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Drug Class Update: Medications for Allergies (Nasal Allergy Inhalers, 1st Generation Antihistamines, 2nd Generation Antihistamines)

Date of Review: February 2026

Date of Last Review: August 2022
Dates of Literature Search: 05/25/2022 – 10/24/2025

Current Status of PDL Class:
See **Appendix 1**.

Purpose for Class Update:
Review new evidence for intranasal allergy inhalers and oral antihistamines for use in chronic rhinosinusitis, allergic rhinitis, and urticaria. The prescription medications have Food and Drug Administration (FDA) approval for management of seasonal and/or perennial allergic rhinitis, which is not currently funded by the Oregon Health Plan (OHP), unless the patient has a co-morbidity such as asthma.

Plain Language Summary:
- Rhinitis refers to inflammation of the nasal passages. This inflammation can cause many symptoms including sneezing, itching, nasal congestion, and runny nose. Allergic rhinitis is caused by a reaction to pollen from trees, grasses, and weeds, dust mites, molds, and animal dander that are breathed in from the environment.
- Treatment of allergic rhinitis includes reducing exposure to allergen and other triggers combined with medicines. Nasal sprays that contain antihistamines or steroids are frequently recommended to relieve symptoms. Some medicines are available without a prescription (over the counter) while others require a prescription.
- Chronic spontaneous urticaria is itching that has lasted for more than 6 weeks with no known cause. Antihistamines such as cetirizine, loratadine, or fexofenadine may relieve the constant itching.
- The Oregon Health Authority (OHA) will pay for fluticasone nasal spray for people who are less than 21 years of age and will pay for the oral antihistamines cetirizine and loratadine without needing documentation as to why it is needed. For all other medicines, providers must explain to the OHA why someone needs the medicine before OHA will pay for it. This process is called prior authorization

Research Questions:
1. Do nasal corticosteroids, antihistamines, or mast cell stabilizers differ in safety or effectiveness when used to treat allergic rhinitis?
2. Do oral antihistamines differ in safety or effectiveness when used to treat allergic rhinitis or urticaria?

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3. Are there subgroups of patients based on demographics (e.g., age, race, gender), concomitant comorbidities and medications, or pregnancy status, for which one nasal inhaler or oral antihistamine is more effective or associated with fewer harms?

Conclusions:

- No recently published, high-quality systematic reviews were identified.
- A 2023 international guideline updated recommendations for evaluation and treatment of allergic rhinitis.[1] Intranasal corticosteroids are strongly recommended as first-line therapy for management of allergic rhinitis.[1] Second-generation oral antihistamines are strongly recommended for management of allergic rhinitis.[1] Intranasal antihistamines are recommended as first- or second-line therapy.[1] Cromolyn is recommended as second-line therapy.[1]
- Canada's Drug Agency (CDA) recommends that RYALTRIS, the combination olopatadine/mometasone nasal spray should not be reimbursed by Canadian public drug plans for the symptomatic treatment of moderate-to-severe seasonal allergic rhinitis and associated ocular symptoms in adults, adolescents, and children aged 6 years and older.[2] Evidence from 3 clinical trials (2 in adolescent and adult patients with seasonal allergic rhinitis and 1 in children with seasonal allergic rhinitis) demonstrated that olopatadine/mometasone nasal spray improved nasal and eye symptoms in people with seasonal allergic rhinitis compared to placebo.[2] However, compared to monotherapy with mometasone nasal spray, the improvements were not clinically meaningful in adolescents and adults, and there was no comparative evidence available in children.[2]
- The 2021 publication from the British Association of Dermatologists provides evidence-based recommendations for the management of chronic spontaneous urticaria.[3] Most of the evidence is derived from studies in adult patients as there is very little published evidence for pediatric patients aged less than 12 years.[3] Recommendations focused on antihistamines include:
    - First-line antihistamines for managing chronic spontaneous urticaria in children include chlorpheniramine, cetirizine, desloratadine, loratadine, and fexofenadine (Expert Opinion).[3]
    - For people with chronic spontaneous urticaria offer a second-generation H_1-antihistamine (cetirizine, desloratadine, fexofenadine, loratadine, levocetirizine) using a regular daily licensed dose (Strong Recommendation).[3]
    - Do not offer first-generation H_1 antihistamines routinely, unless there is no alternative due to concerns about their short- and long-term effects on the central nervous system (Strong Recommendation).[3]
    - Do not increase the dose of first generation H_1 antihistamines (Strong Recommendation).[3]
- In 2024, XHANCE (fluticasone) nasal spray received expanded FDA approval for treatment of adults with chronic rhinosinusitis (CRS) without nasal polyps.[43] Prior to this approval, fluticasone nasal spray was approved for treatment of CRS with nasal polyps.[43]
- There is insufficient evidence to show that there are subgroups of patients based on demographics (based on age, ethnicity, comorbidities, disease duration or severity), for which one treatment for those with allergic rhinitis is more effective or associated with fewer adverse events.

Recommendations:

- After a review of recent evidence, no changes to the Preferred Drug List (PDL) are recommended.
- Create a PDL class for the first-generation oral antihistamines.
- Remove prior authorization (PA) for preferred nasal inhalers in adults.
- After evaluation of costs in executive session the committee voted to:
    - Make general oral hydroxyzine pamoate capsules, hydroxyzine tablets, cyproheptadine tablets, diphenhydramine tablets, diphenhydramine capsules, chlorpheniramine tablets, diphenhydramine liquid and cyproheptadine syrup preferred and all other first generation antihistamines nonpreferred.

- Make levocetirizine, desloratadine, and fexofenadine tablets, and cetirizine solution preferred.
- Make azelastine nasal allergy inhaler preferred.

Summary of Prior Reviews and Current Policy:

- The intranasal allergy drugs were reviewed by the Pharmacy and Therapeutics (P & T) Committee at the August 2022 meeting. No changes were made to the PDL based on review of recently published evidence. Prior authorization criteria were removed for intranasal allergy products in children and adolescents 20 years of age and younger with rhinitis to enhance the ability to grow, develop, or participate in school per the Early and Periodic Screening, Diagnostic and Treatment (EPSDT) Medicaid benefit.
- The second-generation oral antihistamines were last reviewed by the P & T Committee in May 2015. A Drug Effectiveness Review Project (DERP) systematic review summarized the available evidence that was shared with the Committee. Comparative systematic reviews and trials found insufficient evidence to support superior efficacy/effectiveness or harms of any single second-generation antihistamine. The first-generation oral antihistamines have never been reviewed by the P & T Committee.
- All non-preferred intranasal allergy medications and oral antihistamines require PA for Oregon Health Plan (OHP) funded indications. Fluticasone propionate is the only preferred drug on the PDL, and all other intranasal corticosteroids are non-preferred (**Appendix 1**). Non-steroid intranasal allergy drugs are non-preferred due to lack of evidence for OHP-funded conditions. Cetirizine and loratadine are the preferred second-generation oral antihistamines, all other antihistamines are nonpreferred and require PA (**Appendix 1**). Use of non-preferred intranasal corticosteroids and oral antihistamines for OHP-funded conditions is restricted as outlined in the PA criteria in **Appendix 3**.

