidence of adverse events was comparable between the ciclesonide treatment groups and placebo. The incidence of nasal erosions was 1.3% in the 80 µg treatment group and 0.9% in the 160 µg treatment groups. These erosions were assessed as mild in intensity and did not lead to discontinuation from the study. |
| Berger et al[23] (abstract)<br><br>Ciclesonide 74 µg QD (Zetonna®)<br><br>vs<br><br>ciclesonide 148 µg QD (Zetonna®)<br><br>vs | DB, MC, PC, PG, RCT<br><br>Patients ≥12 years of age with a ≥2-year history of PAR | N=1,111<br><br>26 weeks | Primary:<br>Change from baseline in rTNSS, iTNSS, RQLQ and treatment-related adverse events<br><br>Secondary:<br>Not reported | Primary:<br>Patients receiving the 74 µg or 148 µg ciclesonide dose experienced a statistically significant improvement from baseline in rTNSS compared to placebo (LS mean change of 0.65 and 0.52, respectively; *P*≤ 0.01 for both compared to placebo).<br><br>The total scores for iTNSS were significantly improved with both the 74 µg and 148 µg ciclesonide doses compared to placebo (LS mean change of 0.51 and 0.42, respectively; *P*<0.05).<br><br>Both ciclesonide doses were associated with statistically significant improvements in RQLQ scores compared to placebo over 26 weeks (*P*<0.01). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| placebo | | | | The overall incidence of adverse events was comparable between the treatment groups.<br><br>Secondary:<br>Not reported |
| Ratner et al[24] (abstract)<br><br>Ciclesonide 74 µg QD (Zetonna®)<br><br>vs<br><br>ciclesonide 148 µg QD (Zetonna®)<br><br>vs<br><br>placebo | DB, MC, PC, PG, RCT<br><br>Patients ≥12 years of age with a ≥2-year history of SAR from mountain cedar pollen | N=671<br><br>2 weeks | Primary:<br>Change from baseline rTNSS, iTNSS, rTOSS and safety<br><br>Secondary:<br>Not reported | Primary:<br>Patients randomized to either the 74 µg or 148 µg ciclesonide doses experienced a statistically significant improvement from baseline in rTNSS compared to placebo (LS mean change of 1.04 and 1.02, respectively; *P*≤ 0.01 for both compared to placebo).<br><br>Patients who received either the 74 µg or 148 µg ciclesonide dose experienced significant improvements in iTNSS from baseline compared to the placebo group (LS mean change of 0.90 and 0.83 respectively; *P*< 0.001 for both compared to placebo).<br><br>Only the 74 µg ciclesonide treatment group experienced a statistically significant improvement in rTOSS compared with placebo (LS mean change of 0.52; *P*=0.0124).<br><br>The overall incidence of AEs was low and comparable between the treatment groups.<br><br>Secondary:<br>Not reported |
| Mohar et al[25] (abstract)<br><br>Ciclesonide 74 µg QD (Zetonna®)<br><br>vs<br><br>ciclesonide 148 µg QD (Zetonna®) | DB, MC, PC, PG, RCT<br><br>Patients ≥12 years of age with a ≥ 2-year history of PAR | N=1,111<br><br>26 weeks | Primary:<br>Change from baseline to week six in rTNSS, iTNSS, RQLQ scores and adverse events<br><br>Secondary:<br>Not reported | Primary:<br>Patients randomized to either the 74 µg or 148 µg ciclesonide doses experienced a statistically significant improvement from baseline in rTNSS compared to placebo (LS mean change of 0.70 and 0.54, respectively; *P*≤ 0.01 for both compared to placebo).<br><br>After six weeks of treatment, total iTNSS scores were significantly improved in both the 74 µg or 148 µg ciclesonide treatment groups compared to placebo (LS mean change of 0.58 and 0.42, respectively; *P*<0.05 for both compared to placebo). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| vs<br><br>placebo | | | | Six weeks of treatment with either dose of ciclesonide was associated with statistically significant improvements in RQLQ scores compared to placebo (*P*<0.01 for both compared to placebo).<br><br>The overall incidence of adverse events was similar between the ciclesonide treatment groups and placebo over 26 weeks. |
| LaForce et al[26]<br><br>Ciclesonide 300 µg QD (Zetonna®)<br><br>Vs<br><br>ciclesonide 150 µg QD (Zetonna®)<br><br>vs<br><br>ciclesonide 75 µg QD (Zetonna®)<br><br>vs<br><br>placebo | DB, MC, PC, PG, RCT<br><br>Patients ≥12 years of age with SAR for ≥2 years and a sensitivity to grass or tree pollen via skin prick and a rTNSS of ≥6/12 and reported score of ≥2 for rhinorrhea or nasal congestion during the previous seven days of run-in period | N=513<br><br>2 weeks | Primary:<br>Change from baseline in rTNSS<br><br>Secondary:<br>Change from baseline in iTNSS, morning iTNSS, RQLQ, rNNSS, PNSS and safety | Primary:<br>The change from baseline in rTNSS was 0.81 (95% CI, 0.32 to 1.29; *P*=0.001), 0.90 (95% CI, 0.40 to 1.39; *P*<0.001) and 0.66 (95% CI, 0.16 to 1.16; *P*=0.01) for the ciclesonide 300 µg, 150 µg and 75 µg groups, respectively, compared to placebo.<br><br>Secondary:<br>All ciclesonide doses significantly improved the average morning and evening iTNSS during the study period compared to placebo. Treatment differences were 0.75 (95% CI, 0.26 to 1.23; *P*=0.002), 0.86 (95% CI, 0.36 to 1.35; *P*=0.001) and 0.75 (95% CI, 0.25 to 1.25; *P*=0.003) for the ciclesonide 300 µg, 150 µg and 75 µg groups, respectively, compared to placebo.<br><br>Treatment differences for the reduction in the morning iTNSS were 0.86 (95% CI, 0.36 to 1.35; *P*<0.001), 1.03 (95% CI, 0.52 to 1.53; *P*<0.001) and 0.88 (95% CI, 0.37 to 1.39; *P*<0.001) for the ciclesonide 300 µg, 150 µg and 75 µg groups, respectively, compared to placebo.<br><br>Statistically significant improvements in RQLQ scores occurred with ciclesonide 300 µg (0.54; 95% CI, 0.10 to 0.98; *P*=0.02) and 75 µg (0.61; 95% CI, 0.16 to 1.06; *P*=0.008) compared to placebo, but not for the 150 µg treatment group (0.38; 95% CI, -0.06 to 0.81; *P*=0.09).<br><br>Significant improvements in PNSS scores occurred with ciclesonide 300 µg (0.91; 95% CI, 0.25 to 1.58; *P*=0.007), ciclesonide 150 µg (0.73; 95% CI, 0.05 to 1.40; *P*=0.04) and ciclesonide 75 µg (0.94; 95% CI, 0.25 to 1.62; *P*=0.007) compared to placebo. |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| | | | | No differences in the type or severity of adverse events were reported between treatment groups. The most frequently reported adverse events were headache and nasal discomfort. |
| Ratner et al[27]<br><br>Ciclesonide 25 µg QD<br><br>vs<br><br>ciclesonide 50 µg QD<br><br>vs<br><br>ciclesonide 100 µg QD<br><br>vs<br><br>ciclesonide 200 µg QD<br><br>vs<br><br>placebo | DB, MC, PC, PG, Phase II, RCT<br><br>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 | N=726<br><br>2 weeks | Primary:<br>Change from baseline in sum of morning and evening rTNSS<br><br>Secondary:<br>Change from baseline in the sum of morning and evening iTNSS and use of rescue medications | Primary:<br>Ciclesonide 100 and 200 µg/day, significantly improved the sum of morning and evening rTNSS compared to placebo. (*P*=0.04 and *P*=0.003).<br>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.<br><br>Secondary:<br>Both ciclesonide 100 and 200 µg/day demonstrated greater improvements in iTNSS compared to placebo (*P* value not reported).<br><br>There were no appreciable differences in the use of rescue medication, chlorpheniramine, across all treatment groups. |
| Fokkens et al[28]<br><br>Fluticasone furoate 110 µg QD<br><br>vs<br><br>placebo | DB, MC, PC, PG, RCT<br><br>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 | N=285<br><br>2 weeks | Primary:<br>Mean change from baseline over the entire treatment period in daily rTNSS<br><br>Secondary:<br>Mean change from baseline over the entire treatment period in daily rTOSS, morning predose iTNSS, | Primary:<br>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).<br><br>Secondary:<br>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).<br><br>In terms of overall response to therapy, 67% of patients receiving |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| | skin prick test to grass pollen or a positive in vitro test for specific IgE, within 12 months prior to the study | | overall evaluation of response to therapy, mean change from baseline in RQLQ, iTOSS, daily reflective and instantaneous individual symptom scores, time to onset of action | fluticasone furoate reported significant or moderate improvement, compared to 39% of patients given placebo (*P*<0.001).<br><br>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). |
| Gradman et al[29]<br><br>Fluticasone furoate 110 µg QD<br><br>vs<br><br>placebo | DB, NI, PC, RCT, XO<br><br>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<br><br>2 weeks | Primary:<br>Mean growth rate in lower-leg length<br><br>Secondary:<br>Adverse events | Primary:<br>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.<br><br>Secondary:<br>Reported adverse events were similar between the two groups. |
| Kaiser et al[30]<br><br>Fluticasone furoate 110 µg QD<br><br>vs<br><br>placebo | DB, PC, PG, RCT<br><br>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 | N=299<br><br>2 weeks | Primary:<br>Mean change from baseline over the entire treatment period in daily rTNSS<br><br>Secondary:<br>Mean change from baseline over the entire treatment | Primary:<br>Fluticasone furoate significantly reduced nasal symptoms compared to placebo, with a treatment difference of -1.473 (*P*<0.001).<br><br>Secondary:<br>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.<br><br>Fluticasone furoate demonstrated a significant reduction in morning |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| | seasons; positive skin prick test response to ragweed allergen within 12 months prior to start of study; only moderate-to-severe nasal and ocular symptoms; during 2005 fall ragweed allergy season | | period in daily rTOSS, morning predose iTNSS, overall evaluation of response to therapy, HRQL based on RQLQ | predose iTNSS of -1.375 compared with placebo (*P*<0.001).<br><br>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.<br><br>Fluticasone furoate-treated patients reported significant improvements in the overall RQLQ score compared to patients in the placebo group (-0.606; *P*<0.001).<br><br>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[31]<br><br>Fluticasone furoate 110 µg QD<br><br>vs<br><br>placebo | DB, MC, PC, PG, RCT<br><br>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<br><br>4 weeks | Primary:<br>Change from baseline in daily rTNSS<br><br>Secondary:<br>Change from baseline in AM predose iTNSS, AM and PM rTNSS, individual nasal symptoms, ocular symptoms, itching, QOL and response to therapy | Primary:<br>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).<br><br>Secondary:<br>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).<br><br>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.<br><br>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). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| | | | | There was no difference between treatments with regard to ocular symptoms.<br><br>A significantly higher percentage of patients treated with fluticasone furoate reported treatment to be effective compared to patients receiving placebo (*P*=0.005). |
| Meltzer et al[32]<br><br>Fluticasone furoate 110 µg QD<br><br>vs<br><br>fluticasone furoate 55 µg QD<br><br>vs<br><br>placebo | DB, MD, PC, PG, RCT<br><br>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<br><br>2 weeks | Primary:<br>Change from baseline in daily rTNSS<br><br>Secondary:<br>Change from baseline in AM predose iTNSS, response to therapy, adverse events, laboratory tests, nasal examinations, vital signs and ECG | Primary:<br>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).<br><br>Secondary:<br>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).<br><br>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).<br><br>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).<br><br>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[33] | DB, MC, PC, PG, RCT | N=558 | Primary:<br>Mean change from | Primary:<br>Improvements in daily rTNSS over four weeks were not statistically |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| Fluticasone furoate 110 µg QD<br><br>vs<br><br>fluticasone furoate 55 µg QD<br><br>vs<br><br>placebo | Pediatric patients 2 to 11 years of age with a six month or longer history PAR documented by a positive skin prick test against an appropriate perennial allergen | 12 weeks | baseline in daily rTNSS over four weeks<br><br>Secondary:<br>Mean change from baseline in daily iTNSS, overall response to therapy, safety | 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).<br><br>Secondary:<br>Both fluticasone furoate 55 (-0.751) and 110 µg (-0.651) showed significant improvements from baseline in daily iTNSS compared to placebo (*P*=0.002 and *P*=0.009).<br><br>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).<br><br>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[34]<br><br>Fluticasone furoate 55 µg QD<br><br>vs<br><br>fluticasone furoate 110 µg QD<br><br>vs<br><br>fluticasone furoate | DB, PC, PG, RCT<br><br>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<br><br>14 days | Primary:<br>Mean change from baseline in daily rTNSS<br><br>Secondary:<br>Mean change from baseline in morning predose iTNSS, mean change from baseline in daily rTOSS and iTOSS, mean change from | Primary:<br>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).<br><br>Secondary:<br>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). |

