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| MEDICAL POLICY | Allergy Testing (All Lines of Business Except Medicare) | |
| Effective Date: 1/1/2021  1/1/2021 | Section: LAB | Policy No.: 105 |
| | Medical Policy Committee Approved Date: 4/92; 5/95; 10/97; 8/98; 6/99; 5/00; 10/01; 4/03; 11/03; 7/04; 7/05; 5/07; 5/08; 5/10; 11/10; 4/11; 2/13; 12/15; 2/16; 4/16; 8/17; 12/17; 3/18; 4/19; 4/2020; 5/2020; 07/2020 | |
| Medical Officer | Date | |

See Policy CPT CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayn Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:

All lines of business except Medicare

BENEFIT APPLICATION

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

POLICY CRITERIA

In Vivo Allergy Testing

I. The following (A.-F.) in vivo allergy tests are considered **medically necessary and covered**:

- A. Percutaneous Test (Scratch, Prick, or Puncture Test)
- B. Intradermal Test
- C. Skin Patch Test
- D. Photo Test
- E. Bronchial Challenge Test
- F. Oral Food Challenge Test

In Vitro Allergy Testing

MEDICAL POLICY

Allergy Testing (All Lines of Business Except Medicare)

- II. In vitro allergy testing (e.g., RAST/MAST/FAST/ELISA/ImmunoCAP®, CPT: 86003, 86008; or PRIST/RIST, CPT: 82785) may be considered **medically necessary and covered** for the **diagnosis** of suspected IgE-mediated food or inhalant or infectious allergies when **both** of the following (A.-B.) criteria are met:
- A. Clinical documentation of allergic or infectious symptoms (e.g., urticarial, angioedema, ocular pruritus, wheezing, and/or anaphylaxis); **and**
 - B. Any **one or more** of the following (1. or 2.) criteria is met:
 - 1. A skin test has proven inconclusive; **or**
 - 2. Skin testing is not possible due to any **one or more** of the following (a.-d.):
 - a. The patient has widespread skin disease (e.g., dermatographia, ichthyosis, or generalized eczema); **or**
 - b. The patient is receiving skin test suppressive medication therapy that cannot be temporarily discontinued (e.g., antihistamine or beta blocker); **or**
 - c. The patient is unable to cooperate with skin testing (e.g., small child or patient with mental and/or physical disorders); **or**
 - d. When clinical history suggests an unusually greater risk of anaphylaxis from skin testing.
- III. In vitro allergy testing (e.g., RAST/MAST/FAST/ELISA/ImmunoCAP®, CPT: 86003, 86008; or PRIST/RIST, CPT: 82785) is considered **not medically necessary and is not covered** when criterion II. above is not met.

Non-covered Allergy Tests

- IV. Multiallergen IgE screening (CPT: 86005) is considered **not medically necessary and not covered**.
- V. The following (A.-K.) allergy tests are considered **investigational and are not covered** (this list is not all inclusive):
- A. Antigen leukocyte cellular antibody (ALCAT) automated food test
 - B. Applied kinesiology test
 - C. Bead-based epitope assay (BBEA) (e.g., VeriMAP™ Peanut Diagnostic from AllerGenis™)
 - D. Conjunctival or nasal challenge tests
 - E. Cytotoxic food test
 - F. Sublingual provocation
 - G. Iridology
 - H. Hair analysis
 - I. IgG/IgG₄ allergen-specific antibody test
 - J. Leukocyte histamine release test (LHRT)
 - K. Provocation-neutralization food or food additive allergy test (e.g., Rinkel test)

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|-----------------------|--|
| MEDICAL POLICY | Allergy Testing (All Lines of Business Except Medicare) |
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Link to [Policy Summary](#)

BILLING GUIDELINES

Frequency Limits for Medically Necessary Tests

- A cumulative total of 70 percutaneous (scratch, prick, or puncture) allergy tests (CPT: 95004, 95017, 95018) are eligible for reimbursement per calendar year.
- A cumulative total of 40 intracutaneous allergy tests (CPT: 95024, 95027, 95028) are eligible for reimbursement per calendar year.
- A cumulative total of 80 skin patch allergy tests (CPT: 95044) are eligible for reimbursement per calendar year.
- A cumulative total of 40 allergen specific IgE serum tests (CPT: 86003 and 86008, each) for inhalant allergies are eligible for reimbursement per calendar year.
- A cumulative total of 12 allergen specific IgE serum tests (CPT: 86003 and 86008, each) for food allergies are eligible for reimbursement per calendar year.

