RHINITIS

CHI Formulary Indication Review

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Council of Health Insurance

INDICATION UPDATE

ADDENDUM- January 2024

To the CHI Original Rhinitis Clinical Guidance- Issued January 2020

Contents

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Abbreviations

AIT	Allergen-Specific Immunotherapy
AR	Allergic Rhinitis
CADTH	Canadian Agency for Drugs and Technologies in Health
CBS	Consensus Based Statement
CHI	Council of Health Insurance
DSCG	Disodium Cromoglycate
FeNO	Fractional exhaled Nitric Oxide
HAS	Haute Autorite de Sante
HDM	House Dust Mite
HTA	Health Technology Assessment
ILIT	Intralymphatic Immunotherapy
INAH	Intranasal Antihistamines
INCS	Intranasal Corticosteroid
JTFPP	Joint Task Force on Practice Parameters
LTRA	Leukotriene Receptor Antagonist
NAR	Non-Allergic Rhinitis
NARES	Non-Allergic Rhinitis with Eosinophilia Syndrome
nNO	Nasal Nitric Oxide
PROM	Patient Reported Outcome Measure
SCIT	Subcutaneous Immunotherapy
SFDA	Saudi Food and Drug Authority
SLIT	Sublingual Immunotherapy
SPT	Skin Prick Test

Executive Summary

Rhinitis, which occurs most commonly as allergic rhinitis, is an inflammation of the nasal membranes that is characterized by sneezing, nasal congestion, nasal itching, and rhinorrhea, in any combination. Although allergic rhinitis itself is not life-threatening (unless accompanied by severe asthma or anaphylaxis), morbidity from the condition can be significant[1].

Signs and symptoms of allergic rhinitis include sneezing, itchy nose, eyes, ears, palate, rhinorrhea, postnasal drip, congestion, anosmia, headache, earache, tearing, eyes redness or swelling, fatigue, drowsiness, and malaise[1].

Complications include acute or chronic sinusitis, otitis media, sleep disturbance or apnea, dental problems (such as overbite caused by excessive mouth breathing), palatal abnormalities, and eustachian tube dysfunction[1].

Rhinitis may be associated with many etiologic triggers such as infections, immediate-type allergic responses, inhaled irritants, medications, hormonal disturbances, and neural system dysfunction[2].

Rhinitis is basically classified into three major clinical phenotypes: allergic rhinitis (AR), infectious rhinitis, and non-allergic, non-infectious rhinitis (NAR). However, this subdivision may be considered as an oversimplification because a combined (mixed) phenotype exists in many individuals and different endotypes of rhinitis subgroups overlapping. Due to the variety of pathophysiologic mechanisms (endotypes) and clinical symptoms (phenotypes), it is difficult to develop clear guidelines for diagnosis and treatment[2].

Laboratory tests used in the diagnosis of allergic rhinitis include the following: Allergy skin tests (immediate hypersensitivity testing): An in vivo method of determining immediate (IgE-mediated) hypersensitivity to specific allergens, Fluorescence enzyme immunoassay (FEIA): Indirectly measures the quantity of immunoglobulin E (IgE) serving as an antibody to a particular antigen, Total serum IgE: Neither sensitive nor specific for allergic rhinitis, but the results can be helpful in some cases when combined with other factors, Total blood eosinophil count: Neither sensitive nor specific for the diagnosis, but, as with total serum IgE, can sometimes be helpful when combined with other factors[1].

Imaging studies used in the diagnosis and evaluation of allergic rhinitis include radiography which can be helpful for evaluating possible structural abnormalities or to help detect complications or comorbid conditions (such as rhinitis or adenoid hypertrophy), computed tomography (CT) scanning, which may be used to evaluate for acute or chronic sinusitis, and magnetic resonance imaging (MRI)[1].

The management of allergic rhinitis consists of the following 3 major treatment strategies:

1. Environmental control measures and allergen avoidance: these include keeping exposure to allergens such as pollen, dust mites, and mold to a minimum.
2. Pharmacologic management: Patients are often successfully treated with:
    a. Oral antihistamines, decongestants, or both
    b. Regular use of an intranasal steroid spray may be more appropriate for patients with chronic symptoms.
3. Immunotherapy: This treatment may be considered more strongly with severe disease, poor response to other management options, and the presence of comorbid conditions or complications; immunotherapy is often combined with pharmacotherapy and environmental control[1].

Allergic rhinitis prevalence has increased significantly since the 1990s. It is reported to affect approximately 25 and 40% of children and adults globally, respectively. Approximately 80% of AR symptoms develop before the age of 20 years and peak at age 20–40 years before gradually declining. The incidence rate of AR in children over the first 5 years of life was reported to be 17.2%, with a peak age at diagnosis between 24 and 29 months (2.5%). Meta-analysis studies have shown the sex-specific differences in the prevalence of AR with male predominance in childhood and a female predominance in adolescents[3].

The overall prevalence of AR in Saudi Arabia is 21.2% and was comparable in both males and females. However, it was higher in adults than in children and adolescents, and in urban areas than rural areas. Asthma, atopic dermatitis, and eczema co-occurrence with AR are common. AR has a negative impact on the quality of life of the patients in the form of interference with daily activities, sleep problems, difficulty of breath, and school absenteeism[4].

The prevalence of allergic rhinitis in the Kingdom of Saudi Arabia (KSA) has been assessed in a few studies. In a study conducted in Madinah among 6–9 years old children, 24.2% reported ever experiencing rhinitis, and 18.2% reported having current rhinitis symptoms. Among adolescents aged 16 to 18, a remarkably high prevalence of allergic rhinitis was found in Riyadh, reaching 43.8% for participants who said they had experienced rhinitis symptoms and 38.6% for participants who reported current symptoms. In Najran, the overall lifetime prevalence of rhinitis, rhinoconjunctivitis, and physician-diagnosed rhinitis was 34.6%, 14.8%, and 6.3%, respectively, among schoolchildren aged 7–19 years[4].

CHI issued Rhinitis guidelines in January 2020. Updating clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations. Below is a description of sections that need updates.

This report functions as an addendum to the prior CHI Rhinitis clinical guidance and seeks to offer guidance for the effective management of Rhinitis. It provides an **update on the Rhinitis Guidelines** for CHI Formulary with the ultimate objective of updating the IDF (CHI Drug Formulary) while addressing **the most updated best available clinical and economic evidence related to drug therapies.**

Main triggers for the update are summarized, being **the updated guidelines added to the report such as** International consensus statement on allergy and rhinology: Allergic rhinitis **[2023]**, and **the new guidelines added to the report** such as Japanese guidelines for allergic rhinitis **[2020]**, Saudi guidelines on Allergic Rhinitis in Asthma **[2014]**, Ashford and St. Peter's Hospitals NHS Foundation Trust Pediatric Allergic Rhinitis guidelines **[2023]**, Rhinitis 2020: A practice parameter update, ASCIA: Australasian Society of Clinical Immunology and Allergy, Allergic Rhinitis Clinical Update **[2022],** Allergic rhinitis – effective treatment according to the latest recommendations review article **[2022].**

After carefully examining clinical guidelines and reviewing the SFDA drug list, there are NO new SFDA registered drugs to include in the CHI formulary while removing Ebastine and Cetirizine HCL/Pseudoephedrine as they are no longer registered on the SFDA Drug List of November 2023. There have been changes and updates made to the previously listed drugs in terms of drug information and prescribing edits since January 2020.

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) in all tables reflecting specific drug classes' role in the Rhinitis therapeutic management.

Below is a table summarizing the major changes based on the different Rhinitis guidelines used to issue this report:

Table 1. General Recommendations for the Management of Rhinitis

Management of Rhinitis		
General Recommendations	**Level of Evidence/Grade of Recommendation**	**Reference**
<u>Diagnosis</u> • Despite low level evidence specifically addressing this area, history is essential in the diagnosis of AR. • When possible, physical examination should be performed with appropriate personal protective equipment to aid in the diagnosis of AR and exclusion of other conditions. When combined with patient history, it increases diagnostic accuracy and may exclude alternative causes of symptoms. • Skin testing: Regular use of the same SPT device type will allow clinicians to familiarize themselves with it and interpretation of results may therefore be more consistent. The use of standardized allergen extracts can further improve consistency of interpretation.	*Policy level:* Recommendation	International consensus statement on allergy and rhinology: Allergic rhinitis **[2023]**
Oral H1 antihistamines: Newer-generation oral antihistamines can be considered in the treatment of AR.	*Policy level:* Strong recommendation for the use of newer-generation oral antihistamines for AR	International consensus statement on allergy and rhinology: Allergic rhinitis **[2023]**
Intranasal antihistamines: Intranasal antihistamines may be used as first- or second-line therapy in the treatment of AR.	*Policy level*: Strong recommendation	International consensus statement on allergy and rhinology:

		Allergic rhinitis **[2023]**
Intranasal saline: Nasal saline is strongly recommended as part of the treatment strategy for AR.	*Policy level:* Strong recommendation	International consensus statement on allergy and rhinology: Allergic rhinitis **[2023]**
Oral corticosteroids: Although not recommended for routine use in AR, certain clinical scenarios may warrant the use of short courses of systemic corticosteroids, following a discussion of the risks and benefits with the patient. For example, oral steroids could be considered in select patients with significant nasal obstruction that precludes adequate penetration of intranasal agents (corticosteroids or antihistamines). In these cases, a short course of systemic corticosteroids may improve congestion and facilitate access of topical medications. No evidence supports this suggestion, and thus careful clinical judgment and risk discussion are advocated.	*Policy level:* Strong recommendation against routine use	International consensus statement on allergy and rhinology: Allergic rhinitis **[2023]**
Intranasal cromolyn: DSCG (Disodium cromoglycate) may be used as a second-line treatment for AR in patients who fail INCS or intranasal antihistamines, or for short-term preventative benefit prior to allergen exposures.	*Policy level:* Recommendation as a second-line treatment in AR.	International consensus statement on allergy and rhinology: Allergic rhinitis **[2023]**
Combination oral antihistamine and leukotriene receptor antagonist (LTRA): Combination LTRA and oral antihistamines should not be used as first line therapy for AR but can be considered in patients with	*Policy level*: Recommendation against as first line therapy.	International consensus statement on allergy and rhinology: Allergic rhinitis **[2023]**

contraindications to other alternatives. This combination should be used judiciously after carefully weighing potential risks and benefits.		
Allergen immunotherapy for the treatment of allergic rhinitis: **1. Sublingual immunotherapy (SLIT):** General considerations: Recommend tablet or aqueous SLIT in patients (adults and children) with seasonal and/or perennial AR who wish to reduce their symptoms and medication use, as well as possibly reduce the propensity to develop asthma or new allergen sensitizations.	*Policy level:* Strong recommendation for the use of SLIT grass pollen tablet, ragweed tablet, HDM (House Dust Mite) tablet, and tree pollen aqueous solution. Recommendation for SLIT for Alternaria allergy. Option for SLIT for animal allergy. Recommendation for dual-therapy SLIT in bi-allergic patients.	International consensus statement on allergy and rhinology: Allergic rhinitis **[2023]**
2. Conventional subcutaneous immunotherapy (SCIT): SCIT is an appropriate treatment consideration for patients who have not obtained adequate relief with symptomatic therapy or who prefer this therapy as a primary management option, require prolonged weeks of treatment during the year, and/or wish to start treatment for the benefit of the potential secondary disease-modifying effects of SCIT.	Policy level: Strong recommendation for SCIT as a patient preference-sensitive option for the treatment of AR. Strong recommendation for SCIT over no therapy for the treatment of AR. Option for SCIT over sublingual immunotherapy (SLIT) for the treatment of AR	International consensus statement on allergy and rhinology: Allergic rhinitis **[2023]**
Pediatric Allergic Rhinitis:	Not graded	Paediatric Department NHS Ashford and St.

Step up and down to achieve symptom control. Allow 8-12 weeks at each step: Step 1, Allergen Avoidance: Nasal rinsing - with saline solution Step 2, Regular long-acting non-sedating antihistamine: Cetirizine or Loratadine OR Regular nasal corticosteroid spray: Avamys or Mometasone Furoate or Flixonase		Peter's Hospitals - Paediatric Allergic Rhinitis **[2023]**
Pediatric Allergic Rhinitis ***Start with antihistamine if pruritus dominant or nasal corticosteroid if congestion dominant:*** Step 3, Regular oral antihistamine, and nasal corticosteroid Step 4, Switch to 2nd line oral antihistamine: Fexofenadine (from 6yrs) Step 5, Regular nasal antihistamine + corticosteroid spray and oral antihistamine: Dymista nasal spray (from 12yrs) + Fexofenadine Step 6, Add in Leukotriene receptor antagonist: Montelukast. Step 7, Allergen specific immunotherapy	Not graded	Paediatric Department NHS Ashford and St. Peter's Hospitals - Paediatric Allergic Rhinitis **[2023]**
CBS: We suggest that the clinician not select the oral LTRA montelukast for the initial treatment of AR due to reduced efficacy when compared with that of other agents. Furthermore, serious neuropsychiatric events that may include suicidal thoughts or actions have been reported in some patients taking montelukast. As advised by the FDA, montelukast should be used to treat AR only in patients who are	Conditional, very low	A practice parameter update, **[2020]**

not treated effectively with or cannot tolerate other alternative therapies.		
CBS: We recommend that the clinician offer INAH as an initial treatment option for patients with SAR.	Strong, High	A practice parameter update, **[2020]**
CBS: We recommend that when choosing monotherapy for persistent AR, INCS be the preferred medication.	Strong, High	A practice parameter update, **[2020]**
CBS: We suggest that the use of intranasal decongestants to be short term and used for intermittent or episodic therapy of nasal congestion.	Conditional, Low	A practice parameter update, **[2020]**
CBS: We recommend that oral decongestants to be avoided during the first trimester of pregnancy.	Strong, Low	A practice parameter update, **[2020]**
CBS: We suggest that intranasal cromolyn to be offered as an option to be taken just prior to allergen exposure to reduce symptoms of AR from episodic allergen exposures.	Conditional, Very low	A practice parameter update, **[2020]**
GRADE: We suggest that the clinician consider the combination of an INCS and an INAH for the initial treatment of moderate/severe nasal symptoms of SAR in patients ≥12 y old.	Conditional, High	A practice parameter update, **[2020]**
CBS: We suggest that for patients taking an INCS who have persistent rhinorrhea, the clinician may consider the addition of intranasal ipratropium.	Conditional, Moderate	A practice parameter update, **[2020]**
CBS: We suggest that for patients with AR and nasal congestion uncontrolled with an oral antihistamine, the clinician consider the addition of pseudoephedrine, when tolerated.	Conditional, Moderate	A practice parameter update, **[2020]**

CBS: We suggest that AIT (subcutaneous or sublingual tablets) to be considered for patients with controlled mild/moderate asthma with coexisting AR.	Conditional, Moderate	A practice parameter update, **[2020]**
Acupuncture. CBS: We cannot make a recommendation for or against the use of acupuncture for the treatment of AR.	N/A, Very low	A practice parameter update, **[2020]**

At the end of the report, a **key recommendation synthesis section** is added highlighting the latest updates in **the clinical and therapeutic management of rhinitis.**

Section 1.0 Summary of Reviewed Clinical Guidelines & Evidence

This section is divided into two parts: the first includes recommendations from **updated versions of guidelines** mentioned in the previous CHI Rhinitis report, and the second includes **newly added guidelines** that have helped generate this report.

