**Medical Policy**

**Title:** Oral Immunotherapy Agents
(Grastek®, Oralair®, Ragwitek™)

- Prime Therapeutics will review Prior Authorization requests.

**Prior Authorization Form:**

**Link to Drug List (Formulary):**
http://www.bcbsks.com/CustomerService/PrescriptionDrugs/drug_list.shtml

<table>
<thead>
<tr>
<th>Professional</th>
<th>Institutional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original Effective Date: July 23, 2004</td>
<td>Original Effective Date: July 23, 2004</td>
</tr>
<tr>
<td>Revision Date(s): June 7, 2013; August 18, 2014; November 1, 2014; April 14, 2015; October 1, 2015; April 15, 2016; May 15, 2017</td>
<td>Revision Date(s): June 7, 2013; August 18, 2014; November 1, 2014; April 14, 2015; October 1, 2015; April 15, 2016; May 15, 2017</td>
</tr>
<tr>
<td>Current Effective Date: May 15, 2017</td>
<td>Current Effective Date: May 15, 2017</td>
</tr>
</tbody>
</table>

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member’s benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

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**DESCRIPTION**

The intent of the Oral Immunotherapy Agents Prior Authorization (PA) program is to ensure appropriate selection of patients for treatment according to product labeling and guidelines. The PA defines appropriate use based on FDA approved package information.
and current clinical guidelines published by the Joint Task Force on Practice Parameters for Allergy and Immunology. The PA defines appropriate use as immunotherapy of allergic rhinitis in patients who have a positive skin test or pollen specific antibodies who have tried at least two traditional allergy medications, one of which is a nasal corticosteroid or have a documented intolerance, FDA labeled contraindication, or hypersensitivity to traditional treatments. PA criteria also include documentation of provider’s specialty (allergy or immunology), documentation that the patient is to receive the first dose under direct supervision (30 minutes) of that provider and that the patient has epinephrine injection available at home, and initiation of therapy at the required interval before the pollen season. Appropriate dosing based on FDA labeling will be included with a quantity limit of one tablet per day. Requests for oral immunotherapy agents will be reviewed when patient-specific documentation has been provided.

**Target Drugs**
- **Grastek®** (Timothy Grass Pollen Allergen Extract)
- **Oralair®** (Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue grass Mixed Pollens Allergen extract)
- **Ragwitek®** (Short Ragweed Pollen Allergen Extract)

### FDA Labeled Indications

<table>
<thead>
<tr>
<th>Product</th>
<th>Indication(s)</th>
<th>Dosage and Administration*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grastek®</strong> (Timothy Grass Pollen Allergen Extract)</td>
<td></td>
<td></td>
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</tbody>
</table>
| Sublingual tablet – 2800 Bioequivalent Allergy Unit (BAU) | ◦ Treatment of grass pollen-induced allergic rhinitis with or without conjunctivitis confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for Timothy grass or cross-reactive grass pollens.  
◦ Grastek is approved for use in persons 5 through 65 years of age. | Take one tablet daily; place tablet under the tongue and allow it to remain there until completely dissolved. Do not take with food.  
Initiate treatment at least 12 weeks before the expected onset of each grass pollen season and continue throughout the season. For sustained effectiveness Grastek may be taken daily for 3 consecutive years (including intervals between grass pollen seasons).  
Administer the first dose under the supervision of a physician with experience in the diagnosis and treatment of severe allergic reactions. Observe the patients for at least 30 minutes. |
| **Oralair®** (Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue grass Mixed Pollens Allergen extract) | | |
| Sublingual tablet – 100 IR  
300 IR (Index of Reactivity) | ◦ Treatment of grass pollen-induced allergic rhinitis with or without conjunctivitis confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for any of the five grass species contained in this product.  
◦ Oralair is approved for use in persons 10 through 65 years of age. | Adults (age 18-65)  
Take one tablet (300 IR) daily  
Children, Adolescents (age 10-17)  
Increase dose over the first few days:  
Day 1 - 100 IR  
Day 2 - 100 IR x 2  
Day 3 and following – 300 IR  
Place tablet under the tongue and allow it to remain there until completely dissolved. Do not take with food.  
Administer Oralair to children under adult supervision.  
Initiate treatment at least 4 months before the expected onset of each grass pollen season and
<table>
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</thead>
</table>
| **Ragwitek**     | • Treatment of short ragweed pollen-induced allergic rhinitis, with or without conjunctivitis, confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for short ragweed pollen.  
                   • Ragwitek is approved for use in adults 18 through 65 years of age. | Take one tablet daily; place tablet under the tongue and allow it to remain there until completely dissolved. Do not take with food.  
                   Initiate treatment at least 12 weeks before the expected onset of ragweed pollen season and continue throughout the season.  
                   Administer the first dose in a healthcare setting under the supervision of a physician with experience in the diagnosis and treatment of allergic diseases. After receiving the first dose, observe the patient for at least 30 minutes to monitor for signs or symptoms of a severe systemic or a severe local allergic reaction. If the patient tolerates the first dose, the patient may take subsequent doses at home. |

