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## Subject: Allergy Testing and Immunotherapy

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<a href="#">Position Statement</a>	<a href="#">Billing/Coding</a>	<a href="#">Reimbursement</a>	<a href="#">Program Exceptions</a>	<a href="#">Definitions</a>	<a href="#">Related Guidelines</a>
<a href="#">Other</a>	<a href="#">References</a>	<a href="#">Updates</a>			

### DESCRIPTION:

[Allergy](#) is a form of exaggerated sensitivity or hypersensitivity, to a substance that is either inhaled, swallowed, injected, or comes in contact with the skin or eye. A reaction may be caused from exposure to pollens, dust, molds, mites, animal fur or dander, feathers, stinging insect venoms, foods, or drugs. The term allergy is used to describe situations where hypersensitivity results from heightened or altered reactivity of the immune system in response to external substances. Treatment typically consists of avoidance of the offending agent, medication or [immunotherapy](#).

Injections of airborne or insect venom [allergens](#) are prepared for each person individually.

Allergy testing can be broadly subdivided into two methodologies:

[In vivo testing](#) – includes skin allergy testing (i.e., skin prick testing, skin scratch testing, intradermal testing, skin patch testing, and skin endpoint titration), bronchial provocation tests, and food challenges

[In vitro testing](#) – includes various techniques to test the blood for presence of specific IgE antibodies to a particular antigen (i.e., RAST and ELISA tests) and leukocyte histamine release test (LHRT), also referred to as basophil histamine release test.

Allergy immunotherapy is the process of administering progressively increasing doses of an allergen as treatment for a person who has demonstrated sensitivity through allergy testing. The purpose of immunotherapy is to relieve the allergic symptoms by decreasing the reaction to the specific [antigen](#). This clinical intervention has been used over the past 80 years. Immunotherapy begins with injections of the allergen extract (allergen vaccine) in low doses, with gradual increasing doses once or twice weekly as immunity to the antigen develops. Upon reaching a maintenance dose, injections are decreased to every two to six weeks, and may continue for several years.

## POSITION STATEMENT:

### Allergy Testing

The following allergy tests **meet the definition of medical necessity** when performed by or under the direct supervision of a physician for the purpose of establishing a diagnosis of allergy disease:

- Direct nasal mucous membrane test
- Ingestion challenge test (Excluding ingestion challenge food testing; refer to next section below)
- Inhalation bronchial challenge testing with histamine, methacholine or similar compounds
- Intracutaneous (intradermal) tests, sequential and incremental with drugs, biologicals or venoms, immediate type reaction
- Intracutaneous (intradermal) tests, sequential and incremental with drugs, with allergenic extracts for airborne allergens, immediate type reaction
- Intracutaneous (intradermal) tests with allergenic extracts (allergen vaccine), immediate type reaction (i.e., serial endpoint titration/SET)
- Intracutaneous (intradermal) tests with allergenic extracts (allergen vaccine), delayed type reaction, including reading
- Ophthalmic mucous membrane test
- Patch (application) tests with any membrane
- Percutaneous (scratch, puncture, prick) tests with allergenic extracts (allergen vaccine), immediate type reaction
- Percutaneous (scratch, puncture, prick) tests sequential and incremental, with drugs, biologicals or venoms, immediate type reaction
- Photopatch tests
- Provocative testing (e.g., Rinkel test)
- In vitro testing for allergen specific IgE, which includes:
  - ELISA (enzyme linked immunosorbent assay)
  - FAST (Fluorescent allergosorbent test)
  - IP (Immuno-peroxidase test)
  - MAST (Multiple thread allergosorbent test)
  - RAST (Radioallergosorbent test)
  - PRIST (Paper radioimmunosorbent test)
  - CAP assay

Aspirin desensitization **meets the definition of medical necessity** for aspirin sensitive individuals who:

- Require administration of aspirin or aspirin-like drugs, **OR**
- Are unable to avoid aspirin or aspirin-like drugs, **AND**

- **ONE** of the following:
  - Asthma that is poorly controlled
  - Sinus disease with recurrent nasal polyps
  - Require aspirin therapy for primary or secondary prevention of cardiovascular events
  - A chronic inflammatory condition (e.g., arthritis) requiring aspirin or NSAID therapy
  - Antiphospholipid antibodies during pregnancy

The following types of allergy testing are considered **experimental or investigational** as controlled studies have failed to demonstrate the value of these tests for the diagnosis of allergies in clinical practice. This is not an all-inclusive list.

- Administration of allergy immunotherapy outside of a medical facility (e.g., home administration)
- Antigen leukocyte cellular antibody (ALCAT) (automated food allergy testing)
- Applied kinesiology or Nambudripad's allergy elimination test (NAET) (i.e., muscle strength testing or measurement after allergen ingestion)
- Candidiasis test
- Chemical analysis of body tissue (eg, hair)
- Chlorinated pesticides (serum)
- Complement antigen testing (total or components)
- Cytokine and cytokine receptor assay
- Cytotoxic testing for food, environmental or clinical ecological allergy testing (Bryans Test, ACT)
- Electrodermal testing or electrodermal acupuncture
- Food immune complex assay (FICA)
- Ingestion challenge food testing for diagnosing rheumatoid arthritis, depression, or respiratory disorders not associated with anaphylaxis or similar systemic reactions
- Intracutaneous and subcutaneous provocative and neutralization testing for food allergies
- Immune complex assay
- Iridology
- Leukocyte histamine release test (LHRT)/basophil histamine release test
- Lymphocytes (B or T subsets)
- Lymphocyte function assay
- Mediator release test (MRT)
- Prausnitz-Kustner or P-K testing (passive cutaneous transfer test)
- Pulse test (pulse response test, reaginic pulse test)
- Rebuck skin window test

- Sage Complement Antigen Test
- Testing for multiple chemical sensitivity syndrome (a.k.a., idiopathic environmental intolerance (IEI), clinical ecological illness, clinical ecology, environmental illness, chemical AIDS, environmental/chemical hypersensitivity disease, total allergy syndrome, cerebral allergy, 20th century disease)
- Urine autoinjection (autogenous urine immunization)

Routine allergy re-testing **does not meet the definition of medical necessity**.

**Environmental therapy**, also known as idiopathic environmental intolerance therapy or clinical ecology treatment, **does not meet the definition of medical necessity** as there is insufficient peer-reviewed medical literature to support these therapies as being any more effective than the standard care for treatment.

This method of therapy may include the following:

- Aerobic exercise therapy
- Alteration of the individual's household environment
- Environmental care units
- Neutralizing therapy of chemical and food extracts
- Nutritional therapy

### **Allergen Immunotherapy**

Allergen immunotherapy by intradermal or subcutaneous injection **meets the definition of medical necessity** when administered for the treatment of individuals demonstrating hypersensitivity to specific antigens that cannot be managed by medications or avoidance.

Allergen immunotherapy services may include one or more of the following:

- Individual evaluation related to the supply or administration of the allergenic extract (allergen vaccine)
- Supplies (needles, syringes, diluents)
- Monitoring the physical status of the individual during administration of the extract (allergen vaccine.)

