

## News and commentaries

# ARIA in the pharmacy: management of allergic rhinitis symptoms in the pharmacy

## Allergic Rhinitis and its Impact on Asthma

### Members of the workshops\*

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Allergic rhinitis is a symptomatic disorder of the nose induced by an immunoglobulin (IgE)-mediated inflammation of the nasal membranes in response to allergen exposure (1). Predominant symptoms are rhinorrhea, nasal obstruction, nasal itching and sneezing, which improve spontaneously or with treatment (1–3).

The high prevalence of allergic rhinitis and its effect on quality of life have led to its being classified as a major chronic respiratory disease (1, 4). It is reported to affect 10% to 40% of the global population and its prevalence is increasing both in children and adults. Allergic rhinitis can significantly reduce quality of life (5), impairing sleep and adversely affecting leisure, social life, school performance (6) and work productivity (7). The direct and indirect financial costs of allergic rhinitis are substantial. Indirect costs include sick leave, school and work absenteeism and loss of productivity (8, 9).

Asthma and rhinitis are common co-morbidities suggesting the concept of “one airway, one disease” (1). In addition, allergic rhinitis is associated with conjunctivitis and sinusitis.

Recently, advances in our understanding of the mechanisms underlying inflammation of the upper and lower airways have led to improved therapeutic strategies for

managing allergic rhinitis. Practice guidelines incorporating these advances have been developed (1). In addition, a new classification of allergic rhinitis aids the establishment of appropriate initial treatment strategy based on the duration and intensity of the patient's symptoms and lifestyle limitations (1, 10).

Many patients who suffer with allergic rhinitis do not recognise the process as such and do not consult a physician (10, 11). Others commonly seek self-treatment for relief of symptoms using proven or unproven therapies.

Worldwide, pharmacists receive sophisticated clinical training. Given the well-known and well-publicised recognition of iatrogenic disease, pharmacists' skills represent an enormous potential resource to maximise the benefits and minimise the adverse events associated with pharmacotherapy (12). Pharmaceutical care includes prevention, treatment or cure of a disease (13). Interest and expectation that pharmacists provide broader “pharmaceutical care” services has therefore increased (14). Pharmaceutical care for the patient is likely to be optimal when there is collaboration between pharmacists, patients and other health care professionals, specifically physicians.

**In many countries, advice in pharmacies may not necessarily be from a qualified pharmacist but from a member of staff under the supervision of a pharmacist.**

\*Details of workshop members are given in the appendix.

## ARIA in the pharmacy

As trusted healthcare professionals in the community, pharmacists are well placed to identify the symptoms of allergic rhinitis and to recommend appropriate treatment. In some countries, there has recently been an increase in effective and safe medicines available without prescription for the treatment of allergic rhinitis. This guide provides a practical, step-by-step approach to aid pharmacists in advising patients:

- in recognising allergic rhinitis and assessing its severity,
- in understanding the effect of treatment on rhinitis and co-morbidities,
- in determining whether management in the pharmacy is appropriate,
- in initiating an appropriate treatment and monitoring plan,
- and proposing appropriate preventive measures.

This should:

- increase collaboration between pharmacists, physicians and other health care professionals,
- reduce the burden incurred by allergic rhinitis and its co-morbidities,
- aid in the identification of undiagnosed or uncontrolled asthma,
- and improve cost-effectiveness in the management of allergic rhinitis.

This document is a guide. It is not intended to be a mandatory standard of care document for individual countries. It is provided as a basis for pharmacists and their staff, as well as for organisations involved in the treatment of respiratory allergic diseases in various countries to develop relevant local standards of care for their patients. When implementing recommendations, the local plan should consider the infrastructure of pharmacy practice, workforce and regulations in the individual country.

In the present document, the physical examination and testing of patients for allergic rhinitis will not be detailed as relevant information has been published in the ARIA (Allergic Rhinitis and its Impact on Asthma) workshop report (1). Likewise, allergen avoidance, allergen specific immunotherapy and patient education are not emphasised to the extent they are utilised on the overall management. The pharmacist's role in providing education and in recommending strategies for avoiding exposure to allergens and irritants is recognised; however, this document focuses on appropriate initial pharmacotherapy recommendations from the pharmacist. For greater detail about these other areas, the reader is referred to the ARIA workshop report (1).

Medications available without a prescription (over the counter: OTC) from a physician vary in countries throughout the world. Pharmacists can advise and treat patients, depending on the symptoms presented by the patient and the medications which are available. When

there is any doubt about what should or should not be recommended, or if a question exists about an alternative diagnosis, the patient should be referred to a physician for further evaluation.

## Recognising allergic rhinitis in the pharmacy

Recognising allergic rhinitis

Some patients who consult the pharmacist will have had allergic rhinitis previously diagnosed by a physician, others will have made an appropriate self-diagnosis, some will not have any diagnosis of rhinitis or may even have an incorrect diagnosis (e.g. a viral infection, cold). The pharmacist should always therefore ask patients to give an account of his or her symptoms to assist in recognising the disease and assessing the severity. The most commonly reported symptoms are sneezing, an itchy, congested nose (nasal blockage) and runny nose (nasal discharge or rhinorrhea) (Table 1) (11, 15). The eyes, paranasal sinuses and eustachian tube may be affected, resulting in itchy, watery or red eyes, temporary ear fullness and popping, itchy throat and pressure over the cheeks and forehead. Other symptoms may include malaise, headache, weakness, inability to concentrate and fatigue.

If the patient does not give sufficient information about symptoms to arrive at a diagnosis, more information can be elicited by structured questioning (Table 2). It is often relatively easy to differentiate "sneezers and runners" who may have allergic rhinitis from isolated "blockers" who are almost never allergic.

Differentiating allergy from other causes including infection

Allergic rhinitis presents with symptoms similar to those of a number of other conditions and may be confused with a viral infection such as the common cold and with chronic sinusitis. Figure 1 presents an algorithm for differentiating allergic rhinitis from another cause or infectious diseases. The presence of nasal itching, rhinorrhea, sneezing, and eye symptoms are usually consistent with allergic rhinitis.

