PREMERA | BLUE CROSS

An Independent Licensee of the Blue Cross Blue Shield Association

MEDICAL POLICY – 2.01.17

Sublingual Immunotherapy as a Technique of Allergen-Specific Therapy

BCBSA Ref Policy: 2.01.17

Effective Date:	May 1, 2025	RELATED MEDICAL POLICIES:
Last Revised:	Apr. 7, 2025	None
Replaces:	N/A	

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

Clicking this icon returns you to the hyperlinks menu above.

Introduction

Treating allergies often involves giving the person small doses of what they are allergic to. This tends to increase a person's immunity, or tolerance, to the substance. These substances are often given by injections (shots). But a newer method is to put the substance in drops and give them under the tongue. This is called sublingual (which means under the tongue) immunotherapy. This treatment is also sometimes called allergy drops. This policy explains when sublingual immunotherapy is medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Sublingual Immunotherapy	Medical Necessity

• **Oralair**
• **Grastek**
• **Ragwitek**
• **Odactra**
	Sublingual immunotherapy using Oralair, Grastek, or Ragwitek may be considered medically necessary, when used according to US Food and Drug Administration labeling (FDA), for the treatment of pollen-induced allergic rhinitis or rhinoconjuctivitis when the following conditions are met:
	• The individual has a history of rhinitis or rhinoconjunctivitis symptoms related to grass or short ragweed pollen exposure
	• Has a documented positive pollen-specific skin test or pollen-specific immunoglobulin E test
	  ○ Allergy must be confirmed by positive skin test or in vitro testing for pollen-specific immunoglobulin E antibodies to the species contained in the product or, for Grastek, Timothy grass pollen extract, to cross-reactive species
	• The individual's symptoms are not adequately controlled by appropriate pharmacotherapy (see **Related Information**)
	
	Sublingual immunotherapy using Odactra may be considered medically necessary, when used according to FDA labeling, for the treatment of house dust mite-induced allergic rhinitis or rhinoconjunctivitis when the following conditions are met:
	• The individual has a history of rhinitis or rhinoconjunctivitis symptoms related to dust mite exposure
	• Has a documented positive house dust mite-specific skin test or house dust mite-specific immunoglobulin E test
	  ○ Allergy must be confirmed by positive skin test, using licensed house dust mite allergen extracts or in vitro testing for house dust mite-specific immunoglobulin E antibodies to the Dermatophagoides farinae or Dermatophagoides pteronyssinus species
	• The individual's symptoms are not adequately controlled by appropriate pharmacotherapy (see **Related Information**)
	
	Sublingual immunotherapy as a technique of allergy immunotherapy is considered investigational for all other uses.

Documentation Requirements

The individual's medical records submitted for review should document that medical necessity criteria are met. The record should include clinical documentation of:

- Diagnosis/condition
- History and physical examination documenting the severity of the condition
- Name of sublingual immunotherapy that will be used
- Positive pollen or dust mite specific skin test or IgE test
- Pharmacotherapy attempted

Coding

Code	Description
CPT	
95199	Unlisted allergy/clinical immunologic service or procedure

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Use of Oralair, Grastek, and Ragwitek

Contraindications

Contraindications include severe, unstable or uncontrolled asthma; history of any severe local reaction or any severe systemic allergic reaction to sublingual immunotherapy or any severe local reaction to sublingual allergen immunotherapy; and history of eosinophilic esophagitis.

Administration and Dose

- Prescribing information includes a black box warning for severe allergic reactions including anaphylaxis and severe laryngopharyngeal edema. Individuals must be prescribed an epinephrine auto-injector and be trained on how to use it.