Immunotherapy using sublingual drops (also known as sublingual antigen extract drop immunotherapy, sublingual liquid immunotherapy, aqueous extract products) is considered **experimental or investigational**. Data in published medical literature are inadequate to permit scientific conclusions on long-term and net health outcomes.

**NOTE:** For coverage information on sublingual immunotherapy (SLIT) using a specific drug (e.g., Oralair<sup>®</sup>, Grastek<sup>®</sup>, Ragwitek<sup>®</sup>, Odactra<sup>®</sup>), please refer to the member contract pharmacy benefits.

## BILLING/CODING INFORMATION:

### CPT Coding for allergy testing:

0165U	Peanut allergen-specific quantitative assessment of multiple epitopes using enzyme-linked immunosorbent assay (ELISA), blood, individual epitope results and probability of peanut allergy
0178U	Peanut allergen specific quantitative assessment of multiple epitopes using enzyme linked immunosorbent assay (ELISA), blood, report of minimum eliciting exposure for a clinical reaction
86001	Allergen specific IgG quantitative or semiquantitative, each allergen <b>(investigational)</b>
86003	Allergen specific IgE; quantitative or semiquantitative, crude allergen extract, each
86005	Allergen specific IgE; quantitative, multi-allergen screen (e.g., disk, sponge, card)
86008	Allergen specific IgE; quantitative or semiquantitative, recombinant or purified component, each
95004	Percutaneous tests (scratch, puncture, prick) with allergenic extracts, immediate type reaction, including test interpretation and report, specify number of tests
95017	Allergy testing, any combination of percutaneous (scratch, puncture, prick) and intracutaneous (intradermal), sequential and incremental, with venoms, immediate type reaction, including test interpretation and report, specify number of tests
95018	Allergy testing, any combination of percutaneous (scratch, puncture, prick) and intracutaneous (intradermal), sequential and incremental, with drugs or biologicals, immediate type reaction, including test interpretation and report, specify number of tests
95024	Intracutaneous (intradermal) tests with allergenic extracts, immediate type reaction, including test interpretation and report by a physician, specify number of tests
95027 *	Intracutaneous (intradermal) tests, sequential and incremental, with allergenic extracts for airborne allergens, immediate type reaction, including test interpretation and report, specify number of tests
95028	Intracutaneous (intradermal) tests with allergenic extracts, delayed type reaction, including reading, specify number of tests
95044	Patch or application test(s) (specify number of tests)
95052	Photo patch test(s) (specify number of tests)
95056	Photo tests
95060	Ophthalmic mucous membrane tests
95065	Direct nasal mucous membrane test
95070	Inhalation bronchial challenge testing (not including necessary pulmonary function tests), with histamine, methacholine, or similar compounds
95076 *	Ingestion challenge test (sequential and incremental ingestion of test items, e.g., food, drug or other substance); initial 120 minutes of testing
95079 *	Ingestion challenge test (sequential and incremental ingestion of test items, e.g., food, drug or other substance); each additional 60 minutes of testing (List separately in addition to code for primary procedure)

### CPT Coding for Allergy Immunotherapy:

95115	Professional services for allergen immunotherapy not including provision of allergenic extracts; single injection
95117	Professional services for allergen immunotherapy not including provision of allergenic extracts; 2 or more injections
95120	Professional services for allergen immunotherapy in the office or institution of the prescribing physician or other qualified health care professional, including provision of allergenic extract; single injection
95125	Professional services for allergen immunotherapy in the office or institution of the prescribing physician or other qualified health care professional, including provision of allergenic extract; 2 or more injections
95130	Professional services for allergen immunotherapy in the office or institution of the prescribing physician or other qualified health care professional, including provision of allergenic extract; single stinging insect venom
95131	Professional services for allergen immunotherapy in the office or institution of the prescribing physician or other qualified health care professional, including provision of allergenic extract; 2 stinging insect venoms
95132	Professional services for allergen immunotherapy in the office or institution of the prescribing physician or other qualified health care professional, including provision of allergenic extract; 3 stinging insect venoms
95133	Professional services for allergen immunotherapy in the office or institution of the prescribing physician or other qualified health care professional, including provision of allergenic extract; 4 stinging insect venoms
95134	Professional services for allergen immunotherapy in the office or institution of the prescribing physician or other qualified health care professional, including provision of allergenic extract; 5 stinging insect venoms
95144	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy, single or multiple antigens, single dose vials (specify number of vials)
95145	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); single stinging insect venom
95146	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); 2 single stinging insect venoms
95147	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); 3 single stinging insect venoms
95148	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); 4 single stinging insect venoms
95149	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); 5 single stinging insect venoms
95165	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy; single or multiple antigens (specify number of doses)

95170	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); whole body extract of biting insect or other arthropod (specify number of doses)
95180	Rapid desensitization procedure, each hour (e.g., insulin, penicillin, equine serum)

## REIMBURSEMENT INFORMATION:

Reimbursement for allergy testing services includes the following components:

- Supplies (e.g., sterile diluents, syringes, needles)
- Monitoring the physical status of the individual during testing
- Observation, recording, and interpretation of the test results

Reimbursement for allergy testing is based on the number of each type of test performed by the same physician and is subject to the following limitations when the above coverage criteria are met:

### Limitations:

CPT Code:	Type of Test:	Limited To:
86005	Allergen specific IgE; qualitative, multiallergen	1 per year
95004	Percutaneous tests (scratch, puncture, prick) with immediate type reaction	400 in 12 months
95017	Allergy testing with venoms; any combination of percutaneous (scratch, puncture, prick) and intracutaneous (intradermal) testing	120 in 12 months
95018	Allergy testing with drugs and biologicals; any combination of percutaneous (scratch, puncture, prick) and intracutaneous (intradermal) testing	120 in 12 months
95024	Intracutaneous (intradermal) tests with allergenic extracts, immediate type reaction	120 in 12 months
95027	Intracutaneous (intradermal) tests, sequential and incremental, with allergenic extracts for airborne allergens, immediate type reaction	120 in 12 months
95028	Intracutaneous (intradermal) tests with allergenic extracts, delayed type reaction	120 in 12 months
95044	Patch or application test(s)	200 in 12 months
95052	Photo patch test(s)	200 in 12 months
95056	Photo tests	200 in 12 months
95060	Ophthalmic mucous membrane tests	48 in 12 months
95065	Direct nasal mucous membrane test	48 in 12 months
95070, 95071	Inhalation bronchial challenge testing	48 in 12 months
95076 (95079 is an add-on code that is not reported alone)	Ingestion challenge test	4 per year total 1 per year for any given food

The AAAAI practice guidelines make the following recommendations regarding immunotherapy frequency and duration:

- The build-up phase (also called up dosing phase, induction phase or dose-increase phase) involves receiving injections with increasing amounts of allergen, and generally ranges from 1 to 3 times per week. The duration of this phase depends on the frequency of the injections but generally ranges from 3 to 6 months (at a frequency of 2 times and 1 time per week, respectively).
- 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.
- Rush immunotherapy is an accelerated immunotherapy build-up schedule that entails administering incremental doses of allergens at intervals varying between 15 and 60 minutes over 1 to 3 days.
- The maintenance dose or effective therapeutic dose is the dose that provides therapeutic efficacy without significant adverse local or systemic reactions; it may not be the initially calculated projected effective dose.
- The maintenance phase begins when the effective therapeutic dose is achieved; intervals between injections can be progressively increased as tolerated to 4 – 8 weeks for venom, and 2 to 4 weeks for inhalants.
- Venom immunotherapy (VIT) injections generally are given at weekly intervals.
- VIT intervals between maintenance dose injections can increase to 4 weeks the first year of VIT and eventually to every 6 – 8 weeks during subsequent years.
- Clinical improvement is usually observed within one (1) year after the individual reaches maintenance or effective therapeutic dose.
- The decision to continue or stop therapy should be made after 3 – 5 years.
  - Consider discontinuing VIT after 3 – 5 years.
  - The duration of fire ant immunotherapy has not been clearly established, but most allergists recommend continuing therapy 4 – 5 years.