Table 1. Clinical classification of rhinitis (2,10)

	"Sneezers and runners"	"Blockers"
Sneezing	Especially paroxysmal in bouts	Little or none
Rhinorrhea	Always present: watery, anterior and sometimes posterior	Variable, can be thick mucous, and generally more posterior
Nasal itching	Yes, often	No
Nasal blockage	Variable	Often severe
Diurnal rhythm	Worse on awakening, improves during the day and usually worsens again in the evening	Constant day and night, may be worse at night and is often severe
Conjunctivitis	Often present	None

Table 2. Questions to elicit information

- What is your main symptom? (Check for rhinorrhea, sneezing, itchy nose, nasal congestion and/or obstruction, watery or itchy eyes.)
- Has a physician ever diagnosed that you have hay fever, allergic rhinitis or asthma?
- How long have you had these symptoms?
- Do you have the symptoms all the time or do they come and go?
- Are you aware of anything that seems to bring the symptoms on, such as being outdoors, around animals, or related to something you handle at work or at home?
- Is your nasal discharge clear and watery? (Purulent discharge suggests infection)
- Are you experiencing any wheezing or shortness of breath? ("Yes" may indicate asthma.)
- Do you have an earache or pain in your face? ("Yes" may indicate otitis media or sinusitis.)
- Do you have eye symptoms?
- Do you have a family member with allergy problems?
- What medications have you already tried for these symptoms?
- Do you have any other medical conditions or are you on any other medication?

Assessing the severity of allergic rhinitis

A recent classification of allergic rhinitis (intermittent or persistent) has replaced the previous classification of seasonal and perennial forms (1). This classification is more appropriate as it is based on the patient's symptoms and needs, and forms a practical basis for assessing and managing allergic rhinitis (Figure 2).

Management by pharmacists or referral to physician

Once allergic rhinitis has been identified, its severity can be assessed by asking the patient to what extent symptoms affect daily life. Where symptoms are intermittent, i.e. occurring fewer than 4 days per week or for less than 4 weeks, or mild, i.e. causing minimal interference with daily living, pharmacist management may be appropriate depending on medication availability.

Referral to a physician should be considered in cases where:

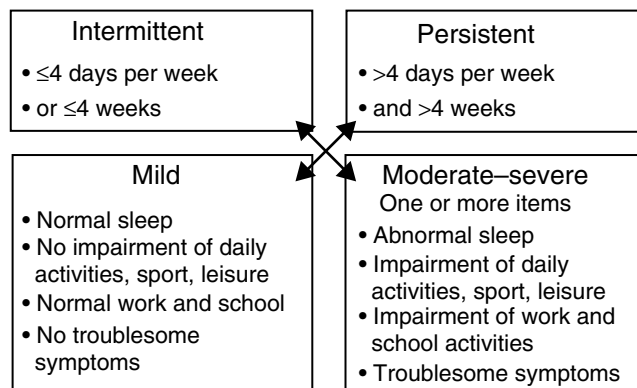


Figure 2. Classification of allergic rhinitis according to ARIA (1).

- persistent, moderate to severe symptoms of rhinitis are present, (although initial treatment might be provided by a pharmacist whilst waiting to see a physician),
- symptoms are suggestive of undiagnosed asthma or uncontrolled asthma in patients with a diagnosis of asthma (e.g. wheezing or shortness of breath),
- symptoms of infection (mucopurulent discharge, sore throat, myalgia, asthenia, fever) are reported,
- subjects whose symptoms do not respond to initial pharmacy management within 2 to 4 weeks,
- bothersome side effects are experienced.

Referral to a physician is also advisable during pregnancy, because some medications should be administered with caution.

Management by a physician is also appropriate for children under 12, because of difficulties in establishing the diagnosis, selecting the proper medications to avoid side effects, and the frequent off-label use of medicines in this age group.

Table 3 lists these and other circumstances in which referral to a physician is desirable.

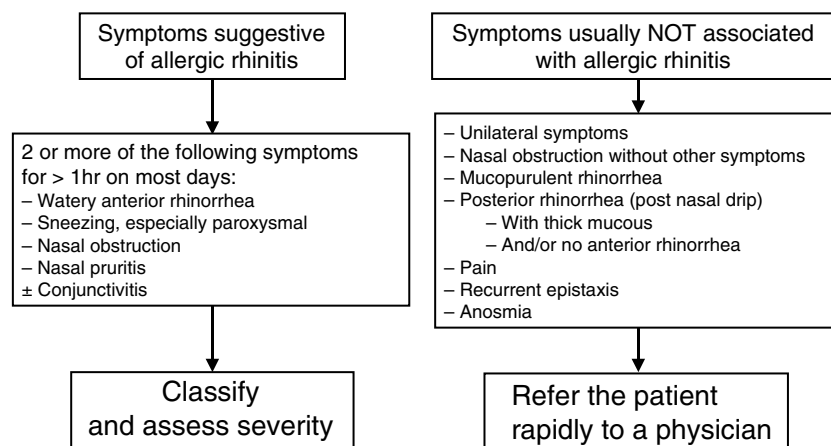


Figure 1. Differentiating allergic rhinitis from other causes.

## ARIA in the pharmacy

Table 3. Circumstances when referral to a physician is advisable before treatment for allergic rhinitis

- Children under 12
- Pregnant or breast-feeding women
- Symptoms not usually associated with allergic rhinitis:
  - Unilateral obstruction
  - Anosmia (loss of smell)
  - Nasal obstruction without rhinorrhea (discharge)
  - Thick green or yellow mucous secretion
  - Posterior rhinorrhea
  - Recurrent epistaxis (nose bleed)
- Severe persistent allergic rhinitis
- Symptoms of undiagnosed asthma
- Symptoms of uncontrolled asthma
- Earache (may indicate otitis)
- Symptoms unresponsive to treatment
- Unacceptable side effects of treatment

### Asthma co-morbidity

Allergic rhinitis and asthma often co-exist. Allergic rhinitis is regarded as a risk factor for the development of asthma (1). In patients with asthma, rhinitis may be associated with a poor control of the disease. Patients with persistent rhinitis should be questioned for symptoms of asthma. Patients with asthma should be questioned for symptoms of rhinitis. Patients with undiagnosed asthma or those

with uncontrolled asthma should be advised to consult a physician for proper evaluation. This is particularly important in children (see also “The management of allergic rhinitis and asthma”).

