MEDICAL POLICY

Excellus
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Medical Policy Title	**Allergy Testing**
Policy Number	**2.01.10**
Current Effective Date	July 17, 2025
Next Review Date	July 2026

Our medical policies are based on the assessment of evidence based, peer-reviewed literature, and professional guidelines. Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. (Link to Product Disclaimer)

POLICY STATEMENT(S)

I. The following **allergy** tests are considered **medically appropriate** in the diagnosis of the allergic patient:

A. Percutaneous test(s) (scratch, puncture, prick) with allergenic extracts;

B. Combination of percutaneous (scratch, puncture, prick) and intracutaneous (intradermal) with venoms, drugs or biologics;

C. Intracutaneous (intradermal) test(s) with allergenic extracts, including airborne allergens;

D. Patch or application tests(s);

E. Photo patch test(s);

F. Photo test(s);

G. Inhalation bronchial challenge testing (not including necessary pulmonary function tests), with histamine, methacholine, or similar compounds;

* If dust, ragweed, or other common allergens are the suspected cause of the problem, this test is **not medically appropriate**, as skin tests can be used in these situations.

H. Ingestion challenge test;

I. Gammaglobulin (immunoglobulin), IgE;

J. Allergen-specific IgE **only** when testing for allergens (e.g., inhalant, food, insect, drug) under the following circumstances:

1. When direct skin testing is impossible due to extensive dermatitis or marked dermatographism;
2. For patients unable to discontinue use of interfering medications (e.g., antidepressants, antihistamines, or beta-blocking agents);
3. For patients who have had a near fatal reaction to an allergen;
4. In children younger than four (4) years of age;
5. In patients who will not or cannot cooperate with percutaneous testing due to mental or physical disease (e.g., Down syndrome, intellectual disability, dementia);

6. To follow patients with food allergies and/or insect sting allergies previously documented by history and in-vivo or in-vitro testing;
7. For patients with suspected latex allergy;
8. For patients with suspected insect sting allergy with prior negative skin testing; **or**
9. For patients with suspected penicillin allergy.

II. The following allergy tests are considered **investigational**:

A. Allergen-specific IgG (when above criteria are not met);
B. Leukocyte histamine release test (LHR);
C. Ophthalmic mucous membrane tests;
D. Direct nasal mucous membrane test;
E. Peanut allergen-specific quantitative assessment of multiple epitopes using enzyme-linked immunosorbent assay (ELISA);
F. Cytotoxicity, Provocative testing (e.g., Rinkel test), Rebuck skin window test.

III. Allergy and laboratory testing for a treatment program (e.g., Southern California Food Allergy Tolerance Induction Program) is considered **investigational**.

RELATED POLICIES

Corporate Medical Policy

2.01.11 Allergen Immunotherapy

11.01.03 Experimental or Investigational Services

POLICY GUIDELINE(S)

Not Applicable

DESCRIPTION

Allergic or hypersensitivity disorders may be manifested by generalized systemic reactions and/or localized reactions in any organ system of the body. The reactions may be acute, subacute, or chronic, and immediate or delayed, and they may be caused by numerous offending agents (e.g., pollen, molds, dust, mites, animal dander, stinging insect venoms, foods, and drugs).

The optimum management of the allergic patient should include a careful history and physical examination and may include confirming the cause of allergic reaction by information from various testing methods. Once the offending allergenic agent(s) is (are) identified, treatment is provided by avoidance, medication, and/or immunotherapy.

Percutaneous Tests

The number of tests required may vary widely from patient to patient, depending upon the patient's history, and may require up to 80 tests. Allergy testing, any combination of percutaneous (scratch, puncture, prick) and intracutaneous is usually used when percutaneous testing is not considered to be sensitive enough to be the cause of an allergic reaction. The number of tests required may vary widely from patient to patient, depending upon the patient's history, and may require up to 40 tests.