* Administer the first dose of these products in a healthcare setting under the supervision of a physician with experience in the diagnosis and treatment of allergic diseases. After receiving the first dose of the product, observe the patient for at least 30 minutes to monitor for signs or symptoms of a severe systemic or a severe local allergic reaction. If the patient tolerates the first dose, the patient may take subsequent doses at home.1-3
POLICY
PRIOR AUTHORIZATION AND QUANTITY LIMIT CRITERIA FOR APPROVAL

A. **Grastek, Oralair, or Ragwitek** will be approved when ALL of the following are met:
   1. The patient has a diagnosis of allergic rhinitis, with or without conjunctivitis
      AND
   2. The patient’s diagnosis is confirmed with ONE of the following:
      a. Positive skin test to ONE of the pollen extracts included in the requested agent OR
      b. Pollen specific antibodies to ONE of the pollen extracts included in the requested agent
         i. Grastek: Timothy grass or cross-reactive grass
         ii. Oralair: Sweet vernal, orchard, perennial rye, Timothy, or Kentucky blue grass
         iii. Ragwitek: Short Ragweed
      AND
   3. The patient is within the FDA labeled age range:
      a. Grastek: between the ages of 5 and 65
      b. Oralair: between the ages of 10 and 65
      c. Ragwitek: between the ages of 18 and 65
      AND
   4. The prescriber has expertise in allergy or immunology or has consulted with an expert in allergy or immunology
      AND
   5. ONE of the following:
      a. The patient has tried and failed at least two traditional allergy medications, one of which was an intranasal corticosteroid
      OR
      b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to at least two standard allergy therapies, one of which was an intranasal corticosteroid
      AND
   6. The patient is not currently using subcutaneous injectable immunotherapy
      AND
   7. The patient is not taking a beta blocker (within the past 90 days)
      AND
   8. The product will be started, or has already been started, 3 to 4 months before the expected onset of the applicable pollen season
      AND
   9. The first dose is given in the clinic/hospital under direct supervision from the provider for a period of at least 30 minutes
      AND
10. The patient has been prescribed epinephrine auto-injector for at home emergency use
   AND
11. The patient does not have any FDA labeled contraindications to the requested agent
   AND
12. ONE of the following:
   a. The requested quantity (dose) is less than or equal to the program quantity limit
      OR
   b. ALL of the following
      i. The requested quantity (dose) is above the set limit
         AND
      ii. ONE of the following
         1) BOTH of the following
            a) The requested quantity (dose) requested is below the FDA labeled dose
               AND
            b) The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit
               OR
         2) BOTH of the following
            a) The requested quantity (dose) requested is above the FDA labeled dose
               AND
            b) The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis

Length of approval: 12 months

B. Sublingual immunotherapy as a technique of allergy immunotherapy is considered experimental / investigational for all other uses.

