EFFECTIVE DATE: 09|01|2021
POLICY LAST UPDATED: 07|01|2021

OVERVIEW

Allergy is a hypersensitive reaction that is usually manifested in the clinical form of allergic asthma, hay fever or eczema developing within minutes to a few hours after exposure to an antigen. The most common types of allergies are rhinitis, asthma, food allergy, insect sting allergy, drug allergy and contact dermatitis. Allergy testing is focused on determining what allergens cause a particular reaction and the degree of the reaction and provides justification for recommendations of specific avoidance measures in the home or work environment or the institution of particular medicines or immunotherapy. Allergy Testing can be broadly subdivided into two methodologies: in vivo testing (skin tests) and in vitro testing (blood serum analysis).

MEDICAL CRITERIA

Not applicable

PRIOR AUTHORIZATION

Not applicable

POLICY STATEMENT

In Vitro (blood serum analysis) Allergy Testing

Medicare Advantage Plans and Commercial Products

The following tests are covered when filed with a covered diagnosis (see Coding Section). All other indications are not covered/not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes:

- ELISA/Act (Enzyme-linked Immunosorbent Assay/Advanced Cell Test) qualitative antibody testing
- IgG and IgG subclass antibody tests for food allergy
- LMRA (Lymphocyte Mitogen Response Assays) by ELISA/Act

Medicare Advantage Plans

The following tests are not covered as the evidence is insufficient to determine the effects of the technology on health outcomes:

- Leukocyte Histamine Release Test (LHRT)
- IgG ELISA, indirect method
- Qualitative multi-allergen screen

The Antigen Leukocyte Antibody Test (ALCAT) is not covered when performed to establish a diagnosis of food allergy, using the diagnosis codes listed in the Coding Section, as the evidence is insufficient to determine the effects of the technology on health outcomes.

Commercial Products

The following tests are not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes:

- Leukocyte Histamine Release Test (LHRT)
- IgG ELISA, indirect method
- Qualitative multi-allergen screen

The Antigen Leukocyte Antibody Test (ALCAT) is not medically necessary when performed to establish a diagnosis of food allergy, using the diagnosis codes listed in the Coding Section, as the evidence is insufficient to determine the effects of the technology on health outcomes.

In Vivo (skin tests) Allergy Testing
Medicare Advantage Plans and Commercial Products
Intradermal and scratch allergy testing is medically necessary when the number of tests are chosen based on the patient's clinical presentation and clinician's judgement, and when the chosen tests are specific to the patients' history and physical examination findings.

ALL ALLERGY TESTING – IN VIVO AND IN VITRO
Medicare Advantage Plans and Commercial Products

The following applies to all allergy testing.

When allergy testing is covered:

- The number and type of antigens used for testing must be chosen judiciously given the patient's presentation and the tester's clinical judgement.
- The number of tests performed must be related to the history, physical findings and clinical judgement specific to each individual patient.

It is not expected that all patients would receive the same series or number of tests.

Retesting with the same antigens should rarely be necessary within a three year period. Routine repetition of skin tests is not indicated (i.e., annually).

Medical Necessity Guidance is criteria used to establish medical necessity for testing and must be based on patient-specific elements identified during the clinical assessment, and documented by the clinician in the patient's medical record and minimally include the following elements:

- Patient history, physical examination and previous laboratory findings;
- Current treatment plan;
- Prescribed medication(s)
- Risk assessment plan

Blue Cross Blue Shield of Rhode Island maintains the right to audit the services provided to our members, regardless of the participation status of the provider. All documentation must be available to BCBSRI upon request. Failure to produce the requested information may result in denial or retraction of payment.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable not medically necessary/not covered benefits/coverage.

BACKGROUND

Allergy is a form of exaggerated sensitivity or hypersensitivity to a substance that is either inhaled, ingested, injected, or comes in contact with the skin or eye. 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. Allergic or hypersensitivity disorders may be manifested by generalized systemic reactions as well as localized reactions in any part of the body. The reactions may be acute, subacute, or chronic, immediate or delayed, and may be caused by a variety of offending agents; pollen, molds, mites, dust, feathers, animal fur or dander, venoms, foods, drugs, etc.

Allergy testing is performed to determine a patient's immunologic sensitivity or reaction to particular allergens for the purpose of identifying the cause of the allergic state, and is based on findings during a complete medical and immunologic history and appropriate physical exam obtained by face-to-face contact with the patient.