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| 220 µg QD<br><br>vs<br><br>fluticasone furoate 440 µg QD<br><br>vs<br><br>placebo | | | baseline in morning and evening rTNSS and iTNSS and overall response to therapy | 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).<br><br>At the end of the treatment period, patients treated with fluticasone furoate rated their overall response to therapy significantly better than those treated with placebo (*P*<0.001). |
| Rosenblut et al[35]<br><br>Fluticasone furoate 110 µg QD<br><br>vs<br><br>placebo | DB, MC, PC, PG, RCT<br><br>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<br><br>12 months | Primary:<br>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<br><br>Secondary:<br>Not reported | Primary:<br>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.<br><br>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.<br><br>There were no clinically meaningful differences between the groups in terms of other safety assessments, including mean changes in ophthalmic parameters.<br><br>Secondary:<br>Not reported |
| Vasar et al[36]<br><br>Fluticasone furoate 110 µg QD<br><br>vs<br><br>placebo | DB, PC, PG, RCT<br><br>Patients 12 years of age and older with a history of PAR for two years or longer and a positive skin-prick | N=302<br><br>6 weeks | Primary:<br>Mean change from baseline in rTNSS<br><br>Secondary:<br>Mean change from baseline in morning predose iTNSS, daily | Primary:<br>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).<br><br>Secondary:<br>The mean change from baseline in morning predose iTNSS was significantly greater in fluticasone furoate patients compared to |

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| | test to an appropriate perennial allergen | | rTNSS, daily PNIF, and RQLQ scores, overall response to therapy and safety | placebo (-3.82 vs -2.36; *P*<0.001).<br><br>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).<br><br>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).<br><br>Treatment was well tolerated over the six week period. |
| Prenner et al[37]<br><br>Mometasone 2 sprays in each nostril QD<br><br>vs<br><br>placebo | DB, MC, PC, PG, RCT<br><br>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<br><br>15 days | Primary:<br>Change from baseline in iTOSS and iTNSS<br><br>Secondary:<br>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:<br>A significant reduction in iTOSS was observed in the mometasone group compared to placebo (*P*=0.026).<br><br>A reduction in iTNSS was observed in the mometasone group compared to placebo (*P*<0.001).<br><br>Secondary:<br>A significant reduction in the LS mean change from baseline in rTOSS was observed in the mometasone group compared to placebo (*P*=0.005).<br><br>A significant reduction in the LS mean change from baseline in rTNSS was observed in the mometasone group compared to placebo (*P*<0.001).<br><br>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).<br><br>No significant difference was observed in the instantaneous eye redness score.<br><br>A significant improvement in individual reflective ocular symptom |

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| | | | | scores was observed in the mometasone group compared to placebo (*P*<0.05).<br><br>A significant improvement in all individual instantaneous and reflective nasal symptoms scores was observed in the mometasone group compared to placebo (*P*<0.05).<br><br>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).<br><br>Greater improvements in the RQLQ were observed in the mometasone group compared to placebo (*P*<0.001).<br><br>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). |
| Makihara et al[38]<br><br>Mometasone 200 µg QD<br><br>vs<br><br>placebo | DB, PC, PG, RCT<br><br>Patients 16 to 65 years of age with a ≥2 year history of Japanese cedar/cypress pollinosis sensitivity assessed by skin price | N=50<br><br>12 weeks | Primary:<br>Change from baseline in TNSS<br><br>Secondary:<br>Change from baseline in TOSS, T5SS, QoL, daytime sleepiness, smell disturbances, frequency of rescue medication use, ECP levels in nasal secretions and safety | Primary:<br>Compared to the placebo group, TNSS scores were significantly lower in the mometasone treatment group following 12 weeks of treatment (*P*<0.05).<br><br>Secondary:<br>After 12 weeks of treatment there was no statistically significant difference between the mometasone and placebo treatment groups with regard to TOSS (*P*=NS).<br><br>Compared to placebo, mometasone was associated with a statistically significant reduction in T5SS at 12 weeks (*P*<0.05).<br><br>A statistically significant improvement in QoL occurred with mometasone compared to placebo at weeks two through 10 (*P*<0.05); however, the difference was not significant at week 12.<br><br>There was no statistically significant difference between mometasone and placebo with regard to daytime sleepiness and smell |