FDA Labeled Contraindications

<table>
<thead>
<tr>
<th>Agent</th>
<th>Contraindications</th>
</tr>
</thead>
</table>
| Grastek | 1. Severe, unstable or uncontrolled asthma  
          2. History of any severe systemic allergic reaction  
          3. History of any severe local reaction to sublingual allergen immunotherapy  
          4. History of eosinophilic esophagitis  
          5. Hypersensitivity to any of the inactive ingredients contained in this product |
| Oralair | 1. Severe, unstable or uncontrolled asthma  
         2. History of any severe systemic allergic reaction  
         3. History of any severe local reaction to sublingual allergen immunotherapy  
         4. History of eosinophilic esophagitis  
         5. Hypersensitivity to any of the inactive ingredients contained in this product |
### Contraindications

<table>
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</table>
| **Ragwitek** | 1. Severe, unstable or uncontrolled asthma  
2. History of any severe systemic allergic reaction  
3. History of any severe local reaction to sublingual allergen immunotherapy  
4. History of eosinophilic esophagitis  
5. Hypersensitivity to any of the inactive ingredients contained in this product |

### Quantity Limits for Target Drugs

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>Quantity Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grastek</strong></td>
<td></td>
</tr>
<tr>
<td>(Timothy Grass Pollen Allergen Extract)</td>
<td></td>
</tr>
<tr>
<td>Tablet, 2800 BAUs</td>
<td>1 tablet/day</td>
</tr>
<tr>
<td>(Bioequivalent Allergy Units)</td>
<td></td>
</tr>
<tr>
<td><strong>Oralair</strong></td>
<td></td>
</tr>
<tr>
<td>(Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue grass Mixed Pollens Allergen extract)</td>
<td></td>
</tr>
<tr>
<td>Tablet, 300 IR (index of reactivity)</td>
<td>1 tablet/day</td>
</tr>
<tr>
<td>Children/Adolescent Starter Pack</td>
<td>1 pack/180 days</td>
</tr>
<tr>
<td><strong>Ragwitek</strong></td>
<td></td>
</tr>
<tr>
<td>(Short Ragweed Pollen Allergen Extract)</td>
<td></td>
</tr>
<tr>
<td>Tablet, 12 Amb a 1-U (Amb a 1-Unit)</td>
<td>1 tablet/day</td>
</tr>
</tbody>
</table>

### RATIONALE

#### Background

Allergic rhinitis (nasal passage inflammation) is characterized by one or more symptoms including sneezing, itching, nasal congestion, and rhinorrhea. Allergic rhinitis (AR) can be characterized as “seasonal” or “perennial” depending on duration and timing of the allergic response.

Current therapy for allergic rhinitis is treated with oral antihistamines, oral corticosteroids, nasal sprays (ie, intranasal corticosteroids, intranasal antihistamines), and leukotriene inhibitors. The Joint Task Force on Practice Parameters on the diagnosis and management of allergic rhinitis state that intranasal corticosteroids are the most effective medications for treating allergic rhinitis. In addition they note that intranasal antihistamines may be considered for use as first-line treatment for allergic and nonallergic rhinitis and are more efficacious and equal to or superior to oral second-generation antihistamines for the treatment of seasonal allergic rhinitis; however, they are generally less effective than intranasal corticosteroids. In addition, inhaled nasal corticosteroids have been found to be more effective in allergy patients than leukotriene modifiers.

When conventional therapy fails (ie, intranasal steroids, antihistamines), immunotherapy is an option. Subcutaneous allergen immunotherapy (SCIT) has represented the main approach of allergen immunotherapy in the US. SCIT may be considered for patients with evidence of symptoms based on allergen exposure, the presence of specific IgE antibodies, and whose allergic rhinitis symptoms are not well controlled by medication and/or avoidance measures.