Coding for Miscellaneous Investigational Tests

When 83516 is billed to represent ALCAT or cytotoxic food testing, it is considered investigational and not covered per this policy.

CPT CODES

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| All Lines of Business Except Medicare | |
| No Prior Authorization Required | |
| Total Serum IgE Testing (e.g., PRIST/RIST) | |
| 82785 | Gammaglobulin (immunoglobulin); IgE |
| Antigen Leukocyte Cellular Antibody (ALCAT) Automated Food Test or Cytotoxic Food Test (Note: This test is considered investigational per this policy) | |
| 83516 | Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method |
| Allergen Specific IgE Testing (e.g., RAST/MAST/FAST/ELISA/ImmunoCAP®) | |
| 86003 | Allergen specific IgE; quantitative or semiquantitative, crude allergen extract, each |
| 86008 | Allergen specific IgE; quantitative or semiquantitative, recombinant or purified component, each |
| Percutaneous Test (Scratch, Prick, or Puncture Test) | |
| 86486 | Skin test; unlisted antigen, each |
| 95004 | Percutaneous tests (scratch, puncture, prick) with allergenic extracts, immediate type reaction, including test interpretation and report, specify number of tests |

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|-----------------------|--|
| MEDICAL POLICY | Allergy Testing (All Lines of Business Except Medicare) |
|-----------------------|--|

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| 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 |
| Intracutaneous Test | |
| 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 |
| Skin Patch Test | |
| 95044 | Patch or application test(s) (specify number of tests) |
| Photo Test | |
| 95052 | Photo patch test(s) (specify number of tests) |
| 95056 | Photo tests |
| Bronchial Challenge Test | |
| 95070 | Inhalation bronchial challenge testing (not including necessary pulmonary function tests); with histamine, methacholine, or similar compounds |
| 95071 | TERMED 12/31/2020 Inhalation bronchial challenge testing (not including necessary pulmonary function tests); with antigens or gases, specify |
| Oral Food Challenge Test | |
| 95076 | Ingestion challenge test (sequential and incremental ingestion of test items, eg, food, drug or other substance); initial 120 minutes of testing |
| 95079 | Ingestion challenge test (sequential and incremental ingestion of test items, eg, food, drug or other substance); each additional 60 minutes of testing (List separately in addition to code for primary procedure) |
| Not Covered | |
| 0165U | Peanut allergen-specific IgE and quantitative assessment of 64 epitopes using enzyme-linked immunosorbent assay (ELISA), blood, individual epitope results and interpretation |
| 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 |
| 86005 | Allergen specific IgE; qualitative, multiallergen screen (eg, disk, sponge, card) |
| 86343 | Leukocyte histamine release test (LHR) |

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|-----------------------|--|
| MEDICAL POLICY | Allergy Testing (All Lines of Business Except Medicare) |
|-----------------------|--|

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| 95060 | Ophthalmic mucous membrane tests |
| 95065 | Direct nasal mucous membrane test |
| Unlisted Codes All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed relative to services addressed in this policy then prior-authorization is required. | |
| 95199 | Unlisted allergy/clinical immunologic service or procedure |

DESCRIPTION

Allergies and Allergy Testing

Allergies are one of the most common chronic conditions in the world.¹⁻³ An allergic reaction arises when the immune system mistakes a substance (e.g., food) as an invader and overreacts to it by producing Immunoglobulin E (IgE) antibodies. These antibodies then cause cells to release histamine (chemical involved in immune response), thus causing an allergic reaction. Common allergens include pollen, dust, food, insects, animal dander, mold, and medications. These allergens typically produce symptoms in the nose, lungs, throat, sinuses, ears, stomach, or skin. Severe allergies can cause asthma or anaphylaxis.