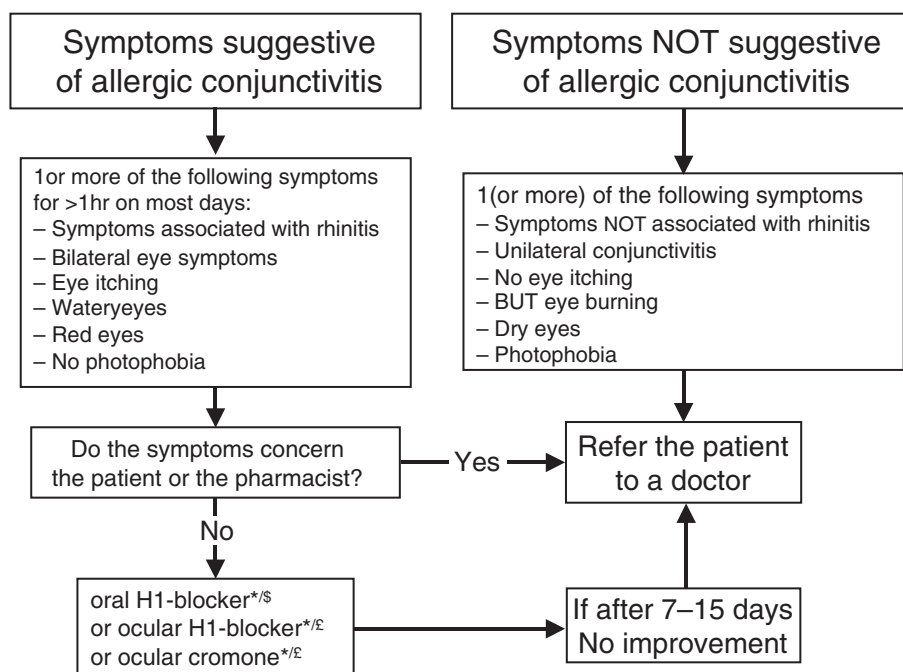
### Conjunctivitis

Eye symptoms are common in patients suffering from allergic rhinitis but do not exist in all patients with rhinitis. In some cases, eye symptoms may predominate over rhinitis (16), hence the term “rhinoconjunctivitis” cannot replace the term “rhinitis”. The presence of conjunctivitis should always be considered. On the other hand, conjunctivitis is not always induced by allergic triggers (Figure 3).

Photophobia (light sensitivity) is an important symptom to be noted and, if present, needs a physician evaluation. Eye itching is common in allergic conjunctivitis. In contrast, eye burning is rarely a sign of allergic conjunctivitis.

### Management of allergic rhinitis

The management of allergic rhinitis should encompass patient education, allergen and pollutant (e.g. tobacco) avoidance when possible, pharmacotherapy and validated allergen specific immunotherapy (1, 17).



\* depending on drug availability not in preferred order  
 \$ non-sedating H1-blockers are preferred  
 £ formulations without preservatives are better tolerated

Figure 3. Differentiating allergic conjunctivitis from other causes and selection of treatment by pharmacists.

### Environmental control

There is some controversy about allergen avoidance. In asthma, a recent meta-analysis showed that some measures were effective in reducing symptoms (18). If avoidance measures are to be considered in allergic rhinitis, allergen sensitivity should be documented. However, a meta-analysis in rhinitis did not show that mite avoidance was clinically effective possibly because of methodological problems (19). More studies are needed to evaluate avoidance measures for other inhaled allergens.

Reduction of active and passive smoking should be advised and assistance provided (pharmacotherapy and support) when appropriate.

### Options for pharmacological treatment of allergic rhinitis

Pharmacological treatment should take into account the efficacy, safety and cost-effectiveness of medications, the patient's preference and the objective of treatment (20), severity of the disease as well as the presence of co-morbidities (Table 4). Medications used for rhinitis are most commonly administered intranasally or orally. The efficacy of medications may differ between patients.

Many medications used in the treatment of allergic rhinitis are available without a medical prescription, although there is a large disparity between countries. There are proposals for harmonisation across the European Union (EU). In many countries, new generation H<sub>1</sub>-antihistamines, intranasal glucocorticosteroids and chromones are available without a prescription. In other countries, only sedating antihistamines and decongestants are available without a prescription. Non-sedating H<sub>1</sub>-oral antihistamines are recommended because of their considerably lower incidence of side effects compared to sedating antihistamines (21, 22). Patients may not always perceive sedation and mental impairment. Common treatments currently available for allergic rhinitis (including prescription-only medicines) are listed in Table 5 (10) and pharmacists are able to advise patients on both prescribed and OTC medications.

The pharmacological treatment of allergic rhinitis proposed by ARIA is an evidence-based (23) and step-wise approach depending on the classification of the symptoms. Figure 4 provides the overall approach to treatment.

Table 4. Responses to commonly asked questions

- Medications are for the relief of symptoms and have no long-lasting effect when stopped. Therefore, in persistent disease, maintenance treatment is required.
- Tachyphylaxis does not usually occur with prolonged treatment except for intranasal decongestants. Continuous treatment with other medications is effective.
- Most medications recommended in this guideline do not have significant long-term side effects and can be administered for prolonged periods.

*Oral and local H<sub>1</sub>-antihistamines.* Both oral and topical (intranasal and ocular) antihistamine preparations are available without prescription for the treatment of allergic rhinitis in many but not all countries. H<sub>1</sub>-blockers or H<sub>1</sub>-antihistamines are medications blocking histamine at the H<sub>1</sub>-receptor level (neutral antagonists or inverse agonists) (24). Some also possess additional anti-allergic properties. During the last 20 years, pharmacological research has produced compounds with minimal sedative effect and impairment: the so-called second-generation H<sub>1</sub>-antihistamines, as opposed to the first generation H<sub>1</sub>-antihistamines (25) (Table 5).

Oral antihistamines are effective against symptoms mediated by histamine, including rhinorrhea, sneezing, nasal itching, and eye symptoms (1, 26), but are less effective on nasal congestion (27, 28). They improve the quality of life of the patient. They are used regularly for the treatment of intermittent and persistent allergic rhinitis, and can also be used to prevent symptoms associated with occasional allergen exposure.

