Clinical Policy Title: Allergy testing

Clinical Policy Number: CCP.1075

Effective Date: June 1, 2014
Initial Review Date: December 18, 2013
Most Recent Review Date: August 30, 2018
Next Review Date: September 2019

Related policies:

CCP.1083 Exhaled nitric oxide for diagnosis of lung disease
CCP.1342 Omalizumab for the treatment of chronic idiopathic urticarial
CCP.1049 Celiac disease — diagnostic testing

About this policy

Prestige Health Choice has developed clinical policies to assist with making coverage determinations. Prestige Health Choice’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Prestige Health Choice when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Prestige Health Choice’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Prestige Health Choice’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Prestige Health Choice will update its clinical policies as necessary. Prestige Health Choice’s clinical policies are not guarantees of payment.

Coverage policy

This policy addresses immediate (immunoglobulin E-mediated) hypersensitivity and delayed (cell-mediated) hypersensitivity allergy testing.

Prestige Health Choice considers the use of allergy testing to be clinically proven and, therefore, medically necessary for members age 2 years and older when the following general and test-specific criteria are met (Golden, 2017; Fonacier, 2015; Seidman, 2015; Sampson, 2014; Boyce, 2010; Joint Task Force, 1995):

- General criteria (all criteria must be met):
  - Clinically significant symptoms documented in an allergy-focused history.
  - Test correlates to the member’s allergy-focused clinical presentation (i.e., testing for antigens to which it is reasonably possible for the member to be exposed).
- Test method and/or allergens tested have been scientifically validated.
- Tests are performed by a licensed provider acting within their scope of practice to perform allergy and immunology services.

- Medically necessary allergy tests and specific criteria:
  - Percutaneous (skin scratch or prick) tests for suspected immunoglobulin E-mediated allergies to foods, inhaled allergens, stinging insect venom, or specific drugs (Golden, 2017; Bernstein, 2008).
  - Skin endpoint titration for members highly allergic to stinging insect venom or inhaled allergens, with both of the following:
    - Determination of starting dose for testing or immunotherapy.
    - Testing in facility equipped to manage anaphylaxis.
  - Intradermal testing for inhalant allergens, either:
    - When percutaneous tests are negative.
    - When using delayed hypersensitivity of the tuberculin type.
  - Patch testing for suspected contact allergy.
  - Repeated open application testing for a negative or inconclusive patch test.
  - Photo testing or photo-patch testing for suspected contact allergy resulting from light exposure.
  - Specific immunoglobulin E in vitro testing, either:
    - After inconclusive percutaneous tests.
    - In lieu of percutaneous skin testing for one of the following:
      - Inability to temporarily discontinue skin test suppressive medication therapy (e.g., antidepressants or beta blockers).
      - Presence of widespread skin disease (e.g., dermatographism or generalized eczema).
      - Uncooperative members.
      - Clinical history suggesting an unusually elevated risk of anaphylaxis from skin testing.
  - Total serum immunoglobulin E testing for:
    - Presence of allergic bronchopulmonary aspergillosis.
    - Select immunodeficiencies (hyper-immunoglobulin E).
    - Eczematous or atopic dermatitis.
    - Suitability and dosing for omalizumab therapy.
  - Double-blind, placebo-controlled oral challenge test (Sampson, 2014).
  - Inhalation challenge for suspected immunoglobulin E-mediated hypersensitivity, either (Joint Task Force, 1995):
    - To establish a causative agent to an occupational exposure.
    - To evaluate therapeutic effectiveness of medications and immunotherapy.
    - When skin tests cannot be performed.
    - In combination with in vitro tests to evaluate specific immunoglobulin E-mediated sensitivity.
Limitations:

Coverage determinations are subject to benefit limitations and exclusions as delineated by the state Medicaid authority. The Florida Medicaid website may be accessed at http://ahca.myflorida.com/Medicaid/.

The number of allergens to be tested per member over a 12-month period is limited to (Centers for Medicare & Medicaid Services Local coverage article A54842; Bernstein, 2008):

- Skin prick/puncture tests — 70 allergens. An additional 70 prick/puncture tests may be approved if the initial tests are negative or inconclusive.
- Intracutaneous tests — 40 allergens.
- Patch tests — 55 allergens.
- In vitro immunoglobulin E testing — 30 allergens.

In vitro allergy testing is not medically necessary for members:

- With no contraindications to skin testing.
- Who respond successfully to empiric therapy for allergy.
- With mild symptoms.
- In combination with a skin test for the same antigen, except in the case of suspected latex sensitivity, hymenoptera, or nut/peanut sensitivity where both tests may be indicated.