#### Guidelines, Reviews

The British Society for Allergy & Clinical Immunology (BSACI) guidelines for immunotherapy for allergic rhinitis note:
• Immunotherapy, both SCIT and sublingual (SLIT), is an effective treatment for adults and children with severe allergic rhinitis that does not respond to conventional pharmacotherapy and allergen avoidance measures.
• SCIT and SLIT have been shown to give long-lasting benefit for some years after stopping treatment.
• The safety profile of SLIT appears to be superior to SCIT in terms of severe systemic reactions although this data comes from indirect comparison not head-to-head trials. It is not yet clear from these studies whether SCIT and SLIT are of equivalent efficacy.

Allergen immunotherapy practice parameter from the Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma & Immunology (AAAAI); the American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy, Asthma & Immunology (written before the FDA approval of SLIT, this formulation was considered investigational at the time of writing):8
• SCIT should be considered for patients who have symptoms of allergic rhinitis/conjunctivitis or asthma with natural exposure to allergens and who demonstrate specific IgE antibodies to the relevant allergen or allergens. Candidates for immunotherapy are patients whose symptoms are not controlled adequately by medications and avoidance measures or those experiencing unacceptable adverse effects of medications or who wish to reduce the long-term use of medications.

A clinical practice guideline from the American Academy of Otolaryngology-Head and Neck Surgery Foundation (endorsed by the American Academy of Family Physicians) recommend that clinicians should offer, or refer to a clinician who can offer, immunotherapy (sublingual or subcutaneous) for patients with AR who have inadequate response to symptoms with pharmacologic therapy with or without environmental controls. The benefits include: altered natural history, improved symptom control, decreased need for medical therapy, long-term cost-effectiveness, may improve or prevent asthma or other comorbidities, and may prevent new sensitizations. The risks, harms, and costs are: local reactions, systemic reactions including anaphylaxis, increased initial cost frequency of treatment (logistics), pain of injection, and delayed onset of symptom control (months). Both SCIT and SLIT have been shown to be efficacious for AR; however, neither has been shown conclusively to be more efficacious than the other.11

An AHRQ review found 74 RCTs (randomized controlled trials) on the efficacy and safety of SCIT, 60 RCTs on the efficacy and safety of SLIT, and 8 RCTs on head-to-head comparisons between both forms of immunotherapy.9
• There is sufficient evidence to support the overall effectiveness and safety of both SCIT and SLIT for treating allergic rhinoconjunctivitis and asthma.
• There is not enough evidence to determine if either SCIT or SLIT is superior.
• SCIT and SLIT are usually safe, although local reactions are commonly reported regardless of the mode of delivery.
• Serious, life-threatening reactions are rare, although they can occur. SLIT studies mainly include patients with allergic rhinitis and/or mild asthma. Safety outcomes for SLIT should not be extrapolated to more severely affected patients.
Most studies use a single allergen for immunotherapy. It may be difficult to extrapolate these results to the use of multiple-allergen regimens, which are commonly used in clinical practice in the US.

**Safety**

All three oral immunotherapy agents carry the same boxed warning:

- Can cause life-threatening allergic reactions such as anaphylaxis and severe laryngopharyngeal edema/restriction.
- Do not administer to patients with severe, unstable or uncontrolled asthma.
- Observe patients in the office for at least 30 minutes following the initial dose.
- Prescribe auto-injectable epinephrine, instruct and train patients on its appropriate use, and instruct patients to seek immediate medical care upon its use.
- May not be suitable for patients with certain underlying medical conditions that may reduce their ability to survive a serious allergic reaction.
- May not be suitable for patients who may be unresponsive to epinephrine or inhaled bronchodilators, such as those taking beta-blockers.

Grastek, Oralair, and Ragwitek have not been studied in subjects who are receiving concomitant allergen immunotherapy. Concomitant dosing with other allergen immunotherapy may increase the likelihood of local or systemic adverse reactions to either subcutaneous or sublingual allergen immunotherapy.¹⁻³

**CODING**

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

<table>
<thead>
<tr>
<th>CPT/HCPCS</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>95199</td>
<td>Unlisted allergy / clinical immunologic service or procedure</td>
</tr>
<tr>
<td>J3490</td>
<td>Unclassified drugs</td>
</tr>
</tbody>
</table>

There are no specific HCPCS codes for the drugs listed in this policy.