Background:

Allergic Rhinitis

Allergic rhinitis is an immunoglobulin (Ig) E-mediated condition that occurs after exposure to indoor or outdoor allergens, such as dust mites, insects, animal dander, molds, and pollen.[4] Symptoms include rhinorrhea, sneezing, nasal congestion, and itching of the nose, eyes, ears, and throat.[5] Allergic rhinitis affects up to 60 million people in the United States annually, can have a major impact on quality of life, and poses a substantial economic burden on society.[6] Self-reported rates of allergic rhinitis are 10% to 30% of adults and as many as 40% of children in the United States.[6] A report from the American Academy of Allergy, Asthma & Immunology (AAAAI) estimates that about 19 million employed adults have allergic rhinitis, and that approximately $4.5 billion in direct costs and 3.8 million in lost work and school days are attributable to this disease annually.[7] Allergic rhinitis is also a significant cause of decreased work productivity/presenteeism (work interference) and school performance.[6] Allergic rhinitis can, by itself, introduce significant inattention, impaired cognition, and decreased daytime school performance.[6] Quality of life issues associated with rhinitis include disturbed sleep; daytime somnolence and fatigue; irritability; depression; impairment of physical and social functioning; and attention, learning, and memory deficits.[6]

Validated clinical surveys for allergic rhinitis often include questions about congestion, rhinorrhea and/or sneezing and may either be representative of current symptoms or reflective of a period of days or weeks.[8] One patient reported outcome measure is the Total Nasal Symptom (TNS-4) score, which is typically administered as a survey comprised of 4 questions about runny nose, nasal itching, sneezing, and congestion.[8] The TNS-4 score is the sum of scores for each of the 4 symptoms, measured on an ordinal scale of 0, 1, 2 or 3 representing no symptoms, mild, moderate, or severe symptoms respectively for a maximum score of 12.[9] The TNS-4 is the most accepted primary efficacy variable that is rated for drug approval in allergic rhinitis by the Food and Drug Administration (FDA).[10] Relatively few articles have calculated minimal clinically important difference (MCID) scores for allergic rhinitis outcome measures, and those that have suggest widely different approaches.[11] The Agency for Healthcare Research and Quality (AHRQ) recommended the MCID be equal to 30% of the maximum TNS-4 score

(i.e., ±3.6 points on a 12 point scale).[11] The 12-hour reflective total nasal symptoms score (rTNSS) has also been reported in clinical studies evaluating efficacy of intranasal products.[11] Both morning and evening assessments are added together so the rTNSS can range from 0 to 24 points.[11] For the rTNSS scale of 0 to 24 points, the comparable MCID thresholds would be 0.46 points (by regression analysis) or 0.56 points (by meta-analysis).[11] Despite the very small change in scoring, which calls into question significant clinical benefit, there are no other validated methods to determine MCID for clinical trials of allergic rhinitis medications.[11]

Symptoms of rhinitis are classified based on the temporal pattern (seasonal, perennial, or episodic), frequency, and severity.[4] Mild rhinitis severity is present when symptoms are not interfering with quality of life such as impairment of daily activities, work or school performance, leisure activities, and sleep.[6] Moderate or severe rhinitis is present when symptoms are troublesome or there is negative impact on any of these quality of life parameters.[6] Symptom frequency has been divided into intermittent (less than 4 days per week or less than 4 consecutive weeks per year) and persistent (4 or more days per week and 4 or more consecutive weeks per year).[6] Allergic rhinitis may also be classified by the temporal pattern of environmental exposure to a triggering allergen: 1) seasonal (e.g., from pollens); 2) perennial (year-round, e.g., dust mites); or 3) from episodic allergen exposures not normally encountered in the patient's environment, such as visiting a home with pets.[6] In the United States, allergic rhinitis has traditionally been viewed as either seasonal or perennial, and it is this classification system that the FDA uses when approving new medications for allergic rhinitis.[6]

Second-generation oral antihistamines (e.g., cetirizine, desloratadine, fexofenadine, levocetirizine, loratadine) are recommended for management of allergic rhinitis.[6] The overall efficacy of first-generation antihistamines (e.g., diphenhydramine, hydroxyzine, chlorpheniramine) compared with second-generation antihistamines for the management of allergic rhinitis symptoms has not been adequately studied.[6] The older first-generation antihistamines are lipophilic and readily cross the blood-brain barrier.[12] This causes unwanted adverse effects such as sedation, drowsiness, fatigue, and impaired concentration, and memory as well as anti-muscarinic effects.[12] The second-generation antihistamines are highly selective for the histamine H_1 receptor, lipophobic, and have limited penetration across the blood-brain barrier which minimizes their adverse effects.[12] Because of significant side effects, first-generation antihistamines have not been recommended for the treatment of allergic rhinitis.[12]

Intranasal pharmacologic options for the treatment of rhinitis include corticosteroids, antihistamines, mast cell stabilizers, and anticholinergics (see **Table 1**). Intranasal corticosteroids are the mainstay of treatment for persistent allergic rhinitis.[5] Specific intranasal corticosteroid agents include beclomethasone, budesonide, ciclesonide, flunisolide, fluticasone, mometasone, and triamcinolone.[13] Mometasone, fluticasone furoate, ciclesonide, and triamcinolone are approved by the Food and Drug Administration (FDA) for use in children 2 years of age and older.[13] They act by decreasing the influx of inflammatory cells and inhibiting the release of cytokines, thereby reducing inflammation of the nasal mucosa.[5] Intranasal corticosteroids also help reduce symptoms of sneezing, itching, rhinorrhea, and congestion.[6] Limited data suggest that intranasal corticosteroids can also reduce allergic eye symptoms, such as itching, tearing, redness, and puffiness.[6] In comparative studies, intranasal corticosteroids have shown superior efficacy to oral antihistamines and leukotriene inhibitors in controlling nasal symptoms, with no significant difference in the relief of ocular symptoms.[14] There is no evidence that one intranasal corticosteroid is superior over another product.[5] Onset of action for intranasal corticosteroids starts at time points ranging from 3 to 5 hours to 60 hours after first dosing.[14] Patients with known seasonal allergic rhinitis should start prophylactic treatment with intranasal corticosteroids several days before the pollen season with an evaluation of the patient's response in 2 weeks.[14]

Table 1. Nasal Allergy Medications: Indications and Age Ranges.[15,16]

Drug Name (Trade Name)	FDA Indication(s)	Formulation	OTC
Intranasal Antihistamines			

Azelastine (ASTEPRO ALLERGY, generic)	Seasonal Allergic Rhinitis; Perennial Allergic Rhinitis ≥6 yo	205.5 mcg/spray	YES
Azelastine (ASTEPRO)	Seasonal Allergic Rhinitis; ≥ 2 yo to 6 yo Perennial Allergic Rhinitis; ≥ 6 months to 6 yo	137 mcg/spray	NO
Olopatadine (PATANSASE, generic)	Seasonal Allergic Rhinitis ≥6 yo	665 mcg/spray	NO
Combination Intranasal Antihistamine/Corticosteroids			
Azelastine-Fluticasone propionate (DYMISTA, generic)	Seasonal Allergic Rhinitis ≥6 yo	137 mcg-50 mcg/spray	NO
Olopatadine-Mometasone (RYALTRIS)	Seasonal Allergic Rhinitis ≥12 yo	665 mcg-25mcg/spray	NO
Intranasal Corticosteroids			
Beclomethasone dipropionate (BECONASE AQ)	Seasonal Allergic Rhinitis; Perennial Allergic Rhinitis; Nonallergic Rhinitis; Nasal Polyps ≥6 yo	42 mcg/spray	NO
Beclomethasone (QNASL)	Seasonal Allergic Rhinitis; Perennial Allergic Rhinitis ≥4 yo	40 mcg and 80 mcg/spray	NO
Budesonide (RHINOCORT ALLERGY, generic)	Seasonal Allergic Rhinitis; Perennial Allergic Rhinitis ≥6 yo	32 mcg/spray	YES
Ciclesonide (OMNARIS)	Seasonal Allergic Rhinitis ≥6 yo Perennial Allergic Rhinitis ≥12 yo	50 mcg/spray	NO
Ciclesonide (ZETONNA)	Seasonal Allergic Rhinitis; Perennial Allergic Rhinitis ≥12 yo	37 mcg/spray	NO
Flunisolide (generic)	Seasonal Allergic Rhinitis; Perennial Allergic Rhinitis ≥6 yo	25 mcg/spray	NO
Fluticasone furoate (FLONASE SENSIMIST)	Allergic Rhinitis ≥2 yo	27.5 mcg/spray	YES
Fluticasone propionate (FLONSASE ALLERGY RELIEF, generic)	Seasonal Allergic Rhinitis; Perennial Allergic Rhinitis; Nonallergic Rhinitis ≥4 yo	50 mcg/spray	YES
Fluticasone propionate (EXHANCE)	Nasal polyps ≥ 18 yo	93 mcg/spray	NO
Mometasone (NASONEX, generic)	Seasonal Allergic Rhinitis ≥2 yo	50 mcg/spray	YES
Triamcinolone (NASACORT ALLERGY 24 HOUR, generic)	Allergic Rhinitis ≥2 yo	50 mcg/spray	YES
Intranasal Mast Cell Stabilizer			
Cromolyn (generic)	Allergic Rhinitis ≥2 yo	5200 mcg/spray	YES
Intranasal Anticholinergics			
Ipratropium (generic)	Rhinorrhea associated with Perennial Allergic Rhinitis; Seasonal Allergic Rhinitis; and Nonallergic Rhinitis ≥5 yo	21 mcg and 42 mcg/spray	NO
Abbreviations: FDA = Food and Drug Administration; mcg = micrograms; mg = milligrams; OTC = over the counter; yo = years old			