Reimbursement for **allergy immunotherapy** is based on the number of procedures performed and is subject to the limitations below:

**Limitations:**

CPT Code	Procedure	Limited to
95115, 95117**	Administration of extract (allergen vaccine)	152 total injections within 12 months
95120, 95125	Allergenic extract (allergen vaccine) including administration	100 total doses within 12 months
95144	Allergenic extract, single dose vials (specify number of vials)	156 doses within 12 months (specify number of vials)

95165	Allergenic extract, single or multiple antigens (specific number of doses)	156 total doses within 12 months
95130 – 95134	Stinging insect venom, including administration	52 total doses within 12 months
95145 – 95149, 95170	Stinging insect venom	52 total doses within 12 months OR 40 total doses within 3 months for rapid desensitization
95180	Rapid desensitization	4 hours for a specific substance (excluding aspirin)
No specific code	Aspirin desensitization	12 hours per year

Allergy testing or immunotherapy services in excess of the above limitations are subject to medical review of documentation supporting medical necessity. The following information may be required documentation to support medical necessity: physician history and physical, care provider notes, and all laboratory studies.

**LOINC Codes:**

<b>DOCUMENTATION TABLE</b>	<b>LOINC CODES</b>	<b>LOINC TIME FRAME MODIFIER CODE</b>	<b>LOINC TIME FRAME MODIFIER CODES NARRATIVE</b>
Physician history and physical	28626-0	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Attending physician visit note	18733-6	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Physician initial assessment	18736-9	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Attending physician progress note	18741-9	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Allergy tests	18716-1	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Laboratory studies (i.e., ELISA, RAST, PRIST, Mast)	26436-6	18805-2	Include all data of the selected type that represents observations made

			six months or fewer before starting date of service for the claim.
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## PROGRAM EXCEPTIONS:

**Federal Employee Program (FEP):** Follow FEP guidelines.

**State Account Organization (SAO):** Follow SAO guidelines.

### Medicare Advantage:

The following National Coverage Determinations (NCDs) were reviewed on the last guideline reviewed date and are located at cms.gov:

Antigens Prepared for Sublingual Administration (110.9)

Food Allergy Testing and Treatment (110.11)

Challenge Ingestion Food (110.12)

Cytotoxic Food Tests (110.13)

The following Local Coverage Determinations (LCDs) were reviewed on the last guideline reviewed date and are located at cms.gov:

Allergy Testing (L33261)

Allergen Immunotherapy (L37800)

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at [Coverage Protocol Exemption Request](#)

## DEFINITIONS:

**ALCAT:** antigen leukocyte cellular antibody) automated food allergy testing; is reported to identify food sensitivity by using a modified Coulter Counter linked to a computer program to measure the change in white blood cells incubated with purified food and mold extract.

**Allergen:** any substance that indicates a state of, or brings on, manifestations of allergy; an antigenic substance capable of producing immediate-type hypersensitivity.

**Allergenic extract (allergen vaccine):** an extract (allergen vaccine) of allergenic components from a crude preparation of an allergen (e.g., weed, grass, mite, animal dander) used for diagnostic skin testing or for immunotherapy (hyposensitization) of allergy.

**Allergy:** an over-reaction of the body's immune system, against particular substances and particles (allergens, antigens) such as pollen, animal dander, dust, insect particles.

**Antigen:** the specific particle that one is allergic to, such as the specific part of pollen.

**Antihistamine:** drug that blocks the allergic reaction.

**Asthma:** a reversible obstructive lung disorder characterized by increased responsiveness of the airways; inflammation and irritation of the airways that may cause wheezing, sneezing, coughing, or shortness of breath.

**Bronchial challenge:** see provocation test; involves the inhalation of agents that trigger respiratory responses (i.e., drugs causing airway constriction, antigens and chemical sensitizers usually related to occupational breathing problems).

**Conjunctival challenge:** see provocation test; small amount of antigen is applied to the lower conjunctival sac.

**Custer immunotherapy:** 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 scheduled (generally within 4 – 8 weeks).

**Cytotoxic testing:** for determining sensitivity to foods believed to cause asthma, arthritis, constipation, diarrhea hypertension, obesity, stomach disorders, and many other conditions; used in the 1980's; controlled clinical studies have failed to demonstrate effectiveness or reliability.

**ELISA (enzyme linked immunosorbent assay):** an in vitro assay for allergen specific IgE antibodies in serum, indicating an allergy to the substance.

**FAST (fluorescent allergosorbent test):** an in vitro assay using a fluoregenic detection system that looks for allergen specific IgE antibodies in serum, indicating an allergy to the substance.

**Food challenge test:** used to confirm or diagnose IgE- mediated hypersensitivity to specific foods, food additives and preservatives (metabisulfite). Increasing amounts of the suspected food allergen is ingested every 15 – 20 minutes for 2 hours or until a reaction occurs or the amount is higher than that expected to produce a reaction. One food item is tested per day.

**Idiopathic environmental intolerance:** The original term, clinical ecology, was replaced by the term multiple chemical sensitivity (MCS). Most recently, it has been replaced by the term idiopathic environmental intolerance, a term reflecting the uncertain nature of the condition and its relationship to chemical exposure. The central focus of the condition is the fact that the individual describes recurrent, nonspecific symptoms referable to multiple organ systems that the sufferers believe are provoked by exposure to low levels of chemical, biologic, or physical agents. The most common environmental exposures include perfumes and scented products, pesticides, domestic and industrial solvents, new carpets, car exhaust, gasoline and diesel fumes, urban air pollution, cigarette smoke, plastics, and formaldehyde. Certain foods, food additives, drugs, electromagnetic fields, and mercury in dental fillings have also been reported as triggering events. However symptoms do not bear any relationship to established toxic effects of the specific chemical and occur at concentrations far below those expected to elicit toxicity.

**Immunotherapy:** allergy injection therapy; the process of injecting small amounts of substances causing the allergy reaction; over a period of time, doses are progressively increased until the body adjusts to

the substance, or becomes desensitized; other treatments include avoidance of the substance or taking medications such as antihistamines to block the allergic reaction.

