Pharmacologic therapy for allergic Rhinitis

- Allergen avoidance
- clinically effective dust mite avoidance includes combination of dust mite covers for bedding, humidity control, high efficiency particulate air (HEPA) vacuuming of carpeting, and acaricides (AAAAI/ACAAI Grade B)

Intranasal and Oral Medications for AR

Corticosteroids

Intranasal[a] (budesonide [OTC], beclomethasone, ciclesonide, flunisolide, fluticasone [propionate and furoate] [OTC], mometasone, triamcinolone [OTC])

Oral (rarely used, eg, prednisone)

Antihistamines

Intranasal[a] (azelastine, olopatadine)

Oral[b]

• First generation/sedating (cautious use in selected patients) (most OTC depending on strength: diphenhydramine, chlorpheniramine, clemastine, and others)

• Second generation/low- or nonsedating[a]: loratadine (OTC), cetirizine (OTC), fexofenadine (OTC), levocetirizine (OTC), desloratadine,

Combination Antihistamine/Corticosteroid

Intranasal (azelastine and fluticasone propionate)

Mast cell stabilizer/cromone

Intranasal (cromolyn [OTC])

LTRA

Oral (montelukast)

Antimuscarinic

Intranasal (ipratropium)

Decongestant

Intranasal (short-term use) (tetrahydrozoline, phenylephrine [OTC], naphazoline [OTC], oxymetazoline [OTC])

Oral[b] (phenylephrine [OTC]; pseudoephedrine [BTC[c]])

Intranasal corticosteroids

- Most effective medication class for controlling symptoms of allergic rhinitis (AAAAI/ACAAI Grade A)
- More effective than combination of antihistamine and leukotriene antagonist in treatment of seasonal allergic rhinitis (AAAAI/ACAAI Grade A)
- May be used on as-needed basis (AAAAI/ACAAI Grade B) but may not be as effective as on continuous basis (AAAAI/ACAAI Grade D)
- As-needed intranasal fluticasone may be more effective than as-needed loratadine in seasonal allergic rhinitis (level 2 [mid-level] evidence)

Antihistamines

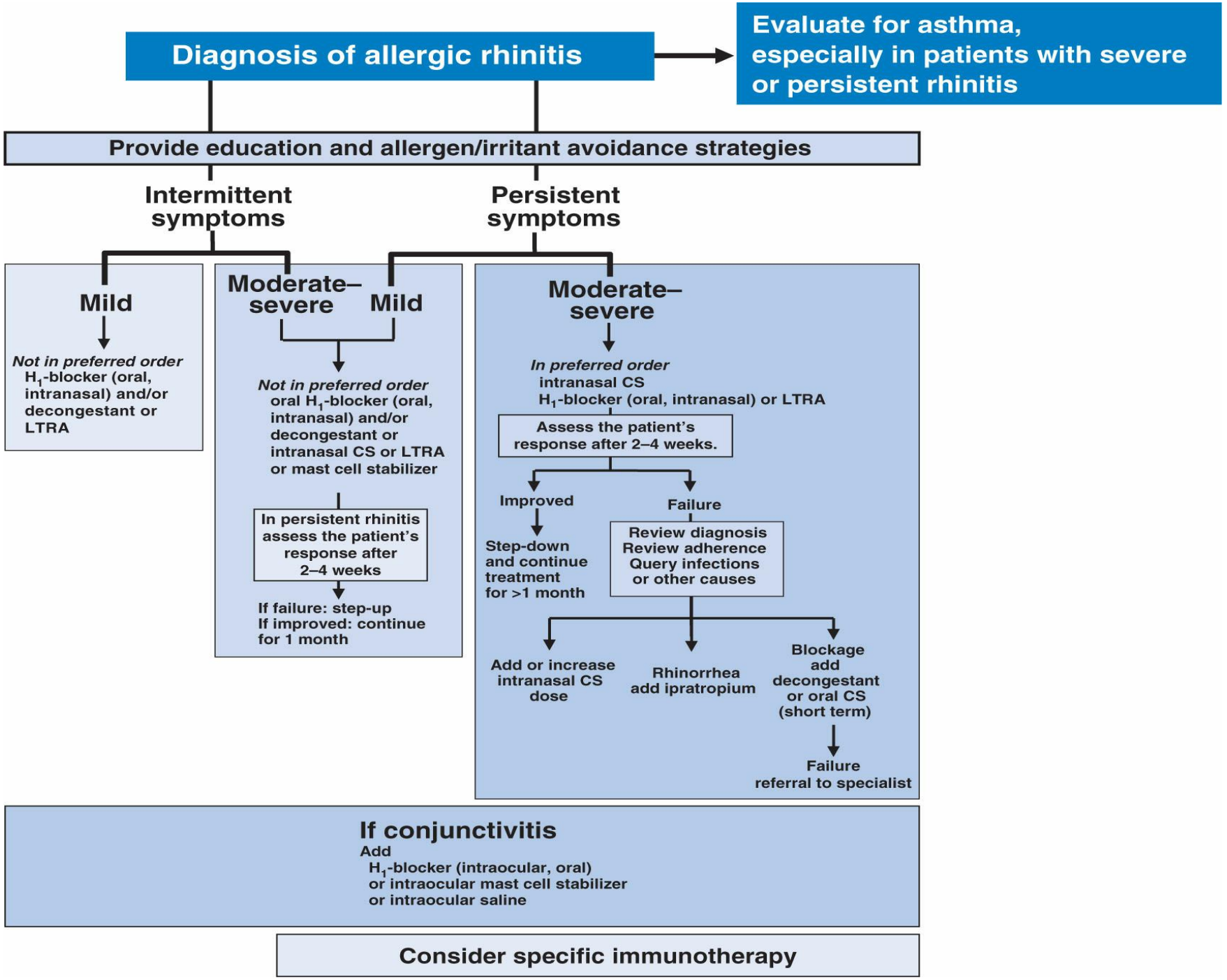
- intranasal antihistamines are equal or superior to oral second-generation antihistamine in treatment of seasonal allergic rhinitis and can be considered first-line treatment (AAAAI/ACAAI Grade A)
- azelastine (intranasal antihistamine) 1 spray per nostril twice daily modestly improves nasal symptoms (level 1 [likely reliable] evidence)
- when using oral antihistamines, second-generation ones generally preferred over first-generation antihistamines because of reduced side effects (AAAAI/ACAAI Grade B)
- use caution with oral and topical decongestants in specific clinical situation (AAAAI/ACAAI Grade C)

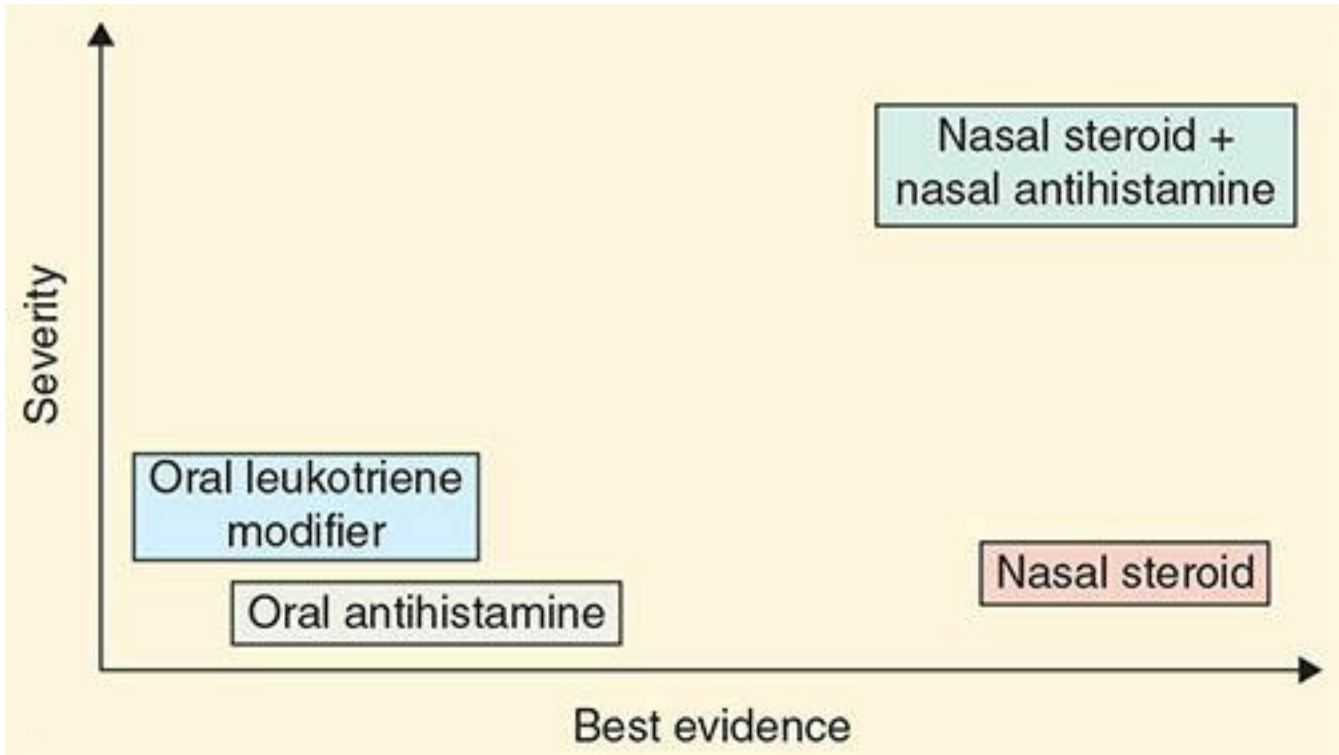
Other agents

- Oral leukotriene receptor antagonists alone, or in combination with antihistamines, have been useful in treatment of allergic rhinitis (AAAAI/ACAAI Grade A); montelukast appears to have small amount of efficacy but less effective than nasal steroids or antihistamines (level 2 [midlevel] evidence)
- Intranasal cromolyn effective in some patients for prevention and treatment of allergic rhinitis (AAAAI/ACAAI Grade A)
- Anticholinergics (such as ipratropium or atropine sulfate nasal spray) may reduce rhinorrhea but not other nasal symptoms (AAAAI/ACAAI Grade A; level 2 [mid-level] evidence)