- The unlisted CPT code 95199 should be used.
- CPT codes for allergen immunotherapy are specific to parenteral administration and should not be used for sublingual immunotherapy.

**ICD-9 Diagnoses**

<table>
<thead>
<tr>
<th>Code</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>477.0</td>
<td>Allergic rhinitis; due to pollen</td>
</tr>
</tbody>
</table>

**ICD-10 Diagnoses (Effective October 1, 2015)**

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<tr>
<th>Code</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>J30.1</td>
<td>Allergic rhinitis due to pollen</td>
</tr>
</tbody>
</table>

**REVISED**

<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>06-07-2013</td>
<td>Policy added to the bcbsks.com web site.</td>
</tr>
</tbody>
</table>
In Policy section:

- Revised policy from experimental / investigational to medically necessary adding, "Sublingual immunotherapy using Oralair®, Grastek®, or Ragwitek® may be considered medically necessary, when used according to FDA-labelling, for the treatment of pollen-induced allergic rhinitis when the following conditions are met:
  1. Patient has a history of rhinitis or rhinoconjunctivitis symptoms related to grass or short ragweed pollen exposure.
  2. Patient has a documented positive pollen-specific skin test or pollen-specific immunoglobulin E (IgE) test (see Policy Guidelines section).
  3. Patient’s symptoms are not adequately controlled by appropriate pharmacotherapy (see Policy Guidelines section)."

- Revised E/I statement adding "for all other uses" to read, "Sublingual immunotherapy as a technique of allergy immunotherapy is considered experimental / investigational for all other uses."

- Added Policy Guidelines:
  "For Oralair®, Grastek®, or Ragwitek® (1-3):
  Documentation of Allergy
  Allergy must be confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies to the species contained in the product or, for Grastek®, Timothy grass pollen extract, to cross-reactive species.
  Contraindications
  Contraindications include severe, unstable or uncontrolled asthma; history of any severe local reaction, or any severe systemic allergic reaction to SLIT; and for Grastek® and Ragwitek®, history of eosinophilic esophagitis.
  Administration and Dose
  1. Prescribing information includes a black box warning for severe allergic reactions including anaphylaxis. Patients must be prescribed an epinephrine auto-injector and be trained on how to use it.
  2. 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).
  3. 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.
  4. All 3 agents are dosed once daily.
  5. For Oralair®, dose titration is required in patients 10 to 17 years of age. Titration can be completed over 3 days at home (after the first dose) according to the schedule in Table 1. In patients between 18 to 65 years, no dose titration is needed; treatment is initiated at the maintenance dose of 300 IR (index of reactivity).
  6. Grastek® and Ragwitek® both are initiated at the maintenance dose (2800 BAU [bioequivalent allergy unit] and 12 Amb a 1 unit, respectively).

Table 1. Oralair® Dosing in Patients Age 10-17 Years (1)

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3 and Following</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 IR</td>
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<td>300 IR</td>
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</tbody>
</table>

IR, index of reactivity, a potency unit defined by the formation of a 7-mm wheal in 30 sensitized individuals during product development. (1)

Pharmacotherapy of Pollen-Induced Allergic Rhinitis

Several clinical practice guidelines describe pharmacologic treatments of pollen-induced allergic rhinitis/rhinoconjunctivitis. (4-8) There is general agreement that:

1. Treatment should be individualized based on symptom severity and duration, comorbidities, and patient age, preference (eg, route of administration, tolerance for adverse effects), and previous treatment history.
2. Measures to increase treatment adherence (eg, shared decision making, consideration of the patient’s school or work schedule, use of a medication calendar or check-off list) are encouraged.

3. Goals of treatment are symptom reduction and improvements in functional capacity and quality of life.

4. A “step-up” (if treatment is inadequate)/“step-down” (if symptom relief is achieved with other interventions, eg, avoidance) approach to treatment is recommended.