**In vitro testing:** within a glass or test tube; in an artificial environment.

**In vivo testing:** used to identify allergic substances that are responsible for producing diseases such as asthma, allergic rhinitis, eczema, urticaria, anaphylaxis, and gastrointestinal reactions.

**In vivo:** within the living body.

**Intradermal or Intracutaneous test:** a small amount (.001 to .05 ml) of antigen extract (allergen vaccine) is injected into the skin with a disposable syringe attached to a 26- to 30- gauge needle or with a tuberculin type syringe; a reaction is recorded 15 – 30 minutes after application. This type of skin testing is more suitable to individuals with lower skin sensitivity or for antigens with lower potency. Because of the added risk of adverse systemic reactions due to the larger volume of antigen extract (allergen vaccine) used, these tests are typically performed on the upper arm or forearm rather than the back, to allow application of a tourniquet if necessary, and are performed in a setting with staff capable of handling adverse reactions and emergencies.

**IP (Immuno-peroxidase test):** an in vitro assay for allergen specific IgE antibodies in serum, indicating an allergy to the substance.

**LEAP:** Lifestyle Eating and Performance disease management program (Don Self & Associates, Inc.) is based on the theory that symptoms of irritable bowel syndrome and other certain conditions are caused by reactions to specific foods and food additives. The program includes individual selection tools, a self-directed stress management program, and assessment tools for determining outcomes.

**MAST (multiple thread allergosorbent test):** an in vitro assay using an enzymatic detection system that looks for allergen specific IgE antibodies in serum, indicating an allergy to the substance.

**Mediator release test (MRT):** primarily used to detect intolerance to foods and additives in individuals with irritable bowel syndrome. Also used in individuals with chronic fatigue syndrome, metabolic conditions (e.g., diabetes, obesity), gastrointestinal disorders (e.g., gastroesophageal reflux disease, chronic ulcerative colitis, and Crohn's disease), neurologic disorders (e.g., migraine headaches, cluster headaches), rheumatologic disorders (inflammatory arthritis, arthralgias, fibromyalgia), otolaryngologic disorders (e.g., perennial rhinitis, chronic sinusitis, chronic otitis media with effusion), dermatologic conditions (e.g., eczema, urticaria, dermatitis), and in individuals with behavioral conditions (e.g., attention deficit disorder, hyperactivity, frequent mood swings, inability to concentrate). This test measures the aggregate release of inflammatory mediators from the individual's immunocytes in vitro after exposure to specific foods and food additives. The results of the mediator release test have been used to design an individual -specific diet to treat irritable bowel syndrome by avoiding foods and additives that trigger significant inflammatory mediator release.

**Nasal challenge:** see provocation test.

**Patch (application) test:** antigen is impregnated into a small piece of gauze or filter paper disc and applied to a strip of aluminum foil or placed within an 8 mm diameter aluminum device (Finn chamber) and applied to the skin and held in place with tape (a test system known as the TRUE test uses multiple

antigens incorporated into a gel delivery system); reactions are observed and recorded at 48 hours after application and may be read again 1 – 5 days after the first reading.

**Prick or puncture test:** a drop of antigen is placed directly on the skin then gently pricked through with a sharp instrument (needle, lancet, or specially designed plastic device) at a 45 – 60 degree angle (prick test) or 90 degree angle (puncture); reactions are recorded at 15 – 20 minutes after application.

**PRIST (paper radioimmunosorbent test):** an in vitro assay for allergen specific IgE antibodies in serum, indicating an allergy to the substance.

**Proteolytic enzyme:** when preparing mixtures of allergen extracts, the prescribing physician must take into account the cross-reactivity of allergen extracts and the potential for allergen degradation caused by proteolytic enzymes (breakdown of proteins).

**Provocation test:** challenge test performed to duplicate the individual's main symptoms or signs by controlled exposure to a suspected antigen; can be delivered by ingestion (food, oral challenge), inhalation (bronchial challenge), or by direct application to the mucosal membrane of nares (nasal challenge) or conjunctiva (conjunctival challenge).

**RAST (radio-allergo-sorbent test):** an in vitro assay for allergen specific IgE antibodies in serum; designed to aid in the diagnosis of IgE-mediated disorders and in the formulation of allergen immunotherapy.

**Rhinitis:** inflammation of the nasal mucosa.

**Rush immunotherapy:** an accelerated immunotherapy build-up schedule that involves administering incremental doses of allergen at intervals varying between 15 and 60 minutes over 1 – 3 days until the targeted therapeutic dose is achieved. A rush immunotherapy schedules for inhalant allergens can be associated with a greater risk of systemic reactions, particularly in high-risk individuals (e.g., those with markedly positive prick/puncture test responses), and premedication with antihistamines and corticosteroids appears to reduce the risk associated with rush immunotherapy.

**SAGE:** a cellular assay that tests for delayed food sensitivity; the SAGE method uses whole blood, rather than serum, and tests simultaneously for multiple pathways.

**Scratch tests:** the skin is superficially scratched with a blunt scarifying device in such a way as to prevent excessive bleeding; a drop of antigen extract (allergen vaccine) is then applied to the scratch; antigen and control sites are recorded 20 minutes after application.

**Skin test:** applying a small amount of an antigen extract (allergen vaccine) directly to the skin either by intradermal tests or by epicutaneous, epidural, or percutaneous tests (scratch, prick, puncture, and patch tests).

## **RELATED GUIDELINES:**

[Peanut \(\*Arachis hypogaea\*\) Allergen Powder-dnfd \(Palforzia\), 09-J3000-69](#)

## **OTHER:**

None applicable.