First-generation oral H<sub>1</sub>-antihistamines are associated with sedation and central nervous system impairment (21). These include performance of cognitive and skilled tasks such as learning and driving. These impairments can be potentiated by alcohol, other sedative medications and compound the sleep disturbance of the disease. Side effects may not always be perceived by the patients. If administered, patients should be advised of the potential side effects of first-generation oral H<sub>1</sub>-antihistamines. First-generation oral antihistamines may also have anticholinergic side effects, including dry mouth, dry eyes, difficulty in urinating and worsening of glaucoma (1, 29). Second-generation H<sub>1</sub>-antihistamines are in general less likely to cause sedation and impairment. They do not have anticholinergic effects. Second generation H<sub>1</sub>-oral antihistamines are recommended because they are equally effective and have fewer side effects, resulting in a better risk-benefit ratio.

Some, but not all, oral H<sub>1</sub>-antihistamines undergo hepatic metabolism via the cytochrome P450 system and may be prone to drug interactions. Certain medications, herbal products, foods and dietary supplements can affect the bioavailability of some second-generation antihistamines.

Major concerns exist about the arrhythmogenic action of terfenadine, astemizole and high doses of diphenhydramine which have exceptionally been associated with fatalities. This is not a class effect (27). The use of terfenadine and astemizole is therefore not advised.

H<sub>1</sub>-antihistamines are also approved for young children (30).

In general, first-generation antihistamines have a short duration of action and require dosing several times daily (31). Most of the second-generation oral H<sub>1</sub>-antihistamines have a rapid onset of action (20 minutes to 2 hours) and a long duration of effect (up to 24 hours) allowing once daily dosing (27). Acrivastine has a shorter duration of action and should be administered twice daily (27).

## ARIA in the pharmacy

Table 5. Medications available for the treatment of allergic rhinitis (including prescription-only medicines) (10)

Classification	Generic names	Mechanism of action	Side effects	Comments
Oral H <sub>1</sub> antihistamines	2nd generation	<ul style="list-style-type: none"> <li>– Blockage of H<sub>1</sub> receptor</li> <li>– Some anti-allergic activity</li> <li>– New generation medications can be used once daily</li> <li>– No development of tachyphylaxis</li> </ul>	<ul style="list-style-type: none"> <li>2nd generation</li> <li>– No sedation for most medications</li> <li>– No anti-cholinergic effect</li> <li>– No cardiotoxicity</li> <li>– Acrivastine has sedative effects</li> <li>– Oral azelastine may induce sedation and has a bitter taste</li> <li>1st generation</li> <li>– sedation is common and may not be perceived</li> <li>– potentiation of impairment induced by alcohol</li> <li>anti-cholinergic effect may occur</li> </ul>	<ul style="list-style-type: none"> <li>– 2nd generation oral H<sub>1</sub>-antihistamines are preferred for their favourable efficacy/safety ratio and pharmacokinetics</li> <li>– 2nd generation medications can be used once daily</li> <li>– Rapidly effective (less than 1 hour) on nasal and ocular symptoms</li> <li>– Poorly effective on nasal congestion</li> <li>– Cardiotoxic medications should be avoided</li> </ul>
	Acrivastine			
	Azelastine			
	Cetirizine			
	Desloratadine			
	Ebastine			
	Fexofenadine			
	Levocetirizine			
	Loratadine			
	Mizolastine			
	1st generation			
	Chlorpheniramine			
	Clemastine			
	Diphenhydramine			
	Hydroxyzine			
	Ketotifen			
	Mequitazine			
	Oxatomide			
	Others			
Local H <sub>1</sub> antihistamines (intranasal, ocular)	Azelastine	<ul style="list-style-type: none"> <li>– Blockage of H<sub>1</sub> receptor</li> <li>– Some anti-allergic activity for azelastine</li> </ul>	<ul style="list-style-type: none"> <li>– Minor local side effects</li> <li>– Azelastine: bitter taste and sedation in some individuals</li> </ul>	<ul style="list-style-type: none"> <li>– Rapidly effective (&lt; 30 mins) on nasal or ocular symptoms</li> </ul>
	Levocabastine			
Intranasal glucocorticosteroids	Beclomethasone	<ul style="list-style-type: none"> <li>– Reduce nasal hyperreactivity</li> <li>– Potently reduce nasal inflammation</li> </ul>	<ul style="list-style-type: none"> <li>– Minor local side effects</li> <li>– Wide margin for systemic side effects</li> <li>– Growth concerns raised by BDP in young children</li> <li>– In young children, consider the combination of intranasal and inhaled medications</li> </ul>	<ul style="list-style-type: none"> <li>– The most effective pharmacological treatment of allergic rhinitis</li> <li>– Effective on nasal congestion</li> <li>– Effect on smell</li> <li>– Effect observed after 7-8 hrs but maximal effect up to 2 weeks</li> </ul>
	Budesonide			
	Ciclesonide			
	Fluticasone			
	Flunisolide			
	Mometasone			
Triamcinolone				
Local chromones (intranasal, ocular)	Sodium cromoglycate	<ul style="list-style-type: none"> <li>– Poorly known</li> </ul>	<ul style="list-style-type: none"> <li>– Minor local side effects</li> </ul>	<ul style="list-style-type: none"> <li>– Intraocular chromones are effective</li> <li>– Intranasal chromones less effective than other therapies; their effect is short-lasting</li> <li>– Overall excellent safety</li> </ul>
	Nedocromil			
Oral decongestants	Ephedrine	<ul style="list-style-type: none"> <li>– Sympathomimetic medications</li> <li>– Relieve symptoms of nasal congestion</li> </ul>	<ul style="list-style-type: none"> <li>– Hypertension</li> <li>– Palpitations</li> <li>– Restlessness</li> <li>– Agitation</li> <li>– Tremor</li> <li>– Insomnia</li> <li>– Headache</li> <li>– Dry mucous membranes</li> <li>– Urinary retention</li> <li>– Exacerbation of glaucoma or thyrotoxicosis</li> </ul>	<ul style="list-style-type: none"> <li>– Use oral decongestants with caution in patients with other diseases</li> <li>– Oral H<sub>1</sub>-antihistamine/decongestant combination products may be more effective than either product alone but side effects are combined</li> </ul>
	Phenylephrine			
	Phenylpropanolamine			
	Pseudo-ephedrine			
	Others			
Intranasal decongestants	Epinephrine	<ul style="list-style-type: none"> <li>– Sympathomimetic medication</li> <li>– Relieve symptoms of nasal congestion</li> </ul>	<ul style="list-style-type: none"> <li>– Same side effects as oral decongestants but less intense</li> <li>– Rhinitis medicamentosa (a rebound phenomena occurring with prolonged use &gt; 10 days)</li> </ul>	<ul style="list-style-type: none"> <li>– Act more rapidly and more effectively than oral decongestants</li> <li>– Limit duration of treatment to &lt; 10 days to avoid rhinitis medicamentosa</li> </ul>
	Naphazoline			
	Oxymethazoline			
	Phenylephrine			
	Tetrahydrozoline			
	Xylomethazoline			
Others				
Intranasal anticholinergics	Ipratropium	<ul style="list-style-type: none"> <li>– Anticholinergics block almost exclusively anterior watery rhinorrhea</li> </ul>	<ul style="list-style-type: none"> <li>– Minor local side effects</li> <li>– Almost no systemic anticholinergic activity</li> </ul>	<ul style="list-style-type: none"> <li>– Effective in allergic and non-allergic patients with rhinorrhea</li> </ul>
Antileukotrienes	Montelukast	<ul style="list-style-type: none"> <li>– Block CystLT receptor</li> </ul>	<ul style="list-style-type: none"> <li>– Well tolerated</li> </ul>	<ul style="list-style-type: none"> <li>– More data needed to position these medications</li> </ul>
	Pranlukast			
	Zafirlukast			