The most common local adverse effects of intranasal corticosteroids include nasal dryness, throat irritation, burning, hoarseness, sneezing, and bitter aftertaste.[17] The effect of intranasal corticosteroids on growth in children has been investigated in controlled studies using both knemometry in short-term studies (2 to 4 weeks) and stadiometry in long-term (12 months) studies.[14] A meta-analysis of 8 randomized controlled trials (n=755) with appropriate controls showed that, compared to children using placebo, mean growth was significantly lower among children using intranasal corticosteroids in trials using knemometry (n = 4 studies) and that there was no significant growth difference in studies using stadiometry (n = 4 studies).[18] The data suggests that intranasal corticosteroids might have deleterious effects on short-term growth in children, but the heterogeneity in the stadiometry studies makes the effects on long-term growth suppression unclear.[14] All intranasal corticosteroids carry a warning that long-term use may restrict growth in children, so using the lowest effective dose is advised to avoid negative growth effects.[19]

Two intranasal antihistamines, azelastine and olopatadine, are FDA-approved for the treatment of allergic rhinitis. Intranasal antihistamines have a rapid onset, are more effective for nasal congestion than oral antihistamines, are more effective for ocular symptoms than intranasal corticosteroids, and show consistent reduction in symptoms and improvement in quality of life in randomized controlled trials (RCTs) compared to placebo.[14] They are less effective for nasal congestion than intranasal corticosteroids.[14] For relief of symptoms of seasonal allergic rhinitis, intranasal antihistamines are equal or superior to oral antihistamines, and may benefit patients for whom oral antihistamine treatment fails.[6] Intranasal antihistamines have a more rapid onset of 15 to 30 minutes compared to 150 minutes for oral antihistamines and have fewer adverse effects than oral therapy.[6] Adverse effects observed with intranasal antihistamines include a bitter aftertaste, headache, nasal irritation, epistaxis, and sedation.[4] Although intranasal antihistamines are an option if symptoms do not improve with nonsedating oral antihistamines, their use as first- or second-line therapy is limited by adverse effects and twice daily dosing.[20] Either intranasal antihistamines or intranasal corticosteroids may be offered as first-line monotherapy for nonallergic rhinitis.[6]

Intranasal cromolyn is available over the counter and is thought to inhibit the degranulation of mast cells, thereby preventing histamine release.[4] Although safe for general use, it is not considered first-line therapy for allergic rhinitis because it is less effective than intranasal corticosteroids and is administered three or four times daily.[21] Although evidence supports the use of intranasal ipratropium, an anticholinergic, for severe rhinorrhea, it is not effective for other nasal symptoms.[22] Adverse effects of ipratropium include dryness of the nasal mucosa, epistaxis, and headache.[4] The recommended administration is two to three times daily.[4]

Oral decongestants are medications that act on adrenergic receptors, which leads to vasoconstriction of small blood vessels (such as those in the nasal mucosa), resulting in relief of nasal congestion symptoms in allergic rhinitis.[1] The most commonly used oral decongestants are pseudoephedrine and phenylephrine, which are sympathomimetic vasoconstrictors that differ in their selectivity to adrenoceptors.[1] Due to the oral administration of pseudoephedrine and phenylephrine, both drugs act systemically and can lead to side effects such as insomnia, headache, nervousness, anxiety, tremors, palpitations, urinary retention, increased blood pressure, and other adverse effects.[1]

Intranasal decongestants (oxymetazoline, xylometazoline, and phenylephrine) are alpha-adrenergic agonists acting as topical vasoconstrictors reducing edema/tissue thickness. Clinically, short-term use results in reduction of nasal congestion/blockage, with little to no effect on allergic symptoms such as sneezing, rhinorrhea, or nasal itching.[1] Onset of action is within 10 minutes , and duration of the effect lasts up to 12 hours.[1] Intranasal decongestants can be helpful for short-term relief of nasal congestion. Intranasal decongestants can provide effective short-term relief of nasal congestion in patients with allergic rhinitis during an acute flare, but chronic use is not recommended due to risk of rhinitis medicamentosa (increased symptomatic nasal congestion secondary to medication overuse).[1]

Leukotriene receptor antagonists (LTRAs) have been studied in the treatment of allergic rhinitis.[1] Montelukast is approved by the FDA for the treatment of seasonal allergic rhinitis in adults and children over 2 years of age, and for perennial allergic rhinitis in adults and children over 6 months of age.[1] While LTRA monotherapy has been consistently shown to be superior to placebo for the treatment of allergic rhinitis, there is now significant evidence that alternative inhaled nasal corticosteroids are superior to LTRAs in terms of symptom reduction and quality of life improvement.[1] In March 2020, the FDA announced a safety concern regarding montelukast and potential serious neuropsychiatric events, including suicidal thoughts.[1] A boxed warning, the FDA's most prominent warning, was added to prescribing information.[1] The FDA advised further that in allergic rhinitis, montelukast should be reserved for patients who are not treated effectively with or cannot tolerate other allergy medications.[1]

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Allergic rhinitis is also often associated with asthma, allergic conjunctivitis, atopic dermatitis, rhinosinusitis, and sleep apnea.[6] Allergic rhinitis, is notably present in about 75% to 80% of all patients with asthma and in nearly 100% with allergic asthma, is associated with increased asthma-related hospitalizations and higher total annual medical costs.[6] Intranasal use of antihistamines and mast cell stabilizers has not been adequately studied in conditions outside of allergic rhinitis. However, intranasal corticosteroids have been studied and used for several other conditions that are currently funded by the Oregon Health Plan (OHP). For example, allergic rhinitis and asthma are often comorbid diseases. An epidemiologic association between allergic rhinitis and asthma has been consistently demonstrated across patient populations. Given the association, it is hypothesized that reducing inflammation in the upper airway with an intranasal corticosteroid may improve asthma symptoms.[23] Attempts have also been made to reduce frequency of episodes of obstructive sleep apnea by changing the characteristics of the upper airway using therapies such as intranasal corticosteroids.[24] Acute sinusitis is frequently caused by a viral infection and is a common reason for primary care visits. Inflammation of nasal mucosa plays an essential role in the development of sinusitis. In addition to treating seasonal and perennial rhinitis, corticosteroids might be beneficial in reducing inflammation in the treatment of sinusitis.[25] Lastly, chronic rhinosinusitis (CRS) is a group of disorders characterized by chronic inflammation of the mucosa of the nose and paranasal sinuses, with symptoms that persist for more than 12 weeks without complete resolution of symptoms.[26] It is most commonly classified as CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP). The use of corticosteroids for the management of CRS is supported by a high level of evidence, with particularly strong evidence for CRSwNP.[26]