- Oralair is approved by the US Food and Drug Administration (FDA) for individuals 10 to 65 years of age. Grastek and Ragwitek have been FDA-approved for individuals 5 to 65 years of age.
- Treatment should begin 12 weeks (16 weeks for Oralair) before the expected onset of the allergy-inducing pollen season. Each product is dosed once daily and continued throughout the pollen season (precoseasonal dosing).
- The first dose is administered under the supervision of a physician experienced in diagnosing and treating severe allergic reactions. Subsequent doses may be taken at home.
- For Oralair, dose titration is required in individuals 5 to 17 years of age. Titration can be completed over 3 days at home, 100 index of reactivity (IR) on day 1, 2 times 100 IR on day 2, and 3 times 100 IR on day 3. In individuals between 18 and 65 years, no dose titration is needed; treatment is initiated at the maintenance dose of 300 IR.
- Grastek and Ragwitek both are initiated at the maintenance dose (2800 bioequivalent allergy unit and 12 Amb a 1-unit, respectively).

Use of Odactra

Contraindications

Contraindications are as listed above for Oralair, Grastek, and Ragwitek.

Administration and Dose

- Prescribing information includes a black box warning for severe allergic reactions including anaphylaxis and severe laryngopharyngeal edema. Individuals must be prescribed an epinephrine autoinjector and be trained on how to use it.
- Odactra is approved by the FDA for individuals 5 through 65 years of age.
- Odactra is dosed at one 12 SQ-HDM tablet daily. Per FDA, "SQ-HDM is the dose unit for ODACTRA. SQ is a method of standardization of biological potency, major allergen content and complexity of the allergen extract. HDM is an abbreviation for house dust mite."
- The first dose is administered under the supervision of a physician experienced in diagnosing and treating severe allergic reactions. Subsequent doses may be taken at home.

Pharmacotherapy of Pollen-Induced Allergic Rhinitis

There is general agreement from clinical practice guidelines on the pharmacologic treatment of pollen-induced allergic rhinitis or rhinoconjunctivitis:

- Treatment should be individualized based on symptom severity and duration, comorbidities and age, preference (e.g., route of administration, tolerance for adverse effects), and previous treatment history.
- Measures to increase treatment adherence (e.g., shared decision making, consideration of the individual's school or work schedule, use of a medication calendar or check-off list) are encouraged.
- Goals of treatment are symptom reduction and improvements in functional capacity and quality of life.
- A "step-up" (if treatment is inadequate) or "step-down" (if symptom relief is achieved with other interventions, e.g., avoidance) approach to treatment is recommended.
- Allergen avoidance is the first step of treatment but may be unrealistic for some individuals.

Medication classes commonly used to treat allergic rhinitis: 1) H_1antihistamines (oral and intranasal); 2) Corticosteroids (oral [short-course for severe disease] and intranasal); 3) Leukotriene receptor antagonists (oral); 4) Sympathomimetic decongestants (oral and intranasal); 5) Chromones (intranasal); 6) Anticholinergic, ipratropium bromide (intranasal).

- Treatment should be symptom-specific, e.g., oral antihistamines may be less effective for prominent congestion than other treatments; prominent rhinorrhea may respond to intranasal ipratropium; rhinitis-only symptoms may be treated with local (intranasal) rather than systemic (oral) therapy.
- For mild or intermittent symptoms, an oral or nasal antihistamine may be considered first-line treatment.
- Newer generation (selective) oral antihistamines are recommended over older (nonselective) antihistamines. Individuals with insomnia and pregnant women may prefer older antihistamines because of their sedating effects and longer safety history, respectively.
- Intranasal corticosteroids may be effective for more severe or persistent symptoms.

- Combination treatment (e.g., oral antihistamine plus intranasal corticosteroid, intranasal antihistamine and corticosteroid, antihistamine [oral or intranasal] plus sympathomimetic [oral or short-course (≤5 days to avoid rebound congestion) intranasal]) may be effective for symptoms nonresponsive to single medications.
- Oral sympathomimetics may cause insomnia; their use is limited in individuals with certain comorbidities (e.g., diabetes, unstable hypertension).
- Oral leukotriene receptor antagonists may reduce asthma exacerbations in individuals with comorbid asthma.