Table 5. Continued

Classification	Generic names	Mechanism of action	Side effects	Comments
Oral/IM glucocorticosteroids	Betamethasone Deflazacort Dexamethasone Hydrocortisone Methylprednisolone Prednisolone Prednisone Triamcinolone	– Potentially reduce nasal inflammation – Reduce nasal hyperreactivity	– Systemic side effects common, in particular with IM medications – Depot injections may cause local tissue atrophy	– When possible, intranasal glucocorticosteroids should replace oral or IM medications – However, a short course of oral glucocorticosteroids may be needed with severe symptoms

Treat in a stepwise approach  
(adolescents and adults)  
Diagnosis of allergic rhinitis  
(history ± skin prick tests or serum specific IgE)

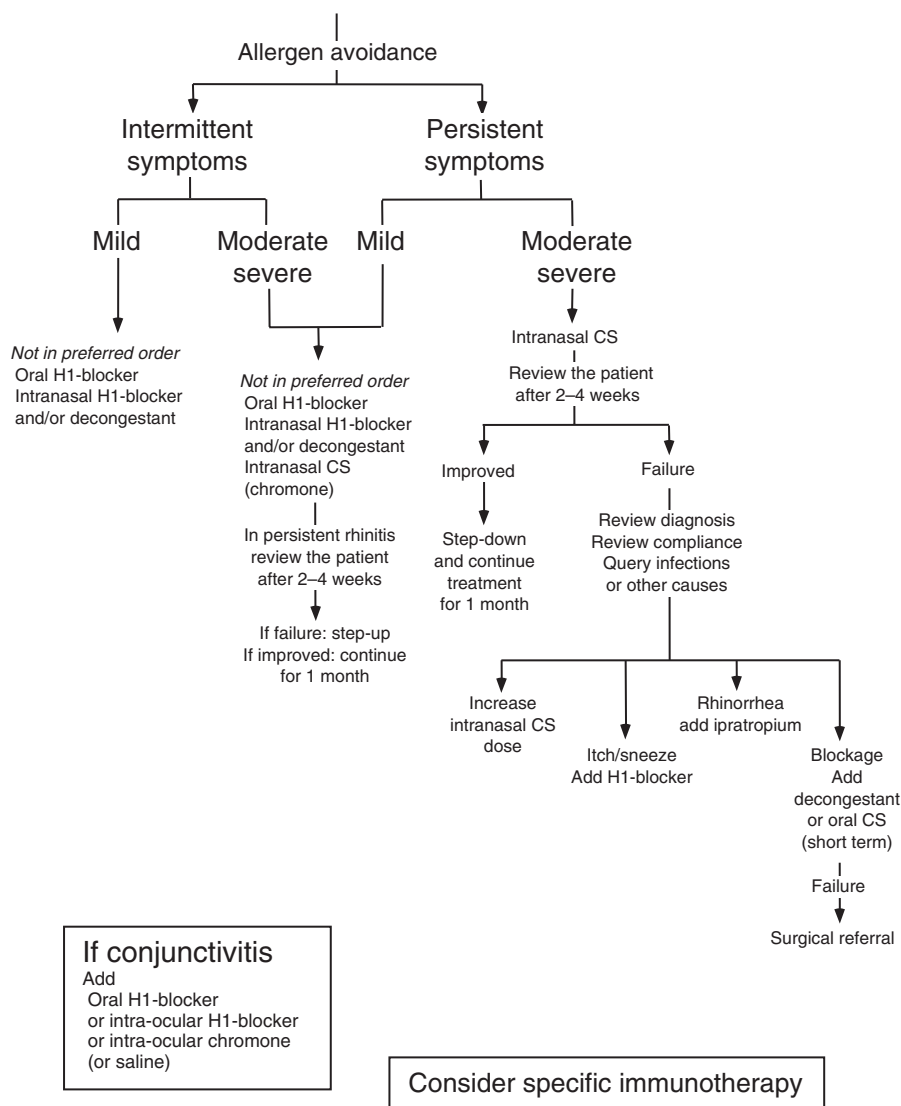


Figure 4. Stepwise approach for the treatment of allergic rhinitis according to ARIA (10).

H<sub>1</sub>-antihistamines given topically (intranasally or ocularly) are as effective as oral antihistamines at the site of their administration in reducing itching, sneezing, runny nose and eye symptoms (1, 26, 27, 32). They can be effective within 20 minutes of administration (33). Topical H<sub>1</sub>-antihistamines require twice-a-day dosing. In general, topical antihistamines are well tolerated. However, intranasal glucocorticosteroids are significantly more effective than oral or topical antihistamines for the treatment of allergic rhinitis (34) and nasal congestion.

