Clinical Policy Title: Allergy testing

Clinical Policy Number: 07.01.03

Effective Date: June 1, 2014
Initial Review Date: December 18, 2013
Most Recent Review Date: January 18, 2017
Next Review Date: January 2018

Related policies:

CP#: 07.01.04 Exhaled nitric oxide for diagnosis of lung disease

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. 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

Prestige Health Choice considers the use of allergy testing to be clinically proven and therefore, medically necessary, when all of the following criteria are met:

- Clinically significant symptoms documented in allergy-focused history.
- Tests are performed by allergists, otorhinolaryngologists (ENT), or pulmonologists.

<table>
<thead>
<tr>
<th>In vivo allergy tests</th>
<th>Indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
<td></td>
</tr>
<tr>
<td>Skin scratch, prick, or puncture:</td>
<td>Suspected immunoglobulin E (IgE)-mediated allergy to:</td>
</tr>
<tr>
<td></td>
<td>• Foods.</td>
</tr>
<tr>
<td></td>
<td>• Stinging insect venom.</td>
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<tr>
<td></td>
<td>• Specific drugs.</td>
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<td></td>
<td>Additional 70 tests, if initial results negative.</td>
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<tr>
<td></td>
<td>Patients highly allergic to stinging insect venom:</td>
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<td></td>
<td>• Determination of starting dose for testing or</td>
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</tbody>
</table>

Policy contains:
- In vivo and in vitro tests.
- Food, inhalant, contact, insect venom, and drug allergies.
immunotherapy.
- Testing in facility equipped to manage anaphylaxis.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin patch</td>
<td>Suspected contact allergy.</td>
</tr>
<tr>
<td>Photo-patch</td>
<td>Suspected contact photo-sensitization.</td>
</tr>
<tr>
<td>Drug bronchial challenge</td>
<td>Suspected IgE-mediated drug hypersensitivity:</td>
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<tr>
<td></td>
<td>- With suggestive history.</td>
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<tr>
<td></td>
<td>- Drug is required for treatment.</td>
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<tr>
<td></td>
<td>- No effective alternative available.</td>
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<tr>
<td>In vitro allergen specific IgE</td>
<td>Testing is limited to that which is determined to be medically necessary on a case by case basis.</td>
</tr>
</tbody>
</table>

**Limitations:**

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

Tests not covered due to insufficient evidence:
- Fractionated exhaled nitric oxide (FeNO) for diagnosis and management of lung disease.
- Sublingual provoked and neutralization for food allergies.
- Allergen-specific immunoglobulin G (IgG).
- Testing and desensitization for poison ivy, oak, or sumac.
- Applied kinesiology.
- Body chemical analysis.
- Candida hypersensitivity syndrome.
- Conjunctival challenge.
- Cytotoxic food test.
- Electrodermal acupuncture.
- Food-specific IgG.
- Vega.
- Facial thermography.
- Hair analysis.
- In vitro:
  - Histamine release or leukocyte histamine release.
  - Lymphocyte proliferation.
- Iridology

There are in vitro tests that are covered, specifically allergen specific IgE; however, a positive test for allergen-specific IgE confirms the presence of the antibody only. Actual reactivity must be determined by history or supervised challenge (Nolte 2016).
**Alternative covered services:**

None.

**Background**

Allergies are acquired, rapid, usually predictable, and exaggerated immune system responses to otherwise harmless environmental substances or allergens that are ingested, inhaled, or contacted. 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).

Others, such as anaphylaxis or severe asthma attacks, may be much more serious. Allergy tests include skin patches or prick tests with candidate allergens, tests involving cell types or chemicals that mediate hypersensitivity reactions (basophils, lymphocytes, or histamines), and blood tests (serum or allergen-specific IgE).

**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 (CMS).

We conducted searches on November 15, 2016. Search terms were: “allergy” and “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**

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 (RCTs) or other study types documenting improved outcomes with testing.

Reviews concur on those tests supported by insufficient evidence (limitations, above).