Allergy testing is used to determine what specific allergens a person is allergic to in order to help prevent and treat allergic reactions. Skin allergy testing is the most common form of allergy testing. The patient's skin is pricked with specific allergens (e.g., cow's milk and strawberries), and skin inflammation at the prick site indicates a positive allergic reaction. Although less common, challenge tests can be used to diagnose food or medication allergies and asthma. For this test, a patient is exposed to a very small amount of the suspected allergen and monitored by an allergist for any allergic reaction.

Allergen-specific IgE blood tests can be used when "skin tests might be unsafe or won't work, such as if you are taking certain medications or have a skin condition that may interfere with skin testing."³ Total IgE blood tests are necessary to diagnosis specific conditions, including: allergic bronchopulmonary aspergillosis, immune disorders (e.g., Wiskott-Aldrich syndrome, hyperimmunoglobulin E syndrome), or malignancies (e.g., IgE myeloma). Also, a total serum IgE level is used in the evaluation of patients with allergic asthma to determine eligibility for treatment with an anti-IgE therapy (i.e., omalizumab). However, "quantification of total serum IgE should not be confused with the measurement of allergen-specific IgE. An elevated total IgE may indicate a patient has allergen sensitivity, but it provides no information about which condition or to what allergens the patient is sensitive. Furthermore, because there is a large degree of overlap between IgE levels in people with and without allergic disease, the utility of total IgE in diagnosing allergic conditions is limited."⁴

REVIEW OF EVIDENCE

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|-----------------------|--|
| MEDICAL POLICY | Allergy Testing (All Lines of Business Except Medicare) |
|-----------------------|--|

A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of in vivo and in vitro allergy testing to diagnose food, inhalant, hymenoptera, and medication allergies. There is a large volume of literature regarding in vivo and in vitro allergy testing; therefore, the rationale for medical necessity will focus on evidence-based clinical practice guidelines. The evidence review for medically necessary tests is primarily limited to systematic reviews, while a complete review of the evidence for investigational tests has been performed. Below is a summary of the available evidence identified through March 2020.

Allergy Testing

Food Allergies

Systematic Reviews

- In 2010, Chafen et al. conducted a systematic review and meta-analysis to evaluate the diagnosis and management of common food allergies.⁵ Independent reviewers systematically identified eligible studies, assessed quality and heterogeneity, and extracted data. The outcomes of interest were sensitivity, specificity, and the receiver operator characteristic (ROC) curves.

A total of 182 publications were identified as eligible for inclusion; however, the authors further restricted the evidence pool to 72 studies that reported data on food allergies to cow’s milk, hen’s egg, peanut, tree nut, fish, and shellfish. Of these 72 studies, 18 were prospective studies of diagnostic tests for allergies. All studies compared skin prick testing (SPT), serum food-specific IgE, or atopy patch testing (APT) with a food challenge reference standard. The authors determined the quality of these studies to be fair. The meta-analysis identified no statistically significant differences for the diagnostic tests overall or for the specific foods. Of the studies that tried to improve diagnostic accuracy by combining tests (n=10), none produced conclusive results. Also, there was insufficient evidence to calculate ROC curves for the APT for peanut, tree nut, fish, or shell fish allergies. Some studies also evaluated other proposed tests for diagnosing food allergies (e.g., Leukocyte Histamine Release Test); however, the authors concluded insufficient evidence was available to evaluate their use for diagnosing food allergies.

The authors stated, “this systematic review of food allergies found that the evidence on the prevalence, diagnosis, management, and prevention of food allergies is voluminous, diffuse, and critically limited by the lack of uniformity for the diagnosis of a food allergy, severely limiting conclusions about best practices for management and prevention.”⁵ Strengths of this study include the systematic identification of evidence by independent authors following a pre-defined protocol, evaluation of quality, and assessment of heterogeneity. A significant limitation is the paucity of high-quality studies evaluating diagnostic tests for allergies. Also, the authors identified between-study heterogeneity in the criteria used for the diagnosis of food allergies, which limits the reliability of comparisons made across studies. There is also potential publication bias due to the author’s stringent inclusion criteria (e.g., English-language only studies). In regards to diagnosing food allergies, the authors concluded, “food challenges, SPT, and serum food-specific IgE all have a role to play in making the diagnosis but no one test has sufficient ease of use or sensitivity or specificity to

