POLICY STATEMENT:

I. Based upon our criteria and assessment of the peer reviewed literature, allergen injection, rush/rapid, cluster, and FDA approved sublingual allergen immunotherapies are considered **medically appropriate** in patients:
   A. with demonstrated hypersensitivity that cannot be adequately managed by medications or avoidance, and
   B. when there is a desire to avoid long-term pharmacotherapy, and
   C. in patients with coexisting allergic rhinitis and asthma where symptoms of asthma occur after natural exposure to aeroallergens and there is demonstrable evidence of clinically relevant specific IgE.

II. Based upon our criteria and assessment of the peer-reviewed literature, the following methods of immunotherapy are considered **investigational**:
   A. Acupuncture;
   B. DNA immunization/vaccination;
   C. Immunization with immunostimulatory sequences;
   D. Intranasal therapy;
   E. Mutated protein therapy;
   F. Peptide therapy;
   G. Provocative-neutralization therapy for food allergies;
   H. Repository emulsion therapy;
   I. Serial dilution endpoint titration therapy (Rinkel therapy);
   J. Sublingual-swallow, sublingual-spit, oral therapy (administration of antigen drops/tablets under the tongue) that has not been approved for marketing by the U. S. Food and Drug Administration (FDA); and
   K. Urine autoinjections, autogenous urine immunization (intramuscular injections of sterilized urine).

III. **Contraindications** to sublingual immunotherapy (SLIT) with FDA approved formulations:
   A. severe, unstable or uncontrolled asthma;
   B. history of any severe local reaction or any severe systemic allergic reaction to SLIT;
   C. history of eosinophilic esophagitis for Grastek® and Ragwitek®;
   D. for Grastek®, the patient is either below the age of five or above the age of sixty-five;
   E. for Oralair®, the patient is either below the age of ten or above the age of sixty-five; and
   F. for Ragwitek®, the patient is either below the age of eighteen or above the age of sixty-five.

This policy does not address Xolair (omalizumab). Refer to the Health Plan Drug policy regarding medical necessity criteria for Xolair.

Refer to Corporate Medical Policy # 2.01.04 regarding Clinical Ecology/ Multiple Chemical Sensitivities/Idiopathic Environmental Intolerance.

Refer to Corporate Medical Policy # 2.01.10 regarding Allergy Testing.

Refer to Corporate Medical Policy # 8.01.20 regarding Acupuncture.

Refer to Corporate Medical Policy # 11.01.03 regarding Experimental and Investigational Services.
POLICY GUIDELINES:

I. Administration of allergen immunotherapy is available in multiple formulations:
   A. Benefits for injections of allergens should be individualized for each patient and are considered under the medical portion of the member’s subscriber contract, when medically appropriate.
   B. Sublingual immunotherapy formulations that have been approved for marketing by the FDA, is dispensed by a pharmacist and benefits are considered under the pharmacy portion of the member’s subscriber contract, when medically appropriate. The first dose of sublingual immunotherapy is administered in a healthcare setting under the supervision of a physician for monitoring of adverse reactions.

II. The Federal Employees Health Benefit Program (FEHBP/FEP) requires that procedures, devices or laboratory tests approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational and thus these procedures, devices or laboratory tests may be assessed only on the basis of their medical necessity.

DESCRIPTION:

Allergen immunotherapy, desensitization or hypo sensitization, may be appropriate in patients not adequately managed with medications and avoidance of the allergen(s), when there is a desire to avoid long-term pharmacotherapy, and in patients with coexisting allergic rhinitis and asthma where symptoms of asthma occur after natural exposure to aeroallergens and there is demonstrable evidence of clinically relevant specific IgE.

Allergen injection immunotherapy involves regular injection(s) of offending allergen(s), in the form of antigen extract(s), over a period of time; with the goal of reducing symptoms. Immunotherapy begins on a weekly or biweekly basis, with low extract dose(s), to prevent untoward reactions, and gradually increases the dose(s) injected as immunity to the antigen(s) develop. After a maintenance antigen dose is achieved, the interval between injection(s) may range from two to six weeks. Immunotherapy may be administered continuously for several years.