- Nasal saline irrigation appears beneficial in treatment of symptoms of chronic rhinorrhea and rhinosinusitis when used as sole modality or for adjunctive treatment (AAAAI/ACAAI Grade A; level 2 [mid-level] evidence)
- butterbur may reduce symptoms of seasonal allergic rhinitis (level 2 [mid-level] evidence)
- limited evidence for effectiveness of acupuncture for prevention or treatment of allergic rhinitis (level 2 [mid-level] evidence)

TREATMENT


Diagnosis of allergic rhinitis
Evaluate for asthma, especially in patients with severe or persistent rhinitis
Provide education and allergen/irritant avoidance strategies
Intermittent symptoms
Persistent symptoms
Mild
Not in preferred order
H1-blocker (oral, intranasal) and/or decongestant or LTRA
Moderate–severe
Mild
Not in preferred order
oral H1-blocker (oral, intranasal) and/or decongestant or intranasal CS or LTRA or mast cell stabilizer
In persistent rhinitis assess the patient's response after 2–4 weeks
If failure: step-up
If improved: continue for 1 month
Moderate–severe
In preferred order
intranasal CS
H1-blocker (oral, intranasal) or LTRA
Assess the patient's response after 2–4 weeks.
Improved
Step-down and continue treatment for >1 month
Failure
Review diagnosis
Review adherence
Query infections or other causes
Add or increase intranasal CS dose
Rhinorrhea
add ipratropium
Blockage
add decongestant or oral CS (short term)
Failure
referral to specialist
If conjunctivitis
Add
H1-blocker (intraocular, oral)
or intraocular mast cell stabilizer
or intraocular saline
Consider specific immunotherapy


Nasal steroid +
nasal antihistamine
Severity
Oral leukotriene
modifier
Nasal steroid
Oral antihistamine
Best evidence

Intranasal corticosteroids

- Intranasal corticosteroids are most effective medication class for controlling symptoms of allergic rhinitis (AAAAI/ACAAI Grade A)
- Intranasal corticosteroids have been shown to be more effective than combination of antihistamine and leukotriene antagonist in treatment of seasonal allergic rhinitis (AAAAI/ACAAI Grade A)
- May be used on as-needed basis (AAAAI/ACAAI Grade B) symptom relief may not be as effective on as-needed basis as on continuous basis (AAAAI/ACAAI Grade D)
- No corticosteroid product is clearly better than others (AAAAI/ACAAI Grade C)
- May be used during pregnancy, with budesonide (Pregnancy Category B) preferred (AAAAI/ACAAI Grade C)

Systemic corticosteroids

- Oral corticosteroids for 5-7 days may be appropriate for very severe or intractable nasal symptoms or to treat nasal polyposis (AAAAI/ACAAI GradeD)
- Single dosing of parental corticosteroid use is discouraged and recurrent parenteral dosing contraindicated (AAAAI/ACAAI Grade D)

Antihistamines Intranasal

- Intranasal antihistamines can be considered first-line treatment intranasal antihistamines are equal or superior to oral second-generation antihistamine in treatment of seasonal allergic rhinitis
- Intranasal antihistamines have been associated with sedation and can inhibit skin test reactions
- Intranasal antihistamines generally less effective than intranasal corticosteroids in treatment of allergic rhinitis
  - azelastine can be considered for patients > 5 years old(2)
  - olopatadine can be considered for patients > 12 years old(2)
  - Antihistamine nasal spray - azelastine (Astelin) 0.1%

Oral antihistamines

- second-generation antihistamines generally preferred over first-generation antihistamines because of reduced side effects (AAAAI/ACAAI Grade B)[1]
- no second-generation antihistamine appears superior to others (AAAAI/ACAAI Grade C)[1]
- patients receiving first-generation antihistamines should be advised of alternatives with lower risk of side effects (AAAAI/ACAAI Grade D)[1]
- sedative properties of second-generation antihistamines vary (AAAAI/ACAAI Grade A)[1]
    - cetirizine and **intranasal**azelastine may cause sedation at recommended dose
    - fexofenadine, loratadine, and desloratadine do not cause sedation at recommended dose
    - loratadine and desloratadine may cause sedation at doses above recommended
- loratadine, desloratadine, and cetirizine may be used in patients > 2 years old[2]

Decongestants

- Oral decongestants (for example, pseudoephedrine [Sudafed]) are effective in treatment of allergic rhinitis.
- Side effects include insomnia, irritability, palpitations
- avoid during first trimester, consider short-term topical decongestants as possible alternative (AAAAI/ACAAI Grade C)

Cautions

caution should be advised when using oral and nasal decongestants in specific clinical situations (AAAAI/ACAAI Grade C)[1, 2]

- adults > 65 years old
- children < 6 years old
- patients with history of
  - cardiac arrhythmia
  - angina pectoris
  - cerebrovascular disease
  - hypertension
  - bladder neck obstruction
  - glaucoma
  - hyperthyroidism
  - prostatic hypertrophy

Leukotriene receptor antagonists

- Oral leukotriene receptor antagonists alone, or in combination with antihistamines, have been useful in treatment of allergic rhinitis (AAAAI/ACAAI Grade A)(1)
- Montelukast is safe treatment option during pregnancy

- adverse effects of montelukast may include
  - agitation
  - anxiety
  - insomnia
  - depression
  - hallucinations
  - tremors
  - dizziness
  - drowsiness
  - seizures
  - suicidal thoughts

Cromolyn (nasal)

- cromolyn generally used prophylactically for seasonal allergic rhinitis[2]
- recommendations from Joint Council of Allergy, Asthma and Immunology (JCAAI) (1)
    - effective in some patients for prevention and treatment of allergic rhinitis (AAAAI/ACAAI Grade A)
    - less effective than corticosteroids (AAAAI/ACAAI Grade A)
    - has not been adequately studied in comparison with leukotriene antagonists and antihistamines (AAAAI/ACAAI Grade A)
    - associated with minimal side effects (AAAAI/ACAAI Grade A)
    - safe treatment option during pregnancy (AAAAI/ACAAI Grade C)

Anticholinergics

- Anticholinergics may reduce rhinorrhea but not effective for other nasal symptoms
- combination ipratropium bromide nasal spray and intranasal corticosteroid is more effective than administration of either alone in treatment of rhinorrhea without any increased incidence of adverse events
- may lead to dryness of nasal membrane
- use ipratropium with caution especially if other anticholinergics are coadministered

Saline

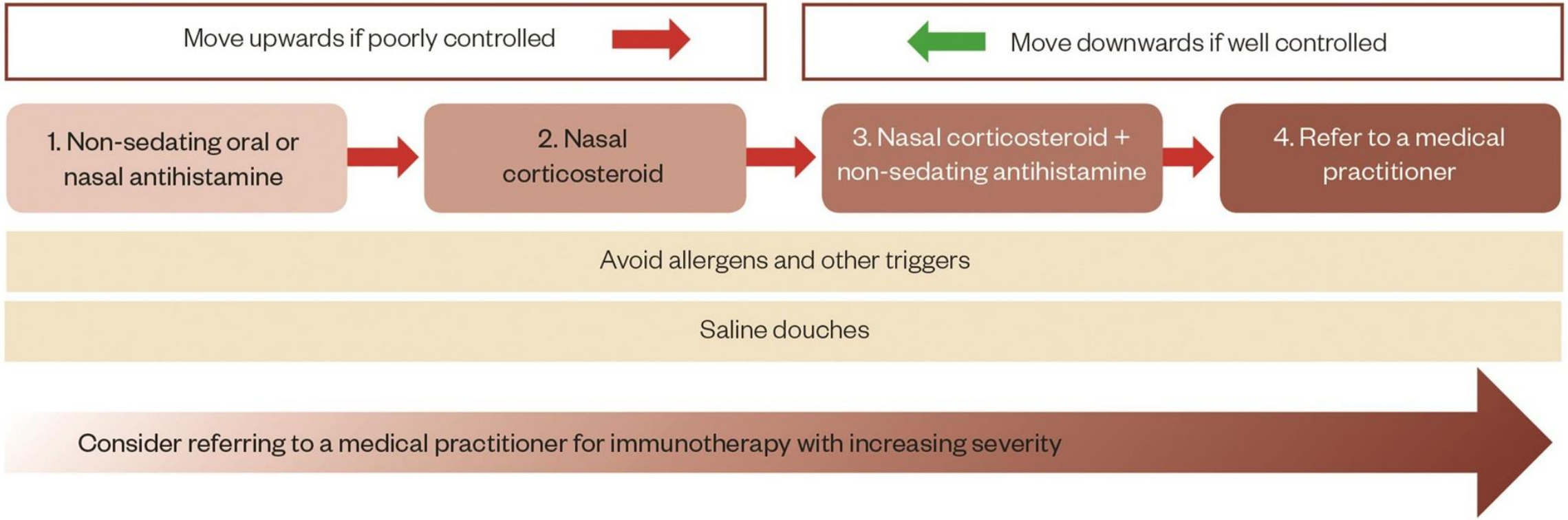
- topical saline
  - beneficial in treatment of symptoms of chronic rhinorrhea and rhinosinusitis when used as sole modality or for adjunctive treatment (AAAAI/ACAAI Grade A)[1]
  - optimal treatment option for seasonal allergic rhinitis in pregnant patients, children, or patients with comorbidities that include hypertension and urinary retention[2]