Allergy Testing can be broadly subdivided into two methodologies:

In vivo testing (skin tests): this testing correlates the performance and evaluation of selective cutaneous and mucous membrane tests with the patient's history, physician examination, and other observations.

- Percutaneous testing (scratch, puncture, prick) and intracutaneous (intradermal) testing are used to evaluate immunoglobulin E (IgE) mediated hypersensitivity to inhalants, foods, hymenoptera (e.g., bee venom), drugs and/or chemicals.
- Patch testing is used to differentiate allergic contact dermatitis (ACD) and irritant contact dermatitis (ICD).
- Photo patch testing is used to evaluate unique allergies resulting from light exposure.
- Photo testing is skin irradiation with a specific range of ultraviolet light. Phots tests are performed for the evaluation of photosensitivity disorders.

In vitro testing (blood serum analysis): immediate hypersensitivity testing by measurement of allergen-specific serum IgE.

Environmental illness refers to a physiologic reaction that is triggered by an exogenous agent, which can be ingested, inhaled, or exposed through direct contact with skin. The physiologic reaction can be an immunologic response or a nonimmunologic response. An adverse physiologic reaction to exogenous antigens has been proposed to play a causative role in a wide variety of illnesses, including allergies, eczema, chronic fatigue, migraine headaches, and gastrointestinal (GI) tract disorders such as irritable bowel syndrome.

Food allergy is the most well-defined type of environmental illness and is estimated to affect 8% of children. In most cases, true food allergy is characterized by a classic immunologic response, i.e., an immunoglobulin E-mediated reaction in response to a specific protein allergen. Reactions can range from mild symptoms to life-threatening anaphylaxis. Current guidelines for the diagnosis and management of food allergies have been developed by National Institute of Allergy and Infectious Disease (NIAID).

Food intolerance is a broader term that overlaps with food allergy but is less well-defined. Food intolerance refers to physiologic reactions that are triggered by a particular food, but which are not immune-mediated. It is hypothesized that physiologic reactions to food may manifest as a range of nonspecific symptoms, such as GI complaints, headache, fatigue, and musculoskeletal complaints and that these symptoms may become chronic with repeated exposure. An example of food intolerance, distinguished from a true food allergy, is lactose intolerance, in which dairy products incite a nonimmunologic reaction that can lead to a constellation of GI symptoms.

Treatment

Treatment of environmental illness primarily involves avoidance of the inciting agent. Acute allergic reactions are treated in the same way as other types of allergies with antihistamines, steroids, and supportive measures. In cases of severe allergy where an agent cannot be definitively avoided, patients can carry and self-administer auto-injectable epinephrine when needed. Prophylactic antihistamines can also be used to prevent or lessen reactions. Allergy immunotherapy may be appropriate for selected allergens.

For patients with food intolerance that is not allergy based, identification of the inciting agent(s) can be difficult because the symptoms are chronic. Use of an elimination diet is considered the best way to identify intolerant agents. In an elimination diet, one specific food or food group is eliminated from the diet for a

specified period, and symptoms are observed. Following the elimination period, a rechallenge can be performed to ascertain whether symptoms return. Elimination diets often need to be done sequentially with a large number of items, so the process can be lengthy and cumbersome.

The umbrella term "food hypersensitivity for food sensitivities" can be used to describe any "adverse reaction to food." The term "food allergy" refers to the subgroup of food-triggered reactions in which immunologic mechanisms have been implicated, whether IgE-mediated, non-IgE mediated, or involving a combination of IgE and non-IgE mediated etiologies. All other reactions to food that were in the past sometimes referred to as "food intolerance" or "food sensitivities" constitute non-allergic food hypersensitivity reactions and are not considered food allergies.

Antigen Leukocyte Antibody Test
The antigen leukocyte antibody test (ALCAT) is intended to diagnose intolerance to foods and other environmental agents. It is a blood test that assesses the response of leukocytes and platelets to a panel of foods and/or other environmental agents, by measuring the change in size and number of cells following exposure to a specific agent.

ALCAT is intended to identify foods and other environmental agents for which an individual may have intolerance. It is not intended to diagnose food allergy. The test is based on the theory that a substantial increase in leukocyte size and number is characteristic of an intolerant response. Identifying the specific inciting agent facilitates avoidance of that agent, which may lead to a reduction in symptoms. In this regard, ALCAT testing has been used as a tool for developing an elimination diet that is targeted to the most likely offending agents.