Consideration of Age

The ages stated in this policy for which Grastek, Ragwitek, Oralair, and Odactra are considered medically necessary are based on the ages approved in the FDA labeling.

Benefit Application

Sublingual immunotherapy may be offered by specialized clinics.

Evidence Review

Description

Sublingual immunotherapy (SLIT) is a potential alternative to subcutaneous immunotherapy (SCIT) for providing allergen-specific therapy. SLIT is proposed as a more convenient alternative delivery route for treating a variety of allergic disorders.

Background

Allergen-specific immunotherapy involves administering well-characterized allergen extracts, the potencies of which are measured and compared with a reference standard.[1] An initial induction or build-up phase progressively increases the allergen dose; this is followed by years of

maintenance injections at the highest dose. Allergen-specific immunotherapy has been used to treat various conditions, including insect allergy, allergic rhinitis, and asthma. SCIT is the standard of care. Due to the inconvenience of multiple injections, particularly in children, alternative delivery routes have been investigated; of these, SLIT is the most prominent. SLIT targets absorption to the sublingual and buccal mucosa. Allergen preparations used for sublingual immunotherapy are held under the tongue for one to several minutes and then swallowed or spit out.

Summary of Evidence

For individuals who have pollen-induced allergic rhinitis or rhinoconjunctivitis who receive SLIT, the evidence includes randomized controlled trials (RCTs) and systematic reviews. The relevant outcomes are symptoms, quality of life, hospitalizations, medication use, and treatment-related morbidity. Three sublingual pollen extracts are approved by the US Food and Drug Administration (FDA) for treatment of pollen-induced allergic rhinitis with or without conjunctivitis. Large, well-designed RCTs supporting the marketing applications for these products have provided consistent evidence of efficacy and safety. Although trials were placebo-controlled, rather than SCIT-controlled, minimum clinically important criteria for demonstrating efficacy were prespecified and were met in most studies. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have house dust mite-specific allergy who receive SLIT, the evidence includes RCTs and systematic reviews. The relevant outcomes are symptoms, quality of life, hospitalizations, medication use, and treatment-related morbidity. One sublingual extract is approved by the FDA for treatment of house dust mite-induced allergic rhinitis with or without conjunctivitis. Most RCTs evaluating SLIT for individuals with dust mite allergies have been placebo-controlled. Meta-analyses have found high levels of heterogeneity among studies. A more recent meta-analysis, published in 2015, had mixed findings; some outcomes but not others favored SLIT over placebo or pharmacologic treatment. However, more recent large, well-designed RCTs supporting the marketing applications for these products have provided consistent evidence of efficacy and safety. Although trials were also placebo-controlled, rather than SCIT-controlled, minimum clinically important criteria for demonstrating efficacy were prespecified and met in the largest studies. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have food allergy who receive SLIT, the evidence includes RCTs, systematic reviews, and an unpublished interventional study. The relevant outcomes are symptoms, quality of life, hospitalizations, medication use, and treatment-related morbidity. A few RCTs have

evaluated SLIT for treatment of food allergies, and these studies have had small sample sizes and tended to be rated as low quality by systematic reviewers. The available RCTs have not consistently found that SLIT is more effective than placebo or oral immunotherapy in patients with non-peanut allergies; in patients with peanut allergy, while available studies indicate efficacy of SLIT relative to placebo or pre-treatment baseline, SLIT has not been found to be as effective as oral immunotherapy. No RCTs were identified that compared SLIT with SCIT. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some currently ongoing or unpublished trials that might influence this review are listed in **Table 1**.

Table 1. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05113394	Preventing Childhood Asthma Using Prophylactic House Dust Mite Allergen Immunotherapy	270	Aug 2029
NCT05476484	Comparative Real World Effectiveness of SQ Sublingual Immunotherapy (SLIT)-Tablets vs. Controls in Allergic Rhinitis and Asthma - Outcomes From a Multinational Register Study	49,844	Jun 2024
NCT05521711	TRADE Trial - Tree Nut Immunotherapy Route Development and Evaluation	60	Jan 2027
Unpublished			
NCT04881461	A Randomised, Parallel-group, Double-blind, Placebo-controlled Phase III Trial Assessing the Efficacy and Safety of 5-grass Mix SLIT-drops in Adults With Grass Pollen-induced Rhinoconjunctivitis	445	Sept 2023

NCT: national clinical trial.