Severity	Mild	Moderate		Severe	
Disease types		Sneezing and rhinorrhea type	Nasal blockage type or combined type with nasal blockage as a chief complaint	Sneezing and rhinorrhea type	Nasal blockage type or combined type with nasal blockage as a chief complaint
Treatments	a. Second-generation antihistamine b. (Mast cell) stabilizer c. Th_2 cytokine inhibitors d. Nasal steroids	a. Second-generation antihistamine b. (Mast cell) stabilizer c. Nasal steroids	a. Anti-LTs agents b. Anti-PGD_2/TXA_2 agents c. Th_2 cytokine inhibitors d. Second-generation antihistamine and vasoconstrictor combination e. Nasal steroids	Nasal steroids + Second-generation antihistamine	Nasal steroids + Anti-LTs agents or anti-PGD_2/TXA_2 agents or Second-generation antihistamine and vasoconstrictor combination
	Choose one of (a), (b), (c), and (d).	Choose one of (a), (b), (c). Combine (a) or (b) with (c), as needed.	Choose one of (a), (b), (c), (d), and (e). Combine (a), (b) or (c), with (e), as needed.		Use vasoconstrictor nasal spray for only 1–2 weeks at the start of treatment as needed.
				Perform surgery for cases with nasal deformities of a nasal blockage type.	
	Allergen-specific immunotherapy				
	Elimination and avoidance of antigens				

Choice of therapy for pollinosis based on severity.

Severity	Primal therapy	Mild	Moderate		Severe	
Disease types			Sneezing and rhinorrhea type	Nasal blockage type or combined type with nasal blockage as a chief complaint	Sneezing and rhinorrhea type	Nasal block age type or combined type with nasal blockage as a chief complaint
Treatments	a. Second-generation antihistamine b. (Mast cell) stabilizer c. Anti-LTs agents d. Anti-PGD_2/TXA_2 agents e. Th_2 cytokine inhibitors f. Nasal steroids	a. Second-generation antihistamine b. (Mast cell) stabilizer c. Anti-LTs agents d. Anti-PGD2/ TXA2 agents e. Th_2 cytokine inhibitors f. Nasal steroids	Second-generation antihistamine + Nasal steroids	Anti-LTs agents or Anti-PGD_2/ TXA_2 agents + Nasal steroids + Second-generation antihistamine or Second-generation antihistamine and vasoconstrictor combination + Nasal steroids	Nasal steroids + Second-generation antihistamine	Nasal steroids + Anti-LTs agents or Anti-PGD_2/TXA_2 agents + Second-generation antihistamine or Nasal steroids + Second-generation antihistamine and vasoconstrictor combination
	Choose one of (a), (b), (f) for sneezing and rhinorrhea type, and (c), (d), (e), (f) for nasal blockage type and combined type	Choose one of (a)–(f). Add (f) at the start of treatment with (a)–(e) as needed.				Use vasoconstrictor nasal spray for only 1–2 weeks as needed. For cases with severe nasal blockage, treatment may be started with oral corticosteroid administration for 4–7 days.
		Antihistamine for eye drops or stabilizer			Antihistamine for eye drops, stabilizer, or steroids	
					Perform surgery for cases with nasal deformities of a nasal blockage type.	
	Allergen-specific immunotherapy					
	Elimination and avoidance of antigens					

A simple algorithm for the treatment of allergic rhinitis



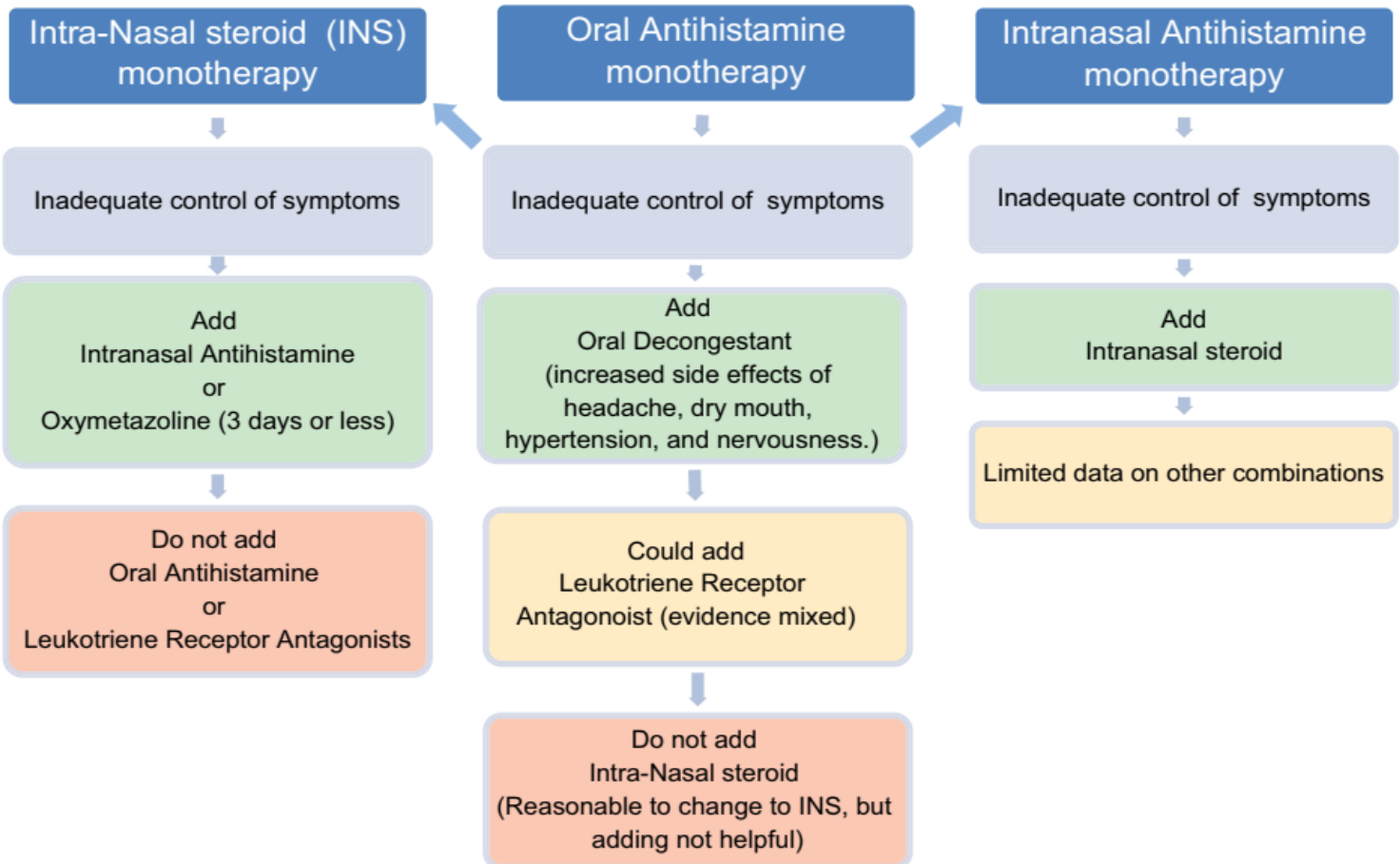


Figure 1. Recommendations for adding a second medication to treat allergic rhinitis.

Classifications

Effectiveness of Agents[a] Used in the Management of Allergic Rhinitis

	Rhinorrhea	Nasal Pruritus	Sneezing	Nasal Congestion	Eye Symptoms	Onset
Antihistamines						
Nasal	Moderate	High	High	Moderate	0	Rapid
Ophthalmic	0	0	0	0	Moderate	Rapid
Oral	Moderate	High	High	0/Low	Low	Rapid
Decongestants						
Nasal	0	0	0	High	0	Rapid
Ophthalmic	0	0	0	0	Moderate	Rapid
Oral	0	0	0	High	0	Rapid
Corticosteroids						
Nasal	High	High	High	High	High	Slow (days)
Ophthalmic	0	0	0	0	High	Slow (days)
Mast-cell stabilizers						
Nasal	Low	Low	Low	0/Low	Low	Slow (weeks)
Ophthalmic	Low	Low	Low	Low	Moderate	Slow (weeks)
Anticholinergics						
Nasal	High	0	0	0	0	Rapid
Leukotriene Modifiers						
Oral	Low	0/Low	Low	Moderate	Low	Rapid

Antihistamines

Generic Name (Example Brand Product)	Adult Dose	Pediatric Dose[c]	Other Effects		
First Generation			**Sedative**	**Antiemetic**	**Anticholinergic**
Chlorpheniramine (Chlor-Trimeton)	4 mg every 4–6 hours	Children 6–12 years: 2 mg every 4–6 hours Children 2–6 years: 1 mg every 4–6 hours	+	0	++
Clemastine (Tavist)	1 mg every 12 hours	Children 6–12 years: 0.67 mg every 12 hours	++	++ to +++	+++
Diphenhydramine (Benadryl)	25–50 mg every 6–8 hours	Children 6–12 years: 12.5–25 mg every 4–6 hours	+++	++ to +++	+++

