Policy Number	**MED206.005**
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Antigen Leukocyte Antibody Test (ALCAT)

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Related Policies (if applicable)
None

Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

The Antigen Leukocyte Antibody Test (ALCAT) **is considered experimental, investigational and/or unproven** for all indications.

Policy Guidelines

There is no specific code for the Antigen Leukocyte Antibody Test (ALCAT) test. There are various sizes of ALCAT panels, and they are likely reported with multiple units of Current Procedural Terminology (CPT) code 83516. For example, the ALCAT Platinum Comprehensive Panel might be reported with 320 units of code 83516.

When 83516 and/or 86160 are billed to represent ALCAT testing, it is considered experimental, investigational and unproven per the coverage section.

Description

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.

Background

Intolerance of Environmental Agents or Food

Environmental illness refers to a physiologic reaction that is triggered by an exogenous agent, which can be ingested, inhaled, or absorbed 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, gastrointestinal tract disorders such as irritable bowel syndrome, eczema, chronic fatigue, and migraine headache. (1)

Food allergy is the most well-defined type of environmental illness and is estimated to affect 8% of children. (2) 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 the National Institute of Allergy and Infectious Disease. (3)

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. (2) It is hypothesized that physiologic reactions to food may manifest as a range of nonspecific symptoms, such as gastrointestinal 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 gastrointestinal symptoms.

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 a 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, 1 specific food or food group is eliminated from the diet for a specified period, and symptoms are observed. Following the elimination period, a re-challenge 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.

Antigen Leukocyte Antibody Test

The ALCAT is intended to identify foods and other environmental agents for which an individual may be intolerant. It is not intended to diagnose food allergies. (4) 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 has been used as a tool for developing an elimination diet that targets 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 then 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. (4)

Regulatory Status

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. The ALCAT is available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

Rationale

Medical polices assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Medical policies assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these policies, and credible information on technical reliability is available from other sources.

Antigen Leukocyte Antibody Test

Clinical Context and Test Purpose

The purpose of the Antigen Leukocyte Antibody Test (ALCAT) in individuals with a suspected intolerance of environmental agents or food is to inform a decision whether to pursue additional diagnostic testing, initiate treatment, or lifestyle and diet management.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals with suspected intolerance to environmental agents or food.

Interventions

The test being considered is ALCAT.

Comparators

The following tests and practices are currently being used to make decisions about diagnosing suspected intolerance of environmental agents or food: antigen or allergen skin testing, antigen or allergen in vitro assays, and elimination dietary changes.

Outcomes

The general outcomes of interest are confirming intolerance to an environmental agent or food and selecting an appropriate intervention. The timing of interest may range from 4 weeks to evaluate test results to 1 to 2 years to evaluate reductions in morbid events and medication use.

Study Selection Criteria

For the evaluation of clinical validity of the ALCAT, studies that met the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores);
- Included a suitable reference standard (describe the reference standard);
- Patient/sample clinical characteristics were described;
- Patient/sample selection criteria were described.

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

There is not a widely accepted criterion standard test for food and environmental intolerance. The double-blind food challenge test may be considered an appropriate reference standard, but there are deficiencies in the definitions and interpretation of food challenge results. No published studies identified have reported on the sensitivity and specificity of ALCAT compared with a double-blind food challenge. One study by Buczylko et al. (1995) compared ALCAT with cytotoxic testing, which is not a test routinely used in clinical care at present, in 56 children

between the ages of 6 months and 16 years. (5) This study reported that results of the 2 tests were consistent in two-thirds of patients.

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials (RCTs).

No RCTs evaluating the clinical utility of ALCAT in a population with suspected intolerance of environmental agents or food were identified.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Randomized Controlled Trials

An RCT by Kaats et al. (1996) evaluated the use of ALCAT in facilitating weight loss, changes in body composition, and health symptoms. (6) One hundred patients were recruited through an advertisement in a fitness newspaper. Eligibility criteria included at least 2 symptoms that had a "severe effect," as measured by the Disease Symptoms Inventory (DSI). Patients were randomized to ALCAT testing followed by dietary modifications or to a control group instructed to pursue a diet of their choosing. The ALCAT group received dietary guidance on dietary changes that were recommended based on ALCAT results. Outcomes were measured after 4 weeks of the intervention and included changes in weight, body composition, and symptoms on the DSI. Eight participants were lost to follow-up, seven in the control group and one in the ALCAT group.