The test is performed by taking a sample of blood, which is first treated to remove the red blood cells and tested to determine the baseline number and size of leukocytes and platelets. Measurement of size and count of cells is performed by the Coulter technique, which is a standard technique in clinical hematology. Next, a small quantity of blood is incubated with multiple agents. Following exposures, change in the number and size of cells is determined for each exposure. A 10% increase in the size of leukocytes is considered characteristic of a response to an intolerant agent.

The ALCAT website (Cell Sciences Systems) lists 11 separate panels consisting of various combinations of foods, herbs, food additives/coloring, and environmental chemicals. The total number of agents tested in these panels ranges from 70 to 357.

For individuals who have a suspected intolerance of environmental agents or food who receive the ALCAT, the evidence includes a randomized controlled trial and case series. Relevant outcomes are morbid events and medication use. There is a lack of published research on the diagnostic accuracy of ALCAT; therefore, it is not possible to determine the sensitivity, specificity, and/or predictive value of the test compared with alternatives. A few low-quality studies have reported improvements in outcomes following the use of ALCAT, but it is not possible to determine whether these changes occurred as a result of the test itself, bias, variation in the natural history of the condition, and/or the placebo effect. The evidence is insufficient to determine the effects of the technology on health outcomes.

Leukocyte Histamine Release Test
The leukocyte histamine release test (LHRT) is designed to provide an in vitro correlate to an in vivo allergic response (i.e., skin prick testing). An allergen is added to the peripheral blood leukocytes of the individual being tested and the in vitro release of histamine from basophils in response to exposure to the allergen is measured. Histamine is normally released as a consequence of the interaction of allergen with cell-bound IgE antibodies. In contrast, the RAST test (radioallergosorbent test) attempts to correlate the presence of allergy to serum levels of antigen-specific IgE as an index of allergic reactivity. Initially, measurements of histamine release required isolation of leukocytes from whole blood followed by the isolation of the released histamine; the laboratory techniques were difficult and time-consuming and thus LHRT was primarily used as a research

tool only. Recently, a special type of glass fiber has been developed that binds histamine with high affinity and selectivity. These glass fibers can be used as a "solid phase" to absorb the histamine that is released directly into the blood. The recent commercial availability of simplified and automated methods of laboratory analysis (i.e., both ELISA and radioimmunoassays) have renewed interest in the clinical applications of LHRT in the evaluation of food, inhalant, and drug allergies. Overall, studies are not sufficient to permit conclusions on the diagnostic accuracy of LHRT, and therefore LHRT is considered not medically necessary.

Serum IgG Testing - Radioallergosorbent Test (RAST) or Enzyme-linked Immunosorbent Assay (ELISA)
Radioallergosorbent test (RAST), fluoroallergosorbent test (FAST), and multiple antigen simultaneous tests are in vitro techniques for determining whether a patient's serum contains IgE antibodies against specific allergens of clinical importance. As with any allergy testing, the need for such tests is based on the findings during a complete history and physical examination of the patient.

The multiple antigen simultaneous testing technique is similar to the RAST/FAST techniques in that it depends upon the existence of allergic antibodies in the blood of the patient being tested. With the multiple antigen simultaneous test system, several antigens may be used to test for specific IgE simultaneously. The qualitative multi-allergen screen is a non-specific test that does not identify a specific antigen.

ELISA (enzyme-linked immunosorbent assay) is another in vitro method of allergy testing for specific IgE antibodies against allergens. This method is also a variation of RAST. ELISA/Act qualitative antibody testing is used to determine the in vitro reaction to various foods and relies on lymphocyte blastogenesis in response to certain food antigens.

IgG and IgG subclass antibody test for food allergy do not have clinical relevance, are not validated, lack sufficient quality control and should not be performed.

CODING

In Vitro Allergy Testing
Medicare Advantage Plans
The following CPT codes are considered medically necessary when filed with the diagnosis codes in the attachment linked below:
86003 Allergen specific IgE; quantitative or semiquantitative, crude allergen extract, each
86008 Allergen specific IgE; quantitative or semiquantitative, recombinant or purified component, each
Note: the above codes can be used for any of the following tests:

- ELISA/Act (Enzyme-linked Immunosorbent Assay/Advanced Cell Test) qualitative antibody testing
- IgG and IgG subclass antibody tests for food allergy
- LMRA (Lymphocyte Mitogen Response Assays) by ELISA/Act

ICD-10 Codes for 86003 and 86008 for Medicare Advantage Plans

Note: The list of ICD-10 diagnosis codes for 86003 and 86008 for Medicare Advantage Plans differs from the ICD-10 diagnosis codes for 86003 and 86008 for Commercial Products.