[a] Denotes industry-sponsored or cosponsored trial.

Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the policy conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Academy of Otolaryngology–Head and Neck Surgery Foundation

In 2024, the American Academy of Otolaryngology-Head and Neck Surgery Foundation (AAO-HNSF) published clinical practice guidelines on allergen immunotherapy in patients with inhalant allergy.[36] They issued a strong recommendation for offering immunotherapy to patients with allergic rhinitis with or without allergic asthma if symptoms are inadequately controlled with medical therapy, allergen avoidance, or both, or have a preference for immunomodulation. A minimum treatment duration of 3 years is recommended for patients who respond. The guidelines recommended patient education on the differences between subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) but did not state a preference for a particular administration route.

In 2015, the AAO-HNSF published clinical practice guidelines on allergic rhinitis that contained the following statement[37]:

"Clinicians should offer, or refer to a clinician who can offer, immunotherapy (sublingual or subcutaneous) for patients with AR [allergic rhinitis] who have inadequate response to symptoms with pharmacologic therapy with or without environmental controls. Recommendation based on RCTs [randomized controlled trials] and systematic reviews, with a preponderance of benefit over harm."

American Academy of Allergy, Asthma and Immunology et al

In 2020, the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma, and Immunology (ACAAI) recommended allergen immunotherapy

(either subcutaneous immunotherapy [SCIT] or sublingual immunotherapy [SLIT]) be offered to individuals with moderate or severe allergic rhinitis who are not controlled with allergen avoidance or pharmacotherapy; prefer immunotherapy; or those who may benefit due to comorbid conditions such as asthma.[38]

In 2017, the AAAAI and the ACAAI jointly published updated practice parameters on SLIT.[39] These recommendations apply to the use of SLIT agents approved by the FDA at time of publication: 5-grass (Oralair), Timothy grass (Grastek), and ragweed (Ragwitek). **Table 2** summarizes statements made.

Table 2. Recommendations on Use of SLIT

Recommendation	SOR	LOE
FDA-approved SLIT should be used to treat allergic rhinitis/rhinoconjunctivitis, and not for any other condition.	Strong	A/B
SLIT may not be suitable for patients who have conditions that reduce their ability to survive a systemic reaction or the associated treatment	Strong	D
Given insufficient information on the safety of initiating or continuing SLIT during pregnancy or breastfeeding, it should be used very cautiously in pregnant or breastfeeding patients	Weak	C
Dosing equivalence should not be assumed between SLIT tablets and extracts of the same allergen; each formulation should have its own safety profile established	Weak	C
First doses of SLIT should be administered in a medical facility under the supervision of a physician or other health care professional with experience in the diagnosis and treatment of anaphylaxis. The patient should be observed in the medical facility for 30 minutes after the administration of SLIT	Strong	D
Epinephrine should be prescribed to patients receiving SLIT tablets, and patients should be trained in its use	Strong	D
The SLIT dose should be reduced if a patient misses treatment for >1 week	Weak	D
Patients receiving SLIT should be scheduled for regular follow-up care with a specialist	Moderate	D

FDA: Food and Drug Administration; LOE: level of evidence: SLIT: sublingual immunotherapy; SOR: strength of recommendation.

Medicare National Coverage

There is no national coverage determination.