Routine or annual use of a large number of skin tests in the absence of a definitive clinical indication is not medically necessary, except venom skin tests, which may require a repeat test at three- to six-month intervals when the initial test is negative (Golden, 2017).

Routine use of in vitro tests for delayed hypersensitivity to contact allergens (e.g., metals and bone cement) is not medically necessary.

If photo patch tests (CPT 95052) are performed for the same antigen and in the same session with patch or application tests (CPT 95044), only the photo patch tests should be reported.

If photo tests are performed with patch or application tests, only the photo tests should be reported.

Tests considered not medically necessary due to insufficient evidence of efficacy include, but are not limited to (Local coverage article A54842; Golden, 2017; Boyce, 2010; Bernstein, 2008):

- Antigen leukocyte cellular antibody automated food allergy testing.
- Applied kinesiology (Nambudripad’s allergy elimination test).
- Atopy patch test, except in patients with pediatric eosinophilic esophagitis to assess potential food triggers.
- Basophil/histamine release or activation.
- Candidiasis test.
- Chemical analysis of body tissue (e.g., hair).
- Chlorinated pesticides (serum).
- Component-resolved testing.
- Conjunctival challenge.
- C-reactive protein.
- Cytokine and cytokine receptor assay.
- Cytotoxicity assays.
- Electrodermal test (vega).
- ELISA/Act qualitative antibody testing.
- Endoscopic allergen provocation.
- Facial thermography.
- Food immune complex assay.
- Gastric juice analysis.
- Ingestion challenge food testing for diagnosing rheumatoid arthritis, depression, or respiratory disorders not associated with anaphylaxis or similar systemic reactions.
- Iridology.
- Lymphocytes (B or T subsets).
- Lymphocyte function assay.
- Lymphocyte stimulation.
- Mediator release assay.
- Prausnitz-Kustner or P-K testing (passive cutaneous transfer test).
- Provocation neutralization tests (subcutaneous or sublingual) for food allergies.
- Pulse test (pulse response test, reaginic pulse test).
- Rebuck skin window test.
- Sage complement antigen test.
- Testing and desensitization for poison ivy, oak, or sumac.
- Multiple chemical sensitivity testing (a.k.a., idiopathic environmental intolerance, clinical ecological illness, clinical ecology, environmental illness, chemical autoimmune deficiency syndrome, environmental/chemical hypersensitivity disease, total allergy syndrome, cerebral allergy, 20th century disease).
- Specific immunoglobulin G testing (e.g., by radioallergosorbert or enzyme-linked immunosorbent assay).
- Total serum immunoglobulin G, immunoglobulin A, or immunoglobulin M testing.

Tests for the following allergens are not clinically proven or medically necessary, including (Local coverage article A54842; Bernstein, 2008):
- Cornstarch.
• Cotton.
• Formaldehyde.
• Newsprint.
• Non-pollen producing flowers (e.g., marigold, dandelion, honeysuckle).
• Orris root.
• Poison ivy, oak, or sumac.
• Smog.
• Sugar.
• Tobacco smoke.

**Alternative covered services:**

Physical examination.

**Background**

Allergies are acquired, rapid, usually predictable, and exaggerated immune system responses to otherwise harmless environmental allergens that are ingested, inhaled, or contacted. They affect as many as 30 percent of adults and 40 percent of children in the United States (Asthma and Allergy Foundation of America, 2015a). The most common allergens include drugs, food, insects, latex, pollen, pets, and mold.

Hypersensitivity to allergens may be immediate (i.e., immunoglobulin E-mediated) or delayed (cell-mediated). Most allergic reactions, such as hay fever or hypersensitivity to animal dander, are relatively mild and non-life-threatening, although accompanied by unpleasant symptoms (sneezing, eye irritation, or itching). Other reactions, such as anaphylaxis or severe asthma attacks, may be much more serious.

Diagnosis of allergies comprises personal and medical history to identify the causative allergen and allergy testing when diagnosis remains uncertain. Diagnostic modalities test for immediate (immunoglobulin E-mediated) and delayed (non-immunoglobulin E- or cell-mediated) hypersensitivity or reaction to rule in or rule out specific allergens. Allergy tests includeskin patches or prick tests and intradermal tests with candidate allergens, tests involving cell types or chemicals that mediate hypersensitivity reactions (basophils, lymphocytes, or histamines), serologic tests (serum or allergen-specific immunoglobulin E), and physician-supervised challenge tests (Asthma and Allergy Foundation of America, 2015b).

**Searches**

Prestige Health Choice searched PubMed and the databases of:
• UK National Health Services Centre for Reviews and Dissemination.
Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.

The Centers for Medicare & Medicaid Services.