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| | | | | disturbances at 12 weeks (*P*>0.05).<br><br>No difference in rescue medication use with loratadine was reported between the treatment groups (*P*>0.05).<br><br>At 12 weeks, there was no statistically significant difference between treatment groups with regard to nasal secretion levels of ECP (*P*=0.063).<br><br>There was no difference in the rate of adverse events between the treatments. There were no patients that discontinued the study medication due to adverse events. |
| Baena-Cagnani et al[39]<br><br>Mometasone 1 spray in each nostril QD<br><br>vs<br><br>placebo | DB, MC, PC, PG, RCT<br><br>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<br><br>4 week efficacy phase followed by 6 month open-label safety period | Primary:<br>Change from baseline to day 15 in physician assessed TNSS<br><br>Secondary:<br>Change from baseline to day 15 in subject assessed TNSS, TSS, TNNSS, individual symptom scores and condition of PAR between baseline and endpoint | Primary:<br>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).<br><br>Secondary:<br>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).<br><br>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).<br><br>At day 15, subject assessed TNNSS scores were not significantly different between the treatment groups.<br><br>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).<br><br>Physician evaluation of the patients' condition favored mometasone |

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| | | | | treatment over placebo at both day 15 (*P*<0.01) and 29 (*P*=0.02). |
| Khanna et al[40]<br><br>Beclomethasone, dose not specified<br><br>vs<br><br>budesonide, dose not specified<br><br>vs<br><br>fluticasone propionate, does not specified<br><br>vs<br><br>mometasone, dose not specified | SB, XO<br><br>Patients with allergic rhinitis | N=114<br><br>Duration not specified | Primary:<br>Sensory perceptions and patient reference<br><br>Secondary:<br>Not reported | Primary:<br>Significantly more patients preferred mometasone and reported less irritation, odor and aftertaste (*P* values not reported).<br><br>Fluticasone propionate was reported by patients as having a significantly higher odor strength and amount of irritation (*P* values not reported).<br><br>Eighty percent of the patients predicted better compliance with their preferred drug.<br><br>Secondary:<br>Not reported |
| Svendsen et al[41]<br><br>Beclomethasone, dose not specified<br><br>vs<br><br>flunisolide, dose not specified | DB, RCT, XO<br><br>Patients with perennial rhinitis | N=23<br><br>8 weeks | Primary:<br>Rhinitis symptoms and patient preference<br><br>Secondary:<br>Not reported | Primary:<br>There were no statistically significant differences in rhinitis symptoms or patient preference between treatments (*P* value not reported).<br><br>Secondary:<br>Not reported |
| Welsh et al[42]<br><br>Beclomethasone 336 µg daily, administered as 2 sprays in each nostril BID | PC, RCT<br><br>Patients 12 to 50 years of age, with at least a two year history of SAR and positive skin test to | N=120<br><br>8 weeks | Primary:<br>Symptomatic relief<br><br>Secondary:<br>Adverse events | Primary:<br>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).<br><br>Beclomethasone and flunisolide significantly reduced hay fever |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| vs<br><br>flunisolide 200 µg daily, administered as 2 sprays in each nostril BID<br><br>vs<br><br>cromolyn 41.6 mg daily, administered as 1 spray in each nostril QID<br><br>vs<br><br>placebo | crude short ragweed extract | | | symptoms compared to cromolyn (*P*<0.001).<br><br>There were no statistically significant differences between beclomethasone and flunisolide in relief of hay fever symptoms (*P* value not reported).<br><br>Secondary:<br>There was significantly more nasal burning with flunisolide than the other treatments (*P*<0.001). |
| Al-Mohaimeid[43]<br><br>Budesonide 200 µg BID<br><br>vs<br><br>beclomethasone 200 µg BID | RCT, SB<br><br>Patients 18 to 70 years of age, with PAR | N=120<br><br>3 weeks | Primary:<br>Nasal symptoms<br><br>Secondary:<br>Not reported | Primary:<br>There were significantly fewer reports of sneezing with budesonide than beclomethasone (*P*=0.04).<br><br>No statistically significant differences in symptoms of blocked nose, runny nose, itchy nose, runny eyes and sore eyes were reported (*P*>0.05).<br><br>After three weeks of treatment, more patients reported being free of symptoms with budesonide compared to beclomethasone (38 vs 27%; no *P* value reported).<br><br>More patients reported the treatment as noticeably, very, or totally effective with budesonide than with beclomethasone (72 vs 58%; *P* value not reported).<br><br>Secondary:<br>Not reported |
| McArthur[44] | DB, RCT | N=88 | Primary: | Primary: |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| Budesonide 200 µg BID<br><br>vs<br><br>beclomethasone 200 µg BID | Adults with SAR | 3 weeks | Nasal and non-nasal symptom score<br><br>Secondary:<br>Adverse events | Budesonide treatment resulted in significantly lower scores for runny 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.<br><br>There was no statistically significant difference between treatment groups in scores for nasal blockage, runny eyes, and sore eyes (*P* value not reported).<br><br>Secondary:<br>Adverse events for both treatments were mild and transient. |
| Vanzieleghem et al[45]<br><br>Budesonide as needed, up to 2 sprays of 50 µg/spray in each nostril QID<br><br>vs<br><br>beclomethasone as needed, up to 2 sprays of 50 µg/spray in each nostril QID | DB, DD, RCT<br><br>Patients with SAR during the ragweed-pollen season | N=61<br><br>7 weeks | Primary:<br>Nasal symptoms, use of chlorpheniramine as rescue medication<br><br>Secondary:<br>Adverse events | Primary:<br>Less budesonide was administered by the subjects than beclomethasone to maintain good control of nasal symptoms (*P*=0.016).<br><br>No statistically significant difference was observed between treatment groups in the amount of oral chlorpheniramine used as rescue medication (*P*=NS).<br><br>Secondary:<br>Reported adverse events with both treatments were mild and transient. |
| Andersson et al[46]<br><br>Budesonide 200 or 400 µg QD<br><br>vs<br><br>fluticasone propionate 200 µg QD<br><br>vs | MC, PC, PG, RCT<br><br>Patients with PAR | N=98<br><br>6 weeks | Primary:<br>Rhinitis symptoms, use of terfenadine as rescue medication<br><br>Secondary:<br>Safety as assessed by rhinoscopy, urine cortisol, adverse events | Primary:<br>There were no significant differences in nasal symptoms or eye symptoms between active treatment groups (*P* value not reported).<br><br>All active treatments reduced the use of terfenadine when compared with baseline, but this was significant with budesonide only (*P*<0.05).<br><br>Secondary:<br>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 |
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| placebo | | | | |
| Day et al[47]<br><br>Budesonide 256 µg QD<br><br>vs<br><br>fluticasone propionate 200 µg QD | DB, MC, PC, PG, RCT<br><br>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<br><br>6 weeks | Primary:<br>Nasal symptoms, patients' overall evaluation of efficacy, and use of rescue medication<br><br>Secondary:<br>Adverse events | Primary:<br>Both treatments resulted in significantly greater improvement in combined nasal symptom scores, runny nose and sneezing from baseline compared with placebo ($P \leq 0.0012$). 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).<br><br>Significant improvements in nasal symptoms were seen at 36 hours with budesonide and 60 hours with fluticasone propionate (*P* value not reported).<br><br>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.<br><br>Secondary:<br>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[48]<br><br>Study 1:<br>Budesonide 32 µg in each nostril for one dose<br><br>vs<br><br>fluticasone propionate 100 µg in each nostril for one dose | MC, RCT, SB, XO<br><br>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)<br><br>N=190 (Study 2)<br><br>1 day | Primary:<br>Sensory Perceptions Questionnaire and patients' product preference<br><br>Secondary:<br>Adverse events | Primary:<br>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.<br><br>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. |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| Study 2:<br>budesonide 32 µg in each nostril for one dose<br><br>vs<br><br>fluticasone propionate 50 µg in each nostril for one dose | | | | More patients perceived the spray in the throat as less wet (*P*<0.004 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.<br><br>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.<br><br>Significantly more patients perceived a less forceful spray with budesonide and therefore preferred budesonide to fluticasone propionate (*P*<0.001).<br><br>Overall, significantly more patients preferred budesonide to fluticasone propionate (*P*=0.02).<br><br>Secondary:<br>Budesonide and fluticasone propionate were both well tolerated. |
| Stern et al[49]<br><br>Budesonide 128 µg or 256 µg QD<br><br>vs<br><br>fluticasone propionate 200 µg QD<br><br>vs<br><br>placebo | MC, PC, PG, RCT<br><br>Patients 18 to 72 years of age, with at least a two-year history of allergic rhinitis | N=635<br><br>4 to 6 weeks | Primary:<br>Nasal and eye symptoms<br><br>Secondary:<br>Adverse events | Primary:<br>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.<br><br>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).<br><br>Secondary:<br>Budesonide and fluticasone propionate were well tolerated, with reported adverse events mild to moderate in severity. |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| Naclerio et al[50]<br><br>Budesonide 32 µg in each nostril QD<br><br>vs<br><br>mometasone 100 µg in each nostril QD | PG, RCT<br><br>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 | N=20<br><br>2 weeks | Primary:<br>Symptomatic relief and quality of life as assessed by the RQLQ and nasal clearance<br><br>Secondary:<br>Not reported | Primary:<br>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).<br><br>Data on nasal clearance could not be interpreted by the authors.<br><br>Secondary:<br>Not reported |
| Aasand et al[51]<br><br>Flunisolide 50 µg in each nostril BID<br><br>vs<br><br>beclomethasone 50 µg in each nostril QID | MC, PG, SB<br><br>Patients with at least a two-year history of seasonal rhinitis | N=47<br><br>4 weeks | Primary:<br>Nasal symptoms<br><br>Secondary:<br>Adverse events | Primary:<br>Flunisolide and beclomethasone improved nasal rhinitis symptoms (88% of patients showed improvement with flunisolide vs 91% with beclomethasone; *P* value not reported).<br><br>No statistical differences were observed between treatment groups (*P* value not reported).<br><br>Secondary:<br>The only reported adverse event with both medications was mild stinging of transient duration. |