Second generations

Second Generation			Sedative	Antiemetic	Anticholinergic
Cetirizine (Zyrtec Allergy)	5–10 mg once daily	Children 6–12 years: 5–10 mg once daily Children 2–5 years: 2.5–5 mg once daily Children 12–23 months: 2.5–5 mg once daily	+	0	±
Fexofenadine (Allegra)	60 mg every 12 hours or 180 mg once daily	Children 2–11 years: 30 mg every 12 hours	±	0	±
Loratadine (Claritin)	10 mg once daily	Children 6–12 years: 10 mg once daily or 5 mg twice daily Children 2–5 years: 5 mg once daily	±	0	±
Levocetirizine[d] (Xyzal)	5 mg once daily in the evening	Children 6–11 years: 2.5 mg once daily in the evening Children 6 months–5 years: 1.25 mg once daily in the evening	±	0	±
Desloratadine[d] (Clarinex)	5 mg once daily	Children 6–11 years: 2.5 mg once daily Children 1–5 years: 1.25 mg once daily Children 6–11 months: 1 mg once daily	±	0	±

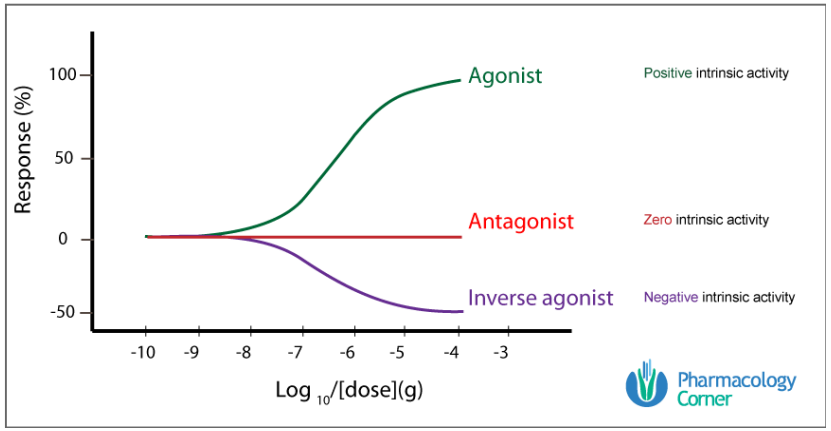
Antihistamines		
Azelastine (Optivar)	Ophthalmic solution: 0.05%	Adults and children ≥3 years: 1 drop in the affected eye(s) every 12 hours
Emedastine (Emadine)	Ophthalmic solution: 0.05%	Adults and children ≥3 years: 1 drop in the affected eye(s) up to 4 times daily
Epinastine (Elestat)	Ophthalmic solution: 0.05%	Adults and children ≥3 years: 1 drop in the affected eye(s) twice daily
Antihistamine/Decongestant Combinations		
Pheniramine + Naphazoline (Naphcon-A, Opcon-A, Visine-A)[a]	Ophthalmic solution: naphazoline HCl 0.025% + pheniramine maleate 0.3%	Adults and children ≥6 years: 1–2 drops in the affected eye(s) every 6 hours for up to 3 days
Antihistamine/Mast-Cell Stabilizers		
Ketotifen (various brand names)[a]	Ophthalmic solution: 0.025%	Adults and children ≥3 years: 1 drop in the affected eye(s) every 8–12 hours
Olopatadine (Pataday, Patanol, Pazeo)	Ophthalmic solution: 0.1%, 0.2%, 0.7%	0.1%: Adults and children ≥3 years 1 drop in affected eye(s) twice daily at an interval of 6–8 hours. 0.2% and 0.7%: Adults and children ≥2 years: 1 drop in the affected eye(s) once daily
Alcaftadine (Lastacaft)	Ophthalmic solution: 0.25%	Adults and children ≥2 years: 1 drop in the affected eyes(s) twice daily
Bepotastine (Bepreve)	Ophthalmic solution: 1.5%	Adults and children ≥2 years: 1 drop in the affected eyes(s) twice daily
Mast-Cell Stabilizers		
Cromolyn Sodium (Crolom)	Ophthalmic solution: 4%	Adults and children ≥4 years: 1–2 drops in the affected eye(s) 4–6 times daily
Lodoxamide (Alomide)	Ophthalmic solution: 0.1%	Adults and children ≥2 years: 1–2 drops in affected eye(s) 4 times daily for up to 3 months
Nedocromil (Alocril)	Ophthalmic solution: 2%	Adults and children ≥3 years: 1–2 drops in the affected eye(s) every 12 hours
Nonsteroidal Anti-Inflammatory Drugs[b]		
Ketorolac (Acular)	Ophthalmic solution: 0.5%	Adults and children ≥3 years: 1 drop in the affected eye(s) 4 times daily
Corticosteroids[c]		
Loteprednol (Alrex)	Ophthalmic suspension: 0.2%	Adults: 1 drop in the affected eye(s) 4 times daily

Decongestants[a],[b] Commonly Used in Allergic Rhinitis

Generic Name (Example Brand Product)	Adult Dose	Pediatric Dose[c]
Oral[a]		
Pseudoephedrine (Sudafed)	60 mg every 4–6 hours (max 240 mg/day)	Children 6–11 years: 30 mg every 4–6 hours (max 120 mg/day) Children 2–5 years: 15 mg every 4–6 hours (max 60 mg/day)
Phenylephrine (Sudafed PE)	10–20 mg every 4 hours (max 120 mg/day)	Children 6–11 years: 10 mg every 4 hours (max 60 mg/day)
Topical[d]		
Naphazoline (Privine)	0.05% solution: 1–2 drops or sprays/nostril every 6 hours	Children <12 years: avoid, unless under physician direction
Phenylephrine (Neo-Synephrine)	0.25%–1.0% solution: 2–3 sprays or drops/nostril every 3–4 hours	Children 6–11 years: 2–3 sprays or drops (0.25% solution)/nostril every 4 hours Children 2–5 years: 2–3 drops (0.125% solution) into each nostril not more than every 4 hours
Oxymetazoline (Afrin)	0.05% solution: 2–3 sprays/nostril every 10–12 hours	Children 6–12 years: 2–3 sprays/nostril every 12 hours
Xylometazoline	0.1% solution: 2–3 sprays into each nostril every 8–10 hours	Children 2–12 years: 1–2 sprays (0.05% solution) into each nostril every 8–10 hours

Antihistamines / efficacy

- They are technically inverse agonists, not competitive antagonists; however, there may be little clinical significance to the difference
- These drugs bind H1 receptors, keeping them in the inactive state. This downregulation of H1 receptor activity results in a decrease in end organ effects.
- Activation of H1 receptors in the nose, upper airway mucosa, and the eye produce the common manifestations of AR (***sneezing, itching, rhinorrhea, nasal congestion, and ocular symptoms***).
- The antihistamines are very effective for the sneezing, itching, and rhinorrhea.
    - There is some improvement of nasal congestion, but less so than for the other symptoms.



- Second- and third-generation antihistamines —The second-generation antihistamines include loratadine, cetirizine, azelastine, and olopatadine.
- These lipophobic agents were developed primarily to avoid the unwanted central nervous system effects of the first-generation drugs.
- Onset of action is within one hour for most agents, and peak serum levels are attained in two to three hours. They are also longer-acting and are dosed once or twice daily.
- Like older H1 antihistamines, they have less impact on nasal congestion compared with glucocorticoid nasal sprays.
- The oral second-generation agents appear to be similarly efficacious to each other.

- Metabolites of second-generation antihistamines, such as fexofenadine (the metabolite of terfenadine), desloratadine (the metabolite of loratadine), and levocetirizine (a purified isomer of cetirizine), are sometimes classified as **"third-generation antihistamines**".
- These compounds were designed to have fewer central nervous system effects than the second-generation agents, although whether this is true has not been confirmed.
- In experimental models, second- and third-generation antihistamines also have a variety of anti-inflammatory properties, including decreased mast cell mediator release and downregulation of adhesion molecule expression. Inhibition of interleukin-4 (IL-4) and interleukin-13 (IL-13) production may explain reports of their dose-dependent beneficial effect in asthma

Role in therapy and efficacy

- Role in therapy and efficacy — Second-generation antihistamines are a popular option for many patients, especially those with mild or intermittent symptoms. Patients who experience adverse effects with the second-generation antihistamines (which is rare) or who prefer a local therapy, are also better treated with glucocorticoid nasal sprays.
- We prefer glucocorticoid nasal sprays for patients with chronic or more significant symptoms, because of their superior efficacy.
- Antihistamines are less effective than glucocorticoid nasal sprays, as previously presented

- Second-generation antihistamines are equally or more efficacious than cromolyn in relieving symptoms.
- There is no evidence that pharmacologic tolerance develops to antihistamines. In addition, the specific allergic sensitivities a patient has does not impact the antihistamine that is prescribed, although agents are sometimes marketed as effective for perennial or seasonal, or indoor or outdoor, allergies. This marketing simply reflects the clinical trials that were performed.
- Clinical studies do not support the use of combinations of H1 and H2 antagonists (such as ranitidine) to treat allergic rhinitis. There is no evidence that doses of second-generation antihistamines greater than those maximally recommended increase efficacy for allergic rhinitis, with higher than recommended doses being associated with sedation in some cases

Dosing of commonly-used agents

- Cetirizine – The standard dose of 10 mg once daily is appropriate for adults and children ages ≥6 years.
- The usual dose for children aged 2 to 5 years is 5 mg once daily. Smaller children aged 6 months to 2 years may be given 2.5 mg once daily. The maintenance dose for patients with significant renal and/or hepatic insufficiency should be reduced by one-half.
- Levocetirizine – Levocetirizine is an active enantiomer of cetirizine and produces effects equivalent to cetirizine at about one-half the dose. For adults and children ≥12 years, the standard dose is 5 mg once daily in the evening or 2.5 mg once daily in the evening for children aged 6 to 11 years. Levocetirizine is unlikely to be effective as an alternative for patients who acquire tolerance to the effects of cetirizine. Significant dose alteration is necessary in renal insufficiency.
- Loratadine – Loratadine is a long-acting selective H1 antihistamine, chemically distinct from cetirizine, and has a standard dose of 10 mg once daily for ages ≥6 years.