1.1 Revised Guidelines

This section contains the **updated versions** of the guidelines mentioned in the January 2020 CHI Rhinitis Report and the corresponding recommendations:

Table 2. Guidelines Requiring Revision

Guidelines Requiring Revision	
Old Versions	**Updated versions**
Section 1.1 **American Academy of Otolaryngology—Head and Neck Surgery** Clinical Practice Guideline: Allergic Rhinitis [**2015**}	N/A*
Section 1.2 **International Consensus** Statement on Allergy and Rhinology: Allergic Rhinitis [**2018**]	Section 1.1.1. **International Consensus** Statement on Allergy and Rhinology: Allergic Rhinitis [**2023**][5]
Section 1.3 British Society of Allergy and Clinical Immunology (**BSACI**) Guideline	N/A*

for the Diagnosis and Management of Allergic and Non-Allergic Rhinitis (Revised Edition 2017; First edition **2007**)	
Section 1.4 Pediatric Rhinitis: Position Paper of the **European Academy of Allergy and Clinical Immunology** [**2013**]	N/A*

*****: *No updated versions available*

1.1.1 International Consensus Statement on Allergy and Rhinology: Allergic Rhinitis [2023]

*Please refer to **Section 1.2** of CHI Rhinitis original clinical guidance.*

In the 5 years that have passed since the publication of the 2018 International Consensus Statement on Allergy and Rhinology: Allergic Rhinitis (ICAR-Allergic Rhinitis 2018), the literature has expanded substantially. ICAR-Allergic Rhinitis 2023 is not intended to be a clinical practice guideline, meta-analysis, or expert panel report. The ICAR authors have carefully reviewed all relevant literature and determined the strength of the available evidence. Based upon this evidence, where applicable, recommendations are made for various diagnostic and treatment options in the realm of AR[5]. ICAR-Allergic Rhinitis 2023 employed established evidence-based review with recommendation (EBRR) methodology to individually evaluate each topic, based on the work of Rudmik and Smith (table 3)[6].

Table 3. American Academy of Pediatrics (AAP) Defined Strategy for Recommendation Development

Level of Evidence	Diagnosis	Therapy/Prevention/Etiology
1	Systematic review of cross-sectional studies with consistently applied reference standard and blinding	Systematic review of randomized trials or n-of-1 trials
2	Individual cross-sectional studies with consistently applied reference standard and blinding	Randomized trial or observational study with dramatic effect
3	Cohort study or control arm of randomized trial	Non-randomized controlled cohort/follow-up study
4	Case-series or case control studies, or poor quality	Case-series, case-control studies, or historically controlled studies*

	prognostic cohort study	
5	Not applicable	Mechanism-based reasoning

*Level may be graded down on the basis of study design, inconsistency between studies, indirectness of evidence, imprecision, or because the absolute effect size is very small; level may be graded up if there is a large or very large effect size or if a significant dose-response relationship is demonstrated. **As always, a systematic review is generally better than an individual study

Aggregate grade of evidence	
Grade	**Research Quality**
A	Well-designed RCTs
B	RCTs with minor limitations Overwhelming consistent evidence from observational studies
C	Observational studies (case control and cohort design)
D	Expert opinion Case reports Reasoning from first principle

AAP (American Academy of Pediatrics) defined strategy for recommendation development			
Evidence Quality	**Preponderance of Benefit over Harm**	**Balance of Benefit and Harm**	**Preponderance of Harm over Benefit**
A. Well-designed RCT's	Strong recommendation	Option	Strong Recommendation Against
B. RCT's with minor limitations; Overwhelmingly consistent evidence from observational studies	Recommendation		Recommendation Against
C. Observational studies (case control and cohort design)			
D. Expert opinion, Case reports, Reasoning from first principles	Option	No Recommendation	Recommendation Against

Evaluation and Diagnosis

History and physical examination

- Despite low level evidence specifically addressing this area, history is essential in the diagnosis of AR. Policy level: Recommendation.
- When possible, physical examination should be performed with appropriate personal protective equipment to aid in the diagnosis of AR and exclusion of other conditions. When combined with patient history, it increases diagnostic accuracy and may exclude alternative causes of symptoms. Policy level: Recommendation.
- **Nasal endoscopy:** Nasal endoscopy may be considered as a diagnostic adjunct in the evaluation of patients with suspected AR. Policy level: Option.
- **Radiologic studies:** Routine use of imaging is not recommended for the diagnosis of AR. Policy level: Recommendation against.
- **Skin testing:** Regular use of the same SPT device type will allow clinicians to familiarize themselves with it and interpretation of results may therefore be more consistent. The use of standardized allergen extracts can further improve consistency of interpretation. Policy level: Recommendation.
- **Serum IgE:** Intervention: Assessment of tIgE may be useful to assess overall atopic status; furthermore, in selected cases it might help guide therapy (i.e., monitor efficacy of AIT). Policy level: Option
- **Nasal provocation testing:** Measurement of nasal sIgE is an option in patients with non-allergic rhinitis suspected of having LAR to support this diagnosis and guide AIT if pharmacologic therapies are inadequate. A consensus for levels of nasal sIgE indicating AR needs to be established. Policy level: Option

Diagnostic modalities for evaluation of allergic rhinitis

Use of validated survey instruments: Validated surveys may be used to screen for AR, follow treatment outcomes and as a primary outcome measure for clinical trials. Specific tests are optimized for various clinicopathological scenarios. Policy level: Recommendation.

Component resolved diagnostic testing: Component resolved diagnostic testing is an option for diagnosis of AR by specialists. Policy level: Option

Nasal provocation testing: Application of nasal provocation testing is useful in local AR and to confirm occupational rhinitis. Policy level: Option for diagnosis of AR when skin or in vitro tests are equivocal or unreliable. Recommendation for diagnosis of local AR and occupational rhinitis

Nasal cytology: Nasal cytology could help in cases of non-allergic rhinitis to suspect local AR or in cases of AR to diagnose a mixed rhinitis. It could be considered an option in cases of negative SPT and/or serum sIgE to evaluate the presence of mucosal eosinophils and consideration of local AR or type 2 inflammation. The cut-off values for determining non-allergic rhinitis with eosinophilia syndrome (NARES) are not yet clear. Policy level: Option

Nasal histology: Nasal histology may be helpful in clinical research or selected cases (e.g., evaluation of tissue eosinophils during surgery). Recommendation against routine clinical practice for AR evaluation due to invasive nature of obtaining a specimen. Policy level: Recommendation against

Rhinomanometry: Rhinomanometry is useful in distinguishing between structural and soft tissue causes of obstruction, when history and examination findings are not congruent, as well as a research tool. Better with individual nasal cavity assessment and four-phase rhinomanometry. Policy level: Option

Acoustic rhinometry: Acoustic rhinometry is most useful in research setting as opposed to as a clinical diagnostic tool. Policy level: Option.

***Peak nasal inspiratory flow*:** Use in conjunction with patient reported outcome measures to improve utility. Policy level: Option.

Fractional exhaled nitric oxide (FeNO), Nasal nitric oxide (nNO): History and physical, diagnostic skin testing, or sIgE testing should be the first-line evaluation of AR. FeNO or nasal NO testing may provide additional diagnostic information if necessary but should not be routinely employed for AR diagnosis. Policy level: FeNO: Recommend against for routine diagnosis of AR. nNO: Recommend against for routine diagnosis of AR.

Pharmacotherapy and procedural options

- *Pharmacologic treatments are frequently employed to control AR symptoms. Depending on the specific therapy and geographic region, these may be available by prescription or over the counter. The evidence for pharmacologic options for AR has been reviewed.*

Oral H1 antihistamines: Newer-generation oral antihistamines can be considered in the treatment of AR. Policy level: Strong recommendation for the use of newer-generation oral antihistamines for AR.

Intranasal antihistamines: Intranasal antihistamines may be used as first- or second-line therapy in the treatment of AR. Policy level: Strong recommendation.

Oral corticosteroids: Although not recommended for routine use in AR, certain clinical scenarios may warrant the use of short courses of systemic corticosteroids, following a discussion of the risks and benefits with the patient. For example, oral

steroids could be considered in selecting patients with significant nasal obstruction that precludes adequate penetration of intranasal agents (corticosteroids or antihistamines). In these cases, a short course of systemic corticosteroids may improve congestion and facilitate access of topical medications. No evidence supports this suggestion, and thus careful clinical judgment and risk discussion are advocated. Policy level: Strong recommendation against routine use.

Intranasal corticosteroids: non-traditional application: No evidence for non-traditional application of intranasal steroids for AR. Policy level: Recommendation against.

Intranasal saline: Nasal saline is strongly recommended as part of the treatment strategy for AR. Policy level: Strong recommendation.

Oral decongestants: Although not recommended for routine use in AR, pseudoephedrine can be effective in reducing nasal congestion in patients with AR; however, it should only be used as short-term/rescue therapy after a discussion of the risks and benefits with the patient (comorbidities) and consideration of alternative intranasal therapy options. Policy level: Strong recommendation against routine use in AR. In certain cases, combination therapy with an oral antihistamine may be beneficial to alleviate severe nasal congestion in short courses.

Intranasal cromolyn: DSCG (Disodium cromoglycate) may be used as a second-line treatment for AR in patients who fail INCS or intranasal antihistamines, or for short-term preventative benefit prior to allergen exposures. Policy level: Recommendation as a second-line treatment in AR.

Biologic therapies: Monoclonal antibody (Biologic) therapies are not currently approved for the treatment of AR. Policy level: Option based upon published evidence, although not currently approved for this indication.

Combination oral antihistamine and intranasal corticosteroid: Current evidence is mixed to support antihistamines as an additive therapy to INCS, as several randomized trials have not demonstrated a benefit over INCS alone for symptoms of AR. Policy level: Option.

Combination oral antihistamine and leukotriene receptor antagonist: Combination LTRA and oral antihistamines should not be used as first line therapy for AR but can be considered in patients with contraindications to other alternatives. This combination should be used judiciously after carefully weighing potential risks and benefits. Policy level: Recommendation against first line therapy.

Combination intranasal corticosteroid and leukotriene receptor antagonist (LTRA): Consider use in patients with AR and asthma, after weighing therapeutic benefits against risks of mental health adverse effects. Policy level: Option as combination therapy if comorbid asthma is present and mental health risks are considered. Not recommended for AR alone.

Combination intranasal corticosteroid (INCS) and intranasal decongestant: Short-term combination therapy with INCS and intranasal decongestant may be considered in patients with AR refractory to combination therapy with INCS and intranasal antihistamine prior to consideration of inferior turbinate reduction or in patients declining surgery. Policy level: Option

Combination intranasal corticosteroid and intranasal ipratropium bromide: Combining IPB with beclomethasone dipropionate can be more effective than either agent alone for the treatment of rhinorrhea in refractory AR in children and adults. Although multiple consensus guidelines have recommended, and there is evidence to support this recommendation, it is important to note that there has only been one randomized controlled trial (RCT) to study the efficacy of combined INCS and IPB therapy compared to either agent alone, and this study was performed in a combined population of patients with AR and non-allergic rhinitis. Policy level: Option.

Allergen immunotherapy for the treatment of allergic rhinitis:

Conventional subcutaneous immunotherapy (SCIT): SCIT is an appropriate treatment consideration for patients who have not obtained adequate relief with symptomatic therapy or who prefer this therapy as a primary management option, require prolonged weeks of treatment during the year, and/or wish to start treatment for the benefit of the potential secondary disease modifying effects of SCIT. Policy level: Strong recommendation for SCIT as a patient preference-sensitive option for the treatment of AR. Strong recommendation for SCIT over no therapy for the treatment of AR. Option for SCIT over sublingual immunotherapy (SLIT) for the treatment of AR.

Rush subcutaneous immunotherapy: Aeroallergen rush SCIT is an option for AR in appropriately selected patients that do not have adequate control of their symptoms with symptomatic therapies. If available at practice location, the use of depigmented-polymerized allergen extracts for rush SCIT has a better safety profile compared with standard extracts. Policy level: Option

Cluster subcutaneous immunotherapy: Cluster SCIT can be safely implemented in clinical practice and offered to those patients eligible for SCIT that may prefer this. Policy level: Option

Sublingual immunotherapy (SLIT): general considerations: Recommend tablet or aqueous SLIT in patients (adults and children) with seasonal and/or perennial AR who wish to reduce their symptoms and medication use, as well as possibly reduce the propensity to develop asthma or new allergen sensitizations. Policy level: Strong recommendation for the use of SLIT grass pollen tablet, ragweed tablet, HDM tablet, and tree pollen aqueous solution. Recommendation for SLIT for Alternaria allergy.

Option for SLIT for animal allergy. Recommendation for dual-therapy SLIT in bi-allergic patients.

Sublingual immunotherapy tablets: SLIT tablets are recommended for patients with severe or refractory AR. Epinephrine auto-injector is recommended in the FDA labeling for approved tablets due to the rare but serious risk of anaphylaxis. Tablets for selecting antigens are available in various countries. Policy level: Strong recommendation.

Aqueous sublingual immunotherapy: High-dose aqueous SLIT is recommended for those patients who wish to reduce their symptoms and rescue medication use. Policy level: Recommendation.

Epicutaneous/transcutaneous immunotherapy: While epicutaneous AIT may potentially have a future clinical application in the treatment of AR, at this juncture there are limited studies that show variable and limited effectiveness, and a significant rate of adverse reactions. Given the above and the availability of alternative treatments, epicutaneous AIT is not recommended at this time. Policy level: Recommendation against

Intralymphatic immunotherapy: More studies are essential to establish the long-term effects of ILIT. Policy level: Option

Combination subcutaneous immunotherapy and biologics: Current evidence supports that anti-IgE may be beneficial as a premedication prior to induction of cluster or rush SCIT protocols, and combination therapy may be advantageous as an option for carefully selected patients with persistent symptomatic AR following AIT. However, at the time of this writing, biologic therapies are not approved by the US FDA for AR alone. An individualized approach to patient management must be considered. Policy level: Option.

1.2 Additional Guidelines

This part includes the added guidelines to the previous CHI Rhinitis report, along with their recommendations.