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|-----------------------|--|
| MEDICAL POLICY | Allergy Testing (All Lines of Business Except Medicare) |
|-----------------------|--|

be recommended over the other tests. Numerous other proposed diagnostic tests are of uncertain value due to lack of evidence.”⁵

- More recent systematic reviews were identified comparing SPT, specific-IgE (sIgE), component-resolved diagnosis, the APT and/or oral food challenge for diagnosing IgE-mediated food allergies. Similar to the Chafen et al. review above, in 2014 Soares-Weiser et al. agreed that the evidence base was weak and difficult to interpret due to between study heterogeneity.⁶ However, the meta-analysis of 24 studies (2831 patients) did indicate that both “SPT and specific-IgE have good sensitivity, but poor specificity with wide variation in estimates for each of the eight food allergies investigated.” Although Soares-Weiser et al. indicated that the evidence for the APT was too limited to draw conclusions, in 2019; Luo et al. conducted a review that found that APT was specific but not sensitive for diagnosing various food allergies in children, especially in children with food allergy-related gastrointestinal symptoms.⁷
- In addition, one recent smaller review was identified that compared the diagnostic sensitivity and specificity of tests for diagnosing cow’s milk allergy, and was able to identify relatively homogenous cut-offs for both SPT and specific IgE tests for children over the age of two.⁸

Inhalation Allergies

Systematic Review

- In 2017, Liu et al. published the results of a systematic review that compared APT to the SPT in the diagnosis of mite-induced atopic dermatitis, including 10 comparative studies (N=669 patients).⁹ In the ten studies analyzed, the percentage of ATP-positive subjects ranged from 14-70% and the SPT was used as the reference standard. Compared to the SPT, the pooled sensitivity, specificity and diagnostic odds ratios for APT were 0.54 (95% CI 0.42-0.66), 0.72 (95% CI 0.56-0.85), and 3.12 (95% CI 1.53-6.39). The area under the summary receiver operating characteristic curve was 0.65 (95% CI 0.61-0.69). The reviewers concluded that the APT was “suitable for identifying mite-sensitization in patients with atopy dermatitis and should be used alongside SPT.”

Allergen-Specific IgE Serum Test (e.g., RAST/MAST/FAST/ELISA/ImmunoCAP®)

Food Allergies

Nonrandomized Studies

- In 2004, Perry et al. conducted a retrospective chart review to evaluate the relationship of allergen-specific IgE levels and oral food challenge outcome.¹⁰ The authors reviewed 604 food challenges in 391 children. All children had food-specific serum IgE levels measured before undergoing a food challenge. The outcome of interest was the relationship between food-specific IgE levels and the food challenge outcome.

MEDICAL POLICY**Allergy Testing
(All Lines of Business Except
Medicare)**

A total of 166 milk challenges were performed with 45% of challenges passed. The patients who passed the milk challenge had a median IgE level of 0.9 kUA/L versus 2.0 kUA/L for those who failed ($P < 0.001$). There was also a statistically significant trend ($P < 0.01$) of increasing challenge failure with increasing milk-specific IgE levels. A total of 138 egg challenges were performed with 57% of challenges passed. The patients who passed the egg challenge had a median IgE level of 0.7 kUA/L versus 1.2 kUA/L for those who failed ($P = 0.02$ passed vs. failed). Of 173 peanut challenges, 59% passed and the median IgE levels for those who passed or failed were 0.5 kUA/L and 1.9 kUA/L, respectively ($P < 0.001$). There was also a statistically significant trend for increasing failure rate with increasing peanut-specific IgE level. “For the 46 wheat challenges, 67% passed, and the medians for those who passed or failed were 4.6 and 19.6 kUA/L, respectively ($P = .01$). For the 81 soy challenges, 72% passed, and the medians for those who passed or failed were 3.2 and 9.3 kUA/L, respectively ($P = .03$).”¹⁰

Although this study includes a large sample size, limitations are present in the retrospective chart review design and lack of randomization. Ultimately, the authors concluded “Allergen-specific IgE concentrations to milk, egg, and peanut and, to a lesser extent, wheat and soy serve as useful predictors of challenge outcome and should be considered when selecting patients for oral challenge to these foods.”