There was a greater reduction in weight in the ALCAT group than in the control group (-1.04 kg vs +0.32 kg; $p<.001$), as well as a greater reduction in the percent body fat (-1.2% vs +0.7%, $p<.001$). There were also significantly better scores on the final DSI outcomes for the ALCAT group. Of 20 symptoms included on the DSI, the final scores were significantly better for the ALCAT group on 18 of 20 symptoms. The results of this trial have limited clinical relevance because the outcomes reported (weight loss, body composition) are not applicable to the main clinical use of the test or relevant to the population assessed in this review. Additionally, the validity of the results was reduced due to limitations in patient selection, lack of blinding, and provision of dietary guidance to the ALCAT group but not the control group.

Case Series

A small number of case series have reported on outcomes following an ALCAT evaluation and treatment based on ALCAT results. These studies are not sufficient to establish efficacy because case series do not control for the natural history of the disorder or for nonspecific factors such as the placebo effect. An example of such a study is Solomon (1992). (1) In this publication, 172 patients with a range of symptoms were tested with ALCAT. Treatment was a food elimination diet and/or allergy immunotherapy, based on ALCAT results. Follow-up allergy testing was performed with serial end point titration at 3 to 6 months after treatment. Outcomes were measured at 1 to 2 years posttreatment by an independent reviewer who asked subjects to rate the effectiveness of treatment on a 1-to-10 scale. For elimination diets, a range of improvement in individual symptoms of 20% to 82% was reported, and for immunotherapy, a range of improvement of 9% to 75% was reported.

Another uncontrolled study that used ALCAT as the basis for an elimination diet is that by Mylek (1995). (7) This study enrolled 72 patients with a range of symptoms considered to be the result of food intolerance. The largest percent improvement in symptoms was reported for arthritis (83%), urticaria (75%), bronchitis (70%), and gastroenteritis (70%). A smaller degree of improvement was reported for the symptoms of hyperreactivity (32%), rhinitis (47%), and atopic dermatitis (49%).

Section Summary: Individuals with Suspected Intolerance of Environmental Agents or Food

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. Because the clinical validity of ALCAT has not been established, a chain of evidence supporting the clinical utility of the test cannot be constructed.

Summary of Evidence

For individuals who have a suspected intolerance of environmental agents or food who receive the Antigen Leukocyte Antibody Test (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 that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

National Institute of Allergy and Infectious Disease

In 2010, the National Institute of Allergy and Infectious Disease published guidelines on the diagnosis and management of food allergy. (3) These guidelines defined and distinguished food

intolerance from food allergy but did not provide recommendations for diagnosis and management of intolerance. For the diagnosis of food allergy, the guidelines stated that "tests selected to evaluate food allergy should be based on the patient's medical history and not comprise large general panels of food allergens."

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov in August 2023 did not identify any ongoing or unpublished trials that would likely influence this medical policy.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	83516, 86160
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

References

1. Solomon BA. The ALCAT Test - A guide and barometer in the therapy of environmental and food sensitivities. Environ Med. 1992; 9(2):1-6.
2. 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
3. Boyce JA, Assa'ad A, Burks AW, 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
4. Cell Sciences Systems. Alcat Test. n.d. Available at <https://cellsciencesystems.com> (accessed August 15, 2023).
5. 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. Jan 1995; 40(3):452-456. PMID 8775289
6. Kaats GR, Pullin D, Parker LK. The short term efficacy of the ALCAT Test of food sensitivities to facilitate changes in body composition and self-reported disease symptoms: a randomized controlled study. Bariatrician. 1996; Spring:18-23.
7. Mylek D. ALCAT Test results in the treatment of respiratory and gastrointestinal symptoms, arthritis, skin and central nervous system. Rocz Akad Med Bialymst. Jan 1995; 40(3):625-629. PMID 8775317

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
12/15/2024	Reviewed. No changes.
12/01/2023	Document updated with literature review. Coverage unchanged. No new references added.
07/15/2022	Reviewed. No changes.
11/01/2021	Document updated with literature review. Coverage unchanged. No new references added.
09/15/2020	Reviewed. No changes.
08/01/2019	New medical document. Information on Antigen Leukocyte Antibody Test (ALCAT) was previously housed on medical policy MED206.001 Allergy Management and remains experimental, investigational and/or unproved. Editorial changes made to the Coverage, intent is unchanged.