Table 4. List of Additional Guidelines

Additional Guidelines
Section 1.2.1 Saudi guidelines on Allergic Rhinitis in Asthma [2014][7]
Section 1.2.2 Japanese guidelines for allergic rhinitis [2020][8]
Section 1.2.3 ASCIA: Australasian Society of Clinical Immunology and Allergy, Allergic Rhinitis Clinical Update [2022][9]

Section 1.2.4 Ashford and St. Peter's Hospitals NHS Foundation Trust Pediatric Allergic Rhinitis guidelines [2023][10]
Section 1.2.5 Current treatment options for allergic rhinitis: a review [2023][11]
Section 1.2.6 Rhinitis [2020]: A practice parameter update[12]

1.2.1 Saudi Clinical Practice Guideline on Allergic Rhinitis in Asthma [2014]

The Ministry of Health (MoH) of Saudi Arabia with the methodological support of the McMaster University working group produced clinical practice guidelines to assist health care providers in evidence-based clinical decision-making. This guideline evaluates the role of inhaled corticosteroids, inhaled antihistamines, and sublingual immunotherapy in the management of allergic rhinitis in this population[7].

The guideline working group developed and graded the recommendations and assessed the quality of the supporting evidence according to the GRADE approach. Quality of evidence (confidence in the available estimates of treatment effects) is categorized as: high, moderate, low, or very low based on consideration of risk of bias, directness, consistency, and precision of the estimates. The strength of recommendations is expressed as either strong ('guideline panel recommends…') or conditional ('guideline panel suggests…') and has explicit implications (table 5).

Table 5. Interpretation of Strong and Conditional (Weak) Recommendations

Implications	Strong recommendation	Conditional (weak) recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	The majority of individuals in this situation would want the suggested course of action, but many would not
For clinicians	Most individuals should receive intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful helping

		individuals making decisions consistent with their values and preferences
For policy makers	The recommendation can be adapted as policy in most situations	Policy making will require substantial debate and involvement of various stakeholders.

Quality of evidence is classified as "high", "moderate", "low", or "very low" based on decisions about methodological characteristics of the available evidence for a specific health care problem.			
High	**Moderate**	**Low**	**Very low**
We are very confident that the true effect lies close to that of the estimate of the effect.	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

The Saudi guidelines' recommendations are assigned the class of recommendations defined in the preceding table:

- The KSA MoH panel recommends intranasal corticosteroids for treatment of adults with seasonal or intermittent allergic rhinitis (**Strong** recommendation; Moderate-quality evidence).
- The KSA MoH panel suggests intranasal corticosteroids for treatment of adults with perennial or persistent allergic rhinitis (Conditional recommendation; Low-quality evidence).
- The KSA MoH panel recommends intranasal corticosteroids rather than intranasal H1- antihistamines for treatment of adults with seasonal or intermittent allergic rhinitis (**Strong** recommendation; High-quality evidence).
- The KSA MoH panel suggests intranasal corticosteroids rather than intranasal H1- antihistamines for treatment of adults with perennial or persistent allergic rhinitis (Conditional recommendation; Very low-quality evidence).

- The KSA MoH panel suggests sublingual immunotherapy for treatment of adults with seasonal or intermittent allergic rhinitis (conditional recommendation; Moderate-quality evidence).
- The KSA MoH panel suggests sublingual immunotherapy for treatment of adults with perennial/persistent allergic rhinitis (conditional recommendation; very low-quality evidence).
- The KSA MoH panel suggests sublingual immunotherapy for treatment of children younger than 18 years old with seasonal or intermittent allergic rhinitis (Conditional recommendation; Moderate-quality evidence).
- The KSA MoH panel suggests sublingual immunotherapy be not used for treatment of children younger than 18 years old with perennial or persistent allergic rhinitis (Conditional recommendation; very low-quality evidence

1.2.2 Japanese Society of Allergology Guidelines for Allergic Rhinitis [2020]

The revised guideline published in 2020 by the Japanese Society of Allergology includes assessment of diagnosis/treatment and prescriptions for children and pregnant women, for broad clinical applications. An evidence-based step-by-step strategy for treatment is also described. No grades of recommendations were outlined[8].

- The aim of treatment is to alleviate symptoms and remove difficulties with everyday life. Choose a treatment based on severity, disease type, and lifestyle.
    1. **Natural courses and communication with patients:** Combinations of pharmacotherapies based on severity and disease types and communication with patients improve patients' satisfaction and QOL.
    2. **Elimination and avoidance of antigens:** In addition to cleaning, lowering humidity with dehumidifier is effective in reducing mites. For Japanese cedar pollinosis, refer to pollen dispersal information to consider measures to prevent pollen inhalation. For pet allergies, avoid contact with causative pets and keep dogs and cats clean.
    3. **Pharmacotherapy:** Therapeutic agents for allergic rhinitis, with different mechanisms of action, are classified as shown in the following (figure 1). Alpha-sympathomimetics (vasoconstrictor nose drops), which temporarily alleviate nasal blockage, are also used.

Table 6. Therapeutic Agents for Allergic Rhinitis. Adapted from the Japanese Society of Allergology 2020 Guideline.

Mast cell stabilizer		
Disodium cromoglycate, tranilast, amlexanox, pemirolast potassium		
Chemical mediator receptor antagonists		
Histamine H1 receptor antagonists (antihistamine)	1st generation	d-chlorpheniramine maleate, clemastine fumarate
	2nd generation	Ketotifen fumarate, azelastine hydrochloride, oxatomide, mequitazine, emedastine difumarate, epinastine hydrochloride, ebastine, cetirizine hydrochloride, levocabastine hydrochloride, bepotastine besilate, fexofenadine hydrochloride, olopatadine hydrochloride, loratadine, fexofenadine & pseudoephedrine
Leukotriene receptor antagonists	Pranlukast hydrate, montelukast sodium	
Prostaglandin D2/thromboxane A2 receptor antagonists (anti-prostaglandin D2/thromboxane A2 agents)	Ramatroban	
Th2 cytokine inhibitor		
Suplatast tosilate		
Steroids		
Nasal	Beclomethasone propionate, fluticasone propionate, mometasone furoate hydrate, dexamethasone cipecilate capsule for external use	
Oral	Compounding agent of betamethasone/d-chlorpheniramine maleate	
Others		
Nonspecific thallassotherapy agents, biological preparations, and herbal medicines		

Mast cell stabilizers

Since the development of disodium cromoglicate (**DSCG**), local agents (eye drops and nasal spray) and oral agents, such as **tranilast, amlexanox, and pemirolast potassium**, have been on the market. They have mild effects. To achieve sufficient clinical effects, 2-week prolonged administration is required. Amelioration rates are increased by continuous administration. Adverse effects, such as sleepiness and dry mouth, do not occur.

Chemical mediator receptor antagonists

Histamine H1 receptor antagonists (antihistamines)

- First-generation antihistamine: First-generation antihistamine often causes adverse effects, such as sleepiness, impaired performance, and dry mouth, but have immediate effects on sneezing and watery rhinorrhea. First-generation antihistamines are contraindicated for patients with glaucoma, prostatic hyperplasia, and asthma because of their potent anticholinergic effects. They have less central nervous system depressant actions in children than in adults. Caution should be exercised for excitatory effects, such as convulsions. Most first-generation antihistamine are marketed as OTC.
- Second-generation antihistamine: Second-generation antihistamine, such as ketotifen fumarate, oxatomide, azelastine hydrochloride, emedastine difumarate, and mequitazine, are effective to some extent for nasal blockage aside from sneezing and watery rhinorrhea. However, they may cause adverse effects, such as sleepiness and impaired performance, in early versions. Thus, caution should be exercised in administering them. The adverse effects of late versions, such as epinastine hydrochloride, ebastine, cetiridine, fexofenadine, loratadine, olopatadine hydrochloride, bepotastine besilate, and levocetirizine, have been reduced. Priority indications are mild to moderate sneezing and rhinorrhea type. Combine them with topical steroids depending on severity. A combination drug containing an antihistamine (**fexofenadine**) and an oral decongestant (**pseudoephedrine**) is now available. However, the priority indication for this combination drug is limited to the moderate to severe nasal blockage type of pollinosis and the severe nasal blockage type of perennial allergic rhinitis.

Leukotriene receptor antagonists (antileukotrienes)

Peptide leukotrienes, produced and released by mast cells, eosinophils, and macrophages, have potent relaxing effects on the vascular smooth muscles of the nasal mucosa, enhancing effects on vascular permeability, and stimulating effects on eosinophil migration. **Pranlukast** and **montelukast** are available. They are effective for nasal blockage. Their effects are increased by prolonged administration.

Comparable effects with those of antihistamines can be achieved for sneezing and rhinorrhea within 4 weeks. Primary indications are treatment of symptoms of the moderate or milder nasal blockage type and those of intermediate type with nasal blockage as the chief complaint. No adverse effects of sleepiness occur.

Prostaglandin D2 and thromboxane A2 receptor antagonist

Ramatroban enhances vascular permeability in the nasal mucosa and suppresses eosinophil migration by blocking thromboxane receptors and suppresses eosinophil migration by blocking CRTh2 (chemoattractant receptor-homologous receptor expressed on Th2 cell), a part of the prostaglandin D2 receptor. They have strong delayed effects on nasal blockage. Primary indications are treatment of symptoms of nasal blockage type and those of combined type with nasal blockage as a chief complaint. The agents interact with some other medicines but cause no adverse effects of sleepiness.

Th2 cytokine inhibitors

IPD inhibits the production of Th2 cytokines, such as IL-4 and IL-5, in T lymphocytes to alleviate allergic inflammation. No adverse effects of sleepiness occur.

Steroids

- Nasal steroids: **Beclomethasone propionate, fluticasone propionate, mometasone furoate, fluticasone furoate, and dexamethasone cipecilate** are available. All agents have strong local effects in small amounts and are poorly absorbed and readily degraded. Thus, they have few systemic adverse effects. They are highly effective for sneezing, watery rhinorrhea, and nasal mucosal swelling, and exert their effects within 1e3 days. A slight feeling of nasal irritation, feeling of dryness, and epistaxis may occur.
- Steroids for internal use: Only for intractable cases with severe nasal blockage and laryngopharynx symptoms, uncontrollable with nasal spray steroids, **prednisolone** (20-40 mg/day) can be administered for 4-7 days at the start of treatment. Caution should be exercised for adverse effects.

Alpha-sympathomimetics (nasal topical vasoconstrictor [decongestant])

Alpha-sympathomimetics act on the a-receptors of vascular smooth muscles to cause vasoconstriction and temporarily alleviate nasal mucosal swelling. Long-term continuous administration causes medicament rhinitis. For the most severe pollinosis, they can be administered 2-3 times a day for 1-2 weeks.

Other pharmacotherapeutic agents

Nonspecific thalassotherapy agents, biological preparation, and herbal medicines can be used.

Adverse effects and drug interactions of therapeutic agents for allergic rhinitis. Therapeutic agents for allergic rhinitis are those for symptomatic treatment, used to alleviate symptoms. Caution should be exercised for harmful adverse effects and drug interactions during treatment. If they occur, take immediate measures and switch to a different treatment.

Specific immunotherapy

Subcutaneous specific immunotherapy (SCIT) has been used over the past century. Its demonstrated effects may be exerted via immunological mechanisms. Of note, local mast cells are decreased, the Th1/Th2 balance is altered, and regulatory T cells are increased. It takes several months to develop effects, requiring routine injection for ≥3 years. Furthermore, a systemic anaphylaxis response may develop in a small number of cases.

Indications: This therapy is indicated for the treatment of patients aged 6 years, without severe systemic symptoms, to whom emergency adrenaline may be administered. Exclude patients on b-blocker therapy or with severe asthma. While this therapy has no harmful effects on pregnant women, it should not be started during pregnancy.

Implementation:

- Specialists should prescribe antigen extracts and take measures against systemic reactions, such as anaphylactic shock.
- In patients with asthma complications, avoid this therapy during a paroxysmal period. In patients with pollinosis, avoid starting this therapy during dispersal of causative pollen.
- For initial injection, reduce the threshold concentration for intradermal reaction to 1/10. Before injection, ask more than one physician or health care professional about concentration and dosage.
- Before increasing an aqueous solution, concentration or changing lots, conduct an intradermal test. For patients with erythema of ≥50 mm diameter, carefully conduct the test and follow-up the patients for 20-30 min after injection.
- Perform therapy for at least 3 years. Therapeutic effects often continue for several years after discontinuation of administration.
- Instruct patients to continue the therapy.

Sublingual immunotherapy (SLIT):

Presently, SLIT is permitted in Japan for reactions to the allergens, Japanese cedar pollen and dust mites. The current indication for SLIT is confirmation of a positive allergen to Japanese cedar pollen or dust mites by a skin reaction or a specific IgE in a patient 5 years of age or older. The allergen is administered as a liquid or tablet every day in a dose escalation manner for at least 2 or 3 years.

The contraindications are serious illnesses that require the use of a b blocker, unstable asthma in which a systemic steroid may be required, treatment with an anti-cancer drug, severe autoimmune disease, or cases in which it is assumed the treatment should not be used in the patient because of the side effects. It cannot be begun from the dispersion period. Sublingual inoculation should be suspended in the case of pregnancy, mouth injury or ulcer, or if severe odonto-therapy is required. However, if pregnancy occurs while this therapy is being administered, allergen immunotherapy, including subcutaneous injection, is generally thought to be safe.

Surgical treatment

Nasal blockage in allergic rhinitis is often caused by nasal deformities, such as deviated septum, hypertrophic rhinitis, and nasal polyps. In this case, corrective surgery of nasal cavity can be performed to improve nasal ventilation. Before pollen season, laser surgery is also performed for Japanese cedar pollinosis, but the effects of this surgery do not continue in the following year. The main purpose is to alleviate nasal blockage. For intractable rhinorrhea, perform posterior nasal neurectomy.

1.2.3 Australasian Society of Clinical Immunology and Allergy (ASCIA) Allergic Rhinitis Clinical Update [2022]

This document published by ASCIA in 2022 is aimed to complement the knowledge of medical practitioners (including general practitioners, pediatricians, and physicians), pharmacists, nurse practitioners and nurses, dietitians and other allied healthcare professionals with information on allergic rhinitis[9]. Grades of recommendations were not outlined.

Aeroallergen minimization

- Avoidance or minimization of confirmed allergens may assist some people in reducing the severity of their allergic rhinitis symptoms.
- This can be difficult to achieve for house dust mite and pollens.
- Avoidance strategies must only be developed if the allergens are clinically significant.

- Realistic consideration must also be given to the family's ability to act in strategies.

Pharmacotherapy and other treatment options

The duration and severity of allergic rhinitis symptoms are useful in guiding therapy, as shown in the table below.

Table 7. Pharmacotherapy and Treatment Options for Allergic Rhinitis. Adapted from the ASCIA 2022 Guideline.