## REFERENCES:

1. Abramson MJ, Puy RM, Weiner JM. Allergen immunotherapy for asthma. *Cochrane Database of Systematic Reviews* 2003, Issue 4. Art. No.: CD001186. DOI: 10.1002/14651858.CD001186.
2. Allergy Diagnostic Testing: An Updated Practice Parameter. I L Bernstein, JT Li, et al. *Ann of Allergy Asthma Immunology*; March 2008; Vol 100, No. 3, Supplement 3 (updated 05/22/09).
3. American Academy of Allergy, Asthma and Immunology (AAAAI). Conditions and Treatments: Food Allergy. Accessed at <https://www.aaaai.org/>.
4. American Academy of Allergy, Asthma and Immunology (AAAAI). Anaphylaxisda practice parameter update 2015. Accessed at <https://www.aaaai.org/>.
5. American Academy of Allergy, Asthma and Immunology (AAAAI) and American College of Allergy, Asthma and Immunology (ACAAI), Joint Council of Allergy, Asthma and Immunology. Cox L, Nelson H, Lockey R, Calabria C, Chacko T, Finegold I, Nelson M, Weber R, Bernstein DI, Blessing-Moore J, Khan DA, Lang DM, Nicklas RA, Oppenheimer J, Portnoy JM, Randolph C, Schuller DE, Spector SL, Tilles S, Wallace D. Allergen immunotherapy: a practice parameter third update. *J Allergy Clin Immunol* 2011 Jan;127(1 Suppl):S1-55.
6. American Academy of Allergy, Asthma and Immunology, American College of Allergy, Asthma and Immunology, Joint Council of Allergy, Asthma and Immunology. Food allergy: A practice parameter update 2014.
7. American Academy of Allergy, Asthma and Immunology (AAAAI) and American College of Allergy, Asthma and Immunology (ACAAI) Task Force. Sublingual immunotherapy: A comprehensive review (05/06)
8. American Academy of Allergy, Asthma and Immunology Position Statement: The Use of Standardized Allergen Extracts, (05/97).
9. American Academy of Allergy, Asthma and Immunology Workgroup Report: Current Approach to the Diagnosis and Management of Adverse Reactions to Foods, (10/03).
10. American Academy of Allergy, Asthma and Immunology. Physician Reference Materials: Position Statement 2, Some Untested Diagnostic and Therapeutic Procedures in Clinical Allergy.
11. American Academy of Allergy, Asthma and Immunology. Physician Reference Materials: Position Statement 10, Skin Testing and Radio Allergosorbent Testing (RAST) for Diagnosis of Specific Allergens Responsible for IgE-Mediated Diseases.
12. American Academy of Allergy, Asthma and Immunology. Physician Reference Materials: Position Statement 21, The Use of In Vitro Tests for IgE Antibody in the Specific Diagnosis of IgE-Mediated Disorders and in the Formulation of Allergen Immunotherapy.
13. American Academy of Allergy, Asthma and Immunology. Physician Reference Materials: Position Statement 24, Allergen Skin Testing From the Board of Directors.
14. American Academy of Allergy, Asthma and Immunology. Physician Reference Materials: Position Statement 35. Idiopathic environmental intolerance. *J Allergy Clin Immunol*. 1999; 103: 36-40.
15. American Academy of Allergy, Asthma, and Immunology Position Statement 8. Controversial Techniques. *J Allergy Clin Immunol*. 1981; 67:333-338.
16. American Academy of Allergy, Asthma & Immunology Position Statement – AAAAI support of the EAACI Position Paper on IgG4. Adverse Reactions to Foods Committee (05/20/10).
17. American Academy of Asthma, Allergy and Immunotherapy (AAAAI). Consultation and referral guidelines citing the evidence: How the allergist-immunologist can help. *J Allergy Clin Immunol* 2006;117:S495-523.

18. American Academy of Allergy, Asthma and Immunology (AAAAI). Allergy Diagnostic Testing: An Updated Practice Parameter. ANNALS OF ALLERGY, ASTHMA, & IMMUNOLOGY March 2008; Volume 100, Number 3, Supplement 3. Accessed at <http://www.aaaai.org>.
19. American Academy of Allergy, Asthma and Immunology (AAAAI). Choosing Wisely Campaign (2014): Ten Things Physicians and Patients Should Question. Accessed at <http://www.aaaai.org>.
20. American Academy of Allergy, Asthma, and Immunology (AAAAI). Allergen immunotherapy: A practice parameter third update (2011). Accessed at <http://www.aaaai.org>.
21. Barrett MD, Stephen. Allergies: Dubious Diagnosis and Treatment, (06/14/03; revised 01/17/08).
22. Berg EA, et al. Drug allergens and food--the cetuximab and galactose- $\alpha$ -1,3-galactose story.
23. Bernstein IL, Li JT, Bernstein DI, Hamilton R, Spector SL, Tan R, Sicherer S, Golden DB, Khan DA, Nicklas RA, Portnoy JM, Blessing-Moore J, Cox L, Lang DM, Oppenheimer J, Randolph CC, Schuller DE, Tilles SA, Wallace DV, Levetin E, Weber R, American Academy of Allergy, Asthma and Immunology, American College of Allergy, Asthma and Immunology. Allergy diagnostic testing: an updated practice parameter. Part 1. Ann Allergy Asthma Immunol. 2008 Mar;100(3 Suppl 3):S15-S66.
24. Biedermann T, et al. Mammalian meat allergy: a diagnostic challenge. Allergo J Int. 2015;24(3):81-83.
25. Blue Cross Blue Shield Association 2003 TEC Assessment; "Sublingual Immunotherapy for Allergies".
26. Blue Cross Blue Shield Association Evidence Positioning System®. 2.01.17 - Sublingual Immunotherapy as a Technique of Allergen Specific Therapy, 11/25.
27. Blue Cross Blue Shield Association Evidence Positioning System®. 2.01.93 - Antigen Leukocyte Antibody Test, 11/25.
28. Burks AW, Calderon MA, Casale T et al. Update on allergy immunotherapy: American Academy of Allergy, Asthma & Immunology/European Academy of Allergy and Clinical Immunology/PRACTALL consensus report. J Allergy Clin Immunol 2013.
29. Cahill KN, et al. Prostaglandin D<sub>2</sub>: a dominant mediator of aspirin-exacerbated respiratory disease. J Allergy Clin Immunol. 2015 Jan;135(1):245-52.
30. Calderon MA, Alves B, Jacobson M, Hurwitz B, Sheikh A, Durham S. Allergen injection immunotherapy for seasonal allergic rhinitis. Cochrane Database of Systematic Reviews 2007, Issue 1. Art. No.: CD001936. DOI: 10.1002/14651858.CD001936.pub2.
31. Canonica GW, Cox L, Pawankar R et al. Sublingual immunotherapy: World Allergy Organization position paper 2013 update. The World Allergy Organization journal 2014; 7(1):6.
32. Carr S, Chan E, Lavine E, Moote W. CSACI Position statement on the testing of food-specific IgG. Allergy Asthma Clin Immunol. 2012 Jul 26;8(1):12.
33. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD): Allergy Testing (L33261) (10/01/15) (Revised 07/11/21).
34. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD): Allergen Immunotherapy (L37800) (10/18/18) (Revised 03/31/24).
35. Centers for Medicare and Medicaid Services (CMS). National Coverage Determination (NCD) for Antigens Prepared for Sublingual Administration (110.9) (11/17/96).
36. Centers for Medicare and Medicaid Services (CMS). National Coverage Determination (NCD) for Food Allergy Testing and Treatment (110.11) (10/31/88).
37. Centers for Medicare and Medicaid Services (CMS) National Coverage Determination (NCD) for Challenge Ingestion Food Testing (110.12) (08/01/78).