Dosing of commonly-used agents

  - For children aged 2 to 5 years, the usual dose is 5 mg once daily. For patients with significant renal and/or hepatic insufficiency, the usual dose is administered every other day.

- Desloratadine – Desloratadine is the major active metabolite of loratadine and produces effects equivalent to loratadine at about one-half the dose. For adults and children ≥12 years, the standard dose is 5 mg once daily.
  - For children aged 6 to 11 years, the dose is 2.5 mg once daily and for those aged 1 to 5 years the dose is 1.25 mg once daily. A lower dose of 1 mg once daily is approved in the United States for small children aged 6 months to 1 year. For patients with significant renal and/or hepatic insufficiency, the usual dose is administered every other day.
- Fexofenadine – The suggested dose of fexofenadine is 180 mg daily for ages ≥12 years or 30 mg twice daily for children aged 2 to 11 years. A lower dose of 15 mg twice daily is approved in the United States for small children aged 6 months to 2 years. For patients with significant renal insufficiency, the adult dose should be reduced to 60 mg once daily. It is best taken without food and specifically not with fruit juices

Adverse effects

- The second-generation antihistamines are less sedating than the first-generation agents, although cetirizine is sedating for approximately 10 percent of patients.
    - Loratadine is nonsedating for most adults at the customary dose of 10 mg once daily, although sedation can occur at higher doses. Fexofenadine is nonsedating at recommended doses and even at higher than recommended doses
    - Varying degrees of anticholinergic effects. Drying of the eyes, in particular, is noticeable to some patients.
- Some oral antihistamines may be associated with weight gain, although it is unclear if this is due to stimulation of appetite or reduced activity secondary to sedation and fatigue. Like other central nervous system effects, weight gain is more prominent with the older, first-generation agents, although it can occur in some patients with the second-generation agents. Weight gain would be predicted to be minimal with fexofenadine (no evidence).

Table 10. Allergic Rhinitis Oral Antihistamines.

Medication	FDA Indications (Seasonal, Perennial)	Contraindications	Approved Ages	Common Side Effects	Dosing	OTC or Prescription
Cetirizine (Zyrtec)	Both	Hypersensitivity to cetirizine, levocetirizine, or hydroxyzine	≥6 months	Occasional sedation, mucosal dryness, urinary retention	Age 2-5 y: 2.5 mg 1 or 2 times per day Age 6-12 y: 5-10 mg/d Age 12-65 y: 10 mg/d Age 66-76 y: 5-10 mg/d Age ≥77 y: 5 mg/d	OTC
Levocetirizine (Xyzal)	Both	Hypersensitivity to levocetirizine, cetirizine, or hydroxyzine	≥6 months	Occasional sedation, mucosal dryness, urinary retention	Age 2-5 y, 1.25 mg/d Age 6-11 y, 2.5 mg/d Age ≥12 y, 2.5-5.0 mg/d	Prescription
Fexofenadine (Allegra)	Seasonal	Hypersensitivity to fexofenadine	≥2 years	Occasional headache	Age 2-11 y, 30 mg twice a day Age ≥12 y, 60 mg twice a day or 180 mg/d	OTC
Loratadine (Claritin, Alavert)	Both	Hypersensitivity to loratadine or desloratadine	≥2 years	Possible sedation with higher than usual doses	Age 2-5 y, 5 mg/d Age ≥6 y, 10 mg/d	OTC
Desloratadine (Clarinex)	Both	Hypersensitivity to desloratadine or loratadine	≥6 months	Possible sedation with higher than usual doses	Age 2-5 y, 1.25 mg/d Age 6-11 y, 2.5 mg/d Age ≥12 y, 5 mg/d	Prescription

Generic Name (Example Brand Product)	Available Dosage Forms/Strength	Dose
Antihistamines		
Azelastine (Optivar)	Ophthalmic solution: 0.05%	Adults and children ≥3 years: 1 drop in the affected eye(s) every 12 hours
Emedastine (Emadine)	Ophthalmic solution: 0.05%	Adults and children ≥3 years: 1 drop in the affected eye(s) up to 4 times daily
Epinastine (Elestat)	Ophthalmic solution: 0.05%	Adults and children ≥3 years: 1 drop in the affected eye(s) twice daily
Antihistamine/Decongestant Combinations		
Pheniramine + Naphazoline (Naphcon-A, Opcon-A, Visine-A)[a]	Ophthalmic solution: naphazoline HCl 0.025% + pheniramine maleate 0.3%	Adults and children ≥6 years: 1–2 drops in the affected eye(s) every 6 hours for up to 3 days
Antihistamine/Mast-Cell Stabilizers		
Ketotifen (various brand names)[a]	Ophthalmic solution: 0.025%	Adults and children ≥3 years: 1 drop in the affected eye(s) every 8–12 hours
Olopatadine (Pataday, Patanol, Pazeo)	Ophthalmic solution: 0.1%, 0.2%, 0.7%	0.1%: Adults and children ≥3 years 1 drop in affected eye(s) twice daily at an interval of 6–8 hours. 0.2% and 0.7%: Adults and children ≥2 years: 1 drop in the affected eye(s) once daily
Alcaftadine (Lastacaft)	Ophthalmic solution: 0.25%	Adults and children ≥2 years: 1 drop in the affected eyes(s) twice daily
Bepotastine (Bepreve)	Ophthalmic solution: 1.5%	Adults and children ≥2 years: 1 drop in the affected eyes(s) twice daily

Antihistamine nasal sprays

- Azelastine and olopatadine are available as prescription nasal sprays.
- These agents appear to have some anti-inflammatory effect and can improve nasal congestion. They are similarly effective.
- Antihistamine nasal sprays have a rapid onset of action (less than 15 minutes) and can be administered "on demand". The onset of action is somewhat faster than that of glucocorticoid nasal sprays.
- Azelastine has a bitter taste that can be bothersome to some patients (which has been corrected in newer preparations) and was mildly sedating in some of the clinical trials performed in getting the medication on the market, although not in others

- Guidelines generally suggest glucocorticoid nasal sprays in preference to antihistamine sprays, based upon the fact that the majority of comparison studies favor glucocorticoids . In noninferiority trials, both olopatadine and azelastine compared favorably with fluticasone propionate.
- First-generation– Beclomethasone, flunisolide, triamcinolone, and budesonide (10 to 50 percent bioavailability)
- Second-generation–Fluticasone propionate (<2 percent), mometasone furoate (<0.1 percent), ciclesonide (<0.1 percent), and fluticasone furoate (<1 percent)

Table 11. Allergic Rhinitis (AR) Intranasal Antihistamines.

Medication	FDA Indications	Contraindications	Approved Ages	Dosing	Common Side Effects	OTC or Prescription
Olopatadine (Patanase) (as HCl) 0.6% (665 µg per spray); aqueous nasal spray	Seasonal AR	None	≥6 y	Age 6-11 y: 1 spray twice a day Age ≥12 y: 2 sprays twice a day	• Bitter taste • Epistaxis • somnolence • Headache	Prescription
Azelastine (Astelin) 0.1% solution (137 µg per spray)	Seasonal AR, vasomotor rhinitis	None	≥6 y	Age 6-11 y: 1 spray twice a day Age ≥12 y: 1-2 sprays twice a day or 2 sprays daily	• Bitter taste • Epistaxis • Somnolence • Headache	Prescription
Azelastine (Astepro) 0.15% solution (205.5 µg per spray)	Seasonal AR, perennial AR	None	≥6 y	Age 6-11 y: 1 spray twice a day Age ≥12 y: 1-2 sprays twice a day or 2 sprays daily	• Bitter taste • Epistaxis • Somnolence • Headache	Prescription
Azelastine plus fluticasone (Dymista) (137 µg of azelastine, 50 µg of fluticasone per spray)	Seasonal AR	None	≥12 y	1 spray per nostril twice a day	• Bitter taste • Epistaxis • Somnolence • Headache	Prescription

Mast-Cell Stabilizers		
Cromolyn Sodium (Crolom)	Ophthalmic solution: 4%	Adults and children ≥4 years: 1–2 drops in the affected eye(s) 4–6 times daily
Lodoxamide (Alomide)	Ophthalmic solution: 0.1%	Adults and children ≥2 years: 1–2 drops in affected eye(s) 4 times daily for up to 3 months
Nedocromil (Alocril)	Ophthalmic solution: 2%	Adults and children ≥3 years: 1–2 drops in the affected eye(s) every 12 hours
Nonsteroidal Anti-Inflammatory Drugs[b]		
Ketorolac (Acular)	Ophthalmic solution: 0.5%	Adults and children ≥3 years: 1 drop in the affected eye(s) 4 times daily
Corticosteroids[c]		
Loteprednol (Alrex)	Ophthalmic suspension: 0.2%	Adults: 1 drop in the affected eye(s) 4 times daily