*Intranasal glucocorticosteroids.* Intranasal glucocorticosteroids are currently the most effective class of medications available for the treatment of allergic and non-allergic rhinitis (35). Intranasal glucocorticosteroids are available without medical prescription in some countries. The effectiveness of intranasal glucocorticosteroids is based on their local activity; the administration of an equivalent amount of medication orally produces no benefit. The rationale for using intranasal glucocorticosteroids in the treatment of allergic rhinitis is that high medication concentrations can be achieved at receptor sites in the nasal mucosa, with minimal risk of systemic adverse effects (1).

Glucocorticosteroids can suppress many stages of the allergic inflammatory process (36) by interacting with transcription factors (37). Due to their mechanism of action, efficacy appears after 7–8 hours of dosing, but maximum efficacy may require up to 2 weeks. These medications are effective at improving all symptoms of allergic rhinitis.

Intranasal glucocorticosteroids have also been shown to improve quality of life, increase a users' sense of well being, improve performance at work and school and reduce sleep problems associated with nasal congestion (38, 39). They may also have a prophylactic effect when administered before the onset of the pollen season (40).

Intranasal glucocorticosteroids are the most appropriate first-line treatment for allergic rhinitis if there is nasal congestion and if symptoms occur frequently or are persistent (41). Intranasal glucocorticosteroids have been shown to be more effective against nasal symptoms than oral or topical antihistamines (35) or topical sodium cromoglycate (42).

In past studies, regular treatment with glucocorticosteroids was found to be more effective than as-needed treatment (43), and regular treatment was thought to be necessary. However, recent studies show that glucocorticosteroids administered as needed (*prn*) have a similar or better efficacy than oral H<sub>1</sub>-antihistamines on nasal symptoms (44), but "as needed" (*prn*) use is less effective than continuous treatment.

In clinical studies, intranasal glucocorticosteroids are well tolerated, and adverse effects are few in number, mild in severity and have the same incidence as placebo (45).

The current intranasal preparations are well tolerated. Crusting, dryness and minor epistaxis may occur in about 5% of patients which are occasionally persistent and may be a reason for stopping treatment. The occurrence of epistaxis under treatment needs physician evaluation. Evidence shows that long-term use of intranasal glucocorticosteroids is free of the concerns associated with long-term use of oral glucocorticosteroids. Even with long-term use, modern formulations of intranasal glucocorticosteroids have no effect on the hypothalamic-pituitary-adrenal axis and do not induce nasal mucosal atrophy (46–48). In children, the rate of growth was slightly reduced in those regularly treated with beclomethasone over one year by intranasal route (49). The clinical significance of this reduced rate of growth is unknown. This effect does not appear to be a class effect since recent studies have shown normal growth rates in children treated with newer intranasal glucocorticosteroids (50). However, it is reasonable to monitor the growth of children receiving long-term treatments with intranasal glucocorticosteroids.

The pharmacist should advise patients on the proper method to administer intranasal glucocorticosteroids; including the importance of directing the spray laterally and not medially (towards the nasal septum).

*Systemic glucocorticosteroids.* Oral glucocorticosteroids are rarely needed to control severe symptoms of allergic rhinitis. Although these medications are effective, they cause unacceptable systemic side effects if used for a prolonged period of time.

The intramuscular injection of glucocorticosteroids is not usually recommended due to the possible occurrence of systemic side effects.

The intranasal injection of glucocorticosteroids is not usually recommended due to the possible occurrence of blindness.

*Chromones.* Intranasal and ocular formulations of chromones, such as sodium cromoglycate, are available without medical prescription in many countries.

Sodium cromoglycate or nedocromil have an excellent safety profile. They reduce the symptoms of allergic rhinitis, but limited efficacy and the need for frequent dosing (as frequent as 4 times daily) are disadvantages. Chromones are generally less effective than other medications used for the treatment of allergic rhinitis (1).

Ocular sodium cromoglycate or nedocromil are effective and have a place in the treatment of allergic conjunctivitis (32). Single-dose formulations without preservatives are often better tolerated by the patients.

N-acetyl-aspartyl glutamic acid (NAAGA), a C3 convertase inhibitor, is used topically as an intranasal or ocular formulation (51). In rhinitis, it was found to have a slightly greater efficacy than cromoglycate, but it was less well tolerated.



*Decongestants.* Oral, intranasal and ocular decongestants are often available without prescription.

Both oral and intranasal decongestants may be used in the treatment of nasal congestion associated with allergic rhinitis. Nasal decongestant sprays have a greater effect on nasal obstruction than oral decongestants (1). However, the use of nasal decongestant sprays is limited by rebound congestion, the potential for irreversible tissue hypertrophy (52) and a decreasing duration of effect after 10 days of use (53). Rhinitis medicamentosa is a condition of nasal hyperreactivity, mucosal swelling and tolerance that is induced or aggravated by the overuse of topical decongestants with or without a preservative. Package inserts for these medications therefore place strict limits on their recommended duration of use. Ocular decongestants can be used in the treatment of conjunctivitis, but they are also capable of causing rebound eye congestion.

Attention should be paid to a range of possible contraindications and warnings associated with oral decongestants, including those regarding use in the elderly, in patients suffering from hypertension, hyperthyroidism, prostate hypertrophy, glaucoma and psychiatric disorders, as well as in patients taking beta-blockers and monoamine oxidase inhibitors (1). Due to its side effects, phenylpropanolamine has been withdrawn in the US and some other countries.

Short courses (less than 10 days) of topical decongestants may be useful in reducing severe nasal blockage when starting the administration of other medications (1).

Oral or ocular combination products containing antihistamines and decongestants are available and are effective for symptomatic relief of nasal and ocular symptoms.

*Anticholinergics.* Anticholinergic agents can help reduce anterior watery rhinorrhea, but they have no effect on nasal blockage or on other symptoms of allergic rhinitis.

*Antileukotrienes.* Antileukotrienes are a new class of medication for the treatment of allergic rhinitis. They modulate inflammation. They have an efficacy comparable to that of oral antihistamines (54).

#### Allergen-specific immunotherapy (vaccination)

Allergen specific vaccination is the practice of administering gradually increasing quantities of an allergen extract to an allergic subject to ameliorate the symptoms associated with the subsequent exposure to the causative allergen. The efficacy of immunotherapy using inhalant allergens to treat allergic rhinitis and asthma is evidence-based when optimally administered (1, 17, 55). Standardised therapeutic vaccines which are available for the most common allergens are favoured.