| Langrick[52]<br><br>Flunisolide 200 µg daily, administered as 2 sprays in each nostril BID<br><br>vs<br><br>beclomethasone 400 µg daily, administered as 2 sprays in each nostril BID | PG, RCT, SB<br><br>Patients 18 to 60 years of age, with a history of moderate to severe hay fever | N=69<br><br>7 weeks | Primary:<br>Signs and symptoms of hay fever, severity of symptoms, and physicians' and patients' evaluation of overall effect of treatment<br><br>Secondary:<br>Adverse events | Primary:<br>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).<br><br>Secondary:<br>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[53] | SB, XO | N=34 | Primary: | Primary: |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| Flunisolide 50 µg in each nostril BID<br><br>vs<br><br>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 | Rhinitis symptoms<br><br>Secondary:<br>Adverse events and *Candida* growth | Treatment with flunisolide and beclomethasone significantly reduced sneezing, stuffiness, runny nose, nose-blowing and interference with routine life when compared with baseline (*P* value not reported).<br><br>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).<br><br>Secondary:<br>Neither treatment resulted in *Candida* growth.<br><br>Reported side effects were minor and were mostly nasal irritation or dryness. |
| Sahay et al[54]<br><br>Flunisolide 50 µg in each nostril BID<br><br>vs<br><br>beclomethasone 50 µg in each nostril QID | OL, PG<br><br>Patients with PAR, with or without SAR | N=56<br><br>4 weeks | Primary:<br>Symptom relief<br><br>Secondary:<br>Detection of *Candida* growths and safety | Primary:<br>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).<br><br>There were no statistically significant differences in control of symptoms between the two treatment groups (*P* value not reported).<br><br>Secondary:<br>There were no signs of adrenal suppression or *Candida* growths in either group.<br><br>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[55]<br><br>Flunisolide 50 µg in each nostril BID<br><br>vs | OL, PG<br><br>Patients with allergic rhinitis and seasonal symptoms for at | N=45<br><br>4 weeks | Primary:<br>Daily symptoms and severity of nasal symptoms<br><br>Secondary: | Primary:<br>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).<br><br>Improvement in the severity of nasal symptoms compared with |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| beclomethasone 50 µg in each nostril QID | least two years | | Adverse events | baseline was similar in both treatment groups (*P* value not reported).<br><br>Secondary:<br>The reported side effects were mild and primarily consisted of local irritation. |
| Kubavat et al[56]<br><br>Fluticasone furoate 110 µg QD<br><br>vs<br><br>fluticasone propionate 200 µg QD | AC, MC, OL<br><br>Patients ≥18 years of age with complaints of allergic rhinitis with nasal/ocular symptoms | N=220<br><br>2 weeks | Primary:<br>Change from baseline in TSS<br><br>Secondary:<br>Change from baseline in TNSS and TOSS, individual nasal and ocular symptoms | Primary:<br>The mean change in TSS score was significantly greater for patients receiving fluticasone furoate compared to fluticasone propionate over two weeks (-10.4 vs -8.9; *P*<0.005).<br><br>A significantly greater proportion of patients experienced complete relief from all nasal and ocular symptoms (i.e. a total symptom score of zero during the course of the study) with fluticasone furoate treatment compared to fluticasone propionate (45.3 vs 31.4%; *P*<0.05).<br><br>Secondary;<br>A statistically significant reduction in TNSS occurred with fluticasone furoate treatment compared to fluticasone propionate (-7.3 vs -6.2; *P*<0.05).<br><br>There was no statistically significant difference in TOSS between fluticasone furoate treatment and fluticasone propionate following two weeks of treatment (-3.1 vs -2.7; *P*=NS).<br><br>There were statistically significant improvements in symptom scores with fluticasone furoate compared to fluticasone propionate for nasal congestion (*P*<0.05), nasal itching (*P*<0.001) and tearing/watery eyes (*P*<0.05). There were no other statistically significant differences in individual symptom scores between the treatments (*P*=NS). |
| Meltzer et al[57]<br><br>Fluticasone furoate 110 µg QD followed by fluticasone propionate 220 µg QD | DB, PC, RCT, XO<br><br>Patients 18 years of age and older with SAR and nasal symptoms during | N=360<br><br>21 days | Primary:<br>Patient preference at the end of the second XO period based on scent or odor | Primary:<br>Twice as many patients preferred fluticasone furoate compared to fluticasone propionate based on scent or odor (*P*<0.001).<br><br>Fifteen percent of patients had no preference for either product based on scent or odor. |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| vs<br><br>fluticasone propionate 200 µg QD followed by fluticasone furoate 110 µg QD<br><br>vs<br><br>fluticasone furoate placebo QD followed by fluticasone propionate placebo QD<br><br>vs<br><br>fluticasone propionate placebo QD followed by fluticasone furoate placebo QD | the two previous fall allergy seasons and a positive skin test result and exposure to fall allergens | | Secondary:<br>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 | Secondary:<br>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 ($P<0.001$).<br><br>No statistically significant differences were observed between products in ease of use, consistency of medication dose delivered, delivery method or device comfort.<br><br>TNSS were similar between treatment groups. Fluticasone furoate and fluticasone propionate significantly reduced TNSS compared to their respective placebo ($P\leq0.01$).<br><br>The proportion of patients with any adverse event was similar between treatments. |
| Meltzer et al[58]<br><br>Fluticasone furoate 2 sprays in each nostril for one dose followed by fluticasone propionate 2 sprays in each nostril for one dose<br><br>vs<br><br>fluticasone propionate 2 sprays in each | DB, MC, RCT, SD, XO<br><br>Patients 18 years of age and older with a diagnosis of allergic rhinitis | N=127<br><br>1 day | Primary:<br>Overall patient preference for fluticasone furoate or fluticasone propionate<br><br>Secondary:<br>Patient preference for individual sensory attributes and their ratings | Primary:<br>Significantly more patients favored fluticasone furoate compared to fluticasone propionate ($P=0.003$).<br><br>Secondary:<br>Significantly more patients favored fluticasone furoate compared to fluticasone propionate based on odor, taste, aftertaste drip down the throat and nose runoff ($P\leq0.037$).<br><br>No significant differences were observed between groups with respect to whether the medication felt soothing, caused nasal irritation or caused sneezing. |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| nostril for one dose followed by fluticasone furoate 2 sprays in each nostril for one dose<br><br>A ten minute washout period occurred between XO treatments. | | | | |
| Haye et al[59]<br><br>Fluticasone propionate 200 µg BID<br><br>vs<br><br>beclomethasone 200 µg BID | DB, MC, PG, RCT<br><br>Patients 16 years of age and older with perennial rhinitis | N=251<br><br>1 year | Primary:<br>Rhinitis symptoms<br><br>Secondary:<br>Safety | Primary:<br>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.<br><br>No significant differences were observed in the amount of sneezing (*P*=0.114) or nasal itching (*P*=0.052) between treatment groups.<br><br>Secondary:<br>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[60]<br><br>Fluticasone propionate 100 µg BID or 200 µg QD<br><br>vs<br><br>beclomethasone 168 µg BID<br><br>vs | DB, MC, PC, PG, RCT<br><br>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 | N=238<br><br>4 weeks | Primary:<br>Nasal symptoms<br><br>Secondary:<br>Adverse events | Primary:<br>Fluticasone propionate reduced patient-rated nasal symptom scores significantly more than beclomethasone (*P*<0.05) and placebo (*P*<0.01) at all time points measured.<br><br>There were no statistically significant differences in clinician-rated nasal symptom scores between treatment groups (*P*=NS).<br><br>Secondary:<br>There were no significant differences in adverse events between treatment groups (*P* value not reported). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| placebo | symptoms | | | |
| Ratner et al[61]<br><br>Fluticasone propionate 200 µg QD<br><br>vs<br><br>beclomethasone 168 µg BID<br><br>vs<br><br>placebo | DB, MC, PC, PG, RCT<br><br>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<br><br>2 weeks | Primary:<br>Nasal symptoms, overall response to treatment, and use of rescue medication (chlorpheniramine)<br><br>Secondary:<br>Adverse events | Primary:<br>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).<br><br>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).<br><br>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).<br><br>Secondary:<br>No clinically significant differences in any of the safety variables between treatment groups were reported. |
| Van As et al[62]<br><br>Fluticasone propionate 100 µg BID or 200 µg QD<br><br>vs<br><br>beclomethasone 168 µg BID<br><br>vs<br><br>placebo | DB, MC, PC, PG, RCT<br><br>Patients 12 to 71 years of age, with PAR and moderate to severe symptoms, nasal eosinophils, and positive skin test to a perennial allergen | N=466<br><br>6 months | Primary:<br>Nasal symptoms and use of antihistamine as rescue medication<br><br>Secondary:<br>Adverse events | Primary:<br>Fluticasone propionate and beclomethasone reduced nasal obstruction, rhinorrhea, sneezing, nasal itching and nasal eosinophilia (*P* value not reported).<br><br>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).<br><br>Secondary:<br>No evidence of systemic effects with drug treatment was reported. |
| Bachert et al[63] | DB, PC, RCT, XO | N=23 | Primary: | Primary: |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| Fluticasone propionate 200 µg QD<br><br>vs<br><br>triamcinolone 220 µg QD<br><br>vs<br><br>placebo | Healthy volunteers 18 to 65 years of age | 12 days | Suppression of the HPA axis as measured by 12 hour overnight urinary cortisol excretion and serum cortisol concentrations<br><br>Secondary:<br>Adverse events | 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.<br><br>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.<br><br>Secondary:<br>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[64]<br><br>Mometasone 100 µg in each nostril QD<br><br>vs<br><br>beclomethasone 100 µg in each nostril BID<br><br>vs<br><br>placebo | DB, DD, MC, PC, PG, RCT<br><br>Patients 12 years of age and older, who are allergic to at least one perennial allergen, with adequate symptomatology | N=427<br><br>12 weeks | Primary:<br>Change from baseline in total morning plus evening diary nasal symptom score over the first 15 days of treatment<br><br>Secondary:<br>Total diary nasal symptom scores averaged over 15-day intervals beyond day 15, composite total and individual diary symptom scores, physician evaluation of response to therapy, and adverse events | Primary:<br>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).<br><br>The difference in reduction from baseline in nasal symptom scores between mometasone and beclomethasone was not significant at any time point (*P*≥0.32).<br><br>Secondary:<br>Physician evaluations of nasal symptoms for mometasone and beclomethasone were not statistically different from each other at any time point (*P* value not reported).<br><br>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[65] | DB, MC, PC, PG, | N=349 | Primary: | Primary: |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| Mometasone 100 µg in each nostril QD<br><br>vs<br><br>beclomethasone 84 µg in each nostril BID<br><br>vs<br><br>placebo | RCT<br><br>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 | 8 weeks | Severity score of nasal and non-nasal symptoms<br><br>Secondary:<br>Adverse events | 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).