Chronic Spontaneous Urticaria

Chronic spontaneous urticaria (also known as chronic idiopathic urticaria) is defined as recurrent pruritic hives with or without angioedema for more than 6 weeks.[27] Chronic urticaria affects about 1% of the world population of all ages, mostly young and middle-aged women.[28] It generally lasts for several years (longer than 1 year in 25–75% of patients) and often takes more than one year before effective management is implemented.[28] Lesions result from degranulation of cutaneous mast cells, which leads to the release of histamine, the major mediator of pruritic wheals and angioedema, as well as the release of leukotrienes, prostaglandins, and platelet-activating factors.[29] Proinflammatory cytokines and vasoactive factors are also released, which results in vasodilatation and leakage of plasma from the vascular system in and below the skin.[29] Although most cases of chronic urticaria are idiopathic, this condition has been reported in association with infections (e.g., hepatitis B and C, Epstein–Barr virus, herpes simplex virus, mycoplasma, Helicobacter pylori, helminthic infestation), rheumatologic diseases (e.g., systemic lupus erythematosus, juvenile rheumatoid arthritis), thyroid disease, neoplasms (particularly lymphoreticular cancers and other lymphoproliferative disorders), ovarian tumors, and oral contraceptive use.[29]

A joint initiative of Dermatology Section of the European Academy of Allergology and Clinical Immunology (EAACI), the EU-founded network of excellence, the Global Allergy and Asthma European Network (GA²LEN), the European Dermatology Forum (EDF), and the World Allergy Organization (WAO) resulted in publication of 2018 guidance for diagnosis and management of chronic urticaria.[30] The use of patient-reported outcome measures such as the urticaria activity score (UAS), the angioedema activity score (AAS), the CU quality of life questionnaire (CU-Q2oL), the angioedema quality of life questionnaire (AE-QoL) and the urticaria control test (UCT) in studies and clinical practice has helped to better define the effects and impact of CU on patients.[30] The UAS7 is based on the assessment of key urticaria signs and symptoms (wheals and pruritus), which are documented by the patient over 7 consecutive days using a 4 point scale. A score of 0 indicates no itching or wheals, while a score of 3 indicates intense wheals (> 50 wheals/24 hours) and intense itching as presented in **Table 2**.[30] The UCT has only 4 items with a clearly defined cut-off for patients with “well-controlled” versus “poorly controlled” disease, and it is thus suited for the management of patients in routine clinical practice.[30] The cut-off value for a well-controlled disease is 12 of 16 possible points.[30]

Table 2. The Urticaria Activity Score for Assessing Disease Activity in Chronic Spontaneous Urticaria[30]

Score	Wheals	Pruritus
0	None	None

1	Mild (< 20/24 hours)	Mild (present but not annoying or troublesome)
2	Moderate (20-50/24 hours)	Moderate (troublesome but does not interfere with normal daily activity or sleep)
3	Intense (> 50/24 hours)	Intense (severe pruritus, which is sufficiently troublesome to interfere with normal daily activity or sleep)

First-line CSU treatment recommendations include oral second-generation antihistamines (cetirizine, loratadine, fexofenadine) taken on a regular basis at standard doses instead of as needed (PRN) for itching.[29] Second-generation antihistamines have advantages over first-generation antihistamines (e.g., chlorpheniramine, cyproheptadine, hydroxyzine, diphenhydramine) because of a slower histamine receptor dissociation rate, thus a longer duration of action; less central nervous system penetration making them less soporific, and minimal activity at nonhistaminic receptors, thus reducing their likelihood for significant side effects.[31] Adults with CSU unresponsive to standard second-generation antihistamine dosing may require dosing increased up to four times the recommended daily dose to manage symptoms (also known as up-dosing).[29] There is less evidence and formal guidance for up-dosing second-generation antihistamines in children.[29]

Methods:
A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. The Medline search strategy used for this review is available in **Appendix 2**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, the Oregon Mental Health Clinical Advisory Group (MHCAG), the Scottish Intercollegiate Guidelines Network (SIGN), and Canada's Drug Agency (CDA-AMA) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

New Systematic Reviews: No recent, high-quality systematic reviews were identified.
After review, 11 systematic reviews were excluded due to poor quality (e.g., indirect network meta-analyses or failure to meet AMSTAR criteria), wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).[32-42]

New Guidelines:
High Quality Guidelines:

International Consensus Statement on Allergy And Rhinology: Allergic Rhinitis
A 2023 international guideline updated recommendations for evaluation and treatment of allergic rhinitis.[1] In this publication, the second and third generation antihistamines are classified as newer-generation antihistamines and include cetirizine, desloratadine, fexofenadine, levocetirizine, and loratadine.[1] First-generation antihistamines (e.g., diphenhydramine and chlorpheniramine) have anticholinergic side effects and can cross the blood–brain barrier, resulting in central nervous system effects such as sedation and drowsiness.[1] These side effects can be more pronounced in the elderly, so first-generation antihistamines should be used with caution in this population.[1] Newer-generation antihistamines block peripheral histamine$_1$-receptors without crossing the blood–brain barrier which prevents central nervous system side effects.[1] Several newer-generation antihistamines are metabolized in the liver by cytochrome P450

enzymes.[1] As a result, prescribers should be conscious of concomitant administration of other drugs that are either processed by cytochrome P450 or drugs that are cytochrome P450 inducers because concurrent administration can either increase or decrease the plasma concentration of the antihistamine.

The data existing on the use of H_2 antihistamines in allergic rhinitis is limited in scope and quality, with very little addition to the literature in the past decade.[1] The objective findings of improved nasal airway resistance suggest that the H_2 histamine receptor does modulate nasal tissue response to histamine.[1] However, the clinical significance of this mechanism is not clear, particularly in the context of modern treatment algorithms.[1] Given the relatively manageable side effect profile and costs of H_2 antihistamines, they may offer patients with otherwise recalcitrant allergic rhinitis symptoms an additional treatment option. However, additional investigation on the efficacy of H_2 antihistamines in combination with other topical medications may be beneficial in the future.[1]

Intranasal antihistamines (azelastine, olopatadine) were compared to oral antihistamine monotherapy in 8 studies, with superiority of intranasal antihistamine in 3 studies, and equivalency in 5 studies.[1] Most of the included studies set a minimum enrollment age of 12 years or older. Three studies that included children aged between 6 and 12 years old found superiority of intranasal antihistamine to placebo in improving symptoms and quality of life.[1] No study reported any serious adverse effects from use of an intranasal antihistamine.[1] These formulations are noted to be generally well tolerated, with taste aversion being the most reported adverse effect.[1] Olopatadine was reported to have better sensory attributes than azelastine in one study.[1] Other reported adverse effects were uncommon, with somnolence, headache, epistaxis, and nasal discomfort each occurring in less than 10% of patients treated with azelastine or olopatadine.[1]

Intranasal corticosteroids are first-line therapy for the treatment of allergic rhinitis by virtue of their superior efficacy in controlling nasal symptoms.[1] The benefits of using intranasal corticosteroids outweigh the risks when used to treat seasonal or perennial allergic rhinitis.[1] Intranasal corticosteroid sprays have undesirable local adverse effects, such as epistaxis, with increased frequency compared to placebo in prolonged administration studies.[1] There are no apparent negative effects on the hypothalamic-pituitary axis.[1]