Rush, or rapid, immunotherapy is an accelerated immunotherapy build-up schedule that entails administering incremental doses of allergen at intervals varying between 15 and 60 minutes over 1 to 3 days until the target therapeutic dose is achieved. Rush immunotherapy schedules for inhalant allergens can be associated with a greater risk of systemic reactions, particularly in high-risk patients (e.g., those with markedly positive prich/ puncture test responses), and premedication with antihistamines and corticosteroids appears to reduce the risk associated with rush immunotherapy. However, rush protocols for administration of Hymenoptera (stinging insect) venom immunotherapy have not been associated with a similar high incidence of systemic reactions.

Cluster immunotherapy is an accelerated build-up schedule that entails administering several injections at increasing doses (generally 2-3 per visit) sequentially in a single day of treatment on nonconsecutive days. The maintenance dose is generally achieved more rapidly than with a conventional (single injection per visit) build-up schedule (generally within 4 to 8 weeks).

Sublingual allergen immunotherapy involves the administration of an allergenic extract tablet that is placed under the tongue and rapidly dissolves. To date, three formulations of sublingual immunotherapy (SLIT) have been approved for marketing in the U. S. by the FDA:

I. On April 1, 2014, the FDA approved Oralair® for treatment of certain grass pollen-induced allergic rhinitis, with or without conjunctivitis, in patients age 10-65, who have grass pollen allergy to Kentucky Blue grass, Orchard grass, Perennial Rye grass, Sweet Vernal grass, and/or Timothy grass. Treatment with Oralair is started four months before the start of the grass pollen season and continued throughout the season.

II. On April 14, 2014, the FDA approved Grastek® for the treatment of Timothy grass pollen-induced allergic rhinitis, with or without conjunctivitis, in patients age 5-65. Treatment with Grastek is started twelve weeks before the start of the grass pollen season and continued throughout the season.
III. On April 17, 2014, the FDA approved Ragwitek® for the treatment of short ragweed pollen-induced allergic rhinitis, with or without conjunctivitis, in patients age 18-65 years. Treatment with Ragwitek is started twelve weeks before the start of the ragweed pollen season and continued throughout the season.

RATIONALE:
Allergen immunotherapy used to treat IgE mediated disease by injection with specific allergenic extracts is a widely accepted medical practice. The efficacy of immunotherapy has been demonstrated in multiple double blind, placebo-controlled studies. Continuing efforts have been made to improve the efficacy of immunotherapy, reduce the risk of reactions and the number of injections necessary through the use of adjuvants, various administration routes, by chemical alteration and modification and polymerization of allergens. However, the results of clinical trials have not proven the safety and efficacy of these methods and remain investigational.

In January 2011, the American Academy of Allergy, Asthma and Immunology (AAAAI), the American College of Allergy, Asthma and Immunology (ACAAI), and the Joint Council of Allergy, Asthma and Immunology (JCAAI) published an update to their practice parameter addressing allergy immunotherapy. In regard to sublingual immunotherapy, the parameter states: “Although several studies have demonstrated the efficacy of sublingual immunotherapy (SLIT), there is no FDA-approved formulation for SLIT, and this treatment route is considered investigational in the United States. Oral immunotherapy and SLIT for food hypersensitivity are also considered investigational.” (Cox, et al, 2011).

Sublingual immunotherapy (SLIT) is a potential alternative to subcutaneous immunotherapy (SCIT) for providing allergen-specific therapy. Despite multiple placebo-controlled studies evaluating SLIT, questions remain about the optimal dosing, duration of treatment, and the use of multiple allergens. Three new sublingual pollen extracts - Oralair®, Grastek® and Ragwitek® -have been approved by the FDA for treatment of pollen-induced allergic rhinitis with or without conjunctivitis. Large, well-designed, randomized controlled trials supporting the marketing applications for these products provide consistent evidence of efficacy and safety. Although trials were placebo-controlled, rather than SCIT-controlled, minimum clinically important criteria for demonstrating efficacy were pre-specified and were met in most studies. Patients in these trials had received previous treatment for their pollen-induced rhinitis or rhinoconjunctivitis symptoms. Scientific literature has also revealed that the use of sublingual immunotherapy in pediatric patients is yet to be established as a safe and efficacious form of treatment. This has been accounted for by the FDA as the recently approved SLITs are contraindicated in pediatric patients. Ineligible age groups vary across products. SLIT is being investigated for other allergies (e.g., other seasonal, food allergies, house dust mite allergies); however, current evidence is insufficient to form conclusions about the use of SLIT for these indications, and no allergy extracts for these uses have been FDA approved.