Regulatory Status

In April 2014, the first sublingual allergen extract tablets were approved by the FDA through the biologics license application process for treatment of pollen-induced allergic rhinitis with or without conjunctivitis:

- On April 1, the FDA approved Oralair (Stallergenes) allergen extract for individuals 10 to 65 years of age. Oralair contains freeze-dried pollen allergen extracts of 5 grasses: Kentucky Blue Grass, Orchard, Perennial Rye, Sweet Vernal, and Timothy.
- On April 11, the FDA approved Grastek (Merck) Timothy grass pollen (Phleum pretense) allergen extract for individuals 5 to 65 years of age. (Grastek is marketed in Europe as Grazax.)
- On April 17, the FDA approved Ragwitek (Merck) short ragweed pollen allergen extract for individuals 18 to 65 years of age. On April 16, 2021, Ragwitek received FDA approval for use in individuals 5 to 17 years of age.

In March 2017, the FDA approved Odactra (Merck) allergen extract for individuals 18 to 65 years of age who have house dust mite-induced allergic rhinitis with or without conjunctivitis. Odactra contains freeze-dried extracts of dust mites (Dermatophagoides farinae and Dermatophagoides pteronyssinus). In February 2025, the FDA expanded the approval to children 5 through 17 years of age.

References

1. Moote W, Kim H, Ellis AK. Allergen-specific immunotherapy. Allergy Asthma Clin Immunol. 2018; 14(Suppl 2): 53. PMID 30275845
2. Meltzer EO, Wallace D, Friedman HS, et al. Meta-analyses of the efficacy of pharmacotherapies and sublingual allergy immunotherapy tablets for allergic rhinitis in adults and children. Rhinology. Oct 01 2021; 59(5): 422-432. PMID 34463311
3. Yang J, Zhang L, Zhao Z, et al. Sublingual immunotherapy for pediatric allergic conjunctivitis: a meta-analysis of randomized controlled trials. Int Forum Allergy Rhinol. Nov 2018; 8(11): 1253-1259. PMID 29782067
4. Di Bona D, Plaia A, Leto-Barone MS, et al. Efficacy of Grass Pollen Allergen Sublingual Immunotherapy Tablets for Seasonal Allergic Rhinoconjunctivitis: A Systematic Review and Meta-analysis. JAMA Intern Med. Aug 2015; 175(8): 1301-9. PMID 26120825
5. Dretzke J, Meadows A, Novielli N, et al. Subcutaneous and sublingual immunotherapy for seasonal allergic rhinitis: a systematic review and indirect comparison. J Allergy Clin Immunol. May 2013; 131(5): 1361-6. PMID 23557834
6. Tie K, Miller C, Zanation AM, et al. Subcutaneous Versus Sublingual Immunotherapy for Adults with Allergic Rhinitis: A Systematic Review with Meta-Analyses. Laryngoscope. Mar 2022; 132(3): 499-508. PMID 33929726

7. Nelson H, Cartier S, Allen-Ramey F, et al. Network meta-analysis shows commercialized subcutaneous and sublingual grass products have comparable efficacy. J Allergy Clin Immunol Pract. 2015; 3(2): 256-266.e3. PMID 25609326

8. Dranitsaris G, Ellis AK. Sublingual or subcutaneous immunotherapy for seasonal allergic rhinitis: an indirect analysis of efficacy, safety and cost. J Eval Clin Pract. Jun 2014; 20(3): 225-38. PMID 24444390

9. Food and Drug Administration (FDA) Center for Drug Evaluation and Research. Statistical Review: Oralair, April 7, 2014. **https://www.fda.gov/media/88419/download**. Accessed November 5, 2024.

10. Didier A, Bons B. Safety and tolerability of 5-grass pollen tablet sublingual immunotherapy: pooled analysis and clinical review. Expert Opin Drug Saf. May 2015; 14(5): 777-88. PMID 25732009

11. Food and Drug Administration (FDA). Statistical review: Grastek. 2014; **http://wayback.archive-it.org/7993/20170722072840/https://www.fda.gov/downloads/BiologicsBloodVaccines/Allergenics/UCM394338.pdf**. Accessed November 5, 2024.