The results in head-to-head comparisons between antihistamine and pseudoephedrine monotherapy are contradictory.[1] While some studies showed that antihistamine monotherapy was more effective than pseudoephedrine, other studies have had different findings.[1] Monotherapy with either treatment (i.e., pseudoephedrine or antihistamine) was more effective than placebo.[1] An analysis of the effectiveness of phenylephrine compared to placebo has shown that phenylephrine (up to 40 mg six times daily) is not superior to placebo in relieving nasal congestion symptoms in allergic rhinitis.[1] Little evidence for benefit in controlling symptoms other than nasal congestion.[1] In certain cases, combination therapy with an oral antihistamine may be beneficial to alleviate severe nasal congestion in short courses.[1] Although not recommended for routine use in allergic rhinitis, pseudoephedrine can be effective in reducing nasal congestion; 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.[1]

Cromolyn is a mast cell stabilizer that inhibits the release of mast cell mediators that promote IgE-mediated inflammation.[1] It has a rapid onset of action with efficacy lasting up to 8 hours, taken as one spray 3-6 times daily.[1] Ultimately, the role of cromolyn as a primary treatment for allergic rhinitis is limited given its lower efficacy when compared to intranasal corticosteroids and potential compliance challenges secondary to a frequent dosing regimen.[1] The medication can also be administered as a preventive strategy, prior to allergen exposure to reduce the development of allergic rhinitis symptoms.[1] A summary of pharmacotherapy recommendations and strength of evidence are presented in **Table 3.**

Table 3. Pharmacotherapy Recommendations for Treatment of Allergic Rhinitis[1]

Medication	Grade of Evidence	Policy	Interpretation
Second Generation Antihistamines	A	Strong Recommendation For Use in Allergic Rhinitis	Newer-generation oral antihistamines are strongly recommended.
Cromolyn	A	Recommend For a Second-Line Treatment Use in Allergic Rhinitis	Primarily used to prevent the onset of symptoms prior to allergen exposure, but it also can be used to treat symptoms once they occur. Less effective for nasal symptoms compared to intranasal antihistamines and intranasal corticosteroids.
Intranasal Antihistamines	A	Recommendation For Use in Allergic Rhinitis	Intranasal antihistamines should be used as first- or second-line therapy.
Intranasal Corticosteroids	A	Strong Recommendation For Use in Allergic Rhinitis	Intranasal corticosteroids should be used as first-line therapy
Intranasal Decongestants	B	Option For Use in Allergic Rhinitis	Option for short-term use
Leukotriene Receptor Antagonists	A	Recommend Against	Leukotriene receptor antagonists should not be used as monotherapy.
Oral Corticosteroids	B	Strong Recommendation Against Use in Allergic Rhinitis	Oral corticosteroids are not recommended.
Oral Decongestants	A	Strong Recommendation Against Use in Allergic Rhinitis	Not recommended for routine treatment. Short-term use of combination H1 antihistamine and oral decongestant may be considered.
First Generation Antihistamines	B	No Recommendation	Insufficient data

Canada's Drug Agency: Recommendations for Coverage of Olopatadine/Mometasone Nasal Spray

Canada's Drug Agency (CDA) recommends that RYALTRIS, the combination olopatadine/mometasone nasal spray should not be reimbursed by Canadian public drug plans for the symptomatic treatment of moderate-to-severe seasonal allergic rhinitis and associated ocular symptoms in adults, adolescents, and children aged 6 years and older.[2] Evidence from 3 clinical trials (2 in adolescent and adult patients with seasonal allergic rhinitis and 1 in children with seasonal allergic rhinitis) demonstrated that olopatadine/mometasone nasal spray improved nasal and ocular symptoms in people with seasonal allergic rhinitis compared to placebo.[2] However, compared to monotherapy with mometasone nasal spray, the improvements were not clinically meaningful in adolescents and adults, and there was no comparative evidence available in children.[2] Based on the evidence reviewed during the initial meeting and the reconsideration meeting, the Canadian Drug Expert Committee (CDEC) could not determine whether olopatadine/mometasone nasal spray would address the unmet needs of patients because of the uncertainty around the benefit of this combination therapy versus appropriate active comparators.[2]

British Association of Dermatologists: Guidance for Management of Chronic Urticaria

The 2021 publication from the British Association of Dermatologists provides evidence-based recommendations for the management of urticaria.[3] Most of the evidence is derived from studies in adult patients as there is very little published evidence for pediatric patients aged less than 12 years.[3] Recommendations focused on antihistamines include:

- Consider using appropriate validated scoring systems to assess disease activity and impact, for example Dermatology Life Quality Index (DLQI), weekly Urticaria Activity Score 7 (UAS7), Angioedema Activity Score (AAS) and/or Urticaria Control Test (UCT) (Expert Opinion).[3]
- First-line antihistamines for managing chronic urticaria in children include chlorpheniramine, cetirizine, desloratadine, loratadine, and fexofenadine (Expert Opinion).[3]
- For people with chronic spontaneous urticaria offer a second-generation antihistamine (cetirizine, desloratadine, fexofenadine, loratadine, levocetirizine) using a regular daily licensed dose (Strong Recommendation).[3]
- Do not offer first-generation H_1 antihistamines routinely, unless there is no alternative, due to concerns about their short- and long-term effects on the central nervous system (Strong Recommendation).[3]
- Do not up dose (i.e. increasing the dose above the licensed dose) first generation antihistamines (Strong Recommendation).[3]
- Offer up dosing (i.e. increasing the dose above the licensed dose) of a single second-generation antihistamine, by up to fourfold the licensed dose, to people whose symptoms are inadequately controlled by the standard licensed dose, provided it is tolerated and there is no caution or contraindication (Strong Recommendation).[3]
- Consider montelukast, in addition to a second-generation H_1-antihistamine, in people whose symptoms are inadequately controlled by standard and increased doses of second-generation H_1-antihistamines (Weak Recommendation).

New Formulations or Indications:

March 2024: XHANCE (fluticasone) nasal spray received expanded FDA-approval for treatment of adults with chronic rhinosinusitis (CRS) without nasal polyps.[43] The recommended dose is 186 mcg (1 spray per nostril) or 372 mcg (2 sprays per nostril) twice daily.[43] Prior to this approval, fluticasone nasal spray was approved for treatment of CRS with nasal polyps.[43] Efficacy of fluticasone nasal spray in patients with CRS without nasal polyps was evaluated in two 24-week, placebo-controlled RCTs.[43] In both trials, patients were randomized 1:1:1 to receive fluticasone 186 mcg twice daily, fluticasone 372 mcg twice daily, or placebo, all administered nasally for 24 weeks.[43] All patients enrolled had at least 2 active nasal symptoms (congestion/obstruction, discharge, facial pain or pressure, reduction or loss of smell) with a minimum nasal congestion score of at least 1.5 out of 3 and a baseline CT scan showing at least 25% opacification of both ethmoid and at least 1 maxillary sinus.[43]

In both trials, the coprimary efficacy endpoints were 1) change from baseline at Week 4 in the composite symptom score (CSS) as determined by patients using a daily diary and 2) change from baseline at Week 24 in percent opacified sinus volume.[43] CSS was the sum of the individual nasal symptom scores for congestion/obstruction, facial pain/pressure, and nasal discharge, each rated by the patient on a 0 to 3 categorical severity scale (0 = none, 1 = mild, 2 = moderate, 3 = severe) in the morning immediately prior to the next dose.[43] Total CSS ranges from 0 to 9.[43] Sinus opacification was measured by CT scan and scored using a 3-dimensional computer-assisted volumetric assessment using software to quantify the average percent of opacified volume in the ethmoid and

maxillary sinuses.[43] In Trial 3 fluticasone was statistically more efficacious than placebo in relieving symptoms and reducing sinus volume. In Trial 4 fluticasone only showed more efficacy in reducing symptoms compared to placebo, but no difference in opacified sinus volume. Results from both trials are presented in **Table 4**. The most common adverse events reported with fluticasone nasal spray in patients with CRS without nasal polyps were epistaxis, headache, and nasopharyngitis.[43]