- In 2001, Sampson and colleagues conducted a prospective nonrandomized study to evaluate the utility of specific IgE concentrations for diagnosing food allergies.¹¹ A total of 100 consecutive children and adolescents referred for evaluation of food allergy were enrolled. Sera was collected and analyzed for specific IgE antibodies to egg, milk, peanut, soy, wheat, and fish. These food-specific IgE values were then compared with clinical history and results of skin prick tests and food challenges in order to determine the diagnostic efficacy.

For egg-specific IgE testing, the results indicated 64% sensitivity, 90% specificity, 96% positive predictive value (PPV), and 39% negative predictive value (NPV). Milk-specific IgE testing had 34% sensitivity, 100% specificity, 100% PPV, and 44% NPV. Peanut-specific IgE testing had 57% sensitivity, 100% specificity, 100% PPV, and 36% NPV. Fish-specific IgE tests had 25% sensitivity, 100% specificity, 100% PPV, and 89% NPV. Soybean-specific IgE tests had a 24% sensitivity, 99% specificity, 86% PPV, and 78% NPV. Wheat-specific IgE tests had a 13% sensitivity, 100% specificity, 100% PPV, and 76% NPV.

Strengths of this study include the larger sample size and comparison to standard diagnostic tests; however, methodological limitations were present in the nonrandomized observational design. The authors concluded “quantification of food-specific IgE is a useful test for diagnosing symptomatic allergy to egg, milk, peanut, and fish in the pediatric population and could eliminate the need to perform double-blind, placebo-controlled food challenges in a significant number of children.”¹¹

- In 2001, Boyano Martinez et al. conducted a prospective nonrandomized study of 81 children in order to evaluate the diagnostic utility of allergen-specific IgE testing.¹² A total of 81 children were enrolled who were under 2 years of age and had a suspected egg allergy. Serum was collected and specific IgE antibodies were analyzed for egg white, egg yolk, ovalbumin, and ovomucoid. These

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| MEDICAL POLICY | Allergy Testing (All Lines of Business Except Medicare) |
|-----------------------|--|

results were then compared to the results of a diagnostic challenge test. The validity of the specific IgE antibodies was analyzed using the children with a negative diagnostic challenge test as the control group. The prevalence of egg allergy was determined to be 79%. The egg white-IgE allergy test had the greatest diagnostic efficacy, reporting a sensitivity and positive predictive value of greater than 95%. "A level of ≥ 0.35 KUA/L for specific IgE antibodies to egg white predicted the existence of reaction in 94% of the cases."¹² Strengths of this study include the comparison to a reference standard and the analysis of diagnostic utility. Limitations were identified in the small sample size and prospective nonrandomized design. The authors concluded that, "in children under 2 years of age with a background of immediate hypersensitivity after egg ingestion and presence of specific IgE antibodies to egg white of ≥ 0.35 KUA/L, diagnostic challenge test is not necessary to establish the diagnosis of allergy to this food."¹²

Inhalation Allergies

Randomized Controlled Trials

In 2008, Niggemann et al. evaluated the diagnostic accuracy of allergen-specific IgE testing in a pediatric population.¹³ A total of 380 consecutive children (< 6 years old) were recruited from 14 different pediatric clinics and randomized to group A or group B. In Group A, the results were provided quickly, so the physicians had them before contacting parents with a diagnosis and advice. In Group B, the physicians made a diagnosis and initial management decisions without the test results but received the results in time for the follow-up visit.

Outcomes of interest were the proportion of uncertain diagnoses at the first visit, the concordance between first-visit diagnosis and in vitro test results, and within Group B only the concordance between second-visit diagnosis and test results. "When diagnosis was made without access to allergen-specific IgE results, 8% of the children were diagnosed as allergic, 6% as non-allergic and in 86% of the cases the physician was uncertain. With access to allergen-specific IgE results the figures were 13%, 65% and 22%, respectively."¹³

Strengths of this study include the large sample size, randomization, and recruitment of patients from several different health centers. A limitation was identified in the lack of follow-up, which did not allow for complete outcome assessment. Also, funding bias is possible due to the study being sponsored by the sIgE manufacturer. Ultimately, the authors concluded that sIgE has an impact on the diagnosis of allergies in children.