In some countries, immunotherapy is dispensed by pharmacists, but it is not recommended to be administered by pharmacists.

Subcutaneous immunotherapy raises contrasting efficacy and safety issues. Thus, the use of optimal doses of vaccines labelled either in biological units or in mass of major allergens has been proposed. Maintenance doses of 5–20 µg of the major allergen are optimal doses for most allergen vaccines.

Subcutaneous immunotherapy should be performed by trained personnel supervised by a physician, and patients should be monitored for 30 minutes after injection. Medications and equipment for treatment of rare but potentially life-threatening acute allergic reactions triggered by subcutaneous immunotherapy should be available.

Subcutaneous specific immunotherapy (not available in all countries) is indicated in patients:

- with moderate-severe or persistent allergic rhinitis who are inadequately controlled by conventional pharmacotherapy,
- who do not wish to be on pharmacotherapy,
- in whom pharmacotherapy produces undesirable side effects,
- who do not want to receive long-term pharmacological treatment.

High dose nasal and sublingual-swallow specific immunotherapy may be used:

- with doses at least 20 to 100 times greater than those used for subcutaneous immunotherapy,
- in patients who had side effects or refused subcutaneous immunotherapy,
- the indications follow those of subcutaneous injections.

Allergen specific immunotherapy interferes with the basic mechanisms of the allergy and alters the natural course of allergic diseases, resulting in symptomatic relief and offering the patient a long-lasting and preventive effect. These are observed using both subcutaneous (56) and sublingual routes (57). Subcutaneous immunotherapy was shown to reduce the onset of new sensitisations (58) as well as the development of asthma in patients with allergic rhinitis (59).

Immunotherapy is now recognised as complementary to the pharmacological treatment for respiratory allergy. It is suggested that immunotherapy should be initiated early in the course of the disease, when irreversible damages are not yet established and when it is still possible to modify the progression of the disease. However, it is usual to start this treatment after the age of 5.

#### Alternative therapies

The use of complementary and alternative therapies (e.g., homeopathy, herbal medicines, acupuncture) for the treatment of rhinitis is increasing. In the ARIA document (1), a review of the literature found that there was insufficient evidence to support the efficacy of alternative therapy. Since then, there have been a few further

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publications, but the design of the trials or their outcome measures did not make it possible to reach a definitive conclusion and recommend their use in the management of allergic rhinitis (60–65). A recent Cochrane Collaboration study has been carried out in asthma and concluded that there is not enough evidence to reliably assess the possible role of homeopathy in asthma (66). There is an urgent need for well-designed, large, randomised, controlled and properly powered clinical trials to evaluate the efficacy and safety of alternative therapies in the management of allergic diseases.

Herbal medicine can induce pharmacological interactions with medications used in the treatment of allergic rhinitis or other illnesses (67). Health care professionals should ask their patients about the use of herbal products and consider the possibility of herb-drug interactions (67).

A pharmacy protocol for treating allergic rhinitis

With recent changes in the regulatory status of some medications for allergic rhinitis symptoms, pharmacists may recommend more therapies which are available without prescription. The use of these medications is likely to result in cost savings for both patient and health care professional (68). The involvement of the pharmacist in the overall management of the patient is also likely to reduce risks of overdosing and drug interactions (69, 70).

Based on the above considerations, a recommended pharmacy protocol for managing allergic rhinitis is shown in Figure 5.

Allergic rhinitis, like other chronic diseases, requires monitoring for:

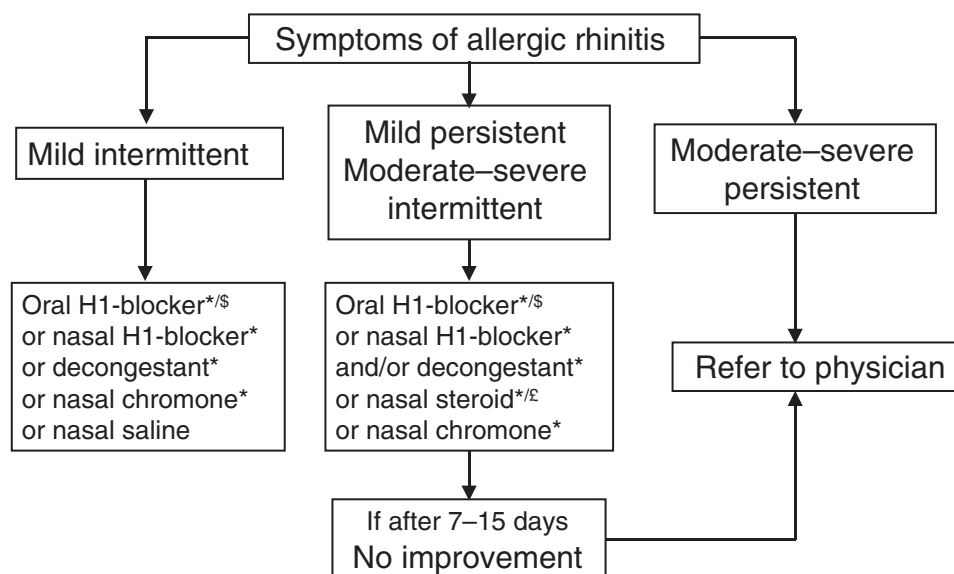
- improvement of symptoms and quality-of-life,
- assessment of safety of OTC and prescribed medications,
- need for referral to a physician,
- need to discontinue or reinstate medications.

### Management of ocular symptoms

With the exception of nasal decongestants and anticholinergics, all the major treatments discussed above are effective against the ocular symptoms of allergic rhinitis (Figure 3). Sodium cromoglycate, nedocromil sodium, NAAGA and H<sub>1</sub>-antihistamines (azelastine, levocabastine, ketotifen, olopatadine) are also available as eye drops. Intranasal glucocorticosteroids have shown some effect in eye symptoms associated with allergic rhinitis (35). Intraocular glucocorticosteroids are effective but, because of known side effects, should only be prescribed and monitored by eye care professionals. The use of antihistamine or chromone eye drops is justified if ocular symptoms are the predominant and/or persistent feature of the patient's allergic rhinitis, persisting despite use of oral H<sub>1</sub>-antihistamines and/or intranasal glucocorticosteroids.