Intracutaneous Tests

This may be used to represent serial endpoint testing (SET), which is a form of intradermal skin testing that uses increasing doses of antigen to determine the concentration at which the reaction changes from negative to positive (the "endpoint"). The test has been used for diagnosing allergic disorders and to guide the initiation of immunotherapy by using the endpoint dilution as the starting antigen dose. A physician or other qualified health care provider uses intracutaneous tests, sequential and incremental, with allergenic extracts for airborne allergens, immediate type reaction, to determine a patient's specific allergies. The number of tests must be specified (each sequential test = 1 unit). This includes test interpretation and provider report.

Patch or Application Tests

Also known as delayed hypersensitivity testing, this testing modality identifies allergens causing contact dermatitis. The suspected allergens are applied to the patient's back under dressings and allowed to remain in contact with the skin for 48 to 72 hours. The area is then examined for evidence of delayed hypersensitivity reactions.

Photo Patch Tests

This test reflects contact photosensitization. The suspected sensitizer is applied to a patch of skin for 48 hours. If no reaction occurs, the area is exposed to a dose of ultraviolet light sufficient to produce inflammatory redness of the skin. If the test is positive, a more severe reaction develops at the patch site than on the surrounding skin.

Inhalation Bronchial Challenge Test

Histamine or methacholine is used to perform this test, when it is necessary to determine whether the patient has hyper-responsive airways. Volatile chemicals are used to perform the test, when the allergy is encountered in an occupational setting.

Ingestion Challenge Test

With these tests, the patient ingests a food, drug or other substance to which sensitivity is suspected. This may be done in an open or blinded manner. Testing may be done at home, but in some instances of extreme suspected hypersensitivity, it may be performed in the office setting.

IgE Test

Total serum IgE concentration testing is not indicated in most allergic patients but may be indicated for patients suspected of having allergic bronchopulmonary aspergillosis, immune deficiency disease characterized by increased IgE levels (e.g., Wiskott-Aldrich syndrome, hyper-IgE staphylococcal

abscess syndrome), IgE myeloma, pemphigoid, or a poorly controlled moderate-to-severe asthmatic patient being considered for possible anti- IgE treatment.

Leukocyte Histamine Release Test

The leukocyte histamine release test is a measurement of the amount of histamine released in-vitro. Varying concentrations of an allergen extract are added to the patient's peripheral blood leukocytes. Histamine is normally released as a consequence of the interaction of allergen with cell-bound IgE antibodies. If an individual is atopic to a specific antigen, the leukocytes will not release the histamine in-vitro. Only a limited number of allergens can be tested from a single aliquot of blood and quality control studies have shown considerable variability in the measurement of histamine results.

SUPPORTIVE LITERATURE

Ferastraoaru et al (2017) reported, in an independent analysis of 75 patients with over 1600 tests between January 2014 and May 2015, for comparison of skin-prick (SPT), intradermal (IDST), and serum-specific immunoglobulin E (ssIgE) testing, that IDST detected more additional environmental sensitizations, compared with ssIgE testing. The authors concluded that IDST may be useful when the SPT and/or ssIgE testing results are negative, but the exposure history indicates relevant allergic sensitization. Serology added only a little more information when both SPT and IDST results were negative, but may be useful in combination with SPT, if IDST cannot be performed.

In a prospective, comparative clinical study (Peltier 2007), 134 subjects were tested for a comparison of intradermal dilutional testing, skin prick testing, and modified quantitative testing for common allergens. The researchers found poor correlation between endpoint and wheal size, as graded on a 1 to 4 system, and concluded that, although a correlation existed, the use of SPT to determine endpoint was inaccurate and dangerous. Modified quantitative testing (MQT) appears to be a safe alternative to IDT for determining starting doses for immunotherapy. The data support the safety and efficacy of MQT (combination SPT and IDT).

In a retrospective review of clinical data (random accrual), Seshul et al (2006) concluded that IDT is an important step in determining the strongest starting dose of immunotherapy that may safely be administered. Initiating immunotherapy in this manner may potentially create significant health care savings by shortening the time required for a patient to reach the patient’s individual, maximally tolerated dose. The use of a relatively large screening panel is cost-effective and does not increase the average number of antigens treated by immunotherapy. Blended allergy testing techniques that include IDT in their protocol are comparable in cost with commonly used allergy testing protocols. Otolaryngologists often favor IDT (SET) because of its well-documented sensitivity, specificity, safety, and reproducibility. IDT has been compared with many testing modalities used by other physicians to validate the technique as a part of mainstream allergy care.