<table>
<tr><th></th><th>Persistent and mild</th><th>Intermittent and moderate-severe</th><th>Persistent and moderate-severe</th></tr>
<tr><td rowspan="2">Intermittent and mild</td><td colspan="3">Intranasal corticosteroid sprays*
Combination treatments (intranasal corticosteroid and antihistamine sprays)*</td></tr>
<tr><td colspan="3">+/- Other therapies (intranasal antihistamines, intranasal chromones, intranasal anticholinergic sprays, leukotriene antagonists)</td></tr>
<tr><td colspan="4">Oral non-sedating or intranasal antihistamines*</td></tr>
<tr><td colspan="4">+/- Nasal saline irrigation</td></tr>
<tr><td colspan="4">Allergen avoidance</td></tr>
<tr><td colspan="2">*Typical first-line treatments recommended</td><td colspan="2">Allergen immunotherapy</td></tr>
</table>

Definitions: *Intermittent: 4 days/week or >4 weeks • Mild: Normal sleep, no impairment of daily activities, normal work, or school performance. • Moderate-severe: One or more of abnormal sleep, impairment of activities, abnormal work or school performance, troublesome symptoms.*

Table 8. Allergic Rhinitis Pharmacotherapy Options. Adapted from the ASCIA 2022 Guideline.

First line treatment options	Other possible treatments	Short term treatment options
Antihistamines (non-sedating oral or intranasal)	Saline treatments	Decongestants (oral or intranasal)
Intranasal corticosteroid sprays	Intranasal chromones	Systemic oral corticosteroids

Combination treatments (intranasal corticosteroid and antihistamine sprays)	Intranasal anticholinergic sprays	Combination treatments (intranasal decongestant and antihistamine sprays)
	Oral leukotriene antagonists	

When symptoms improve, pharmacotherapy doses may be reduced.

A trial of pharmacotherapy initiated by primary care physicians and maintained for at least 4 weeks is recommended before considering referral to a specialist if no improvement.

If a patient is a competitive athlete, it is important to ensure medications suggested are permitted. For example, pseudoephedrine used in some decongestants is subject to certain restrictions.

Non-sedating antihistamines

Table 9. Non-Sedating Antihistamines. Adapted from the ASCIA 2022 Guideline.

Place in therapy	First line treatment for intermittent mild allergic rhinitis or used in conjunction with other therapies.
Route • **Oral** • **Intranasal**	Rapid onset action (1-2 hours) Very rapid onset action (within 30 minutes). May be used as a rescue medication to provide immediate relief of symptoms.
Availability	Over the counter
Type	Non-sedating antihistamines are recommended. Sedating antihistamines are not recommended.
Frequency of use	Once or twice a day.
Benefits • **Ocular symptoms** • **Nasal sneeze/itch/runny nose** • **Nasal congestion**	↓ itchy, watery eyes ↓ sneezing, itchy, runny nose Limited decrease in symptoms

Whilst some nasal antihistamines can reduce nasal congestion, intranasal corticosteroids (INCS) are more effective in reducing nasal congestion. Combination treatments containing an antihistamine and INCS spray offer the combined advantages of both medications.

Intranasal corticosteroids (INCS)

Table 10. Intranasal Corticosteroids (INCS). Adapted from the ASCIA 2022 Guideline.

Place in therapy	First line treatment for persistent and/or moderate to severe allergic rhinitis and treatment failures with antihistamines alone
Availability	Over the counter
Age restriction	Different intranasal corticosteroids often have different minimum age restrictions
Frequency of use	Continuous (more effective; a few days to take effect; maximal effect by 2 weeks) Long-term use if recommended where effective As-needed basis (less effective)
Benefits • **Ocular symptoms** • **Nasal sneeze/itch/runny nose** • **Nasal congestion** • **Cost effective reduction of symptoms**	↓ itchy, watery eyes ↓ sneezing, itchy, runny nose ↓ nasal congestion

Different brands of INCS vary in strength and efficacy. Combination treatments containing an antihistamine and INCS spray offer the combined advantages of both medications.

Other treatment options

- Saline nasal irrigation
    - Clears aeroallergens and inflammatory mucus.
    - Well tolerated and effective in reducing rhinitis symptoms.
    - Safe and inexpensive.
    - Large volume (>60 mL) and positive pressure devices appear to be more effective than simple sprays.
    - Is not a replacement for pharmacotherapy.
- Intranasal chromones such as sodium cromoglycate
    - Are typically used for intermittent rhinitis.

    - Predominantly used for the immediate treatment of itch, sneeze, rhinorrhea.
    - Are more useful for episodic treatment than regular prophylaxis.
    - Duration of action is approximately 4 hours.
    - Are less effective than intranasal corticosteroids
- Intranasal ipratropium
    - Anticholinergic sprays are useful in non-allergic rhinitis.
    - Only decreases watery rhinorrhea.
    - May be used in allergic rhinitis as adjunct treatment for rhinorrhea persisting despite antihistamines or intranasal corticosteroid use.
- Oral leukotriene antagonists
    - Used in children/adolescents with asthma and allergic rhinitis.
    - No additional benefit if used in combination with antihistamines for treatment of allergic rhinitis.
    - The combination of leukotriene antagonists (e.g., Montelukast) and antihistamines are no more effective than intranasal corticosteroids alone for allergic rhinitis.
- Decongestants
    - Oral or nasal decongestants may be used short term (3-5 days) to reduce nasal congestion if severe. This allows more effective administration of intranasal corticosteroids if turbinates are very swollen.
    - Chronic use of intranasal decongestants may lead to rebound nasal obstruction, called rhinitis medicamentosa.
    - Decongestants should not be used in patients with hypertension, coronary artery disease, prostatism or glaucoma. • Decongestants should not be used in pregnancy
- Systemic steroids
    - Brief courses of oral corticosteroids (3-7 days) are rarely indicated but may be considered: If there is severe nasal obstruction. As short-term rescue medication if symptoms are severe, despite conventional therapy, but only up to a maximum limit of 2 or 3 short courses in a 12-month period.

- Depocorticosteroids are NOT recommended due to short duration of benefit and potential for local (subdermal and dermal atrophy) and systemic side effects.
- Patients requiring oral corticosteroids for allergic rhinitis should be referred to a clinical immunology/allergy/specialist for assessment.

Ocular management

- Non-pharmacological therapy: Flush allergen from eyes (saline washes, liquid-tear preparations), Cool compresses.
- Ocular or oral antihistamines or topical mast cell stabilizers may be used to control itchy/watery eyes.
- Intranasal corticosteroids can reduce ocular symptoms of allergic rhinitis.
- Ocular corticosteroids should only be prescribed in consultation with, and regular review by an Ophthalmologist.

Management of allergic rhinitis in pregnancy

- Up to 20% of pregnant women develop symptoms of rhinitis, typically in second trimester, improving 2 weeks after delivery.
- Medications for allergic rhinitis should only be used during pregnancy if the benefit to the mother justifies the potential risk to the fetus.
- There are few well-controlled clinical studies in pregnant women examining the safety of many of the medications used in allergic rhinitis.
- Ideally pharmacotherapy should be avoided in the first trimester of pregnancy. However, there are some oral antihistamines and intranasal corticosteroid sprays with an “A” category used by many pregnant women without any proven increase in harmful effects on fetus.
- Saline nasal irrigation and intranasal chromones are safe in pregnancy.

Management of allergic rhinitis during lactation:

Recommend taking medication after feeding the infant to minimize any potential infant exposure.

➔ Considered safe: Saline nasal treatments, Intranasal sodium cromoglycate (chromone), Intranasal ipratropium (anti-cholinergic), non-sedating oral antihistamines Intranasal corticosteroids.

➔ Evidence for safety lacking (recommend not use): Intranasal azelastine hydrochloride (antihistamine) Intranasal lodoxamide trometamol (chromone).

➔ Crosses into breast milk (recommend not use): Oral or intranasal decongestants Intranasal levocabastine hydrochloride (antihistamine).

Dietary restrictions are not recommended

- There is no evidence that allergic rhinitis is due to food allergies, although conditions may coexist.
- Food elimination is not recommended unless there is a confirmed allergy, and has potential for serious nutritional consequences, especially in young children.
- Restricting cow's milk (dairy) products is often popular, even if there is no confirmed food allergy, but studies do not show any change in mucus production following dietary modification.

Allergen immunotherapy

- Also known as desensitization.
- Involves the regular administration of commercially available allergen preparations to promote clinical tolerance to the allergen/s, administered by subcutaneous injections or sublingual preparations.
- Is usually administered for 3-5 years in order to produce durable effects, to reduce the frequency and severity of allergic rhinitis symptoms.
- Should only be initiated by medical specialists with training in allergy, following a confirmed diagnosis.

Surgery

Surgery plays a limited role in the management of rhinitis.

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

- Nasal irrigation is a widespread first line treatment.
- Intranasal corticosteroids are safe and effective for long term use.
- If short courses of oral corticosteroids are prescribed, both patients and practitioners must remain vigilant to avoid side effects.
- A short course of antibiotics may have a role to play in non-Type 2 CRSwNP, but patient selection is important and side effects need to be managed.
- The effectiveness of allergen immunotherapy in the treatment of CRSwNP remains unclear.
- A few Types 2 targeted biologics have been trialed with positive outcomes.

- These treatments are high cost and need to be used in a cost-effective manner.
- Endoscopic sinus surgery plays a significant role in the management of CRSwNP.
- Surgery is safe, reduces symptom burden, and improves quality of life.
- Refer to an ENT or clinical immunology/allergy specialist for treatment.

1.2.4 National Health Service (NHS) Pediatric Allergic Rhinitis Guideline [2023]

This guideline has been developed by the Ashford and St. Peter's Hospitals to support all clinicians, both allergy specialists and general pediatricians, in managing allergic rhinitis, as well as to guide in decision making as to when to investigate or refer into specialist clinics[10]. No grades of recommendations were outlined.

Step up and down to achieve symptom control. Allow 8-12 weeks at each step.

- ➔ **Step 1, allergen avoidance:** nasal rinsing - with saline solution
- ➔ **Step 2, regular long-acting non-sedating antihistamine:** cetirizine or loratadine **OR regular nasal corticosteroid spray:** fluticasone furoate, mometasone furoate, or fluticasone.

Start with antihistamine if pruritus dominant or nasal corticosteroid if congestion dominant:

- ➔ **Step 3, regular oral antihistamine, and nasal corticosteroid**
- ➔ **Step 4, switch to 2nd line oral antihistamine**: fexofenadine (from 6yrs)
- ➔ **Step 5**, **regular nasal antihistamine + corticosteroid spray and oral antihistamine**: azelastine and fluticasone nasal spray (from 12yrs) + fexofenadine
- ➔ **Step 6, add in leukotriene receptor antagonist:** montelukast.
- ➔ **Step 7, allergen specific immunotherapy**

If eye symptoms – consider sodium cromoglicate eye drops.

Refer for skin prick testing to aid in allergen avoidance and diagnostic uncertainty.

Refer to ENT in case of failed nasal corticosteroid spray + antihistamine for assessment of adenoidal hypertrophy/ consideration of turbinate surgery, or suspected obstructive sleep apnea.

1.2.5 American Academy of Allergy, Asthma & Immunology (AAAAI) Rhinitis Practice Parameter Update [2020]

This comprehensive practice parameter for allergic and nonallergic rhinitis provides updated guidance on diagnosis, assessment, selection of monotherapy and combination pharmacotherapy options, and allergen immunotherapy[12].

Table 11. AAAAI Strength Grading and Certainty of Evidence

Grading the Strength of the Consensus Based Statements (CBSs)	
Strong CBS	The work group and JTFPP are confident that the desirable effects of adherence to the statement outweigh the undesirable effects. This CBS may be appropriate to be used as a practice standard indicator. When making a strong CBS, the wording is "We recommend,' implying that the clinician "should' follow the recommendation. The implications of a strong CBS are: • For patients—most people in your situation would want the recommended course of action and only a small proportion would not; request discussion if the intervention is not offered. • For clinicians—most patients should receive the recommended course of action. • For policy makers—the recommendation can be adopted as a policy in most situations.
Conditional CBS	The work group and JTFPP reached a decision that the desirable effects of adherence to CBS probably outweigh the undesirable effect. When making a conditional CBS, the wording is "We suggest,' implying that the clinician "may' follow the recommendation. The implications of a conditional CBS are: • For patients—most people in your situation would want the recommended course of action, but many would not. • For clinicians—you should recognize that different choices will be appropriate for different patients and that you must help each patient to arrive at a management decision consistent with her or his values and preferences. It is likely that shared decision making will play a major role in arriving at the management decision. • For policy makers—policy making will require substantial debate and involvement of many stakeholders.
Grading the Certainty of Evidence for Each CBS	

High	Further research is very unlikely to change our confidence in the estimate of effect. The recommendation is based on high-quality evidence, such as multiple highly rated randomized controlled trials, systematic reviews, or meta-analyses.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. The recommendation would likely be based on somewhat limited evidence, such as reduced number or quality of randomized controlled trials or controlled trials without randomization.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. The recommendation would likely be based on very weak evidence, such as nonexperimental studies, registries, or comparative studies.
Very Low	Any estimate of the effect is very uncertain. The recommendation is based largely on very low-quality studies and/or on expert opinion. CBS without determination of certainty.
When there are either no published studies, or very limited and/or very weak evidence, a consensus statement without any category of certainty of evidence was developed. The degree of agreement by all JTFPP and work group members is indicated, with voting details provided if there were dissenting votes.	

This guideline contains systematically developed recommendations intended to optimize care of adult and adolescent patients (≥ 12-15 years of age) and to assist physicians and/or other health care practitioners and patients to make decisions regarding diagnosis and therapy for rhinitis. Even though many treatments are approved for younger children, the application of recommendations to children would be partially based on data extrapolation from adult studies and would therefore be less certain.

Clinical history and physical examination

1. CBS: We recommend that the clinician complete a detailed history and a physical examination in a patient presenting with symptoms of rhinitis. Strong Low
2. CBS: We recommend that for patients presenting with rhinitis symptoms, a review of all current medications should be completed to assess whether drug-induced rhinitis may be present. Strong Ungraded

Vasculitis, sarcoidosis, and other systemic diseases

3. CBS: We recommend that aeroallergen skin prick testing or sIgE testing be completed to confirm the diagnosis of AR in a patient with a history consistent with AR. Strong High
4. CBS: We recommend that the clinician not perform food skin prick testing or sIgE for foods in their routine evaluation of a patient presenting with the signs and symptoms compatible with the diagnosis of AR. Strong Ungraded

Severity assessment including QOL by survey instruments and questionnaires

5. CBS: We suggest that the use of a validated instrument (e.g., scoring system, scale, or questionnaire) be considered to help determine the severity of rhinitis and to monitor the degree of disease control. Conditional Low
6. CBS: We recommend against prescribing a first-generation antihistamine and are in favor of a second-generation antihistamine when prescribing an oral antihistamine for the treatment of AR. Strong High

PHARMACOTHERAPY

Oral leukotriene receptor antagonists

7. CBS: We suggest that the clinician not select the oral LTRA **montelukast** for the initial treatment of AR due to reduced efficacy when compared with that of other agents. Furthermore, serious neuropsychiatric events that may include suicidal thoughts or actions have been reported in some patients taking montelukast. As advised by the FDA, **montelukast should be used to treat AR only in patients who are not treated effectively with or cannot tolerate other alternative therapies**. Conditional Very low
8. CBS: We recommend that the clinician not select an oral LTRA for the treatment of NAR. Conditional Ungraded

Systemic corticosteroids

9. CBS: We suggest that for the treatment of very severe or intractable AR, the clinician may consider a short course (5-7 d) of oral corticosteroids. Conditional Very low
10. CBS: We suggest that for the treatment of very severe or intractable AR, the clinician not prescribe a depot parenteral corticosteroid for AR due to the potential risks of systemic and local corticosteroid side effects. Conditional Low .