We conducted searches on July 31, 2018. Search terms were: “Immunologic tests” (MeSH), “Hypersensitivity” (MeSH), “Immune system diseases/chemistry” (MeSH), “Immune system diseases/diagnosis” (MeSH), “Immune system diseases/immunology” (MeSH), and free text terms “allergy test” and “allergy diagnosis.”

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.

- **Guidelines based on systematic reviews.**

- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

Consensus opinion suggests that (National Institute for Health and Care Excellence, 2011; Boyce, 2010; Lieberman, 2010; Bernstein, 2008):

- Available reviews cover all types of allergies in people of all ages, and generally concur that allergy testing should follow an allergy-focused history.

- Cost-effective testing strategies should begin with in vivo tests and progress to in vitro only when initial results are negative or equivocal.

The research literature on allergy testing is restricted to diagnostic accuracy studies. No reviews covered randomized controlled trials or other study types documenting improved outcomes with testing.

**Policy updates:**

The findings from a systematic review and meta-analysis (Nevis, 2016) suggest that skin-prick testing is accurate in discriminating subjects with or without allergic rhinitis; however, the diagnostic accuracy of intradermal testing is not as well established.

In 2018, we added one systematic review of the diagnosis of food allergy (Soares-Weiser, 2014) and several evidence-based guidelines that represent the standard of care for allergy testing (Golden, 2017; Fonacier, 2015; Seidman, 2015; Sampson, 2014; Joint Task Force on Practice Parameters, representing
Policy ID changed from CP# 17.01.03 to CCP.1075.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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</table>
| Golden (2017) for the American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology | **Key points:**  
- Skin or in vitro tests should be performed on patients for whom venom immunotherapy might be indicated.  
- Measurement of basal serum tryptase is highly recommended in patients who had hypotensive reactions to a sting and should be considered in other patients with systemic reactions to stings.  
  - Elevated basal tryptase may indicate the presence of an occult mast cell disorder and may be present in sting allergic patients with negative venom allergy test results. |
| Nevis (2016) | **Key points:**  
- Meta-analysis of seven studies (n = 430 patients) found the sensitivity and specificity for skin-prick testing was 85% and 77%, respectively.  
- Meta-analysis on intradermal testing not done due to low number of studies (four studies).  
- Intradermal testing to confirm skin-prick testing: sensitivity (27% to 50%) and specificity (60% to 100%).  
- Intradermal testing as a stand-alone test: sensitivity (60% to 79%) and specificity (68% to 69%) (two studies). |
| Boyce (2010) for the National Institute of Allergy and Infectious Diseases-Sponsored Expert Panel | **Key points:**  
- Recommended tests in addition to history and physical examination:  
  - Skin-prick test.  
  - Allergen-specific immunoglobulin E using fluorescence enzyme-labeled assays.  
  - Food elimination diets.  
  - Oral food challenges.  
- Tests not recommended:  
  - Intradermal tests.  
  - Atopy patch test.  
  - Skin prick tests, allergen-specific immunoglobulin E tests, and atopy patch tests in combination.  
  - Total serum immunoglobulin E.  
  - Basophil/histamine release or activation.  
  - Lymphocyte stimulation. |
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<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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</thead>
</table>
| Bernstein (2008) for the American Academy of Allergy, Asthma, and Immunology and the American College of Allergy, Asthma, and Immunology Allergy diagnostic testing | - Facial thermography.  
- Gastric juice analysis.  
- Endoscopic allergen provocation.  
- Hair analysis.  
- Applied kinesiology.  
- Provocation neutralization.  
- Allergen-specific immunoglobulin G4.  
- Cytotoxicity assays.  
- Electrodermal test (vega).  
- Mediator release assay.  
| **Key points:** |  
- Use prick/puncture tests to confirm clinical sensitivity induced by aeroallergens, foods, some drugs, and a few chemicals. (Strength of recommendation A – F: B).  
- No clear-cut advantage for any single or multitest device (C).  
- Sensitivity and specificity of prick/puncture tests for both inhalant and food allergens correlate with nasal and oral challenge tests (B).  
- The number of skin tests and the allergens selected for skin testing should be determined based on the patient’s age, history, environment and living conditions (e.g., region of the country), occupation, and activities. Routine use of a large number of skin tests or routine annual testing without a definite clinical indication is clearly not justified (D).  
- The appropriate number of atopic patch tests is indeterminate because they are not routinely performed (D).  
- On initial diagnostic evaluation, 70 prick/puncture and 40 intracutaneous tests for inhalant allergens are justified.  
- Insufficient evidence to justify tests for unproven agents, such as newsprint, sugar, cornstarch, orris root, tobacco smoke, cotton, formaldehyde, and smog.  
- Respiratory challenge tests are used when an objective gold standard for establishing clinical sensitivity is indicated (B).  