12. Food and Drug Administration (FDA), Center for Biologics Evaluation and Research. 26th Meeting of the Allergenic Products Advisory Committee, December 12, 2013. 2013; **https://wayback.archive-it.org/7993/20170114031528/http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/AllergenicProductsAdvisoryCommittee/UCM381421.pdf**. Accessed November 5, 2024.

13. Food and Drug Administration (FDA). Clinical review: Grastek. **https://www.fda.gov/biologicsbloodvaccines/allergenics/ucm393162.htm**. Accessed November 5, 2024.

14. Maloney J, Durham S, Skoner D, et al. Safety of sublingual immunotherapy Timothy grass tablet in subjects with allergic rhinitis with or without conjunctivitis and history of asthma. Allergy. Mar 2015; 70(3): 302-9. PMID 25495666

15. Feng B, Wu J, Chen B, et al. Efficacy and safety of sublingual immunotherapy for allergic rhinitis in pediatric patients: A meta-analysis of randomized controlled trials. Am J Rhinol Allergy. Jan 01 2017; 31(1): 27-35. PMID 28234149

16. Scadding GW, Calderon MA, Shamji MH, et al. Effect of 2 Years of Treatment With Sublingual Grass Pollen Immunotherapy on Nasal Response to Allergen Challenge at 3 Years Among Patients With Moderate to Severe Seasonal Allergic Rhinitis: The GRASS Randomized Clinical Trial. JAMA. Feb 14 2017; 317(6): 615-625. PMID 28196255

17. Valovirta E, Petersen TH, Piotrowska T, et al. Results from the 5-year SQ grass sublingual immunotherapy tablet asthma prevention (GAP) trial in children with grass pollen allergy. J Allergy Clin Immunol. Feb 2018; 141(2): 529-538.e13. PMID 28689794

18. ALK-Abell. Highlights of Prescribing Information: Ragwitek (short ragweed pollen allergen extract). 2022; **https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=70216cba-11b5-40fd-8656-9f27b24f7b60**. Accessed November 5, 2024.

19. Nolte H, Bernstein DI, Nelson HS, et al. Efficacy and Safety of Ragweed SLIT-Tablet in Children with Allergic Rhinoconjunctivitis in a Randomized, Placebo-Controlled Trial. J Allergy Clin Immunol Pract. 2020; 8(7): 2322-2331.e5. PMID 32304832

20. FDA Statistical Review - Ragwitek. **https://www.fda.gov/media/147811/download**. Accessed November 5, 2024.

21. Feng B, Xiang H, Jin H, et al. Efficacy of Sublingual Immunotherapy for House Dust Mite-Induced Allergic Rhinitis: A Meta-Analysis of Randomized Controlled Trials. Allergy Asthma Immunol Res. May 2017; 9(3): 220-228. PMID 28293928

22. Chen L, Lei L, Cai Y, et al. Specific sublingual immunotherapy in children with perennial rhinitis: a systemic review and meta-analysis. Int Forum Allergy Rhinol. Nov 2020; 10(11): 1226-1235. PMID 32329187

23. Liao W, Hu Q, Shen LL, et al. Sublingual Immunotherapy for Asthmatic Children Sensitized to House Dust Mite: A Meta-Analysis. Medicine (Baltimore). Jun 2015; 94(24): e701. PMID 26091451

24. Gendelman SR, Lang DM. Sublingual immunotherapy in the treatment of atopic dermatitis: a systematic review using the GRADE system. Curr Allergy Asthma Rep. Feb 2015; 15(2): 498. PMID 25504262

25. Bae JM, Choi YY, Park CO, et al. Efficacy of allergen-specific immunotherapy for atopic dermatitis: a systematic review and meta-analysis of randomized controlled trials. J Allergy Clin Immunol. Jul 2013; 132(1): 110-7. PMID 23647790