Leukocyte histamine release testing (LHRT) is a technique to evaluate the in vitro release of histamine from leukocytes in response to an allergen. It provides an in vitro correlate to an in vivo allergic response. Published literature reflects that commercially available LHRT studies suffer from not having been performed in a blinded manner or do not indicate whether or not there were blinded

interpretations of the tests. Some studies included patients with known allergies, which did not represent the same population with equivocal allergy histories that would undergo testing. Studies of LHRT are potentially prone to spectrum, referral, and ascertainment bias, and are not sufficient to permit conclusions on the diagnostic accuracy of the tests. It has been suggested that LHRT may be a valuable test in those patients with discordant results of skin prick testing and RAST testing, but studies focusing on this subgroup of patients have not been identified.

Poto et al (2023) stated that mast cells are multi-functional immune cells with complex roles in tissue homeostasis and disease. Cardiac mast cells (HCMCs) are strategically located within the human myocardium and express the high-affinity receptor (FcεRI) for IgE and can be activated by anti-IgE and anti-FcεRI. Autoantibodies to IgE and/or FcεRI have been found in the serum of patients with a variety of immune disorders. The authors compared the effects of different preparations of IgG anti-IgE obtained from patients with atopic dermatitis (AD) with rabbit IgG anti-IgE on the release of preformed (histamine and tryptase) and lipid mediators [prostaglandin D2 (PGD2) and cysteinyl leukotriene C4 (LTC4)] from HCMCs. Functional human IgG anti-IgE from one out of six AD donors and rabbit IgG anti-IgE induced the release of pre-formed (histamine, tryptase) and de-novo synthesized mediators (PGD2 and LTC4) from HCMCs. Human IgG anti-IgE was more potent than rabbit IgG anti-IgE in inducing pro-inflammatory mediators from HCMCs. Human monoclonal IgE was a competitive antagonist of both human and rabbit IgG anti-IgE. The authors concluded that although functional anti-IgE autoantibodies rarely occur in patients with AD, when present, they could powerfully activate the release of pro-inflammatory and vasoactive mediators from HCMCs.

A number of procedures have been shown to be invalid for any clinical purpose. Studies of cytotoxic tests and provocation-neutralization tests have demonstrated that results are not reproducible. Electrodermal diagnosis and applied kinesiology have not been evaluated for efficacy. The “reaginic” pulse test and chemical analysis of body tissues have not been substantiated as valid allergy tests.

According to the 2008 AAAAI and the ACAAI joint practice parameter addressing allergy diagnostic testing, IgG and IgG subclass antibody tests for food allergy do not have clinical relevance, are not validated, lack sufficient quality control, and should not be performed. In addition, although a number of investigators have reported modest increases of IgG4 during venom immunotherapy, confirmation, and validation of the predictive value of IgG4 for therapeutic efficacy of venom immunotherapy are not yet proven. There is insufficient evidence in the published, peer-reviewed, scientific literature to support the use of specific IgG antibody testing by RAST or ELISA in the diagnosis or treatment of allergic disease.

There is a lack of published research on the diagnostic accuracy of peanut allergen-specific quantitative assessment of multiple epitopes using ELISA (e.g., VeriMAP Peanut Diagnostic and VeriMAP Peanut Sensitivity, AllerGenis). The evidence is insufficient to determine the effects of the technology on health outcomes.

Suprun et al (2019) presents the quantification and validation of a Bead-Based Epitope Assay (BBEA) that through multiplexing of epitopes and multiple sample processing enables completion of large experiments in a short period of time, using minimal quantities of patients' blood. Peptides that are uniquely coupled to beads are incubated with serum or plasma samples, and after a secondary fluorophore-labeled antibody is added, the level of fluorescence is quantified with a Luminex reader.