**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.

The findings from two systematic reviews and meta-analyses (Tang 2016, Guo 2016) suggest that diagnostic testing with FeNO achieves a moderate level of performance in the detection of asthma in children.

A systematic review of seven studies (Petsky 2016) concluded that FeNO testing was effective in helping to reduce adult asthma exacerbations, but had no impact on day-to-day clinical symptoms, end-of-study FeNO levels, or inhaled corticosteroid dose. The authors could not advocate FeNO to guide therapy.

A review of five studies (Song 2016) indicated that FeNO, while able to assess airway inflammation, is not a good predictor of responsiveness to inhaled corticosteroids in patients with chronic cough.

Hayes (2015) found FeNO testing is noninvasive, poses no direct risk to patient safety, and may have moderate or moderately high sensitivity and specificity for the diagnosis of asthma. However, cutoff values used for interpretation of FeNO measurements vary widely. The body stated FeNO testing cannot be considered suitable for routine clinical use until a uniform protocol for its interpretation has been established and evaluated in clinical trials demonstrating clinical benefit.

Finally, the high prevalence of food and respiratory sensitization supports the clinical guideline recommendations (Önell 2016) that allergies should be evaluated in all children with suspected asthma as modern microarray platforms demonstrate acceptable accuracy and provide IgE characterization in 47 percent of patients.