<br><br>There was no statistically significant difference in the percentage of days with minimal symptoms between treatment groups (*P* value not reported).<br><br>Nasal symptom scores for the treatment period prior to the allergy season onset were significantly lower with mometasone than beclomethasone (*P*=0.05).<br><br>Secondary:<br>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[66]<br><br>Mometasone 100 or 200 µg QD, administered as 2 sprays of 25 or 50 µg/spray in each nostril QD<br><br>vs<br><br>beclomethasone 100 µg in each nostril BID<br><br>vs<br><br>placebo | DB, DD, MC, PC, PG, RCT<br><br>Patients 18 years of age and older, with moderate to severe SAR for at least two years, who have a positive skin test to at least one tree and/or grass aeroallergen | N=501<br><br>4 weeks | Primary:<br>Nasal symptom score, physicians' and patients' evaluation of response to therapy, and use of loratadine as rescue medication<br><br>Secondary:<br>Adverse events | Primary:<br>Nasal symptoms (*P*≤0.01) and use of rescue medication (*P*≤0.05) were significantly improved in all three treatment groups compared to placebo.<br><br>There were no significant differences between treatment groups in nasal symptom score, physicians' evaluation of nasal symptoms, overall condition, and response to treatment, or use of rescue medication (*P* value not reported).<br><br>Secondary:<br>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). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| Mandl et al[67]<br><br>Mometasone 100 µg in each nostril QD<br><br>vs<br><br>fluticasone propionate 100 µg in each nostril QD<br><br>vs<br><br>placebo | DB, DD, PC, PG, RCT<br><br>Patients 12 to 77 years of age, who are allergic to at least one perennial allergen, and have moderate to severe symptomatology | N=550<br><br>12 weeks | Primary:<br>Nasal symptom score<br><br>Secondary:<br>Physicians' evaluation of nasal symptoms and response to therapy and adverse events | Primary:<br>Both mometasone and fluticasone propionate produced significantly greater improvements in nasal symptoms than placebo (*P*<0.01).<br><br>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).<br><br>Secondary:<br>Physicians' evaluation of nasal symptoms and response to therapy were similar for mometasone and fluticasone propionate (*P* value not reported).<br><br>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[68]<br><br>Mometasone, dose not specified<br><br>vs<br><br>fluticasone propionate 200 µg | DB, RCT, XO<br><br>Patients with allergic rhinitis | N=100<br><br>Duration not specified | Primary:<br>Individual product sensory attributes and overall sensory preference<br><br>Secondary:<br>Not reported | Primary:<br>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).<br><br>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).<br><br>Patients reported significantly larger percentage of expected compliance with mometasone than fluticasone propionate (47 vs 25%; *P*=0.03).<br><br>Secondary:<br>Not reported |
| Lumry et al[69]<br><br>Triamcinolone 220 µg QD | MC, PG, RCT, SB<br><br>Patients at 18 years of age and | N=152<br><br>3 weeks | Primary:<br>Nasal symptoms, eye symptoms, HRQL, and patient | Primary:<br>Significant improvements from baseline in rhinitis related-nasal and eye symptoms were seen with triamcinolone and beclomethasone (*P* value not reported). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| vs<br><br>beclomethasone 168 µg BID | older with at least a two-year history of SAR to ragweed pollen | | preference for sensory attributes<br><br>Secondary:<br>Adverse events | 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).<br><br>Patients rated the taste and odor of triamcinolone as significantly better than beclomethasone ($P \leq 0.05$). 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 ($P > 0.05$).<br><br>Secondary:<br>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[70]<br><br>Triamcinolone 220 µg QD<br><br>vs<br><br>beclomethasone 84 µg BID | MC, PG, RCT, SB<br><br>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 eosinophilia or basophilia | N=169<br><br>4 weeks | Primary:<br>Rhinitis symptoms and global evaluations of treatment by patients and physicians<br><br>Secondary:<br>Adverse events | Primary:<br>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).<br><br>Patients' global evaluation of treatment with triamcinolone was significantly higher than with beclomethasone ($P < 0.05$).<br><br>Secondary:<br>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).<br><br>There was significantly more medication-induced sneezing with triamcinolone compared to beclomethasone ($P = 0.024$).<br><br>There was significantly more medication runoff from the nose and throat with beclomethasone than triamcinolone ($P < 0.05$). |
| Bachert et al[71] | DB, MC, RCT, XO | N=95 | Primary: | Primary: |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| Triamcinolone 110 µg in each nostril QD<br><br>vs<br><br>fluticasone propionate 100 µg in each nostril QD<br><br>vs<br><br>mometasone 100 µg in each nostril QD | Patients 18 years of age or older with at least a two-year history of allergic rhinitis | 1 day | Sensory perceptions, patient preferences, and likelihood of compliance<br><br>Secondary:<br>Not reported | Overall, more patients preferred triamcinolone to fluticasone propionate ($P \leq 0.05$) and mometasone ($P \leq 0.001$).<br><br>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).<br><br>Triamcinolone was preferred more than mometasone for the taste, comfort and less irritation ($P < 0.05$ for all).<br><br>Fluticasone propionate was also preferred more than mometasone in terms of taste, comfort and amount of irritation ($P \leq 0.05$).<br><br>There were no significant differences between fluticasone propionate and mometasone in aftertaste and amount of irritation (*P* value not reported).<br><br>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.<br><br>Secondary:<br>Not reported |
| Gross et al[72]<br><br>Triamcinolone 110 µg in each nostril QD<br><br>vs<br><br>fluticasone propionate 100 µg in each nostril QD | AC, PG, RCT, SB<br><br>Patients 12 to 70 years of age, with fall SAR and positive skin test to ragweed | N=352<br><br>3 weeks | Primary:<br>Nasal symptoms, effects on HRQL as measured by RQLQ, adverse events<br><br>Secondary:<br>Not reported | Primary:<br>No statistically significant differences were reported between the treatment groups in daily TNSS ($P=0.332$), individual symptom 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).<br><br>Secondary:<br>Not reported |
| Small et al[73]<br><br>Triamcinolone 110 µg | MC, PG, RCT, SB<br><br>Patients 12 to 70 | N=233<br><br>21 days | Primary:<br>Rhinitis Index Score and individual | Primary:<br>There were no significant differences between treatment groups in the change from baseline in Rhinitis Index Score ($P=0.23$) or |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| in each nostril QD<br><br>vs<br><br>fluticasone propionate 100 µg in each nostril QD | 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 | | symptom score<br><br>Secondary:<br>Physicians' and patients' global evaluations, patients' acceptance of the study medications, and safety | individual symptoms, such as congestion (*P*=0.58), rhinorrhea (*P*=0.08), sneezing (*P*=0.51) and nasal itching (*P*=0.64).<br><br>Secondary:<br>There were no statistically significant differences between treatment groups in physicians' and patients' global evaluations (*P* value not reported).<br><br>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).<br><br>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[74]<br><br>Triamcinolone 110 µg in each nostril QD<br><br>vs<br><br>fluticasone propionate 100 µg in each nostril QD | AC, MC, PG, SB<br><br>Patients 12 to 70 years of age with seasonal allergic rhinitis for at least two years and a positive epicutaneous or intradermal test to one or more tests of grass pollen, tree pollen, and/or outdoor molds present in their environment | N=295<br><br>21 days | Primary:<br>Mean TNSS<br><br>Secondary:<br>Mean individual symptom scores, dropout rate due to insufficient therapeutic effect, RQLQ scores and SAQ scores | Primary:<br>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).<br><br>Secondary:<br>Both treatments were equally effective at reducing symptom scores from baseline including nasal discharge (*P*=0.9539), nasal stuffiness (*P*=0.7666), sneezing (*P*=0.5559) and nasal itching (*P*=0.7858).<br><br>Zero patients discontinued study the study medications due to lack of therapeutic effect.<br><br>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). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| | | | | 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[75]<br><br>Triamcinolone 220 µg one time<br><br>vs<br><br>fluticasone propionate 200 µg one time<br><br>vs<br><br>mometasone 200 µg one time | DB, MC, RCT, XO<br><br>Patients 18 to 70 years of age, with at least a two-year history of allergic rhinitis, who were symptomatic at baseline | N=215<br><br>1 day | Primary:<br>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<br><br>Secondary:<br>Not reported | Primary:<br>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).<br><br>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).<br><br>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).<br><br>Secondary:<br>Not reported |
| Garris et al[76]<br><br>Fluticasone furoate, dose not specified<br><br>vs<br><br>budesonide, dose not specified<br><br>vs<br><br>mometasone, dose not specified<br><br>vs | RETRO<br><br>Patients four years of age or older with at least one pharmacy claim for a branded intranasal corticosteroid between April 2007 and July 2007 | N=793,349<br><br>10 months | Primary:<br>Time to concomitant use of a prescription non-sedating antihistamine, montelukast, or ocular medications<br><br>Secondary:<br>Cost | Primary:<br>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.<br><br>Patients in the fluticasone furoate cohort had, on average, a 21% lower risk of having a concomitant prescription for allergic rhinitis compared to the other cohorts (*P*<0.05).<br><br>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).<br><br>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. |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| triamcinolone, dose not specified | | | | Secondary:<br>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[77]<br><br>Fluticasone propionate 200 µg QD or BID<br><br>vs<br><br>beclomethasone 200 µg BID<br><br>vs<br><br>placebo | DB, MC, PC, PG, RCT<br><br>Patients with allergic and nonallergic perennial rhinitis | N=not specified<br><br>12 weeks | Primary:<br>Nasal symptoms<br><br>Secondary:<br>Adverse events | Primary:<br>There were no significant differences between active treatment groups in regard to nasal symptoms (*P* value not reported).<br><br>Secondary:<br>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, ECP= eosinophil cationic protein , 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, PNSS=physician-assessed nasal symptom score, rNNSS= reflective non-nasal symptom score, RQLQ=rhinoconjunctivitis quality of life questionnaire, rTNSS=reflective total nasal symptom score, rTOSS=reflective total ocular nasal symptom score, SAR=seasonal allergic rhinitis, T5SS=total five symptom score, TNSS=total nasal symptom score, TOSS=total ocular symptom score, TSS=total symptom score