INTRANASAL AGENTS

Intranasal antihistamines

11. CBS: We recommend that the clinician offer INAH as an initial treatment option for patients with SAR. Strong High
12. CBS: We recommend that the clinician offer INAH as a first-line monotherapy option for patients with NAR. Strong High
13. CBS: We recommend that the clinician offer INAH as a first-line option for patients with intermittent AR. Conditional Ungraded

Intranasal corticosteroids

14. CBS: We recommend that when choosing monotherapy for persistent AR, INCS be the preferred medication. Strong High
15. GRADE: We recommend that for the initial treatment of moderate/severe SAR in patients ≥15 y of age, the clinician use an INCS over an LTRA. (Also see Recommendation 7.) Strong High

Intranasal decongestants

16. CBS: We suggest that the use of intranasal decongestants be short term and used for intermittent or episodic therapy of nasal congestion. (However, see also Recommendation 26.) Conditional Low
17. CBS: We suggest that in patients having severe mucosal edema, which impairs the delivery of other intranasal agents, an intranasal decongestant be considered for up to 5 d of use. Conditional Ungraded

Oral decongestants

18. CBS: We suggest that oral decongestant agents be used with caution in older adults and children younger than 4 y old, and in patients of any age who have a history of cardiac arrhythmia, angina pectoris, cerebrovascular disease, uncontrolled hypertension, bladder outlet obstruction, glaucoma, hyperthyroidism, or Tourette syndrome. Conditional Low
19. CBS: We recommend that oral decongestants be avoided during the first trimester of pregnancy. Strong Low

Intranasal ipratropium

20. CBS: We suggest that patients with PAR and NAR who have rhinorrhea as their main nasal symptom be offered intranasal ipratropium. Conditional Low for PAR; moderate for NAR .

Intranasal cromolyn

21. CBS: We suggest that intranasal cromolyn be offered as an option to be taken just prior to allergen exposure to reduce symptoms of AR from episodic allergen exposures. Conditional Very low

INCS and INAH combined.

22. GRADE: We suggest that the clinician consider the combination of an INCS and an INAH for the initial treatment of moderate/severe nasal symptoms of SAR in patients ≥12 y old. Conditional High
23. CBS: We suggest that the clinician consider the combination of an INCS and an INAH for moderate/severe SAR and PAR that is resistant to pharmacologic monotherapy. * Conditional Moderate
24. CBS: We suggest that the clinician consider the combination of an INCS and an INAH for moderate/severe NAR that is resistant to pharmacologic monotherapy. * Conditional Low

INCS with intranasal ipratropium for control of rhinorrhea

25. CBS: We suggest that for patients taking an INCS who have persistent rhinorrhea, the clinician may consider the addition of intranasal ipratropium. Conditional Moderate

INCS with intranasal decongestant

26. CBS: We suggest that patients with persistent nasal congestion unresponsive to an INCS or to an INCS-INAH combination be offered combination therapy with addition of an intranasal decongestant for up to 4 wk. Conditional Low

Oral antihistamine with oral decongestant

27. CBS: We suggest that for patients with AR and nasal congestion uncontrolled with an oral antihistamine, the clinician consider the addition of pseudoephedrine, when tolerated. (See Recommendation 18.) Conditional Moderate

Oral antihistamines with oral LTRAs

28. CBS: We suggest that for SAR the clinician not combine the oral LTRA montelukast with an oral antihistamine for symptoms not controlled with an oral antihistamine. (See Recommendation 7.) Conditional Moderate

COMBINATION THERAPIES THAT HAVE NOT BEEN SHOWN TO BE CONVINCINGLY SUPERIOR TO MONOTHERAPY

Oral antihistamine with INCS

29. GRADE: We recommend that the clinician not prescribe, as initial treatment, a combination of an oral antihistamine and an intranasal steroid in preference to monotherapy with an intranasal steroid in patients ≥ 12 y of age with symptoms of SAR. Strong Moderate
30. CBS: We suggest that the clinician not prescribe the combination of an oral antihistamine and an INCS in preference to monotherapy with an intranasal steroid in all patients with SAR and PAR. Conditional Very low.

Oral LTRAs with INCS

31. CBS: We suggest against the addition of the oral LTRA montelukast to an INCS for AR, due to the lack of adequate evidence of improved efficacy and concerns for serious neuropsychiatric events from montelukast. (See Recommendation 7.) Conditional Very low

Pharmacotherapy for NAR

32. CBS: We suggest that the clinician offer an INCS as a first-line therapy for NAR. Conditional Low
33. CBS: We suggest that the clinician offer an INAH as a first-line therapy for NAR. Conditional Very low

AIT and AR

34. CBS: We suggest that AIT (subcutaneous or sublingual tablets) be offered through shared decision making to patients with moderate/severe AR who (1) are not controlled with allergen avoidance and/or pharmacotherapy or (2) choose immunotherapy as the preferred method of treatment (e.g., due to the desire to avoid the adverse effects, costs, or long-term use of pharmacotherapy) and/or (3) desire the potential benefit of immunotherapy to prevent or reduce the severity of comorbid conditions, such as asthma. Conditional Moderate
35. CBS: We suggest that AIT (subcutaneous or sublingual tablets) be considered for patients with controlled mild/moderate asthma with coexisting AR. Conditional Moderate

Acupuncture

36. CBS: We cannot make a recommendation for or against the use of acupuncture for the treatment of AR. N/A Very low.

Herbal medications

37. CBS: We cannot make a recommendation for or against the use of specific herbal products for the treatment of AR.

1.2.6 Review Article: Current Treatment Options for Allergic Rhinitis [*International Journal of Research in Medical Sciences*, 2023]

This review article published by Swain et al. in the *International Journal of Research in Medical Sciences* in July 2023 discusses details of current treatment options for AR[11].

TREATMENT OPTIONS

There are several treatment options for AR such as non-pharmacologic and pharmacologic. The goal of the treatment is to eliminate or reduce the present symptoms and prevent future attacks and complications. Appropriate treatment selection should have minimal adverse effects and enable the patient to maintain a normal lifestyle. The treatment options include allergen avoidance, pharmacotherapy, and immunotherapy.

NON-PHARMACOLOGIC INTERVENTIONS

➔ **Allergen Avoidance:** Patients can take measures to reduce exposure to triggers based on specific allergens, whether it is pollen, mold, or animal dander. Allergen avoidance should be part of an overall treatment strategy that includes pharmacotherapy. Pet avoidance shows a clear benefit.

PHARMACOTHERAPY

- The treatment options are usually administered orally or intranasally.
- The treatment options available include *antihistamines*, *corticosteroids*, *decongestants*, *leukotriene receptor antagonists, and anticholinergics*.
- *Immunotherapy* is also an important treatment option for patients who are refractory to pharmacotherapy.

The most common pharmacologic treatment options include intranasal corticosteroids, H1 receptor inverse agonists (antihistamines), and leukotriene receptor antagonists. These medications are effective in the case of seasonal AR and in perineal AR.

Intranasal corticosteroids

- Intranasal corticosteroid sprays are the first-line treatment for moderate to severe AR and are considered the most effective medication for controlling the symptoms of AR.
- Intranasal corticosteroids are highly effective in reducing nasal obstruction and congestion. Intranasal corticosteroids are preferred over all other agents for mild or moderate to severe symptoms of AR.
- The intranasal corticosteroids are *beclomethasone propionate, fluticasone propionate, mometasone furoate, fluticasone furoate, and dexamethasone cipecilate.*
- Intranasal corticosteroids rarely show systemic effects of oral corticosteroids-adrenal suppression, bone fractures (particularly in elderly age), growth suppression, and ocular effects.
- All available intranasal corticosteroids are efficacious in controlling AR symptoms. The product differentiation involves factors like cost, ease of dosing, and sensory issues such as aroma and taste, which can affect patient preference.

Antihistamines

- Antihistamines are most effective against symptoms that are primarily mediated by histamines such as sneezing, pruritus, and ocular symptoms.1 Antihistamines are less effective for nasal congestion and may require a combination with a decongestant or intranasal corticosteroid.
- Oral antihistamines are considered a first-line treatment option for patients with mild to moderate intermittent symptoms of AR.
- *First-generation oral forms of antihistamines* are usually well tolerated but have sedative, cognitive, and anticholinergic effects that can lead to challenges for some patients.
- *Second-generation oral antihistamines* usually have no sedative effects and are well tolerated. Second-generation oral antihistamines such as fexofenadine, loratadine, and desloratadine do not cause sedation at recommended doses. Cetirizine and intranasal azelastine can cause sedation at recommended doses.

Nasal decongestants

- *Use of intranasal decongestants should be limited to no more than three days in a row, as overuse can result in dependence and the patient can experience rebound nasal congestion due to α-receptor downregulation, or rhinitis medicamentosa.*

Leukotrienes receptor antagonists (LTRAs)

- These can be used alone or in combination with antihistamines or intranasal corticosteroids and may be helpful in patients who have comorbid asthma.
- LTRAs have shown efficacy in asthma.
- Montelukast provides statistically significant improvement for nasal symptoms; however, topical corticosteroids and oral antihistamines give a greater reduction in nasal symptom scores.
- Montelukast is considered a safe medication as prophylaxis and treatment for airway allergy including in pediatric age.

Combination of antihistamines and LTRAs

- *Anticholinergics*: These can be used in combination with an antihistamine or intranasal corticosteroid in patients who have primary symptom is rhinorrhea or is refractory to other treatment.
- *Saline douching:* Isotonic solutions are well tolerated, inexpensive, easy to use, and have no side effects.
- *Immunotherapy*: Subcutaneous immunotherapy is effective in decreasing the symptoms and minimizes the medication requirement in long term. It is reserved for patients with a severe type of AR whose symptoms are not sufficiently treated by pharmacotherapy.
- *Probiotics*: Study has shown that probiotics may be very helpful for the treatment or prevention of AR in the pediatric age group. Probiotics promote an improvement to the immune response of the human body and there is satisfactory action on the modulation of the allergic response more as compared to conventional treatment.

AR in pregnancy

- Intranasal corticosteroids are not associated with an increased chance of congenital malformations in humans. These should be considered as first-line therapy in treating AR based on their superiority to oral antihistamines, decongestants, and mast cell stabilizers with respect to efficacy.

- The first-generation antihistamines have not been incriminated as human teratogens. The teratogenicity of second-generation antihistamines has not been studied completely. The fetal safety of loratadine and fexofenadine has not been established in controlled trials and so, their use for AR cannot be used unless first-line therapies have been tried and have failed.

AR in children

- **Mometasone furoate and fluticasone propionate** have been studied in children and found no adverse effects on cortisol levels, the hypothalamic-pituitary-adrenal axis, or growth.
- Nasal douching with isotonic saline solution can reduce the symptoms of children and adults with seasonal rhinitis and is safe and inexpensive. Ipratropium bromide nasal spray reduces rhinorrhea but does not affect another nasal symptom.

Surgical treatment

- Nasal blockage in AR is often caused by deviated nasal septum, hypertrophic rhinitis, and nasal polyps. In this case corrective surgery of the nasal cavity can be performed to relieve nasal obstruction. Corrective surgery to relieve nasal obstruction includes submucosal turbinectomy, septoplasty, inferior turbinectomy, and nasal polypectomy. Vidian neurectomy is helpful to control rhinorrhea.

Section 2.0 Drug Therapy in Rhinitis

This section comprises three subsections: the first contains the newly recommended drugs, the second covers drug modifications, and the third outlines the drugs that have been withdrawn from the market.

2.1 Additions

Since the publication of the previous CHI report in January 2020, no new drugs for the management of rhinitis have been registered by the SFDA.

2.2 Modifications

- *Modifications that have been made since January 2020: Removed PA for LEVOCABASTINE 0.5 mg/ml eye drops suspension- PHENIRAMINE, NAPHAZOLINE HYDROCHLORIDE-ANTAZOLINE SULFATE, NAPHAZOLINE NITRATE- NAPHAZOLINE HYDROCHLORIDE- ANTAZOLINE PHOSPHATE, NAPHAZOLINE HYDROCHLORIDE- SODIUM CROMOGLICATE, TETRAHYDROZOLINE- FLUOROMETHOLONE, SODIUM CROMOGLICATE; All the eye/nose drops, ophthalmic solutions are given over the counter. No need for PA.*

2.3 Delisting

The medications below are no longer SFDA registered[13], therefore, it is advisable to delist the following drugs from CHI formulary. *Please refer to* ***Drugs in the disease - section 2*** *of CHI Rhinitis original clinical guidance*

- Ebastine
- Cetirizine HCL/Pseudoephedrine

Section 3.0 Key Recommendations Synthesis

History and physical examination

- Despite low level evidence specifically addressing this area, history is essential in the diagnosis of AR. Policy level: Recommendation.[5]
- When possible, physical examination should be performed with appropriate personal protective equipment to aid in the diagnosis of AR and exclusion of other conditions. When combined with patient history, it increases diagnostic accuracy. Policy level: Recommendation.[5]

Diagnostic modalities for evaluation of allergic rhinitis

- ***Use of validated survey instruments***: Validated surveys may be used to screen for AR, follow treatment outcomes and as a primary outcome measure for clinical trials. Specific tests are optimized for various clinicopathological scenarios. Policy level: Recommendation.[5]

Pharmacotherapy and procedural options

- **Oral H1 antihistamines:** Newer-generation oral antihistamines can be considered in the treatment of AR. Policy level: Strong recommendation for the use of newer-generation oral antihistamines for AR.[5]
- **Intranasal antihistamines** may be used as first- or second-line therapy in the treatment of AR. Policy level: Strong recommendation.[5]
- **Intranasal cromolyn:** DSCG (Disodium cromoglycate) may be used as a second-line treatment for AR in patients who fail INCS or intranasal antihistamines, or for short-term preventative benefit prior to allergen exposures. Policy level: Recommendation as a second-line treatment in AR.[5]
- **Intranasal corticosteroids**: non-traditional application: No evidence for non-traditional application of intranasal steroids for AR. Policy level: Recommendation against. [5]
- **Oral corticosteroids**: Although not recommended for routine use in AR, certain clinical scenarios may warrant the use of short courses of systemic corticosteroids, following a discussion of the risks and benefits with the patient. For example, oral steroids could be considered in selecting patients with significant nasal obstruction that precludes adequate penetration of intranasal agents (corticosteroids or antihistamines). In these cases, a short course of systemic corticosteroids may improve congestion and facilitate access of topical medications. No evidence supports this suggestion, and thus careful clinical judgment and risk discussion are advocated. Policy level: Strong recommendation against routine use. [5]