**Summary of clinical evidence:**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevis (2016)</td>
<td>Key points:</td>
</tr>
<tr>
<td>Study</td>
<td>Key points</td>
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<td>-------------------------------------------</td>
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</table>
| Diagnostic accuracy of skin-prick testing for allergic rhinitis: a systematic review and meta-analysis. | • A systematic review and meta-analysis from Canada inclusive of 430 patients found the sensitivity and specificity for skin-prick testing was 85% and 77% respectively.  
• The accuracy of intradermal testing in confirming skin-prick testing results was less impressive, with sensitivity ranging from 27% to 50% and specificity ranging from 60% to 100%.  
• The accuracy of intradermal testing as a stand-alone test for diagnosing allergic rhinitis demonstrated sensitivity ranging from 60% to 79% and specificity ranging from 68% to 69%.  
• The study was endorsed by the Ontario Health Technology Assessment Service as accurate and meaningful in a country where allergy testing for rhinitis alone accounts for approximately CAD $3 million per year. |
| Tang (2016)                      | Key points:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Fractional Exhaled Nitric Oxide for the Diagnosis of Childhood Asthma: a Systematic Review and Meta-analysis. | • A systematic review and meta-analysis of fractional exhaled nitric oxide (FeNO) inclusive of 2933 subjects indicated that this non-invasive measure of airway inflammation provides objective data for use in asthma diagnosis.  
• The pooled estimates of sensitivity, specificity, and DOR for the detection of asthma in children were 0.79 [95 % confidence interval (CI), 0.64-0.89], 0.81 (95 % CI, 0.66-0.90), and 16.52 (95 % CI, 7.64-35.71). The SROC was 0.87 (95 % CI, 0.84-0.90). |
| Guo (2016)                        | Key points:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Diagnostic accuracy of FeNO in asthma | • Meta-analysis of 25 studies (n=3983) patients testing accuracy of exhaled nitric oxide for diagnosing asthma.  
• Sensitivity and specificity were 72% and 78% for all patients.  
• Report concludes that exhaled nitric oxide is accurate for diagnosing asthma in steroid-naïve or non-smoking patients, especially those with chronic cough. |
| Petsky (2016)                     | Key points:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Ability of FeNO to guide treatment of adult asthma | • Systematic review of seven studies, 1546 adult asthma patients.  
• Patients who had FeNO had fewer exacerbations vs. controls.  
• No differences between FeNO and control groups in day-to-day clinical symptoms, end-of-study FeNO levels, inhaled corticosteroid dose.  
• Authors conclude FeNO not helpful in guiding therapy in adults with asthma. |
| Song (2016)                       | Key points:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Ability of FeNO to predict corticosteroid response in chronic cough | • Systematic review, 5 studies, patients with chronic cough.  
• Study design heterogeneous, difficult to combine study results.  
• Sensitivity range from 44%–59%, specificity range from 63%–97%.  
• FeNO testing not a good predictor of corticosteroid response. |
| Hayes (2015)                      | Key points:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| FeNO measurement for diagnosis of asthma | • Systematic review evaluating FeNO as an adjunct indicator (seven RCTs) or replacement indicator (three RCTs).  
• FeNO testing is noninvasive and poses no direct risk to patient safety.  
• FeNO may have moderate or moderately high sensitivity and specificity for the diagnosis of asthma. However, cutoff values used for interpretation of FeNO measurements vary widely.  
• FeNO test cannot be considered suitable for routine clinical use until a uniform protocol for its interpretation has been established and evaluated in clinical trials demonstrating clinical benefit. |
<table>
<thead>
<tr>
<th>Reference</th>
<th>Title</th>
<th>Key points</th>
</tr>
</thead>
</table>
| Donohue (2013) | Measuring asthma exacerbations | **Key points:**  
- Meta-analysis of 3 RCTs, comparing FeNO-based and clinically-based adult asthma management programs.  
- Rate of exacerbations measured using both types of algorithms.  
- Asthma exacerbation rate significantly reduced using FeNO-based algorithm. |
| Önell (2016) | Allergy testing in children with persistent asthma: comparison of four diagnostic methods. | **Key points:**  
- A RCT of microarray testing in 71 children with asthma examined serum IgE characterization, which has been projected to be useful in the management of multisensitized patients.  
- Severe (n = 40) and controlled (n = 31) asthmatics were assessed for allergic sensitization by two microarray systems (Microtest and ISAC) and by two standard diagnostic methods (ImmunoCAP and skin prick test).  
- The pairwise concordance between two methods was 90% to 92% independent of methods compared.  
- The sensitivity of the four methods against doctor's diagnosis was 0.77-0.88, and the specificity was 0.97-0.99.  
- Microarray methods provided new information in 47% of the sensitized children in comparison with results obtained by standard diagnostic methods. |
| UK National Institute for Clinical Excellence (NICE) (2011) | Measuring fractional exhaled nitric oxide concentration in asthma | **Key points:**  
- Food allergies in children and young people.  
- Published meta-analyses, March 2010.  
- ≤19 years presenting with:  
  - Atopic eczema.  
  - Anaphylaxis.  
  - Urticaria.  
  - Rhinitis.  
  - Conjunctivitis.  
  - Asthma.  
  - Gastrointestinal symptoms.  
  - Oral allergy syndrome.  
- ≤19 years at higher risk of food allergy:  
  - Existing atopic diseases (asthma, atopic eczema, or allergic rhinitis).  
  - First degree relative (parent or sibling) with food allergy/other atopic disease.  
- Cost analysis: skin prick and IgE blood analysis to confirm food allergy is associated with cost-effectiveness ratio below threshold of £20,000/quality adjusted life years (QALY) gained: robust result with high probability of cost-effectiveness for skin-prick option.  
- Based on results of allergy-focused history, offer skin-prick test and/or blood tests for specific IgE antibodies to suspected foods and co-allergens.  
- Skin-prick only at facilities equipped to deal with anaphylaxis.  
- If non-IgE mediated allergy suspected: try allergen elimination for 2 – 6 weeks and reintroduce after trial; consult with appropriately trained dietician.  
- Tests not recommended:  
  - Vega.  
  - Hair. |
<table>
<thead>
<tr>
<th>Boyce (2010)</th>
<th><strong>Key points:</strong></th>
</tr>
</thead>
</table>
| Guidelines for the diagnosis and management of food allergy | - Diagnosis and management of food allergies.  
- **Recommended tests:**  
  - Symptom recognition and history.  
  - Physical exam.  
  - Skin prick test.  
  - Total serum immunoglobulin E (IgE).  
  - Allergen-specific IgE.  
  - Atopy patch test.  
  - Food elimination diets.  
  - Oral food challenges.  
- **Tests not recommended:**  
  - Intradermal tests.  
  - Basophil/histamine release or activation.  
  - Lymphocyte stimulation.  
  - Facial thermography.  
  - Gastric juice analysis.  
  - Endoscopic allergen provocation.  
  - Hair analysis.  
  - Applied kinesiology.  
  - Provocation neutralization.  
  - Allergen-specific IgG4.  
  - Cytotoxicity assays.  
  - Electrodermal test.  
  - Mediator release assay. |