5. Allergen avoidance is the first step of treatment but may be unrealistic for some patients.

6. Six medication classes are used to treat allergic rhinitis: H1-antihistamines (oral and intranasal), corticosteroids (oral [short-course for severe disease] and intranasal), leukotriene receptor antagonists (oral), sympathomimetic decongestants (oral and intranasal), chromones (intranasal), and the anticholinergic, ipratropium bromide (intranasal).

7. Treatment should be symptom-specific, eg, 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.

8. For mild or intermittent symptoms, oral or nasal antihistamine may be considered first-line treatment.

9. Newer generation (selective) oral antihistamines generally are recommended over older (nonselective) antihistamines. Patients with insomnia and pregnant women may prefer older antihistamines because of their sedating effects and longer safety history, respectively.

10. Intranasal corticosteroids may be effective for more severe or persistent symptoms.

11. Combination treatment (eg, 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.

12. Oral sympathomimetics may cause insomnia; their use is limited in patients with certain comorbidities (eg, diabetes mellitus, unstable hypertension).

13. Oral leukotriene receptor antagonists may reduce asthma exacerbations in patients with comorbid asthma.

Rationale section updated

In Coding section:
- Added ICD-9 Code: 477.0
- Added ICD-10 Code: J30.1
- Removed “Experimental / Investigational on all diagnoses related to this medical policy.”

References updated

11-01-2014 Policy posted 10-02-2014 and effective 11-01-2014, 30 days after posting.

Adopted PTI policy.

Policy title changed to: “Oral Immunotherapy Agents (Grastek®, Oralair®, Ragwitek™)” from “Sublingual Immunotherapy as a Technique of Allergen-Specific Therapy”

Description section revised
- Added FDA Indications

In Policy section
- The policy was revised to the current policy language from:

"A. Sublingual immunotherapy using Oralair®, Grastek®, or Ragwitek® may be considered medically necessary, when used according to FDA-labelling, for the treatment of pollen-induced allergic rhinitis when the following conditions are met:
1. Patient has a history of rhinitis or rhinoconjunctivitis symptoms related to grass or short ragweed pollen exposure."

Contains Public Information
2. Patient has a documented positive pollen-specific skin test or pollen-specific immunoglobulin E (IgE) test (see Policy Guidelines section).
3. Patient’s symptoms are not adequately controlled by appropriate pharmacotherapy (see Policy Guidelines section).

B. Sublingual immunotherapy as a technique of allergy immunotherapy is considered experimental / investigational for all other uses.

Policy Guidelines
For Oralair®, Grastek®, or Ragwitek®(1-3):

Documentation of Allergy
Allergy must be confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies to the species contained in the product or, for Grastek®, Timothy grass pollen extract, to cross-reactive species.

Contraindications
Contraindications include severe, unstable or uncontrolled asthma; history of any severe local reaction, or any severe systemic allergic reaction to SLIT; and for Grastek® and Ragwitek®, history of eosinophilic esophagitis.

Administration and Dose
1. Prescribing information includes a black box warning for severe allergic reactions including anaphylaxis. Patients must be prescribed an epinephrine auto-injector and be trained on how to use it.
2. 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).
3. 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.
4. All 3 agents are dosed once daily.
5. For Oralair®, dose titration is required in patients 10 to 17 years of age. Titration can be completed over 3 days at home (after the first dose) according to the schedule in Table 1. In patients between 18 to 65 years, no dose titration is needed; treatment is initiated at the maintenance dose of 300 IR (index of reactivity).
6. Grastek® and Ragwitek® both are initiated at the maintenance dose (2800 BAU [bioequivalent allergy unit] and 12 Amb a 1 unit, respectively).