- **Oral decongestants:** Although not recommended for routine use in AR, pseudoephedrine can be effective in reducing nasal congestion in patients with AR; however, it should only be used as short-term/rescue therapy after a discussion of the risks and benefits with the patient (comorbidities) and consideration of alternative intranasal therapy options. Policy level: Strong recommendation against routine use in AR. In certain cases, combination therapy with an oral antihistamine may be beneficial to alleviate severe nasal congestion in short courses. [5]
- **Biologic therapies:** Monoclonal antibody (Biologic) therapies are not currently approved for the treatment of AR. Policy level: Option based upon published evidence, although not currently approved for this indication.[5]
- **Combination oral antihistamine and leukotriene receptor antagonist**: Combination LTRA and oral antihistamines should not be used as first line therapy for AR but can be considered in patients with contraindications to other alternatives. This combination should be used judiciously after carefully weighing potential risks and benefits. Policy level: Recommendation against first line therapy. [5]

Allergen immunotherapy for the treatment of allergic rhinitis:

- **Sublingual immunotherapy tablets:** SLIT tablets are recommended for patients with severe or refractory AR. Epinephrine auto-injector is recommended in the FDA labeling for approved tablets due to the rare but serious risk of anaphylaxis. Tablets for selecting antigens are available in various countries. Policy level: Strong recommendation.[5]
- Depocorticosteroids are NOT recommended due to short duration of benefit and potential for local (subdermal/dermal atrophy) and systemic side effects.[9]
- Patients requiring oral corticosteroids for allergic rhinitis should be referred to a clinical immunology/allergy/specialist for assessment.[9]
- Herbal medications: CBS: We cannot make a recommendation for or against the use of specific herbal products for the treatment of AR. [12]

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Rhinitis report** and aims to provide recommendations to aid in the management of Rhinitis. It is important to note that these recommendations should be utilized to support clinical decision-making and not replace it in the management of individual patients with Rhinitis. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

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Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

I. Prescribing Edits (ensure consistent use of abbreviations, e.g., CU, ST)

Some covered drugs may have additional requirements, rules, or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time period
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses, and sequence of therapy

Appendix B. Rhinitis Scope

Section	Rationale/updates
Section 1.1 American Academy of Otolaryngology—Head and Neck Surgery Foundation Clinical Practice Guideline: Allergic Rhinitis [**2015**}	**N/A**
Section 1.2 The American Treatment International Consensus Statement on Allergy and Rhinology: Allergic Rhinitis [**2018**]	**Section 1.1.1. International consensus statement on allergy and rhinology: Allergic rhinitis [2023]**[5] <u>Diagnostic modalities for evaluation of allergic rhinitis</u> Changes in the recommendations related to: Use of validated survey instruments, Component resolved diagnostic testing, Nasal provocation testing, Nasal cytology, Nasal histology, Rhinomanometry, Acoustic rhinometry, Peak nasal inspiratory flow, FeNO, NnO. ***Use of validated survey instruments***: Validated surveys may be used to screen for AR, follow treatment outcomes and as a primary outcome measure for clinical trials. Specific tests are optimized for various clinicopathological scenarios. Policy level: Recommendation. ***Component resolved diagnostic testing:*** Component resolved diagnostic testing is an option for diagnosis of AR by specialists. Policy level: Option ***Nasal provocation testing:*** Application of nasal provocation testing is useful in local AR and to confirm occupational rhinitis. Policy level: Option for diagnosis of AR when skin or in vitro tests are equivocal or unreliable. Recommendation for diagnosis of local AR and occupational rhinitis

	Nasal cytology: Nasal cytology could help in cases of non-allergic rhinitis to suspect local AR or in cases of AR to diagnose a mixed rhinitis. It could be considered an option in cases of negative SPT and/or serum sIgE to evaluate the presence of mucosal eosinophils and consideration of local AR or type 2 inflammation. The cut-off values for determining non-allergic rhinitis with eosinophilia syndrome (NARES) are not yet clear. Policy level: Option ***Nasal histology***: Nasal histology may be helpful in clinical research or selected cases (e.g., evaluation of tissue eosinophils during surgery). Recommendation against in routine clinical practice for AR evaluation due to invasive nature of obtaining a specimen. Policy level: Recommendation against ***Rhinomanometry***: Rhinomanometry is useful in distinguishing between structural and soft tissue causes of obstruction, when history and examination findings are not congruent, as well as a research tool. Better with individual nasal cavity assessment and four-phase rhinomanometry. Policy level: Option ***Acoustic rhinometry***: Acoustic rhinometry is most useful in research setting as opposed to as a clinical diagnostic tool. Policy level: Option. ***Peak nasal inspiratory flow*:** Use in conjunction with patient reported outcome measures to improve utility. Policy level: Option. ***Fractional exhaled nitric oxide (FeNO), Nasal nitric oxide (nNO):*** History and physical, diagnostic skin testing, or sIgE testing should be the first-line evaluation of AR. FeNO or nasal NO testing may provide additional diagnostic information if necessary but should not be routinely employed for AR diagnosis. Policy level: FeNO: Recommend against for routine diagnosis of AR. nNO: Recommend against for routine diagnosis of AR. <u>Pharmacotherapy and procedural options</u> ➢ Pharmacologic treatments are frequently employed to control AR symptoms. Depending on the specific therapy and geographic region, these may be available by prescription or over the counter. The evidence for pharmacologic options for AR has been reviewed. **Oral H1 antihistamines:** Newer-generation oral antihistamines can be considered in the treatment of AR. Policy level: Strong recommendation for the use of newer-generation oral antihistamines for AR.

	Oral corticosteroids: Although not recommended for routine use in AR, certain clinical scenarios may warrant the use of short courses of systemic corticosteroids, following a discussion of the risks and benefits with the patient. For example, oral steroids could be considered in select patients with significant nasal obstruction that precludes adequate penetration of intranasal agents (corticosteroids or antihistamines). In these cases, a short course of systemic corticosteroids may improve congestion and facilitate access of topical medications. No evidence supports this suggestion, and thus careful clinical judgment and risk discussion are advocated. Policy level: Strong recommendation against routine use. **Intranasal corticosteroids**: non-traditional application: No evidence for non-traditional application of intranasal steroids for AR. Policy level: Recommendation against. **Oral decongestants:** Although not recommended for routine use in AR, pseudoephedrine can be effective in reducing nasal congestion in patients with AR; however, it should only be used as short-term/rescue therapy after a discussion of the risks and benefits with the patient (comorbidities) and consideration of alternative intranasal therapy options. Policy level: Strong recommendation against for routine use in AR. In certain cases, combination therapy with an oral antihistamine may be beneficial to alleviate severe nasal congestion in short courses. **Intranasal cromolyn:** DSCG (Disodium cromoglycate) may be used as a second-line treatment for AR in patients who fail INCS or intranasal antihistamines, or for short-term preventative benefit prior to allergen exposures. Policy level: Recommendation as a second-line treatment in AR. **Biologic therapies:** Monoclonal antibody (biologic) therapies are not currently approved for the treatment of AR. Policy level: Option based upon published evidence, although not currently approved for this indication. **Combination oral antihistamine and intranasal corticosteroid:** Current evidence is mixed to support antihistamines as an additive therapy to INCS, as several randomized trials have not demonstrated a benefit over INCS alone for symptoms of AR. Policy level: Option. **Combination oral antihistamine and leukotriene receptor antagonist**: Combination LTRA and oral antihistamines should not be used as first line therapy for AR but can be considered in patients with contraindications to other alternatives. This combination should be used

	judiciously after carefully weighing potential risks and benefits. Policy level: Recommendation against as first line therapy. **Combination intranasal corticosteroid and leukotriene receptor antagonist** (LTRA): Consider use in patients with AR and asthma, after weighing therapeutic benefits against risks of mental health adverse effects. Policy level: Option as combination therapy if comorbid asthma present and mental health risks are considered. Not recommended for AR alone. **Combination intranasal corticosteroid (INCS) and intranasal decongestant**: Short-term combination therapy with INCS and intranasal decongestant may be considered in patients with AR refractory to combination therapy with INCS and intranasal antihistamine prior to consideration of inferior turbinate reduction or in patients declining surgery. Policy level: Option **Combination intranasal corticosteroid and intranasal ipratropium bromide**: Combining IPB with beclomethasone dipropionate can be more effective than either agent alone for the treatment of rhinorrhea in refractory AR in children and adults. Although multiple consensus guidelines have recommended, and there is evidence to support this recommendation, it is important to note that there has only been one randomized controlled trial (RCT) to study the efficacy of combined INCS and IPB therapy compared to either agent alone, and this study was performed in a combined population of patients with AR and non-allergic rhinitis. Policy level: Option. <u>Allergen immunotherapy for the treatment of allergic rhinitis:</u> ***Conventional subcutaneous immunotherapy (SCIT):*** SCIT is an appropriate treatment consideration for patients who have not obtained adequate relief with symptomatic therapy or who prefer this therapy as a primary management option, require prolonged weeks of treatment during the year, and/or wish to start treatment for the benefit of the potential secondary diseasemodifying effects of SCIT. Policy level: Strong recommendation for SCIT as a patient preference-sensitive option for the treatment of AR. Strong recommendation for SCIT over no therapy for the treatment of AR. Option for SCIT over sublingual immunotherapy (SLIT) for the treatment of AR. ***Rush subcutaneous immunotherapy:*** Aeroallergen rush SCIT is an option for AR in appropriately selected patients that do not have adequate control of their symptoms with

	symptomatic therapies. If available at practice location, the use of depigmented-polymerized allergen extracts for rush SCIT has a better safety profile compared with standard extracts. Policy level: Option ***Cluster subcutaneous immunotherapy***: Cluster SCIT can be safely implemented in clinical practice and offered to those patients eligible for SCIT that may prefer this. Policy level: Option ***Sublingual immunotherapy (SLIT):*** general considerations: Recommend tablet or aqueous SLIT in patients (adults and children) with seasonal and/or perennial AR who wish to reduce their symptoms and medication use, as well as possibly reduce the propensity to develop asthma or new allergen sensitizations. Policy level: Strong recommendation for the use of SLIT grass pollen tablet, ragweed tablet, HDM tablet, and tree pollen aqueous solution. Recommendation for SLIT for Alternaria allergy. Option for SLIT for animal allergy. Recommendation for dual-therapy SLIT in bi-allergic patients. ***Sublingual immunotherapy tablets:*** SLIT tablets are recommended for patients with severe or refractory AR. Epinephrine auto-injector is recommended in the FDA labeling for approved tablets due to the rare but serious risk of anaphylaxis. Tablets for select antigens are available in various countries. Policy level: Strong recommendation. ***Aqueous sublingual immunotherapy:*** High-dose aqueous SLIT is recommended for those patients who wish to reduce their symptoms and rescue medication use. Policy level: Recommendation. ***Epicutaneous/transcutaneous immunotherapy:*** While epicutaneous AIT may potentially have a future clinical application in the treatment of AR, at this juncture there are limited studies that show variable and limited effectiveness, and a significant rate of adverse reactions. Given the above and the availability of alternative treatments, epicutaneous AIT is not recommended at this time. Policy level: Recommendation against ***Intralymphatic immunotherapy:*** More studies are essential to establish the long-term effects of ILIT. Policy level: Option ***Combination subcutaneous immunotherapy and biologics:*** Current evidence supports that anti-IgE may be beneficial as a premedication prior to induction of cluster or rush SCIT protocols, and combination therapy may be advantageous as an option for carefully selected patients with

	persistent symptomatic AR following AIT. However, at the time of this writing, biologic therapies are not approved by the US FDA for AR alone. An individualized approach to patient management must be considered. Policy level: Option.
Section 1.3 BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis (Revised Edition **2017**; First edition 2007)	**N/A**
Section 1.4 American Pediatric rhinitis: position paper of the European Academy of Allergy and Clinical Immunology [**2013**]	**N/A**
N/A	**Section 1.2.1.** Saudi guidelines on Allergic Rhinitis in Asthma **[2014]**[7] • The KSA MoH panel recommends intranasal corticosteroids for treatment of adults with seasonal or intermittent allergic rhinitis (**Strong** recommendation; Moderate-quality evidence). • The KSA MoH panel suggests intranasal corticosteroids for treatment of adults with perennial

	or persistent allergic rhinitis (Conditional recommendation; Low-quality evidence). • The KSA MoH panel recommends intranasal corticosteroids rather than intranasal H1-antihistamines for treatment of adults with seasonal or intermittent allergic rhinitis (**Strong** recommendation; High-quality evidence). • The KSA MoH panel suggests intranasal corticosteroids rather than intranasal H1-antihistamines for treatment of adults with perennial or persistent allergic rhinitis (Conditional recommendation; Very low-quality evidence). • The KSA MoH panel suggests sublingual immunotherapy for treatment of adults with seasonal or intermittent allergic rhinitis (conditional recommendation; Moderate-quality evidence). • The KSA MoH panel suggests sublingual immunotherapy for treatment of adults with perennial/persistent allergic rhinitis (conditional recommendation; very low-quality evidence). • The KSA MoH panel suggests sublingual immunotherapy for treatment of children younger than 18 years old with seasonal or intermittent allergic rhinitis (Conditional recommendation; Moderate-quality evidence). • The KSA MoH panel suggests sublingual immunotherapy be not used for treatment of children younger than 18 years old with perennial or persistent allergic rhinitis (Conditional recommendation; very low-quality evidence
N/A	**Section 1.2.2.** Japanese guidelines for allergic rhinitis **[2020]**[8] Step-by-step approach for treatment by ARIA. Modified from ARIA 2008, Japanese version. The aim of treatment is to alleviate symptoms and remove difficulties with everyday life. Choose a treatment based on severity, disease type, and lifestyle. • **Natural courses and communication with patients (Table 3)** Combinations of pharmacotherapies based on severity and disease types and communication with patients improve patients' satisfaction and QOL. Japanese cedar pollinosis, which developed during childhood or early or late Middle Ages, should be treated in view of a prolonged course. • **Elimination and avoidance of antigens (Table 4)** In addition to cleaning, lowering humidity with dehumidifier is effective in reducing mites. For Japanese cedar pollinosis, refer to pollen

	dispersal information to consider measures to prevent pollen inhalation. For pet allergies, avoid contact with causative pets and keep dogs and cats clean. • **Pharmacotherapy (Table 5): Therapeutic agents for allergic rhinitis, with different mechanisms of action, are classified. Alpha- sympathomimetics (vasoconstrictor nose drops), which temporarily alleviate nasal blockage, are also used.** Mast cell stabilizer: Since the development of disodium cromoglicate (**DSCG**), local agents (eye drops and nasal spray) and oral agents, such as **tranilast, amlexanox, and pemirolast potassium**, have been on the market. They have mild effects. To achieve sufficient clinical effects, 2-week prolonged administration is required. Amelioration rates are increased by continuous administration. Adverse effects, such as sleepiness and dry mouth, do not occur. Chemical mediator receptor antagonists a) Histamine H1 receptor antagonists (antihistamine) (i) First-generation antihistamine: First-generation antihistamine often causes adverse effects, such as sleepiness, impaired performance, and dry mouth, but have immediate effects on sneezing and watery rhinorrhea. First-generation antihistamines are contraindicated for patients with glaucoma, prostatic hyperplasia, and asthma because of their potent anticholinergic effects. They have less central nervous system depressant actions in children than in adults. Caution should be exercised for excitatory effects, such as convulsions. Most first-generation antihistamine are marketed as OTC. (ii) Second-generation antihistamine **(Table 6)**: Second-generation antihistamine, such as **ketotifen fumarate, oxatomide, azelastine hydrochloride, emedastine difumarate, and mequitazine**, are effective to some extent for nasal blockage aside from sneezing and watery rhinorrhea. However, they may cause adverse effects, such as sleepiness and impaired performance, in early versions. Thus, caution should be exercised in administering them. The adverse effects of late versions, such as epinastine hydrochloride, ebastine, cetiridine, fexofenadine, loratadine, olopatadine hydrochloride, bepotastine besilate, and levocetirizine, have been reduced. Priority indications are mild to moderate sneezing and rhinorrhea type. Combine them with topical steroids depending on severity. A combination drug containing an antihistamine (**fexofenadine**) and an oral decongestant (**pseudoephedrine**) is now available. However, the priority indication for this combination drug is limited to the