Table 4. Least Square Mean Change in Composite Symptom Scores at Week 4 and Percent Opacified Sinus Volume at Week 24[43]

	Placebo	Fluticasone 186 mcg BID	Fluticasone 372 mcg BID	Difference (95% CI) 186 mcg BID vs. Placebo	Difference (95% CI) 372 mcg BID vs. Placebo
Trial 3	N=75	N=72	N=73		
Baseline Mean CSS	6.2	5.9	6.0	-0.7 (-1.3 to -0.2)	-0.9 (-1.5 to -0.4)
LSM change from baseline in CSS at Week 4	-0.8	-1.5	-1.7		
Baseline Percent of Opacified Sinus Volume	64.1	60.5	61.5	-7.5 (-12.1 to -2.8)	-5.9 (-10.6 to -1.3)
LSM change from baseline in Percent Opacified Sinus Volume at Week 24	0.4	-7.0	-5.5		
Trial 4	N=41	N=41	N=40		
Baseline Mean CSS	5.7	5.5	5.8	-0.9 (-1.6 to -0.2)	-0.9 (-1.6 to -0.2)
LSM change from baseline in CSS at Week 4	-0.7	-1.6	-1.6		
Baseline Percent of Opacified Sinus Volume	61.9	63.0	60.7	-0.5 (-6.8 to 5.9)	-3.2 (-9.5 to 3.2)
LSM change from baseline in Percent Opacified Sinus Volume at Week 24	-5.3	-5.7	-8.4		
Abbreviations: BID = twice daily; CI = confidence interval; CSS = composite symptom score; LSM = least square mean; N=number					

Randomized Controlled Trials:

A total of 136 citations were manually reviewed from the initial literature search. After further review, 136 citations were excluded because of wrong study design (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).

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Appendix 1: Current Preferred Drug List

Nasal Inhalers

Generic	Brand	Route	Form	PDL	OTC
fluticasone propionate	FLUTICASONE PROPIONATE	NASAL	SPRAY SUSP	Y	F
fluticasone propionate	XHANCE	NASAL	AER BR.ACT	N	F
beclomethasone dipropionate	QNASL	NASAL	HFA AER AD	N	F
beclomethasone dipropionate	QNASL CHILDREN	NASAL	HFA AER AD	N	F
ciclesonide	ZETONNA	NASAL	HFA AER AD	N	F
triamcinolone acetonide	24 HOUR NASAL ALLERGY	NASAL	SPRAY	N	O
flunisolide	FLUNISOLIDE	NASAL	SPRAY	N	F
ipratropium bromide	IPRATROPIUM BROMIDE	NASAL	SPRAY	N	F
triamcinolone acetonide	NASAL ALLERGY	NASAL	SPRAY	N	O
flunisolide	NASALIDE	NASAL	SPRAY	N	F
triamcinolone acetonide	TRIAMCINOLONE ACETONIDE	NASAL	SPRAY	N	O
fluticasone propionate	24 HOUR ALLERGY	NASAL	SPRAY SUSP	N	O
fluticasone propionate	ALLERGY RELIEF	NASAL	SPRAY SUSP	N	O
fluticasone propionate	FLUTICASONE PROPIONATE	NASAL	SPRAY SUSP	N	O
mometasone furoate	ALLERGY NASAL	NASAL	SPRAY/PUMP	N	O
azelastine HCl	AZELASTINE HCL	NASAL	SPRAY/PUMP	N	F
azelastine/fluticasone	AZELASTINE-FLUTICASONE	NASAL	SPRAY/PUMP	N	F
budesonide	BUDESONIDE	NASAL	SPRAY/PUMP	N	O
azelastine/fluticasone	DYMISTA	NASAL	SPRAY/PUMP	N	F
mometasone furoate	MOMETASONE FUROATE	NASAL	SPRAY/PUMP	N	F
mometasone furoate	MOMETASONE FUROATE	NASAL	SPRAY/PUMP	N	O
mometasone furoate	NASONEX 24HR ALLERGY	NASAL	SPRAY/PUMP	N	O
olopatadine HCl	OLOPATADINE HCL	NASAL	SPRAY/PUMP	N	F
ciclesonide	OMNARIS	NASAL	SPRAY/PUMP	N	F
olopatadine HCl/mometasone	RYALTRIS	NASAL	SPRAY/PUMP	N	F
budesonide	BUDESONIDE	NASAL	SPRAY/PUMP		O

First Generation Oral Antihistamines

Generic	Brand	Route	Form	PDL	OTC
carbinoxamine maleate	CARBINOXAMINE	ORAL	LIQUID		F
carbinoxamine maleate	CARBINOXAMINE MALEATE	ORAL	LIQUID		F
carbinoxamine maleate	CARBINOXAMINE PD	ORAL	LIQUID		F
carbinoxamine maleate	CARBZAH	ORAL	LIQUID		F
carbinoxamine maleate	CARBINOXAMINE MALEATE ER	ORAL	SUS ER 12H		F
carbinoxamine maleate	KARBINAL ER	ORAL	SUS ER 12H		F

carbinoxamine maleate	CARBINOXAMINE MALEATE	ORAL	TABLET	F
carbinoxamine maleate	RYVENT	ORAL	TABLET	F
chlorpheniramine maleate	ED CHLORPED JR	ORAL	SYRUP	O
chlorpheniramine maleate	CHLO-AMINE	ORAL	TAB CHEW	O
chlorpheniramine maleate	ALLER-CHLOR	ORAL	TABLET	O
chlorpheniramine maleate	ALLERGY	ORAL	TABLET	O
chlorpheniramine maleate	ALLERGY RELIEF	ORAL	TABLET	O
chlorpheniramine maleate	ALLERGY-TIME	ORAL	TABLET	O
clemastine fumarate	CLEMASTINE FUMARATE	ORAL	SYRUP	F
clemastine fumarate	CLEMASTINE FUMARATE	ORAL	TABLET	F
clemastine fumarate	CLEMSZA	ORAL	TABLET	F
cyproheptadine HCl	CYPROHEPTADINE HCL	ORAL	SYRUP	F
cyproheptadine HCl	CYPROHEPTADINE HCL	ORAL	TABLET	F
dexbrompheniramine maleate	ALA-HIST IR	ORAL	TABLET	O
dexchlorpheniramine maleate	RYCLORA	ORAL	SOLUTION	F
dexchlorpheniramine maleate	DEXCHLORPHENIRAMINE MALEATE	ORAL	TABLET ER	F
diphenhydramine HCl	ALLERGY	ORAL	CAPSULE	O
diphenhydramine HCl	ALLERGY RELIEF	ORAL	CAPSULE	O
diphenhydramine HCl	BANOPHEN	ORAL	CAPSULE	O
diphenhydramine HCl	DIPHENHYDRAMINE HCL	ORAL	CAPSULE	F
diphenhydramine HCl	DIPHENHYDRAMINE HCL	ORAL	CAPSULE	O
diphenhydramine HCl	DIPHENHYDRAMINE HCL	ORAL	ELIXIR	F
diphenhydramine HCl	ALLERGY RELIEF	ORAL	LIQUID	O
diphenhydramine HCl	CHILDREN'S ALLERGY	ORAL	LIQUID	O
diphenhydramine HCl	CHILDREN'S ALLERGY RELIEF	ORAL	LIQUID	O
diphenhydramine HCl	DIPHEDRYL	ORAL	LIQUID	O
diphenhydramine HCl	DIPHENHYDRAMINE HCL	ORAL	LIQUID	O
diphenhydramine HCl	M-DRYL	ORAL	LIQUID	O
diphenhydramine HCl	SILADRYL DAS	ORAL	LIQUID	O
diphenhydramine HCl	ANTITUSSIVE COUGH SYRUP	ORAL	SYRUP	O
diphenhydramine HCl	HYDRAMINE	ORAL	SYRUP	O
diphenhydramine HCl	CHILDREN'S ALLERGY RELIEF	ORAL	TAB CHEW	O
diphenhydramine HCl	ALLER-G-TIME	ORAL	TABLET	O
diphenhydramine HCl	ALLERGY	ORAL	TABLET	O
diphenhydramine HCl	ALLERGY RELIEF	ORAL	TABLET	O
diphenhydramine HCl	BANOPHEN	ORAL	TABLET	O
diphenhydramine HCl	DIPHENHYDRAMINE HCL	ORAL	TABLET	O

