BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

ALLERGEN IMMUNOTHERAPY SUBLINGUAL TABLETS: GRASTEK® (Timothy Grass pollen allergen extract) ODACTRA™ House Dust Mite (Dermatophagoides farina & Dermatophagoides pteronyssinus) allergen extract ORALAIR® (Sweet Vernal, Orchard, Perennial Rye, Timothy, Kentucky Blue Grass mixed pollen allergen extract) RAGWITEK™ (Short Ragweed pollen allergen extract) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Grastek, Oralair, Ragwitek, Odactra, and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Allergist or Immunologist

2. Individual's age is **ONE** of the following:
    a. 5 years of age or older **for Grastek, Oralair, or Ragwitek**
    b. 12 years of age or older **for Odactra**

3. Individual has a confirmed diagnosis of allergen-induced allergic rhinitis with or without conjunctivitis

4. There is a positive allergen specific-skin test **OR** positive allergen specific immunoglobulin E (IgE) antibody for **ONE** of the following:
    a. Timothy grass pollen or a cross-reactive allergen **for Grastek**
    b. Mixed grass pollen or cross-reactive allergen **for Oralair**
    c. Short ragweed pollen antigen or cross-reactive allergen **for Ragwitek**
    d. *Dermatophagoides farina* or *Dermatophagoides pteronyssinus* house dust mites **for Odactra**

5. Individual continues to practice allergen avoidance

6. Individual also has a prescription for epinephrine auto-injection

7. Treatment is planned to be initiated within **ONE** of the following:
    a. At least 3 months (12 weeks) prior to expected onset of pollen season and used through the season **for Grastek or Ragwitek**
    b. At least 4 months (16 weeks) prior to expected onset of pollen season and used through the season **for Oralair**

8. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

9. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for at least **ONE** intranasal corticosteroid (over the counter or prescription only) for allergic rhinitis, examples include budesonide (generics), fluticasone (e.g., Flonase Sensimist, Xhance, Flonase Allergy Relief, generics), triamcinolone (e.g., Nasacort Allergy, generics), beclomethasone (e.g., Beconase AQ, Qnasl, generics), ciclesonide (e.g., Omnaris, Zetonna), flunisolide (generics), or mometasone (generics)

10. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for at least **ONE** of the following medications for allergic rhinitis (over the counter or prescription only):
    a. Oral or nasal antihistamine (e.g., cetirizine (Zyrtec, generics), loratadine (e.g., Claritin, generics), fexofenadine (e.g., Allegra Allergy, generics), nasal azelastine (e.g., Astepro, generics), or nasal olopatadine (e.g., Patanase, generics))
    b. Nasal anticholinergic such as ipratropium (generics)
    c. Oral leukotriene modifier such as montelukast (e.g., Singulair, generics) or zafirlukast (e.g., Accolate, generics)
    d. Nasal mast cell stabilizer (e.g., cromolyn (NasalCrom, generics), lodoxamide (Alomide), or nedocromil (Alocril))

11. When applicable, for allergic rhinitis with conjunctivitis individual uses **ONE** ophthalmic anti-allergy medication (over the counter or prescription only) such as ophthalmic azelastine (generics), ketotifen (e.g., Alaway, Zaditor, generics), ketorolac (e.g., Acuvail, Acular LS, generics), or olopatadine (e.g., Pataday, generics)

12. There are **NO** FDA-label contraindications such as:
    a. Severe, unstable, or uncontrolled asthma
    b. History of any severe systemic allergic reaction
    c. History of eosinophilic esophagitis
    d. Severe local reaction or any severe systemic allergic reaction to other types of immunotherapy (SCIT, SLIT-drops, or other SLIT-tabs)

13. Requested agent is not for immediate relief of allergic symptoms

14. Will not be used in combination with other allergen immunotherapy (SCIT, SLIT-drops, or other SLIT-tabs)

Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Grastek, Oralair, Ragwitek, Odactra, and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Allergist or Immunologist

2. Individual's condition has responded while on therapy with response defined as **TWO** of the following:
    a. Achieved and maintains reduction in frequency and severity of nasal symptoms (runny nose, stuffy nose, sneezing, or itchy nose)
    b. When applicable, achieved and maintains reduction in frequency and severity of ocular symptoms (gritty/itchy eyes and watery eyes)
    c. A reduction in the use of or number of additional medications to control symptoms
    d. A reduction in recurrent asthma exacerbations while on therapy