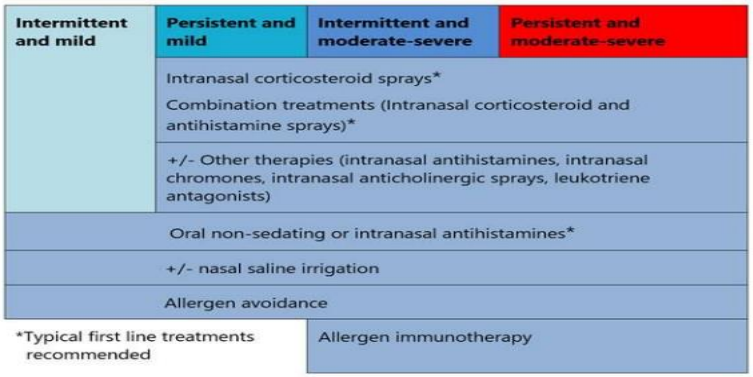
	moderate to severe nasal blockage type of pollinosis and the severe nasal blockage type of perennial allergic rhinitis. • Leukotriene receptor antagonists (antileukotrienes) **(Table 7):** Peptide leukotrienes, produced and released by mast cells, eosinophils, and macrophages, have potent relaxing effects on the vascular smooth muscles of the nasal mucosa, enhancing effects on vascular permeability, and stimulating effects on eosinophil migration. **Pranlukast** and **montelukast** are available. They are effective for nasal blockage. Their effects are increased by prolonged administration. Comparable effects with those of antihistamines can be achieved for sneezing and rhinorrhea within 4 weeks. Primary indications are treatment of symptoms of the moderate or milder nasal blockage type and those of intermediate type with nasal blockage as the chief complaint. No adverse effects of sleepiness, occur. • Prostaglandin D2 and thromboxane A2 receptor antagonist **(Table 8): Ramatroban** enhances vascular permeability in the nasal mucosa and suppresses eosinophil migration by blocking thromboxane receptors and suppresses eosinophil migration by blocking CRTh2 (chemoattractant receptor-homologous receptor expressed on Th2 cell), a part of the prostaglandin D2 receptor. They have strong delayed effects on nasal blockage. Primary indications are treatment of symptoms of nasal blockage type and those of combined type with nasal blockage as a chief complaint. The agents interact with some other medicines but cause no adverse effects of sleepiness. Th2 cytokine inhibitors: IPD inhibits the production of Th2 cytokines, such as IL-4 and IL-5, in T lymphocytes to alleviate allergic inflammation. No adverse effects of sleepiness occur. <u>Steroids</u> a) Nasal steroids **(Table 9): Beclomethasone propionate, fluticasone propionate, mometasone furoate, fluticasone furoate, and dexamethasone cipecilate** are available. All agents have strong local effects in small amounts and are poorly absorbed and readily degraded. Thus, they have few systemic adverse effects. They are highly effective for sneezing, watery rhinorrhea, and nasal mucosal swelling, and exert their effects within 1e3 days. A slight feeling of nasal irritation, feeling of dryness, and epistaxis may occur. b) Steroids for internal use: Only for intractable cases with severe nasal blockage and

	laryngopharynx symptoms, uncontrollable with nasal spray steroids, **prednisolone** (20-40 mg/day) can be administered for 4-7 days at the start of treatment. Caution should be exercised for adverse effects. Alpha-sympathomimetics (nasal topical vasoconstrictor [decongestant]): Alpha-sympathomimetics act on the a-receptors of vascular smooth muscles to cause vasoconstriction and temporarily alleviate nasal mucosal swelling. Long-term continuous administration causes medicament rhinitis. For the most severe pollinosis, they can be administered 2-3 times a day for 1-2 weeks. Other pharmacotherapy: Nonspecific thalassotherapy agents, biological preparation, and herbal medicines can be used. Adverse effects and drug interactions of therapeutic agents for allergic rhinitis **(Table 11, 12):** Therapeutic agents for allergic rhinitis are those for symptomatic treatment, used to alleviate symptoms. Caution should be exercised for harmful adverse effects and drug interactions during treatment. If they occur, take immediate measures and switch to a different treatment. • **Specific immunotherapy:** Subcutaneous specific immunotherapy (SCIT) has been used over the past century. Its demonstrated effects may be exerted via immunological mechanisms. Of note, local mast cells are decreased, the Th1/Th2 balance is altered, and regulatory T cells are increased. It takes several months to develop effects, requiring routine injection for ≥3 years. Furthermore, a systemic anaphylaxis response may develop in a small number of cases.16 The characteristics of this method are shown in **Table 13.** (1) Indications: This therapy is indicated for the treatment of patients aged 6 years, without severe systemic symptoms, to whom emergency adrenaline may be administered. Exclude patients on b-blocker therapy or with severe asthma. While this therapy has no harmful effects on pregnant women, it should not be started during pregnancy. (2) Implementation - Specialists should prescribe antigen extracts and take measures against systemic reactions, such as anaphylactic shock. - In patients with asthma complications, avoid this therapy during a paroxysmal period. In

	patients with pollinosis, avoid starting this therapy during dispersal of causative pollen. - For initial injection, reduce the threshold concentration for intradermal reaction to 1/10. Before injection, ask more than one physician or health care professional about concentration and dosage. - Before increasing an aqueous solution concentration or changing lots, conduct an intradermal test. For patients with erythema of ≥50 mm diameter, carefully conduct the test and follow-up the patients for 20-30 min after injection. - Perform therapy for at least 3 years. Therapeutic effects often continue for several years after discontinuation of administration. - Instruct patients to continue the therapy. • **Sublingual immunotherapy (SLIT)** Presently, SLIT is permitted in Japan for reactions to the allergens, Japanese cedar pollen and dust mites. The current indication for SLIT is confirmation of a positive allergen to Japanese cedar pollen or dust mites by a skin reaction or a specific IgE in a patient 5 years of age or older. The allergen is administered as a liquid or tablet every day in a dose escalation manner for at least 2 or 3 years. • The contraindications are serious illnesses that require the use of a b blocker, unstable asthma in which a systemic steroid may be required, treatment with an anti-cancer drug, severe autoimmune disease, or cases in which it is assumed the treatment should not be used in the patient because of the side effects. It cannot be begun from the dispersion period. Sublingual inoculation should be suspended in the case of pregnancy, mouth injury or ulcer, or if severe odonto-therapy is required. However, if pregnancy occurs while this therapy is being administered, allergen immunotherapy, including subcutaneous injection, is generally thought to be safe. • **Surgical treatment** Nasal blockage in allergic rhinitis is often caused by nasal deformities, such as deviated septum, hypertrophic rhinitis, and nasal polyps. In this case, perform corrective surgery of nasal cavity to improve nasal ventilation. Before pollen season, laser surgery is also performed for Japanese cedar pollinosis, but the effects of this surgery do not continue in the following year. The main purpose is to alleviate nasal blockage. Various techniques shown in **Table 14** are used. For intractable rhinorrhea, perform posterior nasal

	neurectomy. **Choice of therapy** • **Perennial allergic rhinitis** Select a therapy based on severity and disease type. Selection criteria are shown in Table 15. ➢ For mild symptoms, second-generation antihistamines, mast cell stabilizers, Th2 cytokine inhibitors, or nasal topical steroids are the first-line agents. ➢ For moderate symptoms of sneezing and rhinorrhea type, choose one of the following: (i) second-generation antihistamine, (ii) mast cell stabilizer, and (iii) nasal topical steroids. Add (i) or (ii) with (iii) as needed. For symptoms of nasal blockage or combined type, choose an agent from (i) leukotriene receptor antagonists, (ii) prostaglandin D2/thromboxane A2 receptor antagonist, (iii) Th2 cytokine inhibitor, (iv) nasal topical steroids. Combine (i) or (ii) or (iii) with (iv) as needed. ➢ For severe cases with severe sneezing and rhinorrhea, combine second-generation antihistamine with nasal spray steroids. For symptoms of nasal blockage or combined type, add nasal topical steroids with leukotriene receptor antagonists or prostaglandin D2/thromboxane A2 receptor antagonists. Additionally, a combination drug containing an antihistamine and an oral decongestant is suitable for this type. ➢ For all cases, eliminate and avoid antigens. For cases in which treatment can be continued, specific immunotherapy can also be chosen. For cases of nasal blockage type, in which the effects of pharmacotherapy are insufficient, surgical treatment can also be chosen. • **Pollinosis:** Therapy is chosen based on severity and disease type. However, the severity of pollinosis markedly changes with the amount of pollen dispersal. • The table below summarizes the choice of therapy for pollinosis based on severity.

	<table><tr><td>Severity</td><td>Primal therapy</td><td>Mild</td><td>Moderate</td><td></td><td>Severe</td><td></td></tr><tr><td>Disease types</td><td></td><td></td><td>Sneezing and rhinorrhea type</td><td>Nasal blockage type or combined type with nasal blockage as a chief complaint</td><td>Sneezing and rhinorrhea type</td><td>Nasal blockage type or combined type with nasal blockage as a chief complaint</td></tr><tr><td>Treatments</td><td>a. Second-generation antihistamine b. (Mast cell) stabilizer c. Anti-LTs agents d. Anti-PGD_2/TXA_2 agents e. Th2 cytokine inhibitors f. Nasal steroids</td><td>a. Second-generation antihistamine b. (Mast cell) stabilizer c. Anti-LTs agents d. Anti-PGD_2/TXA_2 agents e. Th2 cytokine inhibitors f. Nasal steroids</td><td>Second-generation antihistamine + Nasal steroids</td><td>Anti-LTs agents or Anti-PGD_2/TXA_2 agents + Nasal steroids + Second-generation antihistamine or Second-generation antihistamine and vasoconstrictor combination + Nasal steroids</td><td>Nasal steroids + Second-generation antihistamine</td><td>Nasal steroids + Anti-LTs agents or Anti-PGD_2/TXA_2 agents + Second-generation antihistamine or Nasal steroids + Second-generation antihistamine and vasoconstrictor combination</td></tr><tr><td></td><td>Choose one of (a), (b), (f) for sneezing and rhinorrhea type, and (c), (d), (e), (f) for nasal blockage type and combined type</td><td>Choose one of (a)-(f). Add (f) at the start of treatment with (a)-(e) as needed.</td><td></td><td></td><td></td><td>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.</td></tr><tr><td></td><td></td><td>Antihistamine for eye drops or stabilizer</td><td></td><td></td><td>Antihistamine for eye drops, stabilizer, or steroids</td><td></td></tr><tr><td></td><td></td><td></td><td></td><td></td><td>Perform surgery for cases with nasal deformities of a nasal blockage type.</td><td></td></tr><tr><td></td><td colspan="6">Allergen-specific immunotherapy</td></tr><tr><td></td><td colspan="6">Elimination and avoidance of antigens</td></tr></table> The primary therapy is for introducing the full-scale pollen dispersal period. Therefore, in case of years with small amount of pollen dispersal, the treatment is changed to seasonal treatment according to the severity. Mast cell stabilizer = Chemical mediator release inhibitors, Anti-LTs agents = Leukotriene receptor antagonists, Anti-PGD_2/TXA_2 agents = Prostaglandin D_2/Thromboxane A_2 receptor antagonists.
N/A	**Section 1.2.3**. ASCIA: Australasian Society of Clinical Immunology and Allergy, Allergic Rhinitis Clinical Update [**2022**][11] **<u>Aeroallergen minimization</u>** • Avoidance or minimization of confirmed allergens may assist some people in reducing the severity of their allergic rhinitis symptoms. • This can be difficult to achieve for house dust mite and pollens. • Avoidance strategies must only be developed if the allergens are clinically significant. • Realistic consideration must also be given to the family's ability to act in strategies. **<u>Pharmacotherapy and other treatment options</u>** The duration and severity of allergic rhinitis symptoms are useful in guiding therapy, as shown in the table below.



Definitions: *Intermittent*: 4 days/week or >4 weeks · *Mild*: Normal sleep, no impairment of daily activities, normal work, or school performance. · *Moderate-severe:* One or more of abnormal sleep, impairment of activities, abnormal work or school performance, troublesome symptoms.

- Allergic rhinitis pharmacotherapy options table.
- Allergic rhinitis pharmacotherapy principles.:
  - ➔ When symptoms improve, pharmacotherapy doses may be reduced.
  - ➔ A trial of pharmacotherapy initiated by primary care physicians and maintained for at least 4 weeks is recommended before considering referral to a specialist if no improvement.
  - ➔ If a patient is a competitive athlete, it is important to ensure medications suggested are permitted. For example, pseudoephedrine used in some decongestants is subject to certain restrictions.
- Non-sedating antihistamines, Intranasal corticosteroids (INCS)
- Other treatment options: Saline nasal irrigation, Intranasal chromones such as sodium cromoglycate, Intranasal ipratropium, Oral leukotriene antagonists, Decongestants, Systemic steroids.
- Ocular management:
  - ➔ Non-pharmacological therapy: Flush allergen from eyes (saline washes, liquid-tear preparations), Cool compresses.