hydroxyzine HCl	HYDROXYZINE HCL	ORAL	SOLUTION		F
hydroxyzine HCl	HYDROXYZINE HCL	ORAL	TABLET		F
hydroxyzine pamoate	HYDROXYZINE PAMOATE	ORAL	CAPSULE		F
hydroxyzine pamoate	VISTARIL	ORAL	CAPSULE		F
pyrilamine maleate	PEDIACLEAR-8	ORAL	LIQUID		O
triprolidine HCl	HISTEX PD	ORAL	DROPS		O
triprolidine HCl	HISTEX PD	ORAL	DROPS	N	O
triprolidine HCl	HISTEX PDX	ORAL	DROPS	N	O
triprolidine HCl	PEDIACLEAR PD	ORAL	DROPS		O
triprolidine HCl	TRIPROLIDINE HCL	ORAL	DROPS		O
triprolidine HCl	HISTEX	ORAL	LIQUID		O
triprolidine HCl	HISTEX	ORAL	TAB CHEW	N	O

Second-Generation Antihistamine

Generic	Brand	Route	Form	PDL	OTC
loratadine	ALLERGY RELIEF	ORAL	SOLUTION	Y	O
cetirizine HCl	CETIRIZINE HCL	ORAL	SOLUTION	Y	O
loratadine	CHILDREN'S ALLERGY	ORAL	SOLUTION	Y	O
loratadine	CHILDREN'S ALLERGY RELIEF	ORAL	SOLUTION	Y	O
loratadine	CHILDREN'S LORATADINE	ORAL	SOLUTION	Y	O
loratadine	LORATADINE	ORAL	SOLUTION	Y	O
loratadine	LORATADINE ALLERGY	ORAL	SOLUTION	Y	O
loratadine	ALLERGY RELIEF	ORAL	TAB RAPDIS	Y	O
loratadine	LORATADINE	ORAL	TAB RAPDIS	Y	O
cetirizine HCl	ALL DAY ALLERGY	ORAL	TABLET	Y	O
loratadine	ALL DAY ALLERGY RELIEF	ORAL	TABLET	Y	O
loratadine	ALLERCLEAR	ORAL	TABLET	Y	O
cetirizine HCl	ALLERGY RELIEF	ORAL	TABLET	Y	O
loratadine	ALLERGY RELIEF	ORAL	TABLET	Y	O
cetirizine HCl	CETIRIZINE HCL	ORAL	TABLET	Y	O
loratadine	LORATADINE	ORAL	TABLET	Y	F
loratadine	LORATADINE	ORAL	TABLET	Y	O
cetirizine HCl	ALL DAY ALLERGY RELIEF	ORAL	CAPSULE	N	O
loratadine	ALLERGY RELIEF	ORAL	CAPSULE	N	O
fexofenadine HCl	CHILDREN'S ALLERGY	ORAL	ORAL SUSP	N	O
cetirizine HCl	CETIRIZINE HCL	ORAL	SOLUTION	N	F

cetirizine HCl	CETIRIZINE HCL	ORAL	SOLUTION	N	O
cetirizine HCl	CHILDREN'S ALL DAY ALLERGY	ORAL	SOLUTION	N	O
cetirizine HCl	CHILDREN'S ALLERGY RELIEF	ORAL	SOLUTION	N	O
cetirizine HCl	CHILDREN'S CETIRIZINE HCL	ORAL	SOLUTION	N	O
levocetirizine dihydrochloride	LEVOCETIRIZINE DIHYDROCHLORIDE	ORAL	SOLUTION	N	F
cetirizine HCl	CETIRIZINE HCL	ORAL	TAB CHEW	N	O
loratadine	CHILDREN'S ALLERGY RELIEF	ORAL	TAB CHEW	N	O
cetirizine HCl	CHILDREN'S CETIRIZINE HCL	ORAL	TAB CHEW	N	O
loratadine	CHILDREN'S LORATADINE	ORAL	TAB CHEW	N	O
desloratadine	DESLORATADINE	ORAL	TAB RAPDIS	N	F
levocetirizine dihydrochloride	24HR ALLERGY RELIEF	ORAL	TABLET	N	O
fexofenadine HCl	ALLER-EASE	ORAL	TABLET	N	O
fexofenadine HCl	ALLERGY RELIEF	ORAL	TABLET	N	O
levocetirizine dihydrochloride	ALLERGY RELIEF	ORAL	TABLET	N	O
desloratadine	CLARINEX	ORAL	TABLET	N	F
desloratadine	DESLORATADINE	ORAL	TABLET	N	F
fexofenadine HCl	FEXOFENADINE HCL	ORAL	TABLET	N	F
fexofenadine HCl	FEXOFENADINE HCL	ORAL	TABLET	N	O
levocetirizine dihydrochloride	LEVOCETIRIZINE DIHYDROCHLORIDE	ORAL	TABLET	N	F
levocetirizine dihydrochloride	LEVOCETIRIZINE DIHYDROCHLORIDE	ORAL	TABLET	N	O

Appendix 2: Medline Search Strategy

Ovid MEDLINE(R) ALL <1946 to October 17, 2025> - Steroid Nasal Inhalers

1	exp Beclomethasone/	3147
2	exp Budesonide/	5356
3	ciclesonide.mp.	506
4	flunisolide.mp.	391
5	exp Fluticasone/	3540
6	exp Mometasone Furoate/	962
7	exp Triamcinolone Acetonide/ or exp Triamcinolone/	10371
8	Nasal Absorption/ or Administration, Intranasal/	17788
9	1 or 2 or 3 or 4 or 5 or 6 or 7	22608
10	8 and 9	1027
11	exp Asthma/	150082
12	exp Sleep Apnea Syndromes/	47720
13	exp Sinusitis/	25085
14	exp Rhinitis, Allergic/	25124
15	11 or 12 or 13 or 14	237939
16	10 and 15	730
17	limit 16 to (english language and humans and yr="2022 -Current")	32

Ovid MEDLINE(R) ALL <1946 to October 17, 2025> - Antihistamine Nasal Inhalers

1	azelastine.mp.	851
2	exp Olopatadine Hydrochloride/	318
3	exp Ipratropium/	1934
4	exp Cromolyn Sodium/	4144
5	exp Nasal Absorption/ or exp Administration, Intranasal/	17788
6	1 or 2 or 3 or 4	7104
7	5 and 6	358
8	exp Sleep Apnea Syndromes/	47720
9	exp Sinusitis/	25085
10	exp Asthma/	150082
11	exp Rhinitis, Allergic/	25124
12	8 or 9 or 10 or 11	237939
13	7 and 12	241
14	limit 13 to (english language and humans and yr="2022 -Current")	16

Author: Moretz

Date: February 2026

Ovid MEDLINE(R) ALL <1946 to October 24, 2025> - Oral Antihistamines

1	Histamine H1 Antagonists/ or Histamine Antagonists/ or carbinoxamine.mp.	21868
2	Chlorpheniramine/	2016
3	Clemastine/	357
4	Cyproheptadine/	2276
5	dexchlorpheniramine.mp.	185
6	Diphenhydramine/	4122
7	Hydroxyzine/	1472
8	Pyrilamine/	1797
9	tripolidine.mp.	7
10	Loratadine/	1306
11	Cetirizine/	1490
12	fexofenadine.mp.	1186
13	levocetirizine.mp.	577
14	desloratadine.mp.	780
15	exp Rhinitis, Allergic/th [Therapy]	4864
16	exp Urticaria/th [Therapy]	1683
17	15 or 16	6532
18	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	33068
19	17 and 18 5	51
20	limit 19 to (english language and humans and yr="2015 -Current")	88

Author: Moretz

Date: February 2026

Intranasal Allergy Drugs

Goals:
- Restrict use of intranasal allergy inhalers for conditions funded by the OHP and where there is evidence of benefit.
- Treatment for allergic or non-allergic rhinitis is funded by the OHP only if it complicates asthma, sinusitis or obstructive sleep apnea. Only intranasal corticosteroids have evidence of benefit for these conditions.
- Allow case-by-case review for members covered under the EPSDT program.