38. Centers for Medicare and Medicaid Services (CMS) National Coverage Determination (NCD) for Cytotoxic Food Tests (110.13) (08/05/85).
39. ClinicalTrials.gov. NCT01658475: P. Gingivalis IgG Titer Test for Periodontitis. Okayama University (August 2012).
40. ClinicalTrials.gov. NCT01592071: IgG-mediated Food Test for Weight Loss. Immuno Laboratories (February 2014).
41. ClinicalTrials.gov. NCT01353079: Efficacy and Safety Study Of Short Ragweed Pollen Sublingual-Oral Immunotherapy, Greer Laboratories (February 2015).
42. ClinicalTrials.gov. NCT00599872: Efficacy Study of Sublingual Immunotherapy to Treat Ragweed Allergies. Greer Laboratories (January 2014).
43. ClinicalTrials.gov. NCT00732654: The Safety and Efficacy of Sublingual/Oral Immunotherapy for the Treatment of Milk Protein Allergy. Johns Hopkins University (May 2017).
44. Commins SP, et al. Delayed anaphylaxis, angioedema, or urticaria after consumption of red meat in patients with IgE antibodies specific for galactose-alpha-1,3-galactose. *J Allergy Clin Immunol*. 2009 Feb;123(2):426-33.
45. Commins SP, et al. Delayed anaphylaxis to alpha-gal, an oligosaccharide in mammalian meat. *Allergol Int*. 2016 Jan;65(1):16-20.
46. Commins SP, et al. Delayed clinical and ex vivo response to mammalian meat in patients with IgE to galactose-alpha-1,3-galactose. *J Allergy Clin Immunol*. 2014 Jul;134(1):108-15.
47. Commins SP, et al. The relevance of tick bites to the production of IgE antibodies to the mammalian oligosaccharide galactose- $\alpha$ -1,3-galactose. *J Allergy Clin Immunol*. 2011 May;127(5):1286-93.e6.
48. Commins SP, Platts-Mills TA. Allergenicity of carbohydrates and their role in anaphylactic events. *Curr Allergy Asthma Rep*. 2010 Jan;10(1):29-33.
49. Commins SP, Platts-Mills TA. Delayed anaphylaxis to red meat in patients with IgE specific for galactose alpha-1,3-galactose (alpha-gal). *Curr Allergy Asthma Rep*. 2013 Feb;13(1):72-7.
50. Commins SP, Platts-Mills TA. Tick bites and red meat allergy. *Curr Opin Allergy Clin Immunol*. 2013 Aug;13(4):354-9.
51. Cox L, Nelson H, Lockey R, et al. Allergen immunotherapy: a practice parameter third update. *J Allergy Clin Immunol*. 2011 Jan;127(1 Suppl):S1-55. doi: 10.1016/j.jaci.2010.09.034. Epub 2010 Dec 3. Erratum in: *J Allergy Clin Immunol*. 2011 Mar;127(3):840.
52. Cox LS, Larenas Linnemann D, et al. Sublingual immunotherapy: a comprehensive review. *J Allergy Clin Immunol*. 2006 May;117(5):1021-35.
53. ECRI Trends. Waste in healthcare from the specialist's chair. (04/01/2012).
54. First Coast Service Options (FCSO) Local Coverage Determination LCD# L29057 Allergy Tests, (effective 01/01/13). (Retired 09/30/15)
55. First Coast Service Options (FCSO) Local Coverage Determination LCD# L29056 Allergen Immunotherapy, (effective 10/01/11). (Retired 09/30/15)
56. Fischer J, et al. Clinical spectrum of  $\alpha$ -Gal syndrome: from immediate-type to delayed immediate-type reactions to mammalian innards and meat. *Allergo J Int*. 2016;25:55-62. Epub 2016 Mar 23.
57. Flicker S, Linhart B, Wild C, Wiedermann U, Valenta R. Passive immunization with allergen-specific IgG antibodies for treatment and prevention of allergy. *Immunobiology*. 2013 Jun;218(6):884-91.
58. Flaherty MG, et al. Diagnosis of Life-Threatening Alpha-Gal Food Allergy Appears to Be Patient Driven. *J Prim Care Community Health*. 2017 Oct;8(4):345-348.
59. Fornadley MD, John. Allergy Management for the Otolaryngologist. *Otolaryngologic Clinics of North America*, 31:111-127, 02/98.

60. Gerez IF, Shek LP, Chng HH, Lee BW. Diagnostic tests for food allergy. *Singapore Med J*. 2010 Jan;51(1):4-9.
61. Greenhawt M, Oppenheimer J, et al. Sublingual immunotherapy: A focused allergen immunotherapy practice parameter update (2017). *Ann Allergy Asthma Immunol* 118 (2017) 276e282.
62. Hankin CS, Cox L, et al. Allergy immunotherapy among Medicaid-enrolled children with allergic rhinitis: Patterns of care, resource use, and costs. *The Journal of Allergy and Clinical Immunology*. 2008;1(121):227-32.
63. HAYES Medical Technology Directory; Allergy Testing, In Vitro, RAST, and Other Immunoassays ALLE0403.06 (04/23/98; updated 03/24/03; updated and renamed 8/04 "Allergy Testing for Diagnosis of Allergic Rhinitis, In Vitro, Quantitative"). (08/08/03; updated 10/23/07).
64. HAYES Medical Technology Directory; Allergy Testing, In Vivo, (08/22/06; updated 09/08/07).
65. HAYES Search and Summary. Sublingual Immunotherapy Drops for Allergy Treatment (04/27/07).
66. Hoeks SB, de Groot H, Hoekstra MO. Sublingual immunotherapy in children with asthma or rhinoconjunctivitis: not enough evidence because of poor quality of the studies; a systematic review of literature. *Ned Tijdschr Geneeskd*. 2008 Feb 2;152(5):261-8. PMID: 18333541.
67. Ibrahim C, et al. A retrospective study of the clinical benefit from acetylsalicylic acid desensitization in patients with nasal polyposis and asthma. *Allergy Asthma Clin Immunol*. 2014 Dec 11;10(1):64.
68. Joint Council of Allergy, Asthma and Immunology (JCAAI) Practice Parameter. Stinging insect hypersensitivity: A Practice Parameter Update (10/04).
69. Joint Council of Allergy, Asthma and Immunology (JCAAI). Physician's Instruction Guide for the Preparation of Allergen Extract (02/20/09)
70. Joint Council of Allergy, Asthma and Immunology (JCAAI). Practice Parameters for Allergy Diagnostic Testing. Accessed 08/04/09.
71. Kennedy JL, et al. Galactose- $\alpha$ -1,3-galactose and delayed anaphylaxis, angioedema, and urticaria in children. *Pediatrics*. 2013 May;131(5):e1545-52.
72. Kim JE, Yoo SR, Jeong MG, Ko JY, Ro YS. Hair zinc levels and the efficacy of oral zinc supplementation in patients with atopic dermatitis. *Acta Derm Venereol*. 2014 Sep;94(5):558-62.
73. Kim JM, Lin SY, Suarez-Cuervo C, Chelladurai Y, Ramanathan M, Segal JB, Erekosima N. Allergen-specific immunotherapy for pediatric asthma and rhinoconjunctivitis: a systematic review. *Pediatrics*. 2013 Jun 1;131(6):1155-67.
74. Kollmann D, et al. The quantity and quality of  $\alpha$ -gal-specific antibodies differ in individuals with and without delayed red meat allergy.
75. Lewith GT, Kenyon JN, Broomfield J, Prescott P, Goddard J, Holgate ST. Is electrodermal testing as effective as skin prick tests for diagnosing allergies? A double blind, randomised block design study. *BMJ*. 2001 Jan 20;322(7279):131-4.
76. Lin SY, Erekosima N, Kim JM, et al. Sublingual Immunotherapy for the Treatment of Allergic Rhinoconjunctivitis and Asthma: A Systematic Review. *JAMA*. 2013;309(12):1278-1288. doi:10.1001/jama.2013.2049.
77. Moffitt, JE, Golden, DB, et al. Stinging insect hypersensitivity: a practice parameter update. *J Allergy Clin Immunol* 2004 Oct; 114(4):869-86.
78. Mortuaire G, Michel J, et al. Specific immunotherapy in allergic rhinitis. *European annals of otorhinolaryngology, head and neck diseases*. 2017 Sep 1;134(4):253-8.
79. Mullin RJ, et al. Relationship between red meat allergy and sensitization to gelatin and galactose- $\alpha$ -1,3-galactose. *J Allergy Clin Immunol*. 2012 May;129(5):1334-1342.e1.