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2. Measures to increase treatment adherence (eg, shared decision making, consideration of the patient’s school or work schedule, use of a medication calendar or check-off list) are encouraged.
3. Goals of treatment are symptom reduction and improvements in functional capacity and quality of life.
4. A “step-up” (if treatment is inadequate)/“step-down” (if symptom relief is achieved with other interventions, eg, avoidance) approach to treatment is recommended.
5. Allergen avoidance is the first step of treatment but may be unrealistic for some patients.
6. Six medication classes are used to treat allergic rhinitis: H1-antihistamines (oral and intranasal), corticosteroids (oral [short-course for severe disease] and intranasal), leukotriene receptor antagonists (oral), sympathomimetic decongestants (oral and intranasal), chromones (intranasal), and the anticholinergic, ipratropium bromide (intranasal).

7. Treatment should be symptom-specific, eg, 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.

8. For mild or intermittent symptoms, oral or nasal antihistamine may be considered first-line treatment.

9. Newer generation (selective) oral antihistamines generally are recommended over older (nonselective) antihistamines. Patients with insomnia and pregnant women may prefer older antihistamines because of their sedating effects and longer safety history, respectively.

10. Intranasal corticosteroids may be effective for more severe or persistent symptoms.

11. Combination treatment (eg, 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.

12. Oral sympathomimetics may cause insomnia; their use is limited in patients with certain comorbidities (eg, diabetes mellitus, unstable hypertension).

13. Oral leukotriene receptor antagonists may reduce asthma exacerbations in patients with comorbid asthma."

- Added Contraindications chart
- Added Quantity Limits chart

Rationale section updated
Coding section reviewed with no changes
References updated

04-14-2015
In Policy section:
- In Item 12 a, removed "prescribed dosage", "within", and "(FDA approved labeled dosage)", and added "requested quantity (dose), "less than or equal to", and "quantity", to read, "The requested quantity (dose) is less than or equal to the program quantity limit."
- In Item 12 b, added "ALL of the following,
  i. The requested quantity (dose) is above the set limit AND,
  ii. One of the following,
    1) BOTH of the following,
      a) The requested quantity (dose) requested is below the FDA labeled dose AND,
      b) The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit OR,
    2) BOTH of the following,
      a) The requested quantity (dose) requested is above the FDA labeled dose AND"
- In Item 12 b i 2 b, removed "The quantity (dose) requested is greater than the maximum dose recommended in FDA approved labeling, and", to read, "The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist."

Updated References section.

10-01-2015
Published 11-10-2015; effective 10-01-2015.
In Policy section:
| 04-15-2016 | Updated Description section. |
|  | In Policy section: |
|  | In Item A 11, removed “therapy” and added “the requested agent” to read, "The patient does not have any FDA labeled contraindications to the requested agent." |
|  | Added Item B, “Sublingual immunotherapy as a technique of allergy immunotherapy is considered experimental / investigational for all other uses.” |
|  | Updated FDA Labeled Contraindications table. |
|  | Updated Quantity Limits for Target Drugs table. |
|  | Updated Rationale section. |
|  | Updated References section. |
| 05-15-2017 | Updated Description section: |
|  | Updated FDA Labeled Indications table. |
|  | In Policy section: |
|  | In Item A 4, added "with" to read, "The prescriber has expertise in allergy or immunology or has consulted with an expert in allergy or immunology" |
|  | In Item A 8, added ", or has already been started," to read, "The product will be started, or has already been started, 3-4 months before the expected onset of the applicable pollen season" |
|  | Added "4. History of eosinophilic esophagitis" to Oralair in the FDA Labeled Contraindications table. |
|  | Updated Rationale section. |
|  | Updated References section. |

**REFERENCES**

9. AHRQ-Effective Health Care Program. Subcutaneous and sublingual immunotherapy to treat allergic rhinitis/rhinoconjunctivitis and asthma.

**Other References**


4. Blue Cross and Blue Shield of Kansas Otolaryngology Liaison Committee Consent Ballot, October 2012.

5. Blue Cross and Blue Shield of Kansas CB: Family Practice Liaison Committee, Pediatric Liaison Committee, Otolaryngology Liaison Committee, October 2014.