26. Kim JY, Jang MJ, Kim DY, et al. Efficacy of Subcutaneous and Sublingual Immunotherapy for House Dust Mite Allergy: A Network Meta-Analysis-Based Comparison. J Allergy Clin Immunol Pract. Dec 2021; 9(12): 4450-4458.e6. PMID 34464748
27. Demoly P, Emminger W, Rehm D, et al. Effective treatment of house dust mite-induced allergic rhinitis with 2 doses of the SQ HDM SLIT-tablet: Results from a randomized, double-blind, placebo-controlled phase III trial. J Allergy Clin Immunol. Feb 2016; 137(2): 444-451.e8. PMID 26292778
28. Nolte H, Bernstein DI, Nelson HS, et al. Efficacy of house dust mite sublingual immunotherapy tablet in North American adolescents and adults in a randomized, placebo-controlled trial. J Allergy Clin Immunol. Dec 2016; 138(6): 1631-1638. PMID 27521719
29. de Silva D, Geromi M, Panesar SS, et al. Acute and long-term management of food allergy: systematic review. Allergy. Feb 2014; 69(2): 159-67. PMID 24215577
30. Romantsik O, Bruschettini M, Tosca MA, et al. Oral and sublingual immunotherapy for egg allergy. Cochrane Database Syst Rev. Nov 18 2014; (11): CD010638. PMID 25405335
31. Narisety SD, Frischmeyer-Guerrerio PA, Keet CA, et al. A randomized, double-blind, placebo-controlled pilot study of sublingual versus oral immunotherapy for the treatment of peanut allergy. J Allergy Clin Immunol. May 2015; 135(5): 1275-82.e1-6. PMID 25528358
32. Kim EH, Yang L, Ye P, et al. Long-term sublingual immunotherapy for peanut allergy in children: Clinical and immunologic evidence of desensitization. J Allergy Clin Immunol. Nov 2019; 144(5): 1320-1326.e1. PMID 31493887
33. Burks AW, Wood RA, Jones SM, et al. Sublingual immunotherapy for peanut allergy: Long-term follow-up of a randomized multicenter trial. J Allergy Clin Immunol. May 2015; 135(5): 1240-8.e1-3. PMID 25656999
34. Kim EH, Keet CA, Virkud YV, et al. Open-label study of the efficacy, safety, and durability of peanut sublingual immunotherapy in peanut-allergic children. J Allergy Clin Immunol. Jun 2023; 151(6): 1558-1565.e6. PMID 36828080
35. Seidman MD, Gurgel RK, Lin SY, et al. Clinical practice guideline: Allergic rhinitis. Otolaryngol Head Neck Surg. Feb 2015; 152(1 Suppl): S1-43. PMID 25644617
36. Dykewicz MS, Wallace DV, Amrol DJ, et al. Rhinitis 2020: A practice parameter update. J Allergy Clin Immunol. Oct 2020; 146(4): 721-767. PMID 32707227
37. Greenhawt M, Oppenheimer J, Nelson M, et al. Sublingual immunotherapy: A focused allergen immunotherapy practice parameter update. Ann Allergy Asthma Immunol. Mar 2017; 118(3): 276-282.e2. PMID 28284533

History

Date	Comments
11/05/97	Add to Medicine Section - New Policy
11/03/98	Replace Policy - Scheduled review, no criteria changes.
08/12/03	Replace Policy - Policy regarding sublingual immunotherapy and SET-guided immunotherapy reviewed; policy statement unchanged.
08/09/05	Replace Policy - Policy revised with literature search; policy retitled, now focuses solely on sublingual immunotherapy; other forms of immunotherapy no longer addressed.
06/16/06	Update Scope and Disclaimer - No other changes.