Nonrandomized Studies

In 2008, Van Kampen and colleagues conducted a prospective nonrandomized study to evaluate the clinical utility of allergen specific IgE (sIgE) testing and skin prick testing (SPT) to diagnose occupational allergy to wheat and rye.¹⁴ The authors recruited 107 bakers with either work-related symptoms suggesting rhinitis and/or allergy or patients making worker's compensation claims for occupational asthma. All patients underwent skin prick testing, in vitro testing (sIgE), and challenge testing (reference

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| MEDICAL POLICY | Allergy Testing (All Lines of Business Except Medicare) |
|-----------------------|--|

standard). Outcomes of interest included sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and receiver operating characteristic (ROC) analysis.

When calculated for a specific IgE cut-off value of 0.35 kU/l, wheat and rye flour specificity was 68% and 62%, PPV 74% and 82%, and NPV was 82% and 71%, respectively. Sensitivity was 87% for both flours. The sIgE concentrations were significantly higher in bakers with a positive challenge test compared to those with negative challenge tests.

Strengths of this study include the prospective design with the use of a reference standard; however, limitations were identified due to the small sample size and lack of randomization. The authors concluded, “a high concentration of flour-specific IgE in the sera of bakers suffering from work-related symptoms is a good indicator for a positive inhalation challenge test with flours.”¹⁴

Allergy Tests Considered Investigational

The following tests have either (1) not been evaluated in a clinical trial; (2) have been evaluated in a clinical trial but reported inconclusive results or were not compared to a reference standard and/or; (3) were recommended against in clinical practice guidelines. There is not enough evidence to conclude these tests are accurate or reliable for the diagnosis of allergies. Further studies of good methodological quality are required in order to confirm the diagnostic utility of these tests.

1. Antigen leukocyte cellular antibody (ALCAT) automated food test¹⁵
2. Applied kinesiology allergy test¹⁶⁻¹⁸
3. Bead-Based Epitope Assay (BBEA)
4. Cytotoxic food test¹⁹⁻²²
5. Sublingual provocation^{23,24}
6. Iridology^{25,26}
7. Hair analysis^{27,28}
8. IgG/IgG4 allergen specific antibody test²⁹⁻³²
9. Provocation-neutralization food or food additive allergy test (e.g., Rinkel test)³³
10. Leukocyte histamine release test (LHRT)³⁴⁻⁴⁰
11. Conjunctival or nasal challenge tests⁴¹⁻⁵³

CLINICAL PRACTICE GUIDELINES

The American Board of Internal Medicine’s (ABIM) Foundation Choosing Wisely® Initiative (2019)

The Choosing Wisely® initiative includes the following recommendations:⁵⁴

- Don’t perform unproven diagnostic tests, such as immunoglobulin G (IgG) testing or an indiscriminate battery of immunoglobulin E (IgE) tests, in the evaluation of allergies
- Don’t routinely do diagnostic testing in patients with chronic urticaria.
- Don’t perform food IgE testing without a history consistent with potential IgE-mediated food allergy.
- Don’t perform screening panels for food allergies without previous consideration of medical history.

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|-----------------------|--|
| MEDICAL POLICY | Allergy Testing (All Lines of Business Except Medicare) |
|-----------------------|--|

- Don't use skin prick tests or blood tests such as the radioallergosorbent test (RAST) for the routine evaluation of eczema

Food Allergies

American Academy of Allergy, Asthma & Immunology/American College of Allergy, Asthma, & Immunology/Joint Council of Allergy, Asthma, & Immunology (AAAAI/ACAAI/JCAAI)

The 2014 AAAAI/ACAAI/JCAAI evidence-based practice parameter gave the following recommendations regarding food allergy testing:⁵⁵