## Special Populations

**Table 5. Special Populations[3-12,14]**

| 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.<br><br>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.<br><br>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.<br><br>Omnaris® is approved for use in children six years of age and older.<br><br>Zetonna® is approved for use in children 12 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.<br><br>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.<br><br>Approved for use in children two years of age and older. | No dosage adjustment required. | No dosage adjustment required.<br><br>Monitoring is recommended with severe hepatic dysfunction. | C | Unknown |
| Fluticasone propionate | No dosage adjustment required | Not studied in renal | Not studied in hepatic | C | Unknown |

| Generic Name | Population and Precaution | | | | |
|---|---|---|---|---|---|
| | Elderly/ Children | Renal Dysfunction | Hepatic Dysfunction | Pregnancy Category | Excreted in Breast Milk |
| | in the elderly population.<br><br>Approved for use in children four years of age and older. | dysfunction. | dysfunction. | | |
| Mometasone | No dosage adjustment required in the elderly population.<br><br>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.<br><br>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[3-12,14]**

| Adverse Events | Beclomethasone | Budesonide | Ciclesonide | Flunisolide | Fluticasone Furoate | Fluticasone Propionate | Mometasone | Triamcinolone |
|---|---|---|---|---|---|---|---|---|
| **Cardiovascular** | | | | | | | | |
| Chest pain | - | - | - | - | - | - | 2 to <5 | - |
| Palpitations | - | a | - | - | - | - | - | - |
| **Central Nervous System** | | | | | | | | |
| Dizziness | - | - | a | - | - | 1 to 3 | - | a |
| Headache | <5 | - | 6.0 to 6.6 | ≤5 | 8 to 9 | 6.6 to 16.1 | 26 | 5.5 |
| Insomnia | - | - | - | - | - | - | - | a |
| 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 | a |
| Vomiting | - | - | - | ≤5 | - | 2.6 to 4.8 | 5 | - |
| **Hypersensitivity reactions** | | | | | | | | |
| Anaphylaxis | a | a | - | - | a | a | a | - |
| Angioedema | a | a | - | - | a | a | a | - |
| Bronchospasm | a | 2 | - | - | - | a | - | - |
| Dermatitis | - | a | - | - | - | - | - | - |
| Dyspnea | - | - | - | - | - | a | - | a |
| Edema of face/tongue | - | - | - | - | - | a | - | - |
| Pruritus | - | a | - | - | - | a | - | a |
| Rash | a | a | - | - | a | a | - | 2.5 |
| Wheezing | a | a | - | - | - | a | 2 to <5 | - |
| Urticaria | a | a | - | - | a | a | - | - |
| **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 | a | - |
| Nasal discomfort | 5.2* | | | | | | | |
| Nasal dryness | a | - | - | >1 | - | - | - | - |
| Nasal irritation | a | 2 | ≥3 | ≤5 | - | - | 2 to <5 | a |
| Nasal mucosal ulceration | a | - | a | ≤1 | 1 | a | a | - |
| Nasal septal perforation | a | a | a | a | - | a | a | a |
| Nasal stuffiness/ congestion | <3 | - | a | ≤5 | - | - | - | a |
| 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) | - | a | - | ≤5 | - | a | - | - |
| Throat dryness/irritation | a | a | - | - | - | a | - | - |
| Upper respiratory tract infection | - | - | - | - | - | - | 5 to 7 | - |
| **Special senses** | | | | | | | | |
| Aftertaste | - | - | - | 8 to 17 | - | - | - | - |
| Blurred vision | - | - | - | - | - | a | - | - |
| Cataracts | a | a | a | - | a | a | a | a |
| Conjunctivitis | - | - | - | - | - | a | 2 to <5 | - |
| Dry/irritated eyes | - | - | - | - | - | a | - | - |
| Earache | - | - | 2.2 | - | - | - | 2 to <5 | - |
| Glaucoma | a | a | a | - | a | a | a | a |
| Hoarseness | - | - | - | ≤1 | - | a | - | - |
| Increased intraocular pressure | a | a | - | - | - | a | - | a |
| Loss of taste/smell | a | a | - | a | - | a | - | - |
| Otitis media | - | - | - | - | - | - | 2 to <5 | - |
| Unpleasant taste/smell | a | - | - | - | - | - | a | a |
| Watery eyes | <3 | - | - | ≤5 | - | - | - | - |
| **Miscellaneous** | | | | | | | | |
| Aches and pains | - | - | - | - | - | 1 to 3 | - | - |
| Arthralgia | - | - | - | - | - | - | 2 to <5 | - |
| Back pain | - | - | ≥3 | - | 1 | - | - | - |