Date	Comments
11/14/06	Replace Policy - Policy updated with literature review; policy statement unchanged. References added.
05/13/08	Replace Policy - Policy updated with literature search; no change to the policy statement. References added.
05/12/09	Replace Policy - Policy updated with literature search; no change to the policy statement.
05/11/10	Replace Policy - Policy updated with literature search; no change to the policy statement. References added.
06/13/11	Replace Policy - Policy updated with literature review; no change in policy statement. References 8 and 11 added; other references renumbered/removed. ICD-10 codes added to policy.
05/22/12	Replace policy. Policy updated with literature review; no change in policy statement. References 2, 4, 5, 10-12 added; other references renumbered/removed.
07/25/12	Related Policies Update – Title to 2.01.01 has been changed to include: (i.e., Multiple Chemical Sensitivities)
08/24/12	Update Coding Section – ICD-10 codes are now effective 10/01/2014.
05/28/13	Replace policy. Policy updated with literature review through January 22, 2013; no change in policy statement. References 4, 8 and 14 added; other references renumbered/removed.
07/24/13	Replace policy. Policy updated with literature review through April 20, 2013. No change in policy statement. References 2, 3, 14, 17 and 18 added; other references renumbered/removed.
07/14/14	Annual Review. Policy statement changed to medically necessary for Oralair, Grastek, and Ragwitek to treat grass or short ragweed pollen allergies when criteria are met. These medications are investigational for all other uses. Policy updated with literature review through April, 2014. References 1-8, 14-16, 20-42, 47, 52, and 55 added, 10 and 54 updated; 22 deleted; others renumbered/removed. Policy statement changed as noted. Coding update: CPT codes 95144-95165 and ICD-9 and ICD-10 diagnosis and procedure codes removed from policy.
06/17/15	Annual Review. Policy updated with literature review through March 11, 2015; references 12, 29-30, 42, 44-47, 51-54, 57-58, and 69-70 added; reference 41 updated. Policy statements unchanged.
08/28/15	Update Related Policies. Remove 2.01.01 as it was archived.
12/01/16	Annual Review, approved November 8, 2016. Policy updated with literature review through August 11, 2016; references 2, 9, 13, 15, and 24-26 added. Policy statements unchanged. Language added to the Rationale section to indicate that the age application of the policy is based on FDA-labeling.
03/03/17	Policy moved to new format. No change to policy statement.

Date	Comments
12/01/17	Annual Review, approved November 9, 2017. Policy updated with literature review through August 24, 2017; references 15-17 and 25 added; note 11 updated. Policy statements unchanged.
01/01/19	Annual Review, approved December 13, 2018. Policy updated with literature review through August 2018; references 22-24, 34, and 37 added; references 7 and 14 updated. Policy statement added that sublingual immunotherapy using Odactra may be considered medically necessary, when used according to Food and Drug Administration labeling, for the treatment of house dust mite-induced allergic rhinitis or rhinoconjunctivitis when the specified conditions are met.
03/01/19	Minor update, added Documentation Requirements section.
01/01/20	Annual Review, approved December 10, 2019. Policy updated with literature review through August 2019; references added, Policy statements unchanged.
12/01/20	Annual Review, approved November 19, 2020. Policy updated with literature review through August 23, 2020; references added. Policy statements unchanged.
04/01/21	Update Related Policies. Policy 2.04.76 archived and removed.
01/01/22	Annual Review, approved December 2, 2021. Policy updated with literature review through August 24, 2021; references added. Updated Ragwitek prescribing information to note April 2021 FDA approval for use in children aged 5-17 years.
12/01/22	Annual Review, approved November 21, 2022. Policy updated with literature review through August 22, 2022; references added. Minor editorial refinements to policy statements; intent unchanged. Changed the wording from "patient" to "individual" throughout the policy for standardization.
01/01/24	Annual Review, approved December 11, 2023. Policy updated with literature review through August 17, 2023; references added. Policy statements unchanged.
01/01/25	Annual Review, approved December 9, 2024. Policy updated with literature review through August 12, 2024; references added. Policy Guidelines updated to align with current FDA age approvals for Oralair and Odactra.
05/01/25	Interim Review, approved April 7, 2025. Dosage and administration and Regulatory Status sections updated for Odactra to include the expanded FDA indication for children 5 through 17 years of age. Policy statement unchanged as it denotes "used according to FDA labeling."

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.