Some evidence from clinical trials has been published on the comparative effectiveness of SLIT versus SCIT, but the quantity and quality of evidence is less than that for efficacy versus placebo. Several 2013 systematic reviews tended to find better outcomes with SCIT than with SLIT, but findings were inconclusive due to small numbers of trials and variability in study design. There also are insufficient data to draw firm conclusions about the relative safety of SLIT versus SCIT.

CODES: Number Description
Eligibility for reimbursement is based upon the benefits set forth in the member’s subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key: Experimental/Investigational = (E/I), Not medically necessary/appropriate = (NMN).
<table>
<thead>
<tr>
<th>CPT</th>
<th>Description</th>
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<tbody>
<tr>
<td>95115</td>
<td>Professional services for allergen immunotherapy, not including provision of allergenic extracts; single injection</td>
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<tr>
<td>95117</td>
<td>two or more injections</td>
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<tr>
<td>95144</td>
<td>Professional services for the supervision and provision of antigens for allergen immunotherapy, single or multiple antigens, single dose vials (specify number of vials)</td>
</tr>
<tr>
<td>95145</td>
<td>Professional services for the supervision and provision of antigens for allergen immunotherapy (specify the number of doses); single stinging insect venom</td>
</tr>
<tr>
<td>95146</td>
<td>two single stinging insect venoms</td>
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<tr>
<td>95147</td>
<td>three single stinging insect venoms</td>
</tr>
<tr>
<td>95148</td>
<td>four single stinging insect venoms</td>
</tr>
<tr>
<td>95149</td>
<td>five single stinging insect venoms</td>
</tr>
<tr>
<td>95165</td>
<td>Professional services for the supervision and provision of antigens for allergen immunotherapy; single or multiple antigens (specify number of doses)</td>
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</tbody>
</table>

*Note: Not appropriate for sublingual immunotherapy.*

| 95170    | whole body extract of biting insect or other arthropod (specify number of doses) |
| 95180    | Rapid desensitization procedure, each hour (eg, insulin, penicillin, horse serum) |
| 95199    | Unlisted allergy/clinical immunologic service or procedure |

*Note: Used for FDA approved formulations of sublingual immunotherapy.*

<table>
<thead>
<tr>
<th>HCPCS: No code(s)</th>
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<tbody>
<tr>
<td>ICD9:</td>
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*Proprietary Information of YourCare Health Plan*
ICD10: H10.411-H10.419 Chronic giant papillary conjunctivitis (code range)
H10.45 Other chronic allergic conjunctivitis
J30.0-J30.2, J30.81-J30.9 Allergic rhinitis (code range)
J45.20-J45.909 Asthma (code range)
J45998 Other asthma
L500 Allergic urticaria
L503 Dermatographic urticarial
Z91.010-Z91.09 Allergy status (code range)

REFERENCES:


Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. Drug allergy: an updated practice parameter. Ann Allergy Asthma Immunol 2010 Oct;105(4):259-273.


Proprietary Information of YourCare Health Plan


Wessel F, et al. Safety and tolerability of an SQ-standardized GRAss ALlergy immunotherapy tablet (GRAZAX®) in a real-life setting for three consecutive seasons - the GRAAL trial. *Clin Drug Investig* 2012 Jul 1;32(7):451-63


New York State Medicaid criteria. August 2016 Medicaid Update, Volume 32, Number 8, pg. 19.

**KEY WORDS:**

Allergy shots, Allergen/Allergy Immunotherapy, Grastek®, Oralair®, Ragwitek®, Sublingual immunotherapy (SLIT).
CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a Local Coverage Determination for Allergy Immunotherapy. Please refer to the following websites for Medicare Members: http://apps.ngsmedicare.com/lcd/LCD_L28451.htm.