	➔ Ocular or oral antihistamines or topical mast cell stabilizers may be used to control itchy/watery eyes.
	➔ Intranasal corticosteroids can reduce ocular symptoms of allergic rhinitis.
	➔ Ocular corticosteroids should only be prescribed in consultation with, and regular review by an Ophthalmologist.
	• Management of allergic rhinitis in pregnancy
	  • Up to 20% of pregnant women develop symptoms of rhinitis, typically in second trimester, improving 2 weeks after delivery.
	  • Medications for allergic rhinitis should only be used during pregnancy if the benefit to the mother justifies the potential risk to the fetus.
	  • There are few well-controlled clinical studies in pregnant women examining the safety of many of the medications used in allergic rhinitis.
	  • Ideally pharmacotherapy should be avoided in the first trimester of pregnancy. However, there are some oral antihistamines and intranasal corticosteroid sprays with an "A" category used by many pregnant women without any proven increase in harmful effects on fetus.
	  • Saline nasal irrigation and intranasal chromones are safe in pregnancy.
	• Management of allergic rhinitis during lactation: Recommend taking medication after feeding the infant to minimize any potential infant exposure. (table)
	<u>Dietary restrictions are not recommended.</u>
	• There is no evidence that allergic rhinitis is due to food allergies, although conditions may coexist.
	• Food elimination is not recommended unless there is a confirmed allergy, and has potential for serious nutritional consequences, especially in young children.
	• Restricting cow's milk (dairy) products is often popular, even if there is no confirmed food allergy, but studies do not show any change in mucus production following dietary modification.
	• Allergen immunotherapy

	• Surgery • Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)
N/A	**Section 1.2.4.** Ashford and St. Peter's Hospitals NHS Foundation Trust Pediatric Allergic Rhinitis guidelines [**2023**][10] Step up and down to achieve symptom control. Allow 8-12 weeks at each step. ➔ **Step 1, Allergen Avoidance:** Nasal rinsing - with saline solution ➔ **Step 2, Regular long-acting non-sedating antihistamine:** Cetirizine or Loratadine **OR Regular nasal corticosteroid spray:** Avamys or Mometasone Furoate or Flixonase Start with antihistamine if pruritus dominant or nasal corticosteroid if congestion dominant: ➔ **Step 3, Regular oral antihistamine, and nasal corticosteroid** ➔ **Step 4, Switch to 2nd line oral antihistamine**: Fexofenadine (from 6yrs) ➔ **Step 5**, **Regular nasal antihistamine + corticosteroid spray and oral antihistamine**: Dymista nasal spray (from 12yrs) + Fexofenadine ➔ **Step 6, Add in Leukotriene receptor antagonist:** Montelukast. ➔ **Step 7, Allergen specific immunotherapy** If eye symptoms – consider sodium cromoglicate eye drops. Who to refer for Skin prick testing: To aid allergen avoidance, Diagnostic uncertainty. Who to refer to ENT: Failed nasal corticosteroid spray + antihistamine for assessment of adenoidal hypertrophy/ consideration of turbinate surgery, Suspected Obstructive Sleep Apnoea.
N/A	**Section 1.2.5.** Rhinitis **2020**: A practice parameter update[12] This guideline contains systematically developed recommendations intended to optimize care of adult and adolescent patients (>_12-15 years of age) and to assist physicians and/or other health care practitioners and patients to make decisions regarding diagnosis and therapy for rhinitis. Even though many treatments are approved for younger children, the application of recommendations to children would be partially based on data extrapolation from adult studies and would therefore be less certain. 38. CBS: We recommend that the clinician complete a detailed history and a physical

	examination in a patient presenting with symptoms of rhinitis. Strong Low 39. CBS: We recommend that for patients presenting with rhinitis symptoms, a review of all current medications should be completed to assess whether drug-induced rhinitis may be present. Strong Ungraded 40. CBS: We recommend that aeroallergen skin prick testing or sIgE testing be completed to confirm the diagnosis of AR in a patient with a history consistent with AR. Strong High 41. CBS: We recommend that the clinician not perform food skin prick testing or sIgE for foods in their routine evaluation of a patient presenting with the signs and symptoms compatible with the diagnosis of AR. Strong Ungraded 42. CBS: We suggest that the use of a validated instrument (e.g., scoring system, scale, or questionnaire) be considered to help determine the severity of rhinitis and to monitor the degree of disease control. Conditional Low 43. CBS: We recommend against prescribing a first-generation antihistamine and are in favor of a second-generation antihistamine when prescribing an oral antihistamine for the treatment of AR. Strong High 44. CBS: We suggest that the clinician not select the oral LTRA montelukast for the initial treatment of AR due to reduced efficacy when compared with that of other agents. Furthermore, serious neuropsychiatric events that may include suicidal thoughts or actions have been reported in some patients taking montelukast. As advised by the FDA, montelukast should be used to treat AR only in patients who are not treated effectively with or cannot tolerate other alternative therapies. Conditional Very low 45. CBS: We recommend that the clinician not select an oral LTRA for the treatment of NAR. Conditional Ungraded 46. CBS: We suggest that for the treatment of very severe or intractable AR, the clinician may consider a short course (5-7 d) of oral corticosteroids. Conditional Very low 47. CBS: We suggest that for the treatment of very severe or intractable AR, the clinician not prescribe a depot parenteral corticosteroid for AR due to the potential risks of systemic and local corticosteroid side effects. Conditional Low

	48. CBS: We recommend that the clinician offer INAH as an initial treatment option for patients with SAR. Strong High 49. CBS: We recommend that the clinician offer INAH as a first-line monotherapy option for patients with NAR. Strong High 50. CBS: We recommend that the clinician offer INAH as a first-line option for patients with intermittent AR. Conditional Ungraded 51. CBS: We recommend that when choosing monotherapy for persistent AR, INCS be the preferred medication. Strong High 52. GRADE: We recommend that for the initial treatment of moderate/severe SAR in patients ≥15 y of age, the clinician use an INCS over an LTRA. (Also see Recomendation 7.) Strong High 53. CBS: We suggest that the use of intranasal decongestants be short term and used for intermittent or episodic therapy of nasal congestion. (However, see also Recommendation 26.) Conditional Low 54. CBS: We suggest that in patients having severe mucosal edema, which impairs the delivery of other intranasal agents, an intranasal decongestant be considered for up to 5 d of use. Conditional Ungraded 55. CBS: We suggest that oral decongestant agents be used with caution in older adults and children younger than 4 y old, and in patients of any age who have a history of cardiac arrhythmia, angina pectoris, cerebrovascular disease, uncontrolled hypertension, bladder outlet obstruction, glaucoma, hyperthyroidism, or Tourette syndrome. Conditional Low 56. CBS: We recommend that oral decongestants be avoided during the first trimester of pregnancy. Strong Low 57. CBS: We suggest that patients with PAR and NAR who have rhinorrhea as their main nasal symptom be offered intranasal ipratropium. Conditional Low for PAR; moderate for NAR 58. CBS: We suggest that intranasal cromolyn be offered as an option to be taken just prior to allergen exposure to reduce symptoms of AR from episodic allergen exposures. Conditional Very low 59. GRADE: We suggest that the clinician consider the combination of an INCS and an INAH for

	the initial treatment of moderate/severe nasal symptoms of SAR in patients ≥12 y old. Conditional High 60. CBS: We suggest that the clinician consider the combination of an INCS and an INAH for moderate/severe SAR and PAR that is resistant to pharmacologic monotherapy. * Conditional Moderate 61. CBS: We suggest that the clinician consider the combination of an INCS and an INAH for moderate/severe NAR that is resistant to pharmacologic monotherapy. * Conditional Low 62. CBS: We suggest that for patients taking an INCS who have persistent rhinorrhea, the clinician may consider the addition of intranasal ipratropium. Conditional Moderate 63. CBS: We suggest that patients with persistent nasal congestion unresponsive to an INCS or to an INCS-INAH combination be offered combination therapy with addition of an intranasal decongestant for up to 4 wk. Conditional Low 64. CBS: We suggest that for patients with AR and nasal congestion uncontrolled with an oral antihistamine, the clinician consider the addition of pseudoephedrine, when tolerated. (See Recommendation 18.) Conditional Moderate 65. CBS: We suggest that for SAR the clinician not combine the oral LTRA montelukast with an oral antihistamine for symptoms not controlled with an oral antihistamine. (See Recommendation 7.) Conditional Moderate 66. GRADE: We recommend that the clinician not prescribe, as initial treatment, a combination of an oral antihistamine and an intranasal steroid in preference to monotherapy with an intranasal steroid in patients ≥ 12 y of age with symptoms of SAR. Strong Moderate 67. CBS: We suggest that the clinician not prescribe the combination of an oral antihistamine and an INCS in preference to monotherapy with an intranasal steroid in all patients with SAR and PAR. Conditional Very low. 68. CBS: We suggest against the addition of the oral LTRA montelukast to an INCS for AR, due to the lack of adequate evidence of improved efficacy and concerns for serious neuropsychiatric events from montelukast. (See Recommendation 7.) Conditional Very low 69. CBS: We suggest that the clinician offer an INCS as a first-line therapy for NAR. Conditional

	Low 70. CBS: We suggest that the clinician offer an INAH as a first-line therapy for NAR. Conditional Very low 71. CBS: We suggest that AIT (subcutaneous or sublingual tablets) be offered through shared decision making to patients with moderate/severe AR who (1) are not controlled with allergen avoidance and/or pharmacotherapy or (2) choose immunotherapy as the preferred method of treatment (e.g., due to the desire to avoid the adverse effects, costs, or long-term use of pharmacotherapy) and/or (3) desire the potential benefit of immunotherapy to prevent or reduce the severity of comorbid conditions, such as asthma. Conditional Moderate 72. CBS: We suggest that AIT (subcutaneous or sublingual tablets) be considered for patients with controlled mild/moderate asthma with coexisting AR. Conditional Moderate 73. CBS: We cannot make a recommendation for or against the use of acupuncture for the treatment of AR. N/A Very low. 74. CBS: We cannot make a recommendation for or against the use of specific herbal products for the treatment of AR
N/A	**Section 1.2.6.** Current treatment options for allergic rhinitis: a review [**2023**][11]

Appendix C. MeSH Terms PubMed

C.1 PubMed Search for Rhinitis:

Query	Filters	Search Details	Results
((((((Rhinitis[MeSH Terms]) AND (Rhinitis[Title/Abstract])) OR (Rhinitides[Title/Abstract])) OR (Nasal Catarrh[Title/Abstract])) OR (Catarrh, Nasal[Title/Abstract])) OR (Catarrhs, Nasal[Title/Abstract])) OR (Nasal Catarrhs[Title/Abstract])	Guideline, in the last 5 years	(("Rhinitis"[MeSH Terms] AND "Rhinitis"[Title/Abstract]) OR "Rhinitides"[Title/Abstract] OR "nasal catarrh"[Title/Abstract] OR "catarrh nasal"[Title/Abstract] OR (("catarrhal"[All Fields] OR "common cold"[MeSH Terms] OR ("common"[All Fields] AND "cold"[All Fields]) OR "common cold"[All Fields] OR "Catarrh"[All Fields] OR "Catarrhs"[All Fields]) AND "Nasal"[Title/Abstract]) OR (("nasalance"[All Fields] OR "nasality"[All Fields] OR "nasalization"[All Fields] OR "nasalized"[All Fields] OR "nasally"[All Fields] OR "nose"[MeSH Terms] OR "nose"[All Fields] OR "Nasal"[All Fields] OR "nasals"[All Fields]) AND "Catarrhs"[Title/Abstract])) AND ((y_5[Filter]) AND (guideline[Filter]))	5

Appendix D. Treatment Algorithm

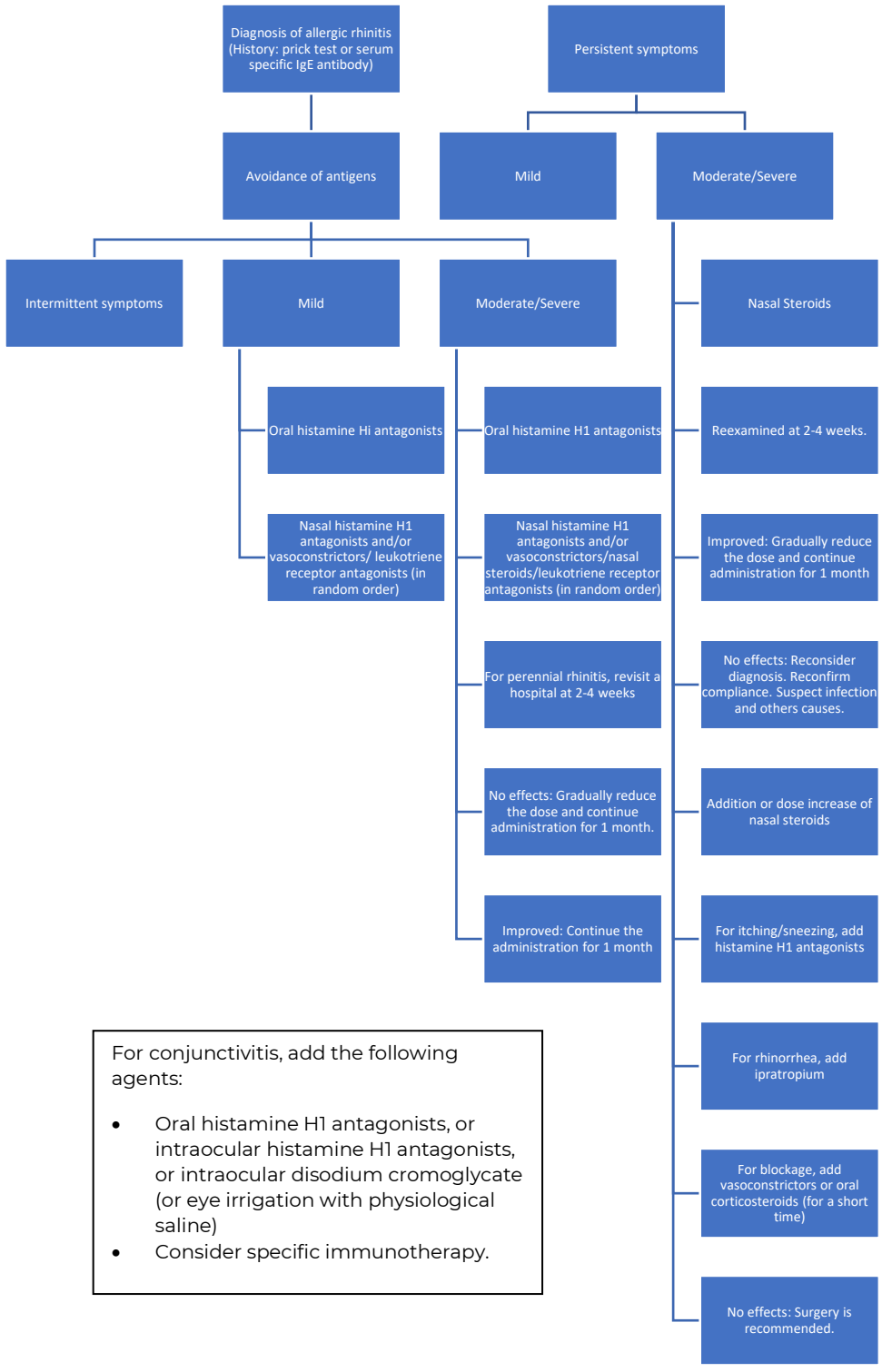


Figure 1. *Step by step approach for the treatment of allergic rhinitis (AR)*