Additional Oral and Intranasal Agents for Rhinitis

Additional Oral and Intranasal Agents for Rhinitis

Generic (Brand Product)	Available Dosage Forms/Strength	Adult Dose	Pediatric Dose
Oral			
Leukotriene modifiers Montelukast (Singulair)	Tablets: 10 mg Tablets, chewable: 4 mg, 5 mg Oral granules: 4 mg	10 mg once daily	Children 6–14 years: 5 mg once daily Children 2–5 years: 4 mg once daily Children 6–23 months: 4 mg once daily
Intranasal			
Antihistamine Azelastine (Astepro)	Nasal spray: 0.1% 0.15%	Perennial: 0.15%: 2 sprays/nostril twice daily Seasonal: 0.1%: 1–2 sprays/nostril twice daily 0.15%: 1–2 sprays/nostril twice daily or 2 sprays/nostril once daily.	Perennial: Children 6 months–5 years (0.1%) 1 sp EN BID Children ≥2 years: 0.15%: 2 sprays/nostril twice daily Children 6–11 years: 0.1% or 0.15%: 1 spray/nostril twice daily Seasonal: Children 6–11 years: 0.1% or 0.15%: 1 spray/nostril twice daily Children 2–5 years: 0.1%: 1 spray/nostril twice daily
Olopatadine (Patanase)	Nasal Solution: 0.6%	Two sprays per nostril twice daily	6–11 years: 1 spray per nostril twice daily
Mast-cell stabilizer Cromolyn sodium (Nasalcrom)[a]	Nasal spray: 5.2 mg/spray	1 spray/nostril 3–4 times/day (every 4–6 hours; max 6 times daily)	Children ≥2 years: 1 spray/nostril 3–4 times/day (every 4–6 hours; max 6 times daily)
Anticholinergic Ipratropium bromide (Atrovent)[b]	Nasal spray: 21 mcg/spray (for perennial symptoms), 42 mcg/spray (for seasonal symptoms)	2 sprays/nostril up to 4 times daily (max = 672 mcg/day)	Children ≥6 years: 42 mcg/spray: 2 sprays/nostril 2–3 times/day Children 5–11 years: 84 mcg/spray: 2 sprays/nostril 3 times daily

- The older intranasal corticosteroids (beclomethasone, flunisolide, and budesonide) have significant absorption, whereas, among the newer products, fluticasone and mometasone, have bioavailability of less than 2%
- Most patients tolerate intranasal corticosteroids very well.

Major side effects of INCSs

- The older INCSs (beclomethasone, flunisolide, and budesonide) have significant absorption, whereas, among the newer products, fluticasone, ciclesonide, and mometasone have bioavailability of less than 1% to 2%
- The decreased absorption minimizes systemic side effects. However, there is still some concern for hypothalamic–pituitary–adrenal (HPA) axis suppression (growth suppression), osteoporosis, and ocular effects (glaucoma, cataracts).
- **There is no confirmation that INCSs cause posterior subcapsular cataracts, increased intraocular pressure, or decreased bone density; however, those with risk factors for these conditions should be monitored carefully for their development.**
- Additionally, clinicians should examine total corticosteroid exposure (ie, from all sources, inhaled, oral, etc) in assessing potential risk for adverse effects from systemic exposure
- Ultimately, patient preference for a specific INCS may be determined more by cost, availability, and formulation differences that affect odor and aftertaste

Name	Formulation	FDA Indications	Contraindications	Age Approved	Dosing	Common Side Effects	OTC or Prescription
Triamcinolone acetonide[a] (Nasacort Allergy 24HR), 55 µg per spray	Propellant, aqueous	Seasonal and perennial AR	History of hypersensitivity to medication or components	≥2 y	Age 2-5 y: 1 spray per nostril every day Age 6-11 y: 2 sprays per nostril every day Age ≥12 y: 2 sprays per nostril 1 or 2 times per day	Pharyngitis, epistaxis, cough	OTC
Budesonide (Rhinocort AQ) 32 µg per spray	Propellant	AR and nonallergic rhinitis	History of hypersensitivity to medication or components	≥6 y	Age ≥6 y: 2 sprays per nostril twice a day or 4 sprays per nostril in the morning	Epistaxis, pharyngitis, bronchospasm, coughing, nasal irritation	Prescription
Flunisolide[b] (Nasalide or Nasarel), 25 µg per spray	0.025% solution	Seasonal and perennial AR	History of hypersensitivity to medication or components	≥6 y	Age 6-14 y: 1 spray per nostril 3 times per day or 2 sprays per nostril twice a day Age >14 y: 2 sprays per nostril 2 or 3 times per day	Epistaxis, pharyngitis, cough, aftertaste, nasal burning or stinging	Prescription
Fluticasone propionate[b] (Flonase), 50 µg per spray	0.05% nasal spray (aqueous)	AR and nonallergic rhinitis	History of hypersensitivity to medication or components	≥4 y	Age 4 y to adult: 1 spray per nostril every day Adult: 2 sprays per nostril every day	Headache, pharyngitis, epistaxis, nasal burning or irritation, nausea or vomiting, asthma symptoms, cough	Prescription

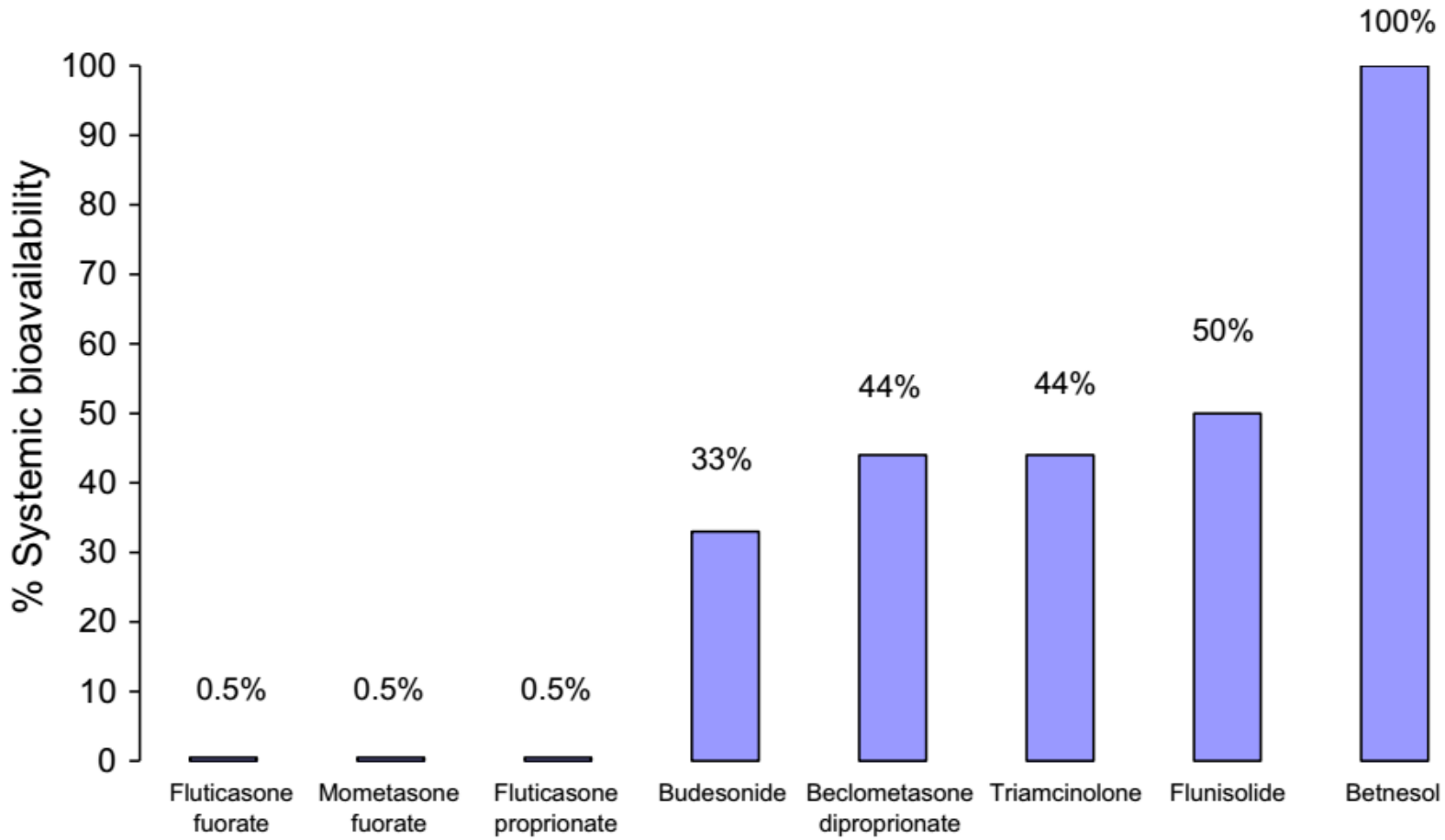
Mometasone furoate (Nasonex), 50 µg per spray	Aqueous	Seasonal and perennial AR, nasal polyps	History of hypersensitivity to medication or components	≥2 y	Age 2-11 y: 1 spray per nostril every day Age ≥12 y: 2 sprays per nostril every day Age ≥18 y with polyps: 2 sprays per nostril twice a day	Headache, viral infection, pharyngitis, epistaxis, cough	Prescription
Ciclesonide (Omnaris), 50 µg per spray	Aqueous suspension	Seasonal and perennial AR	History of hypersensitivity to medication or components	≥6 y	Age ≥6 y: 2 sprays per nostril every day	Epistaxis, headache, nasopharyngitis, ear pain, pharyngolaryngeal pain	Prescription
Fluticasone furoate (Veramyst), 27.5 µg per spray	Suspension	Seasonal and perennial AR	History of hypersensitivity to medication or components	≥2 y	Age 2-11 y: 1-2 sprays per nostril every day Age >11 y: 2 sprays per nostril every day	Epistaxis, headache, pharyngolaryngeal pain, nasal ulceration, back pain, pyrexia, cough	Prescription
(Qnasl), 80 µg per spray	HFA nonaqueous aerosol	Seasonal and perennial AR	History of hypersensitivity to medication or components	≥12 y	Age ≥12 y: 2 sprays per nostril every day	Nasal discomfort, epistaxis, headache	Prescription
Ciclesonide (Zetonna), 37 µg per spray	HFA-propelled aerosol	Seasonal and perennial AR	History of hypersensitivity to medication or components	≥12 y	Age ≥12 y: 1 spray per nostril every day	Nasal discomfort, epistaxis, headache	Prescription