Commercial Products
The following CPT codes are considered medically necessary when filed with the diagnosis codes in the attachment linked below:
86003 Allergen specific IgE; quantitative or semiquantitative, crude allergen extract, each
86008 Allergen specific IgE; quantitative or semiquantitative, recombinant or purified component, each
Note: the above code can be used for any of the following tests:

- ELISA/Act (Enzyme-linked Immunosorbent Assay/Advanced Cell Test) qualitative antibody testing

- IgG and IgG subclass antibody tests for food allergy
- LMRA (Lymphocyte Mitogen Response Assays) by ELISA/Act

ICD-10 Codes for 86003 and 86008 for Commercial Products

Note: The list of ICD-10 diagnosis codes for 86003 and 86008 for Commercial Products differs from the ICD-10 diagnosis codes for 86003 and 86008 for Medicare Advantage Plans.

Medicare Advantage Plans and Commercial Products
The following CPT codes are not covered for Medicare Advantage Plans and not medically necessary for Commercial Products:
86001 Allergen specific IgG quantitative or semiquantitative, each allergen
86005 Allergen specific IgE; qualitative, multiallergen screen (eg, disk, sponge, card)
86343 Leukocyte histamine release test (LHR)
Note: the above codes can be used for

- IgG ELISA, indirect method (LCD 86001)
- Qualitative multi-allergen screen (LCD 86005)
- Leukocyte Histamine Release Test (LHRT) (BCA 86343)

The following CPT code is not covered for Medicare Advantage Plans and not medically necessary for Commercial Products when filed with the diagnosis codes listed below:
83516 Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method
Note: the above code can be used for:

- Antigen Leukocyte Antibody Test (ALCAT)

*NOTE: There are various sizes of ALCAT panels and they are likely reported with multiple units of CPT code 83516.

ICD-10 Diagnosis Codes Not Covered/Not Medically Necessary with CPT 83516
K52.21-K52.29
Z91.010-Z91.018
Z91.02

In Vivo Allergy Testing
Medicare Advantage Plans and Commercial Products
The following CPT codes are covered, ***at the limits found in the grid below***, when performed according to the guidelines in the policy statement.

CPT Code and Explanation	Type of Test	Annual Maximum Allowed Units	Units Explanation
95004 – A physician or other qualified health care provider scratches, punctures, or pricks the skin to introduce specific allergy extracts to determine a patient's allergies. The immediate skin reaction is documented. This code includes test interpretation and provider report.	Scratch/Percutaneous	70	A total of 70 scratch, puncture, or prick allergy tests are eligible for reimbursement per calendar year.
95017 - Allergy testing, any combination of percutaneous (scratch, puncture, prick) and	Scratch/percutaneous and Intradermal	27	A total of 27 tests filed under 95017 are eligible for

intracutaneous (intradermal), sequential and incremental, with venoms, immediate type reaction, including test interpretation and report, specify number of tests.			reimbursement per calendar year.
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.	Scratch/percutaneous and Intradermal	19	A total of 19 tests filed under 95018 are eligible for reimbursement per calendar year.
95027 - 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. This code includes test interpretation and provider report.	Intradermal/ intracutaneous	80	A total of 80 tests filed under 95027 are eligible for reimbursement per calendar year.
95024 - A physician or other qualified health care provider injects suspected allergenic substances into the skin to determine the patient's specific allergies. The immediate skin reaction is documented. This code includes test interpretation and provider report.	Intradermal/ intracutaneous	40	A total of 40 intracutaneous allergy tests are eligible for reimbursement per calendar year. 40 units is the maximum allowed for codes 95024 and 95028. (Example: 40 units for 95024, or 20 units for 95024 **AND** 20 units for 95028). **NOTE:** Intracutaneous allergy tests should only follow negative scratch, punture or prick tests.
95028 - Intracutaneous (intradermal) tests with allergenic extracts, delayed type reaction, including reading, specify number of tests.	Intradermal/ intracutaneous	40	A total of 40 intracutaneous allergy tests are eligible for reimbursement per calendar year. 40 units is the maximum allowed for codes 95024 and

			95028. (Example: 40 units for 95024, or 20 units for 95024 **AND** 20 units for 95028). **NOTE:** Intracutaneous allergy tests should only follow negative scratch, puncture or prick tests.
95052 - Photo patch test(s) (specify number of tests).	Photo	20	A total of 20 photo tests are eligible for reimbursement per calendar year.