- Manage non-IgE-mediated reactions to foods with appropriate avoidance and pharmacotherapy as indicated with the understanding that the specific role of immunity (e.g., IgA, IgM, IgG, and IgG subclasses) in these forms of food allergy has not been demonstrated. [Strength of recommendation: Strong; B Evidence]
- The clinician should obtain a detailed medical history and physical examination to aid in the diagnosis of food allergy. [Strength of recommendation: Strong; D Evidence]
- The clinician should use specific IgE tests (skin prick tests, serum tests, or both) to foods as diagnostic tools; however, testing should be focused on foods suspected of provoking the reaction, and test results alone should not be considered diagnostic of food allergy. [Strength of recommendation: Strong; B Evidence]
- The clinician should consider oral food challenges (OFCs) to aid in the diagnosis of IgE-mediated food allergy. [Strength of recommendation: Strong; A Evidence]
- Do not routinely obtain total serum IgE levels for the diagnosis of food allergy. [Strength of recommendation: Strong; C Evidence]
- Unproved tests, including allergen specific IgG measurement, cytotoxicity assays, applied kinesiology, provocation neutralization, and hair analysis, should not be used for the evaluation of food allergy. [Strength of recommendation: Strong; C Evidence]
- Measurement of food-specific IgG and IgG4 antibodies in serum are not recommended for the diagnosis of non-IgE-mediated food-related allergic disorders.

National Institute for Health and Care Excellence (NICE)

The 2011 NICE evidence-based clinical practice guideline for food allergies in patients under 19 years old recommended the following:⁵⁶

- Based on the results of the allergy-focused clinical history, if IgE-mediated allergy is suspected, offer the child or young person a skin prick test and/or blood tests for specific IgE antibodies to the suspected foods and likely co-allergens
- Tests should only be undertaken by healthcare professionals with the appropriate competencies to select, perform and interpret them
- Skin prick tests should only be undertaken where there are facilities to deal with an anaphylactic reaction.

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|-----------------------|--|
| MEDICAL POLICY | Allergy Testing (All Lines of Business Except Medicare) |
|-----------------------|--|

National Institute for Allergies and Infectious Diseases

The 2011 National Institute for Allergies and Infectious Diseases evidence-based guideline for the diagnosis and management of food allergy (FA) in the United States recommended the following:⁵⁷

- Perform a skin prick/puncture test to assist in the identification of foods that may be provoking IgE-mediated food-induced allergic reactions
- The routine use of measuring total serum IgE should not be used to make a diagnosis of FA.
- Allergen-specific serum IgE (sIgE) tests can be used for identifying foods that potentially provoke IgE-mediated food-induced allergic reactions. Serum testing can be especially useful when SPTs cannot be done (for example, due to extensive dermatitis or dermatographism), or when antihistamines cannot be discontinued.
- Oral food challenges can be used for diagnosing FA. The DBPCFC is the gold standard.
- The guideline recommended not using any of the following non-standardized tests for the routine evaluation of IgE-mediated FA:
 - Basophil histamine release/activation
 - Lymphocyte stimulation
 - Facial thermography
 - Gastric juice analysis
 - Endoscopic allergen provocation
 - Hair analysis
 - Applied kinesiology
 - Provocation neutralization
 - Allergen-specific IgG4
 - Cytotoxicity assays
 - Electrodermal test (Vega)
 - Mediator release assay (LEAP diet)

Allergic Dermatitis

American Academy of Dermatology (AAD)

The 2014 AAD evidence-based guidelines for the care and management of atopic dermatitis (AD) stated, “patch testing should be considered in patients with AD who have persistent/recalcitrant disease and/or a history or physical examination findings consistent with allergic contact dermatitis.”⁵⁸

Hymenoptera (Stinging Insects) Hypersensitivity

American Academy of Allergy, Asthma & Immunology (AAAAI)

The 2017 AAAAI evidence-based practice parameter for stinging insect hypersensitivity gave the following recommendations:⁵⁹

- Referral to an allergist is appropriate for any patient who has had an allergic reaction to an insect sting.

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|-----------------------|--|
| MEDICAL POLICY | Allergy Testing (All Lines of Business Except Medicare) |
|-----------------------|--|

- Patients might have venom specific IgE not detected by skin testing, even though skin testing is the most reliable and preferred diagnostic method to identify venom specific IgE. Therefore, it is recommended that further evaluation for detection of venom specific IgE be performed if the skin test response is negative. This would include serum IgE assays for venom IgE and repeat skin tests.