3. Individual has been adherent with the medication and allergen avoidance

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Oral inflammation, oral ulcerations, or oral wounds
        ii. Persistent and escalating adverse reactions in the mouth or throat
        iii. Eosinophilic esophagitis

6. Requested agent is not for immediate relief of allergic symptoms

7. Will not be used in combination with other allergen immunotherapy (SCIT, SLIT-drops, or other SLIT-tabs)

Renewal duration: 12 months

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- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

Description:

Grastek, Oralair, and Ragwitek are allergen extracts used as allergen immunotherapy for the treatment of pollen-induced allergic rhinitis with or without conjunctivitis confirmed by positive skin test or *in vitro* testing for pollen-specific immunoglobulin E (IgE) antibodies. Grastek is used for allergies to Timothy grass pollen. Oralair is used for five mixed grass pollen (Kentucky bluegrass, Orchard grass, Perennial Ryegrass, Sweet Vernal grass, and Timothy grass). Ragwitek is used for allergies to short ragweed pollen.

Odactra House Dust Mite (*Dermatophagoides farina & Dermatophagoides pteronyssinus*) allergen extract is indicated in adults as immunotherapy for house dust mite (HDM)-induced allergic rhinitis, with or without conjunctivitis, confirmed by *in vitro* testing for immunoglobulin E (IgE) antibodies to *Dermatophagoides farinae* or *Dermatophagoides pteronyssinus* HDMs, or skin testing to licensed HDM allergen extracts. Odactra is not indicated for the immediate relief of allergic symptoms.

HDM allergies are a reaction to tiny bugs found in house dust on bedding, upholstered furniture, and carpeting. Individuals with HDM allergies experience a cough, runny nose, nasal itching, nasal congestion, sneezing, and itchy and watery eyes.

Allergen immunotherapy (AIT) for the treatment of allergic symptoms has traditionally been administered by subcutaneous injection therapy (SCIT) or as an aqueous or liquid extract of allergen, generally administered as drops, and held under the tongue for a specified period of time and then the residual is swallowed (SLIT-drops). A new alternative approach is administration of allergens using a dissolvable sublingual tablet (SLIT-tabs).

Each SLIT-tab has a risk for anaphylaxis, and they are not used in combination with other immunotherapy (other SLIT-tab, SLIT-drops, or SCIT) due to an increased risk for hypersensitivity reactions. Use of SLIT-tab in individuals with severe, unstable, or uncontrolled asthma is contraindicated.

SLIT-tab therapy must be initiated before the start of the expected allergy season. Initial dose of SLIT-tab is given in the office setting, where the individual can be observed for 30 minutes after the first dose. Individuals require a prescription of epinephrine for home use for severe allergic reactions if they develop. SLIT tab is not used to control acute symptoms or to provide immediate relief of symptoms. It should be noted that other long-established therapeutic options mentioned above can be given at any time to control acute and chronic symptoms.

Six medication classes are available for use to treat allergic rhinitis: antihistamines (oral and intranasal), corticosteroids (oral and intranasal), leukotriene receptor antagonists (oral), sympathomimetic decongestants (oral and intranasal), cromolyn (intranasal), and the anticholinergic, ipratropium bromide (intranasal). Selection of any particular agent or combination of agents should be based on type of symptoms needed to control and other medical conditions of the individual.

Oral antihistamines may be less effective than other treatments for prominent congestion symptoms. For mild or intermittent symptoms, use of an oral or intranasal antihistamine may be considered first-line treatment. Due to

less sedating effects, newer selective oral antihistamines are recommended over older nonselective antihistamines. Rhinorrhea may respond to intranasal ipratropium and rhinitis-only symptoms may be treated with intranasal rather than oral therapy. Intranasal corticosteroids may be effective for more severe or persistent symptoms.