The signal is then normalized and converted to epitope-specific antibody binding values. The authors show that the effect of technical artifacts, i.e. well position or reading order, is minimal and batch effects can be easily estimated and eliminated from the data. The authors analyzed the relationship between IgE and IgG4 binding to 50 peanut epitopes in a cohort of 160 children. The authors state they showed that epitope-specific IgE alone was sufficient to distinguish between peanut allergic and non-allergic children; with IgG4 and IgG4-IgE ratio providing no additional information. Larger studies of epitope-specific antibody responses might be helpful in determining the role of IgG4 and different levels of peanut reactivity. To further advance the molecular allergy diagnostics and potentially bring it to the clinic, the authors have developed a Bead-Based Epitope Assay (BBEA) that allows high-throughput screening of samples and epitopes with significantly smaller volumes of serum or plasma compared to current molecular assays. BBEA provides greater sensitivity and reproducibility than microarrays and better resolution than component resolved diagnostics, making it a promising tool for the development of diagnostic and prognostic biomarkers. The authors concluded that epitope-specific antibody binding quantified with BBEA is highly reliable, reproducible and has greater sensitivity of epitope detection compared to peptide microarrays. IgE directed at allergenic epitopes is a sensitive biomarker of food allergy and can be used to predict allergy severity and phenotypes; and quantification of the relationship between epitope-specific IgE and IgG4 can further improve our understanding of the immune mechanisms behind allergic sensitization.

There is lack of published research showing the efficacy of Tolerance Induction Programs (e.g., Southern California Food Allergy Institute's Tolerance Induction Program) to treat food allergies. These treatment programs and the extensive testing required to participate in the treatment is considered investigational.

PROFESSIONAL GUIDELINE(S)

According to a March 2008 American Academy of Allergy, Asthma, and Immunology (AAAAI) practice parameter addressing Allergy Diagnostic Testing, IgE antibody assay technology has improved, with new high-binding capacity, solid-phase matrices, non-isotopic labels for detection antibodies, and standards calibrated to the World Health Organization IgE reference preparation. These enhancements have led to an evolution in assay methods from the first-generation qualitative assays (e.g., RAST, MAST, EAST), through the second generation semi-quantitative IgE assays (e.g., AutoCAP, Alastat, HYTech, Matrix, MagicLite), to the present state-of-the-art quantitative third generation autoanalyzers. Two third-generation immunoassays are the Immunocaptured System (Phadia) and the Immulite 2000 (Diagnostic Products Corp.), the chemistry of which is similar to the original RAST, but which employ non-isotopic labels and have more rapid throughput with improved precision, accuracy, and analytical sensitivity. Their automated chemistries report out allergen specific IgE antibody quantitatively.

In a 2022 publication on Practice Parameters for Drug Allergy, a joint task force of the AAAAI, the American College of Allergy, Asthma and Immunology (ACAAI), and the Joint Council of Allergy, Asthma & Immunology included in its executive summary a statement validating the use of intracutaneous (intradermal) tests, which are generally used for specific allergens (e.g. Hymenoptera venoms and penicillin), but may also be applied if prick/puncture test results are negative, and there is a strong historical likelihood of clinical allergy to specific allergens.

REGULATORY STATUS

The United States Food and Drug Administration (FDA) provides oversight of laboratory developed tests, now considered medical devices under the Federal Food, Drug, and Cosmetic Act. Refer to the FDA Medical Device website. Available from: https://www.fda.gov/medical-devices [accessed 2025 Jun 26]

CODE(S)

- Codes may not be covered under all circumstances.
- Code list may not be all inclusive (AMA and CMS code updates may occur more frequently than policy updates).
- (E/I)=Experimental/Investigational
- (NMN)=Not medically necessary/appropriate

CPT Codes

Code	Description
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, 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 (E/I)	Ophthalmic mucous membrane tests
95065 (E/I)	Direct nasal mucous membrane test

Code	Description
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.)
82785	Gammaglobulin (immunoglobulin), IgE
86001 (E/I)	Allergen-specific IgG; quantitative or semiquantitative, each allergen
86003	Allergen-specific IgE; quantitative or semiquantitative, crude allergen extract, each
86005	Allergen-specific IgE; qualitative, multi-allergen screen (e.g., disk, sponge, card)
86008	Allergen-specific IgE; quantitative or semiquantitative, recombinant or purified component, each
86343 (E/I)	Leukocyte histamine release test (LHR)
0165U (E/I)	Peanut allergen-specific quantitative assessment of multiple epitopes using enzyme-linked immunosorbent assay (ELISA), blood, individual epitope results and probability of peanut allergy
0178U (E/I)	Peanut allergen-specific quantitative assessment of multiple epitopes using enzyme-linked immunosorbent assay (ELISA), blood, report of minimum eliciting exposure for a clinical reaction