80. National Guideline Clearinghouse. Institute for Clinical Systems Improvement (ICSI) Diagnosis and management of asthma, (01/08).
81. National Guideline Clearinghouse. Joint Task Force on Practice Parameters, American College of Allergy, Asthma and Immunology, American College of Allergy, Asthma and Immunology, Joint Council of Allergy, Asthma and Immunology. Allergen immunotherapy: a practice parameter second update, (09/07).
82. National Guideline Clearinghouse. Moffitt JE, et al. Stinging insect hypersensitivity: a practice parameter update. *J Allergy Clin Immunol* 2004 Oct; 114(4):869-86.
83. National Guideline Clearinghouse; American College of Allergy, Asthma, & Immunology. Food allergy: a practice parameter. *Ann Allergy Asthma Immunol* 2006 Mar;96(3 Suppl 2):S1-68. This is the current release of the guideline (accessed 09/23/14).
84. National Guideline Clearinghouse. Consultation and referral guidelines citing the evidence: how the allergist-immunologist can help. (06/18/06; accessed 09/23/14).
85. NIAID-Sponsored Expert Panel, Boyce JA, Assa'ad A, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. *J Allergy Clin Immunol* 2010;126(6 Suppl):S1-5S8.
86. Pieniawska-Śmiech K, Lewandowicz-Uszyńska A, Zemelka-Wiacek M, Jutel M. Serum Allergen-Specific IgE among Pediatric Patients with Primary Immunodeficiency. *Children (Basel)*. 2022 Mar 25;9(4):466. doi: 10.3390/children9040466.
87. Platts-Mills TA, et al. Anaphylaxis to the carbohydrate side chain alpha-gal. *Immunol Allergy Clin North Am*. 2015 May;35(2):247-60. *Allergy*. 2017 Feb;72(2):266-273.
88. Platts-Mills TA, et al. Delayed Anaphylaxis Involving IgE to Galactose-alpha-1,3-galactose. *Curr Allergy Asthma Rep*. 2015 Apr;15(4):12.
89. Ramsey N, Berin MC. Pathogenesis of IgE-mediated food allergy and implications for future immunotherapeutics. *Pediatr Allergy Immunol*. 2021 Oct;32(7):1416-1425. doi: 10.1111/pai.13501. Epub 2021 Jun 17.
90. Saleh H, Embry S, Nauli A, Atyia S, Krishnaswamy G. Anaphylactic reactions to oligosaccharides in red meat: a syndrome in evolution. *Clin Mol Allergy*. 2012 Mar 7;10(1):5.
91. Santos AF, Lack G. Basophil activation test: food challenge in a test tube or specialist research tool? *Clin Transl Allergy*. 2016 Mar 15;6:10.
92. Scadding GW, Calderon MA, 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*. 2017 Feb;317(6):615-25.
93. Severino MG, Cortellini G, et al. Sublingual immunotherapy for large local reactions caused by honeybee sting: a double-blind, placebo-controlled trial. *J Allergy Clin Immunol*. 2008 Jul;122(1):44-8. doi: 10.1016/j.jaci.2008.03.031. Epub 2008 May 12.
94. Shady MM, Fathy HA, Ali A, Galal EM, Fathy GA, Sibaii H. Comparison of Serum IgG Antibody Test with Gastric Biopsy for the Detection of Helicobacter Pylori Infection among Egyptian Children. *Open Access Maced J Med Sci*. 2015 Jun 15;3(2):303-6.
95. Shaker MS, Wallace DV, Golden DBK, Oppenheimer J, et al. Anaphylaxis-a 2020 practice parameter update, systematic review, and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) analysis. *J Allergy Clin Immunol*. 2020 Apr;145(4):1082-1123. doi: 10.1016/j.jaci.2020.01.017.
96. Shakoor Z, AlFaifi A, AlAmro B, AlTawil LN, AlOhalay RY. Prevalence of IgG-mediated food intolerance among patients with allergic symptoms. *Ann Saudi Med*. 2016 Nov-Dec;36(6):386-390.

97. Sieber J, Köberlein J, Mösges R. Sublingual immunotherapy in daily medical practice: effectiveness of different treatment schedules - IPD meta-analysis. *Curr Med Res Opin.* 2010 Apr;26(4):925-32. doi: 10.1185/03007991003659483. PMID: 20163297.
98. Skoner D, Gentile D, et al. Sublingual immunotherapy in patients with allergic rhinoconjunctivitis caused by ragweed pollen. *J Allergy Clin Immunol.* 2010 Mar;125(3):660-6, 666.e1-666.e4. doi: 10.1016/j.jaci.2009.12.931. Epub 2010 Feb 11.
99. Slayden TA, Shakir MKM, Hoang TD. A BULL IN A PILL SHOP: ALPHA-GAL ALLERGY COMPLICATING TREATMENT OPTIONS FOR POSTPROCEDURAL HYPOTHYROIDISM. *AACE Clin Case Rep.* 2020;6(3):e101-e104. Published 2020 May 11. doi:10.4158/ACCR-2019-0495.
100. Spies JW, et al. The role of aspirin desensitization in patients with aspirin-exacerbated respiratory disease (AERD). *Braz J Otorhinolaryngol.* 2016 May-Jun;82(3):263-8.
101. Stapel SO, Asero R, Ballmer-Weber BK, Knol EF, Strobel S, Veiths S, Kleine-Tebbe J. Position Paper: Testing for IgG4 against food is not recommended as a diagnostic tool: EAACI Task Force Report. *Allergy* 2008;63:793-796.
102. Steinke JW, et al. The alpha-gal story: lessons learned from connecting the dots. *J Allergy Clin Immunol.* 2015 Mar;135(3):589-96; quiz 597.
103. Stone CA Jr. et al. Anaphylaxis after zoster vaccine: Implicating alpha-gal allergy as a possible mechanism. *J Allergy Clin Immunol.* 2017 May;139(5):1710-1713.e2.
104. Tripathi A, et al. Delayed anaphylaxis to red meat masquerading as idiopathic anaphylaxis. *J Allergy Clin Immunol Pract.* 2014 May-Jun;2(3):259-65.
105. UpToDate. Overview of in vitro allergy tests. 2024. Accessed at [uptodate.com](https://www.uptodate.com).
106. UpToDate. Overview of skin testing for IgE-mediated allergic disease. 2024. Accessed at [uptodate.com](https://www.uptodate.com).
107. U.S. Department of Health and Human Services, US Food and Drug Administration (FDA), Center for Biologics Evaluation and Research (CBER). Guidance for Industry; Testing Limits in Stability Protocols for Standardized Grass Pollen Extracts. Nov. 2000.
108. U.S. Department of Health and Human Services, US Food and Drug Administration (FDA), Center for Biologics Evaluation and Research (CBER). Guidance for Industry; On the Content and Format of Chemistry Manufacturing and Controls Information and Establishment Description Information for an Allergenic Extract or Allergen Patch Test. April 1999.
109. U.S. Food and Drug Administration (FDA); Vaccines, Blood, and Biologics. Standardized Allergenic Extracts. Accessed 08/04/09.
110. U.S. Food and Drug Administration (FDA) Approval, Oralair (04/2014).
111. U.S. Food and Drug Administration (FDA) Approval, Grastek (04/2014).
112. U.S. Food and Drug Administration (FDA) Approval, Ragwitek (04/2014).
113. Viswanathan RK, Biagtan MJ, Mathur SK. The role of autoimmune testing in chronic idiopathic urticaria. *Ann Allergy Asthma Immunol.* 2012 May;108(5):337-341.e1.
114. Wilson DR, Torres Lima M, Durham SR. Sublingual immunotherapy for allergic rhinitis. *Cochrane Database of Systematic Reviews* 2003, Issue 2. Art. No.: CD002893. DOI: 10.1002/14651858.CD002893.
115. Wilson JM, et al. Galactose- $\alpha$ -1,3-Galactose: Atypical Food Allergen or Model IgE Hypersensitivity? *Curr Allergy Asthma Rep.* 2017 Jan;17(1):8.
116. Wilson JM, Schuyler AJ, Workman L, et al. Investigation into the  $\alpha$ -Gal Syndrome: Characteristics of 261 Children and Adults Reporting Red Meat Allergy. *J Allergy Clin Immunol Pract.* 2019;7(7):2348-2358.e4. doi:10.1016/j.jaip.2019.03.031. PMID: 30940532.

