BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 10/31/14
LAST REVIEW DATE: 8/15/19
LAST CRITERIA REVISION DATE: 8/15/19
ARCHIVE DATE:

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

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 10/31/14
LAST REVIEW DATE: 8/15/19
LAST CRITERIA REVISION DATE: 8/15/19
ARCHIVE DATE:

ALLERGEN IMMUNOTHERAPY SUBLINGUAL TABLETS

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

Criteria:

- **Criteria for initial therapy:** Grastek, Oralair, Ragwitek, or Odactra is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in allergy or immunology or is in consultation with an Allergist or Immunologist

  2. Age is **ONE** of the following:
     - 5 years of age or older **for Grastek**
     - 10 years of age or older **for Oralair**
     - 18 years of age or older **for Ragwitek**
     - 18 years of age or older **for Odactra**

  3. 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:
     - Timothy grass pollen or a cross-reactive allergen **for Grastek**
     - Mixed grass pollen or cross-reactive allergen **for Oralair**
     - Short ragweed pollen antigen or cross-reactive allergen **for Ragwitek**
     - *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:
     - At least 3 months (12 weeks) prior to season onset and used through the season **for Grastek**
     - At least 4 months (16 weeks) prior to season onset and used through the season **for Oralair**
     - At least 3 months (12 weeks) prior to season onset and used through the season **for Ragwitek**

  8. Individual has failure, contraindication or intolerance to at least **ONE** intranasal corticosteroid (over the counter or prescription only) for allergic rhinitis:

ALLERGEN IMMUNOTHERAPY SUBLINGUAL TABLETS

- Individual has failure, contraindication or intolerance to **ONE** of the following medication for allergic rhinitis (over the counter or prescription only): Oral or nasal antihistamine
- Nasal Anticholinergic
- Oral Leukotriene modifier
- Nasal mast cell stabilizer

9. When applicable, for allergic rhinitis with conjunctivitis use of **ONE** ophthalmic anti-allergy medication (over the counter or prescription only)

10. There are **NO** contraindications
    - Contraindications include:
      - Severe, unstable or uncontrolled asthma
      - History of any severe systemic allergic reaction
      - History of eosinophilic esophagitis
      - Hypersensitivity to any of the inactive ingredients contained in the product
      - Severe local reaction or any severe systemic allergic reaction to other types of immunotherapy (SCIT, SLIT-drops, or other SLIT-tabs)

11. Will not be used 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, or Odactra is considered ***medically necessary*** and will be approved with documentation of **ALL** of the following:

1. Individual continues to be seen by a physician specializing in allergy or immunology or is in consultation an Allergist or Immunologist

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

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

4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use, such as:
   - Contraindications as listed in the criteria for initial therapy section
   - Significant adverse effect such as:
     - Oral inflammation, oral ulcerations, or oral wounds

ALLERGEN IMMUNOTHERAPY SUBLINGUAL TABLETS

- Persistent and escalating adverse reactions in the mouth or throat

5. There are no significant interacting drugs

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

Renewal duration: 12 months

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), chromolyn (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.

Resources:

Grastek. Package Insert. Revised by manufacturer 6/2014, accessed 10-22-2014. Revised by manufacturer 04/2017, accessed 08-22-2017. Revised by manufacturer 10/2017, accessed 07-19-2018.

Oralair. Package Insert. Revised by manufacturer 10/2014, accessed 10-22-2014. Revised by manufacturer 12/2016, accessed 08-22-2017, 07-19-2018.

Ragwitek. Package Insert. Revised by manufacturer 6/2014, accessed 10-22-2014. Revised by manufacturer 3/2016, accessed 07-22-2016. Revised by manufacturer 03/2017, accessed 08-22-2017. Revised by manufacturer 04/2017, accessed 07-19-2018.

Odactra. Package Insert. Revised by manufacturer 03/2017, accessed 03-20-2017. Revised by manufacturer 04/2017, 01/2018, accessed 03-14-2018.

Odactra product information accessed 04-27-18 at DailyMed:
https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=71ca220d-78d5-47d4-be84-8d6e844b24b3

Calderon MA, Kleine-Tebbe J, Linneberg A, et al.: House Dust Mite Respiratory Allergy: An Overview of Current Therapeutic Strategies. J Allergy Clin Immunol Pract 2015; 3(6):843-855

UpToDate: Sublingual immunotherapy for allergic rhinoconjunctivitis and asthma. Current through Jul 2017.
https://www-uptodate-com.mwu.idm.oclc.org/contents/sublingual-immunotherapy-for-allergic-rhinoconjunctivitis-and

ALLERGEN IMMUNOTHERAPY SUBLINGUAL TABLETS

asthma?source=search_result&search=sublingually%20administered%20allergy%20immunotherapy%20tablets&selectedTitle=1~17#H523955

UpToDate: Sublingual immunotherapy for allergic rhinoconjunctivitis and asthma. Current through Mar, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/sublingual-immunotherapy-for-allergic-rhinoconjunctivitis-and-asthma?search=house%20dust%20mite&source=search_result&selectedTitle=6~87&usage_type=default&display_rank=6

UpToDate: Pharmacotherapy of allergic rhinitis. Current through Jul 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/pharmacotherapy-of-allergic-rhinitis?source=search_result&search=allergen%20specific%20immunotherapy&selectedTitle=20~150#H25107621