Intranasal Corticosteroids[a] Commonly Used for Rhinitis

Beclomethasone dipropionate (Beconase AQ) QNasal (HFA) QNasal (Children's)	42 mcg/spray 80 mcg/spray 40 mcg/spray	42 mcg: 1–2 sprays/nostril twice daily 80 mcg: 2 sprays/nostril once daily	Children 6–12 years: 42 mcg: 1 spray/nostril twice daily (max 2 sprays/nostril daily) Children 4–11 years: 40 mcg: 1 spray/nostril once daily (max 2 sprays/nostril daily)
Budesonide (Rhinocort Aqua) (Rhinocort Allergy) (Children's Rhinocort)	32 mcg/spray	1 spray/nostril once daily (max 4 sprays/nostril daily)	Children 6–12 years: 1 spray/nostril once daily (max 2 sprays/nostril daily)
Ciclesonide (Omnaris) Zetonna (HFA)	50 mcg/spray 37 mcg/spray	50 mcg: 2 sprays/nostril once daily 37 mcg: 1 spray/nostril once daily	50 mcg: Children 6–12 years: 2 sprays/nostril once daily (approved for seasonal symptoms in ages >6, and for perennial symptoms for ages >12) 37 mcg: do not use in children <12.
Fluticasone propionate (Flonase Allergy Relief) (Clarispray) (Children's Flonase) (GoodSense Nasoflow) (Ticaspray)	50 mcg/spray	2 sprays/nostril once daily or 1 spray/nostril twice daily	Children 4–11 years: 1 spray/nostril once daily (max 2 sprays/nostril daily)
Fluticasone furoate (Flonase Sensimist)	27.5 mcg/spray	2 sprays/nostril once daily	Children 2–11 years: 1 spray/nostril once daily (max 2 sprays/nostril daily)
Flunisolide (no brand product available)	0.025%	>15 years: 2 sprays/nostril 2 or 3 times daily (max 8 sprays/nostril daily)	Children 6–14 years: 1 spray/nostril 3 times daily or 2 sprays/nostril twice daily (max 4 sprays/nostril daily)
Mometasone furoate (Nasonex)	50 mcg/spray	2 sprays/nostril once daily	Children 2–11 years: 1 spray/nostril once daily
Triamcinolone acetonide (Nasacort AQ) (Nasacort Allergy)	55 mcg/spray	2 sprays/nostril once daily	Children 2–5 years: 1 spray/nostril once daily (max 1 spray/nostril daily) Children 6–11 years: 1–2 sprays/nostril once daily (max 2 sprays/nostril daily)
Azelastine HCl/fluticasone propionate (Dymista)	137/50 mcg/spray	1 spray/nostril twice daily	Children ≥6 years: 1 spray/nostril twice daily

- Local side effects include nasal burning, irritation, and dryness, which may occur in 2% to 10% of patients.
- Also, 2% to 12% of patients may experience mild epistaxis.
- There is still some concern for hypothalamic–pituitary–adrenal (HPA) axis suppression (growth suppression), osteoporosis, and ocular effects (glaucoma, cataracts)
    - There is no confirmation that intranasal corticosteroids cause posterior subcapsular cataracts, increased intraocular pressure, or decreased bone density

- Intranasal corticosteroids (INCSs) have potent anti-inflammatory
- Properties that reduce symptoms of sneezing, itching, rhinorrhea, and congestion


% Systemic bioavailability
100
90
80
70
60
50
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30
20
10
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33%
44%
44%
50%
100%
Fluticasone fuorate
Mometasone fuorate
Fluticasone proprionate
Budesonide
Beclometasone diproprionate
Triamcinolone
Flunisolide
Betnesol

Ipratropium bromide —

- Ipratropium bromide, in the form of a 0.03 percent nasal spray, can be useful for decreasing rhinorrhea. It is a congener of atropine and may act by decreasing the release of substance P. However, it is less effective than glucocorticoid nasal sprays for sneezing, pruritus, or nasal obstruction. Ipratropium bromide is also available in a stronger formulation (0.06 percent), although this is specifically labeled for reduction of rhinorrhea associated with colds.
- Ipratropium is not recommended as a first-line drug in allergic rhinitis. It is sometimes useful in children or adults who have profuse rhinorrhea not otherwise controlled with topical nasal glucocorticoids, a complaint most commonly observed in adult patients with concomitant allergic and nonallergic (or vasomotor) rhinitis.

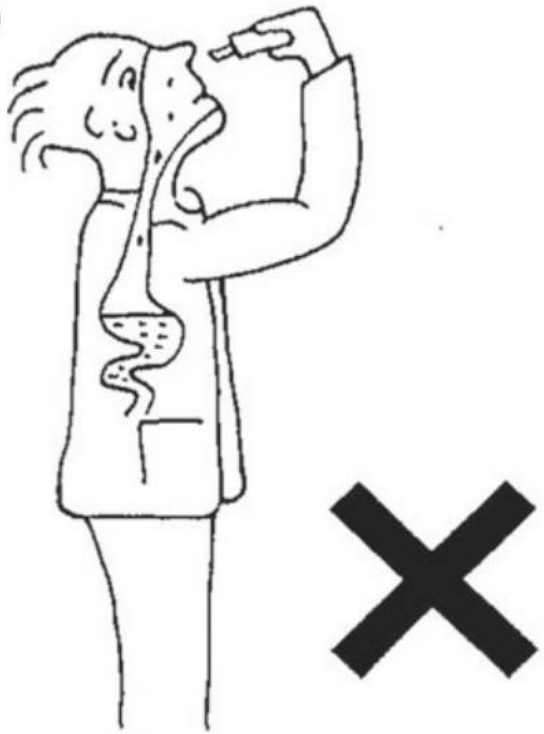
Administration Instructions for Intranasal Solution Medications (Not HFA MDP Products)

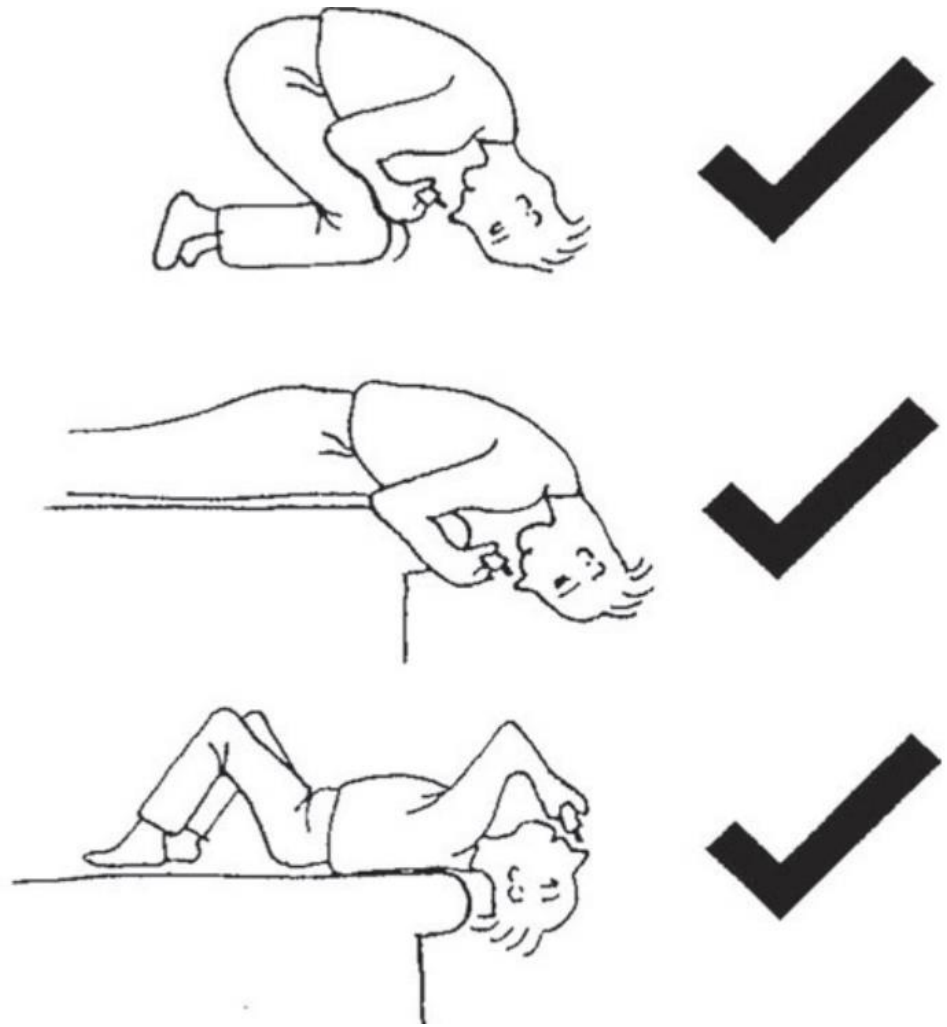
1. Clear the nose of mucus and debris.
2. Consult product labeling for preadministration instructions (eg, shaking the container, priming the spray pump).
3. Do not tilt head backward. This increases drug lost down the esophagus. This decreases efficacy and increases the potential for systemic absorption and thus systemic side effects.
4. Bend the head forward (flex the chin onto the chest) so that the nose is the lowest portion of the head. This is best for nasal sprays. If possible, lie down with the stomach on a flat surface or kneel down. Then, flex chin onto neck, so that the open nostrils are pointing upward, toward the ceiling. This position may be best for nose drops (more volume than sprays). An alternate position is to lie supine on a flat surface, then bend the neck backward (extend the head), so that the open nostrils point upward toward the ceiling.
5. Use the contralateral hand to insert the spray nozzle or dropper into one nostril (ie, the left hand for right nostril).
6. Use the other hand to occlude the opposite nostril (the one not being medicated).
7. Aim the spray or drops toward the outer (lateral) inside surface of each nostril and away from the nasal septum.
8. Breath in slowly but deeply through the medicated nostril.
9. Repeat this procedure to apply medication to the other nostril.
10. Consult the product labeling for instructions on cleaning the device.
11. See the text for information about preparation and use of saline irrigation.

