2.01.93 Antigen Leukocyte Antibody Test

Original Policy Date: May 29, 2015
Effective Date: May 1, 2017
Section: 2.0 Medicine
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Policy Statement

The Antigen Leukocyte Antibody Test (ALCAT) is considered not medically necessary for all indications.

Policy Guidelines

There are various sizes of Antigen Leukocyte Antibody Test (ALCAT) panels. ALCAT panels are likely reported with multiple units of the following CPT code:

- **83516**: Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method (e.g., ALCAT Platinum Comprehensive Panel might be reported with 320 units of code 83516)

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.

Related Policies

- N/A

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates [e.g., Federal Employee Program (FEP)] prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

ALCAT is a laboratory-developed test that is not subject to U.S. Food and Drug Administration approval. Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; such tests must meet the general regulatory standards of the Clinical Laboratory Improvement Act.

Rationale

Background

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, gastrointestinal (GI) 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 NIAID.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 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 nonimmunologic reaction that can lead to a constellation of GI 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 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 allergic in nature, identification of the inciting agent(s) can be difficult because the symptoms are chronic in nature. 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 of time and symptoms 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 that the process can be lengthy and cumbersome.

Antigen Leukocyte Antibody Test (ALCAT)
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.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 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, Deerfield Beach, FL) 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 range from 70 to 320.⁴

Literature Review
Assessment of a diagnostic technology typically focuses on 3 categories of evidence: (1) technical performance (test-retest reliability or interrater reliability); (2) diagnostic accuracy
(sensitivity, specificity, and positive and negative predictive value) in relevant populations of patients; and (3) demonstration that the diagnostic information can be used to improve patient outcomes. In addition, subsequent use of a technology outside of the investigational setting may also be evaluated. These categories of evidence, although not always evaluated in sequence, can be considered similar to the 4 phases of therapeutic studies.

There is lack of full-length, peer-reviewed publications that evaluate the utility of the Antigen Leukocyte Antibody Test (ALCAT). Many citations from the manufacturer’s website and other internet sources were abstracts presented at scientific meetings or articles published in non-peer-reviewed journals that are not indexed in MEDLINE. The following literature review summarizes the most relevant publications that were identified through MEDLINE and supplemental searches.

Technical Performance
The technical performance of the test refers to the ability of the test to accurately identify changes in the number and size of leukocytes and platelets. The technology uses the “Coulter Counter” technique that is in widespread use in clinical medicine, and thus is expected to have an accuracy that is similar to standard technology for counting and measuring cells.

The reproducibility of the test is uncertain. There were no publications identified that evaluated test-retest reproducibility over time.

Diagnostic Accuracy
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. There were no published studies identified that reported on the sensitivity and specificity of ALCAT, in comparison with a double-blind food challenge. One study from 1995 compared ALCAT and cytotoxic testing, which is not a test routinely used in clinical care at present, in 56 children between the ages of 0.5 and 16 years. This study reported that results of the 2 tests were consistent in two thirds of the patients.

Impact on Health Outcomes
One randomized controlled trial was identified that evaluated the use of ALCAT in facilitating weight loss, changes in body composition, and health symptoms. 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 versus a control group that was instructed to pursue a diet of their own 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, 7 in the control group and 1 in the ALCAT group.

There was a greater reduction in weight in the ALCAT group compared with the control group (-1.04 kg vs. +0.32 kg, p<0.001), as well as a greater reduction in the percent body fat (-1.2% vs. +0.7%, p<0.001). 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 study have limited clinical relevance because the outcomes reported (weight loss and body composition) are not applicable to the main clinical use of the test. Also, the validity of the results is reduced by limitations in patient selection, lack of blinding, and provision of dietary guidance to the ALCAT group but not the control group.

A small number of case series have been published, reporting outcomes following ALCAT testing and treatment based on ALCAT results. These studies are not sufficient to establish efficacy.
because they cannot control for the natural history of the disorder or for nonspecific factors such as the placebo effect. An example of 1 such study is by Solomon. 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 post treatment 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 was published by Mylek in 1995. This study enrolled 72 patients with a range of symptoms that were 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%).

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in January 2015 found no relevant ongoing studies of the ALCAT test.

Summary of Evidence
The Antigen Leukocyte Antibody Test (ALCAT) is a blood test that is intended to diagnose intolerance to foods and other environmental agents. There is a lack of published research on the diagnostic accuracy of the test; 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 report improvement in outcomes following use of ALCAT, but it is not possible to determine whether these changes occur as a result of test itself, versus bias, variation in the natural history of the condition, and/or the placebo effect. Guidelines for the diagnosis of food allergy from the National Institute of Allergy and Infectious Disease do not discuss use of ALCAT. Due to the limitations of the evidence base, and lack of acceptance of the test as a component of standard care by experts in this area, ALCAT is considered not medically necessary for all indications.

Supplemental Information
Practice Guidelines and Position Statements
There were no clinical practice guidelines identified for the diagnosis and management of food intolerance.

The National Institute of Allergy and Infectious Disease published guidelines on the diagnosis and management of food allergy in 2010. These guidelines define and distinguish food intolerance from food allergy, but do not provide recommendations for diagnosis and management of intolerance. For the diagnosis of food allergy, the guidelines state 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."

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.
References

7. Kaats GR PD, 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. The Bariatrician. 1996;Spring:18-23.

Documentation for Clinical Review

Please provide the following documentation (if when requested):
- History and physical and/or consultation notes from referring provider including:
  - Previous diagnostic testing(s) and response(s) including duration
  - Reason for request of procedure

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement.

NMN

The following services may be considered not medically necessary.

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<thead>
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<th>Type</th>
<th>Code</th>
<th>Description</th>
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<td>CPT®</td>
<td>83516</td>
<td>Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method</td>
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<td>HCPCS</td>
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Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

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<td>05/29/2015</td>
<td>BC BSA Medical Policy adoption</td>
<td>Medical Policy Committee</td>
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<tr>
<td>05/01/2017</td>
<td>Policy revision without position change</td>
<td>Medical Policy Committee</td>
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Definitions of Decision Determinations

**Medically Necessary:** A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

**Investigational/Experimental:** A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.