Length of Authorization:
- 30 days to 12 months

Requires PA:
- Non-preferred intranasal corticosteroids and antihistamines
- Intranasal ipratropium and cromolyn sodium

Covered Alternatives:
- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/
- Preferred intranasal corticosteroids, preferred antihistamines DO NOT require prior authorization for children and adolescents up to their 21st birthday.

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code	
2. Does patient have an evidence-supported and co-morbid condition funded by the OHP? • Chronic Sinusitis (J320-J329) • Acute Sinusitis (J0100; J0110; J0120; J0130; J0140; J0190) • Sleep Apnea (G4730; G4731; G4733; G4739)	**Yes:** Document ICD10 code(s) and approve for up to 12 months for chronic sinusitis or sleep apnea and approve for no more than 30 days for acute sinusitis	**No:** Go to #3

Approval Criteria		
2. Is there a diagnosis of asthma or reactive airway disease in the past 1 year (J4520-J4522; J45901-J45998)?	**Yes:** Go to #4	**No:** Go to #5
3. Is there a claim for an *orally* inhaled corticosteroid in the past 90 days? Note: Asthma-related outcomes are not improved by the addition of an intranasal corticosteroid to an orally inhaled corticosteroid.	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Approve for up to 6 months
4. Has the patient had lack of benefit, intolerance, or have a contraindication a preferred products? Note: Preferred products are reviewed for comparative effectiveness and safety by the Oregon Pharmacy & Therapeutics Committee	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness
5. Is the patient eligible for EPSDT review AND is there documentation that the condition is of sufficient severity that it impacts the patient's health (e.g., quality of life, function, growth, development, ability to participate in school, perform activities of daily living, etc.)?	**Yes:** Approve for 6 months	**No:** Go to #6

Approval Criteria		
6. RPh only: Is the diagnosis funded by the OHP?	**Funded:** Deny; medical appropriateness. (e.g, COPD; Obstructive Chronic Bronchitis; or other Chronic Bronchitis [J449; J40; J410-418; J42; J440-449]), Use clinical judgment to APPROVE for 1 month to allow time for appeal. Message: "The request has been denied because it is considered medically inappropriate; however, it has been APPROVED for 1 month to allow time for appeal."	**Not Funded:** Deny; not funded by the OHP. (e.g, allergic rhinitis (J300-J309); chronic rhinitis (J310-312); allergic conjunctivitis (H1045); upper respiratory infection (J069); acute nasopharyngitis (common cold) (J00); urticaria (L500-L509); etc.)

P&T / DUR Review: *2/26 (DM);8/22 (DM);11/15 (AG); 7/15; 9/08; 2/06; 9/04; 5/04; 5/02*
Implementation: *3/1/26; 10/1/22; 10/13/16; 1/1/16; 8/25/15; 8/09; 9/06; 3/06; 5/05; 10/04; 8/02*

Antihistamines (Oral)

Goals:

- Approve antihistamines only for conditions funded by the OHP in adults. Allow case-by-case review for members covered under the EPSDT program.
- Allergic rhinitis treatment is covered by the OHP only when complicated by other diagnoses (e.g. asthma, sleep apnea).
- Promote use that is consistent with Oregon Asthma Guidelines and medical evidence. http://public.health.oregon.gov/DiseasesConditions/ChronicDisease/Asthma/Pages/index.aspx

Length of Authorization:

- Up to 12 months

Requires PA:

- Non-preferred oral antihistamines and combinations

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Will the prescriber consider a change to a preferred product? Message: • Preferred products do not require a PA. • Preferred products are evidence-based reviewed for comparative effectiveness and safety by the Oregon Pharmacy & Therapeutics Committee.	**Yes:** Inform prescriber of covered alternatives in class.	**No:** Go to #3
3. Does patient have a diagnosis of allergic rhinitis, allergic conjunctivitis, or chronic rhinitis/pharyngitis/nasopharyngitis?	**Yes:** Go to #4	**No:** Go to #8
4. Does the patient have asthma or reactive airway disease exacerbated by chronic/allergic rhinitis or allergies?	**Yes:** Go to #5	**No:** Go to #6

Approval Criteria		
5. Does the drug profile show an asthma controller medication (e.g. ORAL corticosteroid, etc.) and/or inhaled rescue beta-agonist (e.g. albuterol, ICS/formoterol) within the last 6 months? *Keep in mind: albuterol may not need to be used as often if asthma is controlled on other medications.*	**Yes:** Approve for 6 months	**No:** Pass to RPh. Deny; medical appropriateness. *Oregon Asthma guidelines recommend all asthma clients have access to rescue inhalers and those with persistent disease should use anti-inflammatory medicines daily (preferably orally inhaled corticosteroids).*
6. Does patient have other co-morbid conditions or complications that are funded? • Acute or chronic inflammation of the orbit • Chronic Sinusitis • Acute Sinusitis • Sleep apnea • Wegener's Granulomatosis	**Yes:** Document ICD-10 codes. Go to #7	**No:** If not eligible for EPSDT review: Pass to RPh. Deny; not funded by the OHP If eligible for EPSDT review: Go to #10
7. Does patient have contraindications (e.g. pregnancy), or had insufficient response to available treatment alternatives for the funded condition? Document.	**Yes:** Approve for up to 6 months	**No:** Pass to RPh. Deny; medical appropriateness
8. Is the diagnosis COPD or Obstructive Chronic Bronchitis?	**Yes:** Pass to RPh. Deny; medical appropriateness. Antihistamine not indicated.	**No:** Go to #9

Approval Criteria		
9. Is the diagnosis funded? Note: Chronic Bronchitis, acute upper respiratory infections, and urticarial are not funded by the OHP	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** If not eligible for EPSDT review: Pass to RPh. Deny; not funded by the OHP If eligible for EPSDT review: Go to #10
10. Is there documentation that the condition is of sufficient severity that it impacts the patient's health (e.g., quality of life, function, growth, development, ability to participate in school, perform activities of daily living, etc.)?	**Yes:** Go to #11	**No:** Pass to RPh. Deny; medical necessity.
11. Is the request for a preferred product OR has the patient failed to have benefit with, or have contraindications or intolerance to, at least 2 preferred products? Message: Preferred products are evidence-based reviewed for comparative effectiveness and safety by the Oregon Pharmacy & Therapeutics Committee.	**Yes:** Approve for 12 months.	**No:** Pass to RPh. Deny; medical appropriateness. Inform prescriber of covered alternatives in class.

P&T Review: *2/26 (DM); 12/22; 5/15 (AG); 9/10; 9/08; 2/06; 9/04; 5/04; 2/02*
Implementation: *1/1/23; 5/1/16; 7/15, 1/11, 7/09, 7/06, 3/06, 10/04, 8/02, 9/06*