RELATED POLICIES
Not applicable

PUBLISHED
Provider Update, August 2021
Provider Update, February 2021
Provider Update, February 2020
Provider Update, January 2019
Provider Update, November 2016
Provider Update, October 2016

REFERENCES

1. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD): RAST Type Tests (L33591). National Government Services, Inc.
2. Solomon B.A. The ALCAT Test - A guide and barometer in the therapy of environmental and food sensitivities. Environmental Medicine. 1992;9(2):1-6.
3. Gupta RS, Dyer AA, Jain N, et al. Childhood food allergies: current diagnosis, treatment, and management strategies. Mayo Clin Proc. May 2013;88(5):512-526. PMID 23639501
4. 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. Dec 2010;126(6 Suppl):S1-58. PMID 21134576
5. ALCAT test website. http://www.alcat.com/. Accessed December 3, 2014.
6. Wuthrich B. Unproven techniques in allergy diagnosis. J Investig Allergol Clin Immunol. 2005;15(2):86-90. PMID 16047707
7. Buczylko K, Obarzanowski T, Rosiak K, et al. Prevalence of food allergy and intolerance in children based on MAST CLA and ALCAT tests. Rocz Akad Med Bialymst. 1995;40(3):452-456. PMID 8775289
8. Kleine-Tebbe J, Werfel S, Roedsgaard D et al. Comparison of fiberglass-based histamine assay with a conventional automated fluorometric histamine assay, case history, skin prick test, and specific serum IgE in patients with milk and egg allergic reactions. Allergy 3; 48(1):49-53.
9. Kleine-Tebbe J, Galleani M, Jeep S et al. Basophil histamine release in patients with birch pollen hypersensitivity with and without allergic symptoms to fruits. Allergy 1992; 47(6):618-23.
10. Paris-Kohler A, Demoly P, Persi L et al. In vitro diagnosis of cypress pollen allergy by using cytofluorimetric analysis of basophils (Bastotest). J Allergy Clin Immunol 2000; 105(2 pt 1):339-45.
11. American Academy of Allergy: Position Statements-Controversial techniques. Journal of Allergy and Clinical Immunology 67:333-338 1980. Reaffirmed 2012.

12. Sicherer, SH. Manifestations of food allergy: Evaluation and management. American Family Physician 59:415-424, 1999
13. Boyles JH Jr. A comparison of techniques for evaluating IgE-mediated allergies. Ear Nose Throat J. 2011 Apr; 90(4):164-9.
14. Bernstein IL, Li JT, Bernstein DI et al. Allergy diagnostic testing: an updated practice parameter. Part 1. Ann Allergy Asthma Immunol 2008 Mar; 100(3 Suppl 3):S15-S66.
15. ECRI Institute. [Product Overview] Complement Antigen Technology for Testing Food Sensitivity. 02/13/2013.
16. Adkinson: Middleton's Allergy: Principles and practice, 8th ed. Saunders, an inmrint of Elsevier, 2013.
17. Boyce JA. National institute of allergy and infectious diseases: Guidelines for the diagnosis and management of food allergy in the United States: summary of the NIAID sponsored expert panel report. Nutr Res. 2011 Jan; 31(1):61-75.
18. Chafen JJ, Newberry SJ, Riedl MA, Bravata DM, Maglione M, Suttorp MJ et al. Diagnosing and managing common food allergies: a systematic review. JAMA 2010;303:1848–1856.
19. Keet CA, Wood RA, Matsui EC. Limitations of reliance on specific IgE for epidemiologic surveillance of food allergy. J Allergy Clin Immunol 2012;130:1207–1209.
20. Muraro A, Roberts G, Worm M, Bilò M, Brockow K, Fernández-Rivas M et al. Anaphylaxis: guideline from the European Academy of Allergology and Clinical Immunology. Allergy 2014; doi: 10.1111/all.12437.