Combination treatment may consist of oral antihistamine with intranasal corticosteroid, intranasal antihistamine and intranasal corticosteroid, and oral or intranasal antihistamine plus sympathomimetic. Combination therapy may be effective for symptoms nonresponsive to single medications.
Oral sympathomimetics may cause insomnia and their use may be limited in patients with certain comorbidities; intranasal sympathomimetics may cause rebound nasal congestion when used beyond 5 days. Oral leukotriene receptor antagonists may reduce asthma exacerbations in patients with comorbid asthma.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Comparison and characteristics of SLIT-tab agents:

	Grastek	Oralair	Ragwitek	Odactra
Components	Timothy grass pollen extract Cross-reactive with: Timothy Orchard Kentucky Blue Perennial Rye Sweet Vernal Fescue Redtop	Pollen extracts of 5 grasses: Timothy Orchard Kentucky Blue Perennial Rye Sweet Vernal	Short ragweed pollen extract	House dust mite allergen extract from *Dermatophagoides farinae* and *D. pteronyssinus*
Indications	Grass pollen-induced allergic rhinitis with or without conjunctivitis		Short ragweed pollen-induced allergic rhinitis with or without conjunctivitis	Dust mite-induced allergic rhinitis with or without conjunctivitis
Approved for ages	5 to 65 years			12 to 65 years
Required testing	Positive skin test **or** in vitro testing for IgE antibodies to Timothy grass **or** any of the cross-reactive grass species	Positive skin test **or** in vitro testing for IgE antibodies to any of the 5 grass species in the table	Positive skin test **or** in vitro testing for IgE antibodies to short ragweed	Positive skin test with a house dust mite extract **or** in vitro testing for IgE antibodies to *Dermatophagoides farinae* or *D. pteronyssinus*
Initiation	12 weeks prior to grass season	16 weeks prior to grass season	12 weeks prior to ragweed season	Can be started anytime
Duration	Prior to and through relevant grass season; may be continued on a perennial basis over 3 years for sustained effectiveness	Prior to and through relevant grass season	Prior to and through relevant ragweed season	Year-round
Data on safety of reinitiating treatment after a missed dose	In clinical trials, treatment interruptions for up to 7 days were allowed	Data not available	In clinical trials, treatment interruptions for up to 7 days were allowed	

Contraindications	Severe unstable or uncontrolled asthma History of any severe systemic allergic reaction History of any severe local reaction after taking SLIT Hypersensitivity to inactive ingredients in the product History of eosinophilic esophagitis		
Asthma patients	Not studied in patients with moderate or severe asthma or in patients who require daily medication to treat asthma	Trials allowed patients who required daily low doses of inhaled glucocorticoids to treat asthma	Trials allowed patients with mild-to-moderate asthma that required, at most, a medium daily dose of an inhaled glucocorticoid to treat asthma

Timing relative to pollen seasons:
Pre-seasonal treatment: SLIT-tablet therapy for pollen allergy is initiated 3-4 months prior to the allergen season

Co-seasonal treatment: Daily therapy is then maintained through the end of the pollen season

Continuous year-round: Studies that showed persistent benefit two years after completion of a three-year course of therapy used continuous year-round treatment

Resources:

Grastek (timothy grass pollen allergen extract) product information, revised by ALK-Abello AS. 09-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 31, 2024.

Odactra (dermatophagoides pteronyssinus and dermatophagoides farina) product information, revised by ALK-Abello AS. 05-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 31, 2024.

Oralair (sweet vernal, orchard, perennial rye, timothy, and Kentucky blue grass mixed pollens allergen extract) product information, revised by Stallergenes SAS. 11-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 31, 2024.

Ragwitek (Short ragweed (ambrosia artemisiifolia) pollen) product information, revised by ALK-Abello AS. 09-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 31, 2024.

Creticos PS. Sublingual immunotherapy for allergic rhinitis and conjunctivitis: SLIT-tablets. In: UpToDate, Corren J, Feldweg AM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through June 2024. Topic last updated September 17, 2023. Accessed July 05, 2024.

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Roberts G, Pfaar O, Akdis CA, et al.: EAACI Guidelines on Allergen Immunotherapy: Allergic rhinoconjunctivitis. Allergy 2018;73:765–798. Accessed June 17, 2022. Re-evaluated July 05, 2024.

Greenhawt M, Oppenheimer J, Nelson M, et al.: Sublingual immunotherapy A focused allergen immunotherapy practice parameter update. Ann Allergy Asthma Immunol 2017; 118: 276-282. Accessed June 07, 2023. Re-evaluated July 05, 2024.