| Adverse Events | Beclomethasone | Budesonide | Ciclesonide | Flunisolide | Fluticasone Furoate | Fluticasone Propionate | Mometasone | Triamcinolone |
|---|---|---|---|---|---|---|---|---|
| Dysmenorrhea | - | - | - | - | - | - | 5 | - |
| Excoriation | - | - | - | - | - | - | - | 2.5 |
| Fatigue | - | - | - | - | - | - | - | a |
| Fever | - | - | - | - | 4 to 5 | 1 to 3 | - | - |
| Flu-like symptoms | - | - | - | - | - | 1 to 3 | 2 to <5 | - |
| Growth suppression | a | a | a | a | a | a | a | a |
| Immunosuppression | - | a | a | - | a | - | a | a |
| Impaired wound healing | - | a | a | - | a | - | a | a |
| Infection | a | a | a | a | a | a | a | a |
| 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 | - | - | - | - | - | a | - | - |

a Percent not specified.
- Event not reported.

## Contraindications

**Table 7. Contraindications[3-12,14]**

| Contraindication | Beclometh-asone | Budesonide | Ciclesonide | Flunisolide | Fluticasone Furoate | Fluticasone Propionate | Mometasone | Triamcinolone |
|---|---|---|---|---|---|---|---|---|
| Hypersensitivity to any ingredient of the preparation | a | a | a | a | a | a | a | a |
| Presence of an untreated infection of the nasal mucosa | - | - | - | a | - | - | - | - |

## Warnings/Precautions

**Table 8. Warnings and Precautions[3-12,14]**

| Warning | Beclometh-asone | Budesonide | Ciclesonide | Flunisolide | Fluticasone Furoate | Fluticasone Propionate | Mometasone | Triamcinolone |
|---|---|---|---|---|---|---|---|---|
| Candida albicans infection have rarely occurred; when an infection develops it may require treatment | a | a | a | a | a | a | a | a |

| Warning | Beclometh-asone | Budesonide | Ciclesonide | Flunisolide | Fluticasone Furoate | Fluticasone Propionate | Mometasone | Triamcinolone |
|---|---|---|---|---|---|---|---|---|
| and the corticosteroid should be discontinued | | | | | | | | |
| Corticosteroids may inhibit wound healing and should not be used in patients with recent nasal septal ulcers, nasal surgery or trauma | - | a | a | a | a | a | a | a |
| Excessive doses of beclomethasone intranasal may suppress HPA function; avoid larger than recommended doses | a | a | a | a | a | a | a | a |
| Epistaxis was observed in clinical trials more frequently compared to placebo | - | a | a | - | a | - | a | a |
| Hypersensitivity reactions including anaphylactic reaction, urticaria, rash, dermatitis, angioedema and pruritus may occur | a | a | - | - | a | a | a | - |
| Instances of nasal septum perforation have been reported | a | a | a | a | a | - | a | - |
| Intranasal corticosteroids may cause a reduction in growth velocity when administered to pediatric patients | a | a | a | a | a | a | a | a |
| Intranasal corticosteroids should be used with caution in patients with active infections of the respiratory tract | a | - | a | - | a | a | a | a |
| Rare instances of wheezing, cataracts, glaucoma and increase intraocular pressure have been reported following administration | a | a | a | - | a | a | a | a |
| Replacing systemic corticosteroids with a topical corticoid may be accompanied by signs of adrenal insufficiency | a | a | a | a | a | a | - | - |
| Strong CYP3A4 inhibitors may | - | a | - | - | a | - | - | - |

| Warning | Beclometh-asone | Budesonide | Ciclesonide | Flunisolide | Fluticasone Furoate | Fluticasone Propionate | Mometasone | Triamcinolone |
|---|---|---|---|---|---|---|---|---|
| increase exposure when used concomitantly | | | | | | | | |
| Temporary loss of taste and smell have been reported with use | - | - | - | a | - | - | - | - |
| Use with caution in patients receiving prednisone treatment for any disease | - | - | - | a | - | - | - | - |

## 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 9. Drug Interactions[3-12,14]**

| 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 10. Dosing and Administration[3-12,14]**

| Generic Name | Adult Dose | Pediatric Dose | Availability |
|---|---|---|---|
| Beclomethasone | Nasal polyps, nonallergic (vasomotor) rhinitis:<br>Suspension:1 to 2 inhalations in each nostril BID<br><br>Perennial allergic rhinitis, seasonal allergic rhinitis:<br>Aerosol: 2 inhalations in each nostril QD, suspension: 1 to 2 inhalations in each nostril BID | Nasal polyps, nonallergic (vasomotor) rhinitis, perennial allergic rhinitis, seasonal allergic rhinitis in children 6 to 12 years old:<br>Suspension: Initial, 1 inhalation in each nostril BID; maximum, 2 inhalations in each nostril BID<br><br>Perennial allergic rhinitis, seasonal allergic rhinitis in children ≥12 years old:<br>Aerosol: 2 inhalations in each nostril QD, suspension: 1 to 2 inhalations in each nostril BID | Aerosol for nasal inhalation: 80 µg/actuation (120 actuations)<br><br>Suspension for nasal inhalation: 42 µg/inhalation (180 metered doses) |
| Budesonide | Perennial allergic rhinitis, seasonal allergic rhinitis:<br>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:<br>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:<br>Aerosol: 1 inhalation in each nostril QD, suspension: 2 inhalations in each nostril QD | Perennial allergic rhinitis, seasonal allergic rhinitis in children ≥12 years old:<br>Aerosol: 1 inhalation in each nostril QD, suspension: 2 inhalations in each nostril QD | Aerosol for nasal inhalation: 37 µg/actuation (60 actuations)<br><br>Suspension for nasal inhalation: |