HCPCS Codes

Code	Description
No code(s)	

ICD10 Codes

Code	Description
B44.0-B44.9	Aspergillosis (code range)
B48.4	Penicillosis
D80.3	Selective deficiency of immunoglobulin G (IgG) subclasses

Code	Description
D82.0	Wiskott-Aldrich syndrome
H10.411-H10.419	Chronic giant papillary conjunctivitis (code range)
H10.45	Other chronic allergic conjunctivitis
J30.0	Vasomotor rhinitis
J30.1-J30.9	Allergic rhinitis (code range)
J45.20-J45.998	Asthma (code range)
L23.0-L23.9	Allergic contact dermatitis (code range)
L24.0-L24.9	Irritant contact dermatitis (code range)
L25.0-L25.9	Unspecified contact dermatitis (code range)
L27.0-L27.9	Dermatitis due to substances taken internally (code range)
L30.0	Nummular dermatitis
L30.2	Cutaneous autosensitization
L30.8	Other specified dermatitis
L30.9	Dermatitis, unspecified
L50.0	Allergic urticaria
L50.3	Dermatographic urticaria
T36.0X5A-T36.0X5S	Adverse effect of penicillins (code range)
T36.1X5A-T36.1X5S	Adverse effect of cephalosporins and other beta-lactam antibiotics (code range)
T39.015A-T39.015S	Adverse effect of aspirin (code range)
T39.095A-T39.095S	Adverse effect of salicylates (code range)
T63.001A-T63.94XS	Toxic effect of contact with venomous animals and plants (code range)

Code	Description
T65.811A-T65.814S	Toxic effect of latex (code range)
T78.00XA-T78.09XS	Anaphylactic reaction due to food (code range)
T78.2xxA	Anaphylactic shock, unspecified, initial encounter
T78.3xxA	Angioneurotic edema, initial encounter
T78.40XA	Allergy, unspecified, initial encounter
T78.41xA	Arthus phenomenon, initial encounter
T78.49xA	Other allergy, initial encounter
T88.2xxA	Shock due to anesthesia, initial encounter
T88.52XA	Failed moderate sedation during procedure, initial encounter
T88.59xA	Other complications of anesthesia, initial encounter
T88.6XXA	Anaphylactic reaction due to adverse effect of correct drug or medicament properly administered, initial encounter
Z91.010-Z91.09	Allergy status other than drugs & biologicals (code range)

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SEARCH TERMS

Not Applicable

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

NCD - Food Allergy Testing and Treatment (110.11) [accessed 2025 Jun 9]

NCD - Cytotoxic Food Tests (110.13) [accessed 2025 Jun 9]

NCD - Challenge Ingestion Food Testing (110.12) [accessed 2025 Jun 9]

LCD - RAST Type Tests (L33591) [accessed 2025 Jun 9]

PRODUCT DISCLAIMER

- Services are contract dependent; if a product does not cover a service, medical policy criteria do not apply.
- If a commercial product (including an Essential Plan or Child Health Plus product) covers a specific service, medical policy criteria apply to the benefit.
- If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.
- If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.
- If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.

POLICY HISTORY/REVISION

Committee Approval Dates

01/20/00, 10/18/01, 10/16/02, 10/15/03, 09/16/04, 11/17/05, 09/21/06, 12/20/07, 09/18/08, 09/17/09, 09/16/10, 09/15/11, 09/20/12, 09/19/13, 09/18/14, 09/17/15, 09/15/16, 11/16/17, 01/17/19, 01/16/20, 08/20/20, 02/18/21, 01/20/22, 01/19/23, 06/22/23, 07/18/24, 07/17/25

Date	Summary of Changes
07/17/25	• Annual review; policy intent unchanged.
01/01/25	• Summary of changes tracking implemented.
01/20/00	• Original effective date