Environmental/Inhalation Allergies

Institute for Clinical Symptoms Improvement (ICS)

The 1994 (revised 2013) ICSI evidence based clinical practice guideline for the diagnosis and treatment of respiratory illness in children and adults recommended the following:⁶⁰

- Skin tests are presently the preferred test for the diagnosing of IgE-mediated inhalation allergies.
- A limited panel of two to four radioallergosorbent (RAST) tests can be considered. If a greater number of specific allergens are to be identified, skin tests are the preferred diagnostic tests.
- Skin tests require experience in application and interpretation, and carry the risk of anaphylactic reactions. Therefore, only specially trained providers should perform them.
- The guideline recommended not using any of the following tests for the routine evaluation of IgE-mediated inhalation allergies:
 - Blood eosinophilia
 - Total IgE serum concentrations
 - Sublingual provocation testing
 - Rinkel method of skin titration

Medication Allergies

American Academy of Allergy, Asthma & Immunology/American College of Allergy, Asthma, & Immunology/Joint Council of Allergy, Asthma, & Immunology (AAAAI/ACAAI/JCAAI)

The 2010 AAAAI/ACAAI/JCAAI evidence-based practice parameter on drug allergies gave the following recommendations:⁶¹

- The most useful test for detecting IgE-mediated drug reactions caused by many large-molecular-weight biologicals and penicillin is the immediate hypersensitivity skin test.
- Relatively few studies with small numbers of patients have evaluated the specificity and sensitivity of third-generation assays (e.g., RAST/MAST) for detection of penicillin specific IgE in vitro. These studies demonstrate relatively high specificity (97%- 100%) but lower sensitivity (29%-68%) for penicillin specific IgE. Therefore, although a positive in vitro test result for penicillin specific IgE is highly predictive of penicillin allergy, a negative in vitro test result does not adequately exclude penicillin allergy.
- Patch testing is the most reliable technique for diagnosis of contact dermatitis caused by topically applied drugs.
- The guideline recommended against the use of the basophil activation test for evaluating patients with possible allergies to lactam antibiotics and nonsteroidal anti-inflammatory drugs (NSAIDs).

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| MEDICAL POLICY | Allergy Testing (All Lines of Business Except Medicare) |
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Allergic Bronchopulmonary Aspergillosis (ABPA)

Infectious Diseases Society of America (IDSA)

The 2016 IDSA evidence-based clinical practice guidelines for the diagnosis and management of aspergillosis recommended the use of aspergillus immunoglobulin E (IgE) and total IgE to establish the diagnosis of allergic bronchopulmonary aspergillosis (ABPA).⁶²

Allergic Asthma

American Thoracic Society (ATS)/European Respiratory Society (ERS)

The 2014 ERS/ATS evidence-based clinical practice guideline for the evaluation and treatment of severe asthma recommended a therapeutic trial of omalizumab in both children and adults with severe allergic asthma.⁶³ The guideline also stated “adults and children (aged ≥6 years) with severe asthma who are considered for a trial of omalizumab, should have confirmed IgE-dependent allergic asthma uncontrolled despite optimal pharmacological and non-pharmacological management and appropriate allergen avoidance, if their total serum IgE level is 30–700 IU·mL⁻¹.”⁶³

POLICY SUMMARY

Percutaneous, intracutaneous, and challenge allergy tests are a common clinical practice and widely used for the diagnosis of IgE-mediated allergies. The evidence supports the use of allergen-specific IgE serum testing for the diagnosis of IgE-mediated food or inhalant allergies. Although the evidence does not indicate one test is superior to the other, the high sensitivity, high negative predictive value, and fast results make skin testing an ideal first-line investigation of IgE-mediated allergies. Total serum IgE testing is necessary to evaluate specific conditions, including: allergic bronchopulmonary aspergillosis, immune disorders (e.g., Wiskott-Aldrich syndrome, hyperimmunoglobulin E syndrome), or malignancies (e.g., IgE myeloma). Also, a total serum IgE level is used in the evaluation of patients with allergic asthma to determine eligibility for treatment with an anti-IgE therapy (i.e., omalizumab). Multiallergen testing does not identify specific antigens; therefore, it is considered not medically necessary. There are several allergy tests that do not have sufficient evidence to confirm their diagnostic utility; therefore, they are considered investigational.

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

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| MEDICAL POLICY | Allergy Testing (All Lines of Business Except Medicare) |
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The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

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MEDICAL POLICY**Allergy Testing
(All Lines of Business Except
Medicare)**

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