(A)

1. Shake bottle well
2. Look down
3. Using right hand for left nostril put nozzle just inside nose aiming towards outside wall
4. Squirt once or twice (2 different directions ↗→)
5. Change hands and repeat for other side
6. Breathe in gently through the nose
7. Do not sniff

(B)



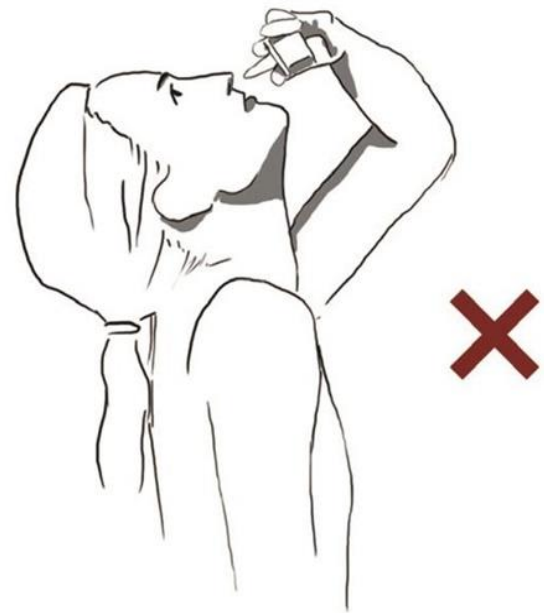


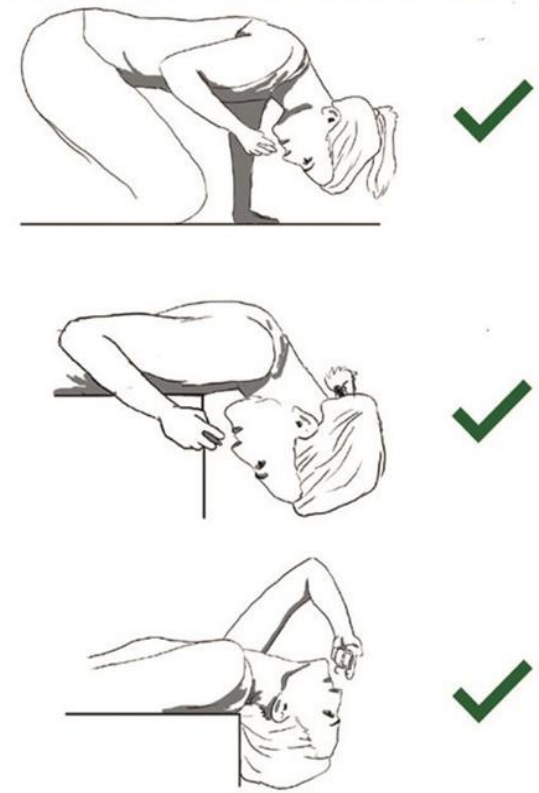
A

1. Shake bottle well
2. Look down
3. Using RIGHT hand for LEFT nostril put nozzle just inside nose aiming towards outside wall
4. Squirt once or twice (2 different directions)
5. Change hands and repeat for other side
6. Do not sniff hard

B

Choose any position you feel comfortable with





Saline

- This therapy may benefit any patient with rhinitis, including those with vasomotor rhinitis.5 Saline may be administered as drops or a spray, but the irrigation mode of administration is popularly known by several terms, including neti pot, nasal wash, nasal douche, n irrigation.

- Although less effective than intranasal corticosteroids, it has been shown to improve sneezing and nasal congestion
- Iodized salt is not recommended as it may be irritating. Hypertonic saline seems to have no advantage over 0.9% sodium chloride.
- The head is bent forward and downward, then tilted to the side opposite the treated nostril. Then, with a bulb syringe or similar device, slowly introduce about 4 oz (118 mL) of the warm saline solution

  into one nostril. Soon, the solution will run out of the opposite nostril. The position of the head should be adjusted as necessary to avoid the solution running into the ears or down the throat

Efficacy and properties of drug treatments used in allergic rhinitis				
Characteristic	**Oral antihistamine**	**Nasal steroid**	**Nasal decongestant**	**Nasal cromone**
Rhinorrhea	++	+++	-	+
Sneezing	++	+++	-	+
Itching	++	+++	-	+
Blockage	+	+++	++++	+
Eye symptoms	++	++	-	-
Onset of action	1 hr	12 hrs	5–15 min	Variable
Duration	12–24 hrs	12–48 hrs	3–6 hrs	2–6 hrs

-, no effect; +, marginal effect; ++++, substantial effect (under natural exposure conditions).
(Reproduced with permission from Farooque S. Allergic rhinitis: Guide to diagnosis, allergen avoidance and treatment. The Prescriber 2012;5th May:380-39.

Risks of medication in pregnant women with allergic rhinitis.

Generic name	Trade name	Australian standards	FDA standards
Antiallergics (for internal use)			
d-chlorpheniramine maleate	Polaramin®	A	B
d-chlorpheniramine maleate	Allergin®	A	B
Diphenhydramine hydrochloride	Vena®, Restamin®	A	B
Cyproheptadine hydrochloride	Periactine®	A	B
Promethazine hydrochloride	Pyrethia®, Hiberna®		C
Clemastine fumarate	Tavegyl®	A	B
Diphenylpyraline teoclate	Agiell®, Plokon®	B2	
Loratadine	Claritin®	B1	B
Cetirizine hydrochloride	Zyrtec®	B2	B
Fexofenadine hydrochloride	Allegra®	B2	C
Amlexanox	Solfa®		B
Epinastine hydrochloride	Alesion®		C
Azelastine hydrochloride	Azeptin®		C
Ketotifen fumarate	Zaditen®		C
Nasal sprays			
Beclomethasone propionate	Aldecin® AQ Nasal, Rhinocort®	B3	C
Fluticasone propionate	Flunase®	B3	C
Disodium cromoglycate	Intal®		B
Amlexanox	Solfa®		B
Ketotifen fumarate	Zaditen®		C

Adverse effects of therapeutic agents for allergic rhinitis.

Medicines	Adverse effects
First-generation antihistamine	Sleepiness, systemic malaise, dry mouth, etc. (asthma, dysuria, glaucoma, and contraindication to driving)
Second-generation antihistamine	Hepatic and gastrointestinal disorders, sleepiness, and myocardiopathy for some agents
Oral mast cell stabilizer	Hepatic and gastrointestinal disorders, rash, and cystitis for some agents
Leukotriene receptor antagonists	Leukopenia, thrombocytopenia, hepatic disorders, rash, diarrhea, abdominal pain, etc.
Prostaglandin D_2/thromboxane A_2 receptor antagonists	Bleeding tendency, hepatic disorders, rash, abdominal pain, headache, etc.
Th2 cytokine inhibitors	Hepatic disorders, jaundice, nephrosis, etc.
Oral corticosteroids	Infection, adrenocortical insufficiency, diabetes, peptic ulcer, moon face, glaucoma, etc. (contraindicated for treatment of infection, peptic ulcer, hypertension, diabetes, glaucoma, etc.)
Nasal steroids	Nasal irritation, feeling of dryness, epistaxis, etc.
Mast cell stabilizer and antihistamine for nasal spray	Nasal irritation and sleepiness (for some agents)
Vasoconstrictor nose spray	Habituation, rebound phenomena, hyporesponsiveness, etc.