| Joint Task Force on Practice Parameters, representing: the American Academy of Allergy, Asthma, and Immunology; the American College of Allergy, Asthma, and Immunology; and the Joint Council of Allergy, Asthma and Immunology (1995) Practice parameters for the diagnosis and treatment of asthma | **Key points:**  
- Percutaneous and intracutaneous techniques are the most sensitive methods for detecting specific immunoglobulin E antibody.  
- Indications for in vitro testing:  
  - Presence of dermatographism or extensive dermatitis.  
  - When medications that influence skin tests (e.g., H1 histamine receptor antagonists or certain tricyclic antidepressants) cannot be discontinued.  
  - In certain children with chronic or recurrent respiratory symptoms.  
- Indications for skin tests and in vitro tests:  
  - To establish an allergic basis for symptoms.  
  - To establish specific causes of symptoms.  
  - To evaluate the degree of sensitivity to a specific allergen.  
- Indications for inhalation challenge:  
  - To assess airway responsiveness to a specific antigen.  
  - To establish a causative agent to an occupational exposure.  


Citation | Content, Methods, Recommendations
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- To evaluate therapeutic effectiveness of medications and immunotherapy.
- When skin tests cannot be performed.
- In combination with in vitro tests to evaluate specific immunoglobulin E-mediated sensitivity.

References

Professional society guidelines/other:


- Practice parameters for the diagnosis and treatment of asthma. Joint Task Force on Practice Parameters, representing the American Academy of Allergy Asthma and Immunology, the


**Peer-reviewed references:**


**Centers for Medicare & Medicaid Services National Coverage Determinations:**

110.11 Food allergy testing and treatment.

**Local Coverage Determinations:**

L33261 Allergy Testing.

L33417 Allergy Skin Testing.

L34313 Allergy Testing.

L36241 Allergy Testing.

L36402 Allergy Testing.

A54842 Response to Comments: Allergy Testing (L36402).

**Commonly submitted codes**
Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comments</th>
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<tbody>
<tr>
<td>86003</td>
<td>Allergen specific immunoglobulin E; quantitative or semiquantitative, each allergen</td>
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<tr>
<td>86005</td>
<td>Allergen specific immunoglobulin E; qualitative, multiallergen screen (dipstick, paddle, or disk)</td>
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<tr>
<td>95004</td>
<td>Intra-dermal scratch/prick</td>
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<tr>
<td>95017</td>
<td>Serial endpoint titration</td>
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<tr>
<td>95018</td>
<td>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</td>
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<tr>
<td>95024</td>
<td>Intracutaneous (intradermal) tests with allergenic extracts, immediate type reaction, including test interpretation and report, specify number of tests</td>
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<td>95027</td>
<td>Intracutaneous (intradermal) tests, sequential and incremental, with allergenic extracts for airborne allergens, immediate type reaction, including test interpretation and report, specify number of tests</td>
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<td>95028</td>
<td>Intracutaneous (intradermal) tests with allergenic extracts, delayed type reaction, including reading, specify number of tests</td>
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<tr>
<td>95044</td>
<td>Patch or application test(s) (specify number of tests)</td>
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<tr>
<td>95052</td>
<td>Photo patch test(s) (specify number of tests)</td>
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<tr>
<td>95070</td>
<td>Inhalation bronchial challenge testing (not including necessary pulmonary function tests); with histamine, methacholine, or similar compounds</td>
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<tr>
<td>95071</td>
<td>Inhalation bronchial challenge testing (not including necessary pulmonary function tests); with antigens or gases, specify</td>
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<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
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<tr>
<td>J30.1 - J30.9</td>
<td>Allergic rhinitis</td>
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<td>L20.84</td>
<td>Intrinsic (allergic) eczema</td>
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<tr>
<td>L25.4</td>
<td>Unspecified contact dermatitis due to food in contact with skin</td>
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<tr>
<td>L27.2</td>
<td>Dermatitis due to ingested food</td>
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<td>L50.0</td>
<td>Allergic urticarial</td>
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<td>T50.995+</td>
<td>Adverse effect of other drugs, medicaments and biological substances</td>
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<tr>
<td>T63.001+</td>
<td>Toxic effect of contact with venomous animals and plants</td>
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<td>T63.94x+</td>
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<tr>
<td>T78.00+</td>
<td>Anaphylactic shock due to adverse food reaction</td>
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<td>T78.09+</td>
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<td>T78.1+</td>
<td>Other adverse food reactions, not elsewhere classified</td>
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<tr>
<td>HCPCS Level II Code</td>
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<td>Comments</td>
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