117. Wolver SE, et al. A peculiar cause of anaphylaxis: no more steak? The journey to discovery of a newly recognized allergy to galactose-alpha-1,3-galactose found in mammalian meat. *J Gen Intern Med.* 2013 Feb;28(2):322-5.
118. Zeng ZC et al. Detection of Cytomegalovirus (CMV) Infection in Wheezing Infants by Urine DNA and Serum IgG Testing. *Med Sci Monit.* 2017 Mar 11;23:1242-1246.
119. Zhong C, Yang W, et al. Clinical evaluation for sublingual immunotherapy with *Dermatophagoides farinae* drops in adult patients with allergic asthma. *Ir J Med Sci.* 2018 May;187(2):441-446. doi: 10.1007/s11845-017-1685-x. Epub 2017 Oct 14. PMID: 29032417.

## COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy and Coverage Committee on 01/22/26.

## GUIDELINE UPDATE INFORMATION:

05/15/01	Medical Coverage Guideline Reformatted and Revised.
01/01/02	HCPCS coding changes.
01/01/03	HCPCS coding changes.
05/15/03	Reviewed; limitation changed for allergenic extract.
05/15/04	Scheduled review; added "mediator release test" to list of non-covered services; formatting revisions.
05/15/05	Scheduled review; no change in coverage statement.
10/15/05	Revision consisting of adding information regarding SAGE food allergy test.
05/15/06	Scheduled review: added investigational statement for sublingual immunotherapy for allergies and added additional tests and immunotherapies for idiopathic environmental illness; updated references.
09/15/06	Revision consisting of adding 83516, 83518, 83519, 83520, and 86005 to the list of allergy tests.
01/01/07	Annual HCPCS coding update (deleted 95078.)
05/15/07	Scheduled review; reformatted guideline; no change in coverage statement.
01/01/08	Annual HCPCS coding update: descriptor revisions for codes 95004, 95024, and 95027.
07/15/08	Scheduled review; no change in position statement; updated references.
01/01/09	Annual HCPCS coding update: revised descriptors for 95010 and 95015.
01/09/09	Revisions consisting of addition of criteria regarding IgG food allergy testing; reference added.
11/15/09	Scheduled review; no position statement changes; medical society information added regarding mixing of allergen extracts; reimbursement limitations revised; definitions added; references updated.
01/01/10	Annual HCPCS coding update: revised descriptors for 83516, 83518, 83519, and 83520.
04/15/10	Revision to Billing/Coding and Reimbursement sections regarding 83516, 83518, and 83519.
12/15/10	Scheduled review; Position Statement unchanged; added information regarding LEAP program; coding section revised; related ICD-10 codes added; references updated; formatting changes.

04/15/11	Revision to Reimbursement section of the guideline regarding allergen extracts.
07/15/11	Revision; formatting changes.
10/01/11	Revision to Reimbursement section.
12/15/11	Revisions to Billing/Coding (deleted code 83520) and Reimbursement sections.
03/15/12	Revision; Reimbursement section updated.
11/15/12	Annual review; position statement reformatted, references updated, formatting changes.
01/01/13	Annual HCPCS coding update: added 95017, 95018, 95076, and 95079; revised descriptors for 95004, 95027, 95120, 95125, 95130, 95131, 95132, 95133, and 95134; deleted 95010, 95015, and 95075.
11/15/13	Annual review; position statements unchanged; Program Exceptions section updated; references updated.
11/15/14	Annual review; position statement regarding sublingual immunotherapy revised; references updated; formatting changes.
06/15/16	Added CPT code 86001.
08/15/17	Scheduled review. Deleted "In vitro testing for allergen specific IgG" from the list of testing considered medically necessary. Added additional testing considered experimental or investigational. Deleted coverage statement for sublingual immunotherapy (SLIT) using Oralair®, Grastek®, or Ragwitek®. Revised Reimbursement Information section. Updated references. Reformatted guideline.
11/10/17	Revision: Added note regarding coverage of sublingual immunotherapy.
01/01/18	Annual CPT/HCPCS coding update: added 86008; revised 86003, 86005.
03/15/18	Revision: added criteria for aspirin desensitization; revised Reimbursement Information section; updated references.
08/15/18	Unscheduled review. Maintained position statement and updated references.
11/15/19	Revision. Added (E/I) coverage statement for sublingual immunotherapy antigen drops. Updated references.
04/01/20	Quarterly CPT/HCPCS coding update: added 0165U.
07/01/20	Quarterly CPT/HCPCS coding update: added 0178U; revised code descriptor 0165U.
08/15/20	Scheduled review. Revised list of allergy tests considered E/I. Updated references.
01/01/21	Annual CPT/HCPCS coding update. Revised 95070; deleted 95071.
08/15/21	Revision. Updated list of services considered environmental therapy.
07/15/22	Scheduled review. Added non-coverage statement for allergy immunotherapy administered outside a medical facility. Updated references.
05/22/23	Update to Program Exceptions section.
07/15/24	Scheduled review. Maintained position statement and updated references.
02/15/26	Position statements maintained.