### The management of allergic rhinitis and asthma

Asthma may be severe and even life threatening. When pharmacists identify patients with undiagnosed or untreated asthma, or asthma which is not optimally

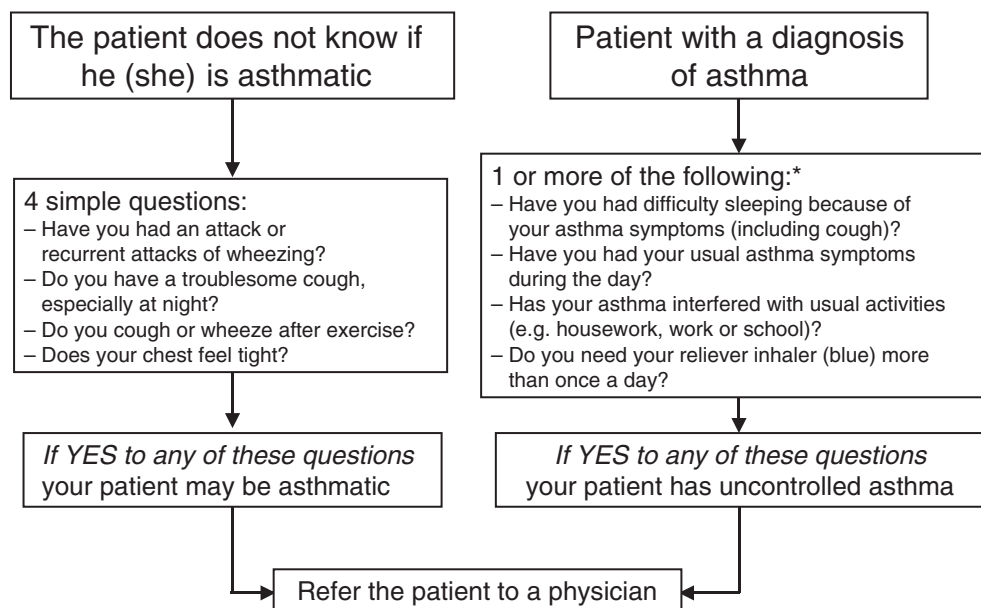


\* depending on drug availability and not in preferred order

\$ non-sedating H1-blockers should be preferred

£ if nasal obstruction predominates, intranasal steroids are the first-line treatment

Figure 5. Selection of allergic rhinitis treatment by pharmacists.



From the National Asthma Campaign, «conquering asthma»

Figure 6. Assessing asthma in a patient with persistent allergic rhinitis. \*From the National Asthma Campaign, “conquering asthma”.

controlled, they should encourage these individuals to obtain appropriate medical care.

There are many similarities between the nasal and bronchial mucosa, the major difference being the rich vascular supply to the nose that accounts for nasal obstruction being a symptom of allergic rhinitis. In the bronchi, smooth muscle accounts for the bronchospasm seen in asthma. The upper and lower airways may well be affected by a common inflammatory process (71) with interconnected mechanisms, suggesting the concept of “one airway, one disease” (72).

Epidemiological studies consistently show that allergic rhinitis and asthma often co-exist: at least 75% of patients with asthma complain from rhinitis symptoms, and 20–30% of those with allergic rhinitis also have asthma (73). Allergic rhinitis is also a risk factor for asthma (74). Therefore, patients with persistent symptoms of allergic rhinitis should be referred to their physician to be evaluated for asthma. In the ARIA document (1), it is recommended that evaluation should include a medical history, chest examination and assessment of airflow obstruction before and after taking a bronchodilator. The diagnosis of asthma should follow the guidance in the recent update of the GINA guidelines (75).

If a patient has persistent allergic rhinitis, the patient should be questioned about his or her symptoms of asthma (Figure 6 and Table 6). If there is any suspicion of undiagnosed asthma, the patient should be referred to a physician.

Table 6. Questions that should be asked if a patient is suspected of having asthma (76)

- Do you find yourself short of breath?
- Do you make whistling noises (wheeze) when you breathe?
- Does your chest feel tight?
- Do you have a cough regularly?
- Are these symptoms particularly noticeable first thing in the morning, during the night or with exercise?

Table 7. Questions to ask patients diagnosed with asthma to reveal the level of asthma control (77)

In the last month:

- Have you had difficulty sleeping because of your asthma symptoms (including cough)?
- Have you had your usual asthma symptoms during the day (cough, wheeze, chest tightness or breathlessness)?
- Has your asthma interfered with your usual activities (e.g. housework, work, school)?
- Have you used your  $\beta_2$ -agonist more than once a day in the past week?

If a patient has a diagnosis of asthma, he/she should be questioned to assess the level of asthma control (Table 7).

If there is poor control (any positive answer to the Table 7 questions), the patient should be advised to consult a physician.

The treatment of asthma should follow the recently published guidelines (75, 76).

It is important to manage co-morbidity of allergic rhinitis and asthma. Treatment of allergic rhinitis has been associated with improved outcomes from asthma (78).

**Conclusion**

Allergic rhinitis is an increasing global health problem. The ARIA classification distinguishes between intermittent and persistent allergic rhinitis. Allergic rhinitis that is intermittent or mild may be appropriate for management by the pharmacist. Referral to a physician should be considered in cases of symptoms that are moderate to severe-persistent, suggestive of undiagnosed or uncon-

trolled asthma, suggestive of infection or non-allergic rhinitis, and for symptoms poorly responsive to treatment after 2 to 4 weeks.

The management of allergic rhinitis represents a collaboration between pharmacists, physicians, other health care professionals and patients. The cost-effectiveness of these approaches should be tested in allergic rhinitis as it has been for asthma (79), reactive airway diseases (80, 81) and other chronic diseases (68).

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## Appendix

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Endorsing organisations

APhA: American Pharmacists Association

ARIA: Allergic Rhinitis and its Impact on Asthma

CESPHARM

EAACI: European Academy of Allergology and Clinical Immunology

EFA: European Federation of Allergy and Airways Diseases Patients' Associations

IPCRG: International Primary Care Respiratory Group