| Generic Name | Adult Dose | Pediatric Dose | Availability |
|---|---|---|---|
| | | Seasonal allergic rhinitis in children ≥6 years old:<br>Suspension: 2 inhalations in each nostril QD | 50 µg/inhalation (120 metered doses) |
| Flunisolide | Perennial allergic rhinitis, seasonal allergic rhinitis:<br>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:<br>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:<br>25 µg/inhalation (200 metered doses)<br><br>29 µg/inhalation (200 metered doses) |
| Fluticasone furoate | Perennial allergic rhinitis, seasonal allergic rhinitis:<br>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:<br>Suspension: 1 inhalation in each nostril QD; maximum, 2 inhalations in each nostril QD | Suspension for nasal inhalation:<br>27.5 µg/inhalation (120 metered doses) |
| Fluticasone propionate | Nonallergic (vasomotor) rhinitis, perennial allergic rhinitis, seasonal rhinitis:<br>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:<br>Suspension: 1 inhalation in each nostril QD; maximum, 2 inhalations in each nostril QD | Suspension for nasal inhalation:<br>50 µg/inhalation (120 metered sprays) |
| Mometasone | Nasal congestion associated with seasonal allergic rhinitis:<br>Suspension: 1 inhalation in each nostril QD<br><br>Nasal polyps in adults ≥18 years old:<br>Suspension: 2 inhalations in each nostril QD to BID<br><br>Perennial allergic rhinitis, seasonal allergic rhinitis:<br>Suspension: 2 inhalations in each nostril QD<br><br>Prophylaxis of seasonal allergic rhinitis in individuals >12 years old:<br>Suspension: 2 inhalations in each nostril QD | Nasal congestion associated with seasonal allergic rhinitis in children 2 to 11 years old:<br>Suspension: 1 inhalation in each nostril QD<br><br>Perennial allergic rhinitis, seasonal allergic rhinitis in children 2 to 11 years old:<br>Suspension: 1 inhalation in each nostril QD | Suspension for nasal inhalation:<br>50 µg/inhalation (120 metered doses) |
| Triamcinolone | Perennial allergic rhinitis, seasonal allergic rhinitis:<br>Suspension: 2 inhalations in each nostril QD; maintenance, | Perennial allergic rhinitis, seasonal allergic rhinitis in children 2 to 5 years old:<br>Suspension: 1 inhalation in | Suspension for nasal inhalation:<br>55 µg/inhalation (120 metered |

| Generic Name | Adult Dose | Pediatric Dose | Availability |
|---|---|---|---|
| | 1 inhalation in each nostril QD | each nostril QD<br><br>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 | doses) |

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

## Clinical Guidelines

**Table 11. 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<br>· The diagnosis of allergic rhinitis is based upon the concordance between typical history of allergic symptoms and diagnostic response.<br>· Typical symptoms of allergic rhinitis include rhinorrhea, sneezing, nasal obstruction and pruritus.<br>· Diagnostic tests are based on the demonstration of allergen-specific immunoglobulin E (IgE) in the skin or blood.<br>· Many asymptomatic patients can have positive skin tests or detectable serum levels of IgE.<br><br>Treatment<br>· 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.<br>· A stepwise approach depending on the severity and duration of rhinitis is proposed.<br>· Not all patients with moderate/severe allergic rhinitis are controlled despite optimal pharmacotherapy.<br>· Intranasal glucocorticoids are recommended over oral H1-antihistamines 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.<br>· Second-generation oral or intranasal H1-antihistamines are recommended for the treatment of allergic rhinitis and conjunctivitis in adults and children.<br>· First generation oral H1-antihistamines are not recommended when second-generation ones are available, due to safety concerns.<br>· 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.<br>· Intramuscular glucocorticoids and long-term use of oral glucocorticoids are not recommended due to safety concerns.<br>· Topical chromones are recommended in the treatment of allergic rhinitis but they are only modestly effective.<br>· 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. |

| Clinical Guideline | Recommendations |
|---|---|
| | · Intranasal ipratropium is recommended for the treatment of rhinorrhea associated with allergic rhinitis.<br>· 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.<br>· 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.<br>· 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)**[2] | Diagnosis<br>· 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.<br>· A physical examination with emphasis on the upper respiratory tract should be performed in patients with a history of rhinitis.<br>· 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.<br>· 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.<br>· The measurement of total IgE should not be routinely performed.<br>· Cytotoxic tests, provocation-neutralization, electrodermal testing, applied kinesiology, iridology, and hair analysis are not recommended diagnostic procedures.<br><br>Treatment<br>· The management and monitoring of rhinitis should be individualized and based on symptoms, physical examination findings, comorbidities, patient age and patient preferences.<br>· Environmental control measures include avoidance of known allergic triggers when possible.<br>· 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.<br>· 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.<br>· Intranasal antihistamines are efficacious and equal to or "superior" to oral second-generation antihistamines for treatment of seasonal allergic rhinitis.<br>· Intranasal antihistamines may be considered for use as first-line treatment for allergic and nonallergic rhinitis.<br>· Leukotriene receptor antagonists alone or in combination with antihistamines are effective in the treatment of allergic rhinitis.<br>· Topical decongestants are not recommended for regular daily use but can be considered for short-term management of nasal congestion.<br>· Intranasal corticosteroids are the most effective medication class for |

| Clinical Guideline | Recommendations |
|---|---|
| | controlling symptoms of allergic rhinitis and all are considered equally efficacious.<br>· Intranasal corticosteroids can provide significant relief of symptoms when used on a regular basis as well as an as-needed basis.<br>· Intranasal corticosteroids may be useful in the treatment of some forms of nonallergic rhinitis.<br>· A short course of oral corticosteroids may be appropriate for very severe or intractable nasal symptoms or significant nasal polyposis.<br>· Intranasal cromolyn sodium may be effective for the prevention and treatment of allergic rhinitis.<br>· Intranasal anticholinergics may be effective in reducing rhinorrhea and are more effective when used in combination with intranasal corticosteroids.<br>· 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.<br>· 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] | <u>Diagnosis</u><br>· Patients can present with any of the following symptoms: congestion, rhinorrhea, pruritus, sneezing, posterior nasal discharge, and sinus pressure/pain.<br>· 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.<br>· The most common physical findings suggestive of rhinitis tend to be swollen nasal turbinates, rhinorrhea and pruritus however allergic conjunctivitis may also be present.<br>· 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.<br>· Diagnostic testing should be considered if the results would change management.<br>· 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.<br>· A nasal smear for eosinophils is a good predictor of a patient's response to treatment topical nasal corticosteroids.<br>· Peripheral blood eosinophil count, total serum IgE level, Rinkel method of skin titration and sublingual provocation testing are not recommended.<br><br><u>Treatment</u><br>· If a clinical diagnosis is obvious, symptomatic treatment, which consists of education on avoidance and medication therapy, should be initiated.<br>· Avoidance of triggers is recommended.<br>· 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.<br>· Regular daily use of intranasal corticosteroids is required to achieve optimal results.<br>· It may be best to start treatment one week prior to the start of the allergy |

| Clinical Guideline | Recommendations |
|---|---|
| | season for prophylaxis.<br>· Clinical response does not seem to vary significantly between the available intranasal corticosteroids.<br>· Systemic corticosteroids should be reserved for refractory or severe cases of rhinitis. Injectable steroids are not generally recommended.<br>· Antihistamines are effective at controlling all symptoms associated with allergic rhinitis except nasal congestion.<br>· Antihistamines are somewhat less effective than intranasal corticosteroids but they can be used on a daily or as needed basis.<br>· Second-generation antihistamines are recommended because they are less sedating and cause less central nervous system impairment.<br>· Leukotriene inhibitors may be as effective as second-generation antihistamines for the treatment of allergic rhinitis and less effective than intranasal corticosteroids.<br>· Oral decongestants are effective in reducing nasal congestion. Oral decongestants can be a useful addition to antihistamines.<br>· Topical decongestants, which have the potential to induce rebound congestion after three days, are effective for the short-term relief of nasal congestion.<br>· Cromolyn is less effective than intranasal corticosteroids and is most effective when used prior to the onset of allergic symptoms.<br>· Cromolyn is a good alternative for patients who are not candidates for corticosteroids.<br>· Intranasal anticholinergics are effective in relieving anterior rhinorrhea in allergic and nonallergic rhinitis.<br>· Reserve immunotherapy for patients with significant allergic rhinitis in which avoidance activities and pharmacotherapy are insufficient to control symptoms.<br>· If adequate relief is achieved appropriate follow-up should include further education on avoidance activities and medications.<br>· If patients anticipate unavoidable exposure to known allergens they should begin the use of medications prior to exposure.<br>· If adequate relief is not achieved within two to four weeks consider a trial of another medication, allergen skin testing by a qualified physician, a complete nasal examination, or a diagnosis of nonallergic rhinitis.<br>· Treatment options for nonallergic rhinitis include intranasal corticosteroids, oral decongestants and antihistamines, topical antihistamines, and nasal strips. |

**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. [2,15,16] All of the ten available intranasal corticosteroids have demonstrated safety and efficacy for their respective indications.[18-77] 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 into improved outcomes. The results of multiple head-to-head trials have generally failed to demonstrate clinically significant differences between products.[41-55,57-76]

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.[3-12,14] Two nasal aerosol formulations of existing drugs, beclomethasone (QNASL®) and ciclesonide (Zetonna®), have recently been approved by the FDA for the relief of symptoms associated with perennial and season allergic rhinitis. The other intranasal corticosteroid products are formulated as aqueous suspensions which may be bothersome to patients due to the potential of the suspension to drip down or out of the nose following administration. There are currently three intranasal corticosteroids that are available generically: flunisolide, fluticasone propionate and triamcinolone.[14]

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