<table>
<thead>
<tr>
<th>Lieberman (2010)</th>
<th><strong>Key points:</strong></th>
</tr>
</thead>
</table>
| The diagnosis and management of anaphylaxis | - Diagnosis and management of anaphylaxis.  
- **Diagnosis:**  
  - History.  
  - Evaluation of signs and symptoms.  
  - Skin-prick.  
  - Food challenge.  
  - In vitro IgE. |

<table>
<thead>
<tr>
<th>Schneider-Chaffen (2010)</th>
<th><strong>Key points:</strong></th>
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</thead>
</table>
| Diagnosing and Managing common food allergies | - Diagnosing and managing common food allergies.  
- Diagnostic accuracy studies, 9/2009.  
- Eighteen prospective studies (N = 2806); generally fair quality.  
- No significant (NS) differences, skin-prick vs. food challenge or serum food-specific IgE.  
- Conclusions hindered by lack of uniform diagnostic criteria. |
<table>
<thead>
<tr>
<th>Hayes (2009)</th>
<th>Key points:</th>
</tr>
</thead>
</table>
| Allergy testing for diagnosis of respiratory allergy in vitro | • Diagnosis of respiratory allergy, in vitro: quantitative in vitro assay for allergen-specific IgE.  
• Fair-to-good evidence for agreement with skin testing in patients referred to allergy clinic.  
• No evidence for impact on decision making in clinic, in primary care, or on patient outcomes. |

<table>
<thead>
<tr>
<th>Hayes (2009a)</th>
<th>Key points:</th>
</tr>
</thead>
</table>
| Allergy testing for diagnosis of respiratory allergy in vivo | • Allergy testing, in vivo.  
• Remaining questions re: most effective skin tests.  
• Evidence ratings: (A) for skin-prick/puncture, suspected inhalant; (B) intradermal, suspected inhalant; (C) skin-prick+ history/physical, suspected food; (D) intradermal, suspected food (high rate of false-positive reactions). |

<table>
<thead>
<tr>
<th>Lewis (2008)</th>
<th>Key points:</th>
</tr>
</thead>
</table>
| Diagnostic evaluation of inhalant allergies | • Cost-effectiveness of diagnostic evaluation of inhalant allergies.  
• Three approaches to suspected IgE-mediated inhalant allergies:  
  – Modified quantitative.  
  – Intra-dermal dilution.  
  – In vitro.  
• Modified quantitative most effective and least costly.  
• May not be generalized to all laboratories. |

**References**

**Professional society guidelines/other:**


**Peer-reviewed references:**


**CMS National Coverage Determinations (NCDs):**

110.11 National Coverage Determination (NCD) for Food allergy testing and Treatment. CMS Medicare Coverage Database Web site. https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=266&ncdver=1&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&KeyWord=Allergy+Testing&KeyWordLookUp=Title&KeyWordSearchType=And&list_type=ncd&bc=gAAAAACAAAAAAA%3d%3d&. Accessed November 15, 2016.

**Local Coverage Determinations (LCDs):**


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>
</tr>
</thead>
<tbody>
<tr>
<td>86003</td>
<td>Allergen specific IgE; quantitative or semiquantitative, each allergen</td>
<td></td>
</tr>
<tr>
<td>86005</td>
<td>Allergen specific IgE; 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>
<td></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>
<td></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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<tr>
<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>
<td></td>
</tr>
<tr>
<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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ICD-10 Code | Description | Comments |
|------------|-------------|----------|

<table>
<thead>
<tr>
<th>HCPCS Level II</th>
<th>Description</th>
<th>Comments</th>
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<tbody>
<tr>
<td>No codes</td>
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