Subject: Allergy Testing and Immunotherapy

Background: Immunotherapy for allergic diseases involves gradual administration and introduction of allergens to which the individual is sensitive to, for the purpose of modulating an immune response and alleviating allergic symptoms.

In vivo allergy testing may be performed to confirm possible triggers for the individual's symptoms based on clinical history that suggests diagnosis of immunoglobulin E (IgE)-mediated allergic disorders. Skin testing, which is a form of in vivo testing, directly introduces the antigen or allergen into the skin through percutaneous methods (e.g. prick, puncture, scratch on skin surface) or by the intradermal or intracutaneous route (e.g. injection into dermal layer). A bronchial challenge test requires an individual to breathe in the allergen to provoke bronchoconstriction or narrowing of the airways to evaluate the presence the allergic response. Patch testing involves apply patches with the allergen in small chambers or discs to an individual's back to measure the allergic response. A photo test assesses an individual's degree of photosensitivity by exposing the skin to various degrees of radiation (e.g., UVA or UVB). An oral or ingestion food challenge involves an individual eating a specific food slowly and in gradually increasing amounts to diagnose or rule out a food allergy. These tests may be used to confirm IgE-mediated diseases, such as allergic rhinitis, allergic asthma, anaphylaxis to insect venoms, drugs, and food. Anaphylaxis is a severe allergic response that involves more than one system of the body and can present as swelling, hives, lowered blood pressure and in some severe cases, shock.

In vitro allergy testing for the presence of allergen-specific immunoglobulin E (IgE) may also be provided to individuals who experience symptoms upon exposure to an allergen. The test requires analysis to detect hypersensitivity by measurement of allergen specific IgE in the blood serum. These tests may be used for inhalant allergens (e.g. pollen, mold, dander or dust), foods, insect stings for younger children or when direct skin testing is impossible due to extensive dermatitis, or dermatographism or conditions where antihistamines cannot be stopped for skin testing, such as chronic hives.

Policy and Coverage Criteria:

Allergy Immunotherapy

Harvard Pilgrim Health Care (HPHC) considers allergy immunotherapy as reasonable and medically necessary when administered under the supervision of an appropriately trained physician and when documentation confirms ALL the following indications:

- Results of allergy testing show immediate hypersensitivity to skin tests or in vitro tests for specific immunoglobulin E (IgE); AND
- Diagnosis of ANY of the following conditions:
  - Allergic asthma
  - Allergic conjunctivitis
  - Allergic rhinitis

    - Stinging insect hypersensitivity
- Documentation must confirm contraindication to or failed maintenance by pharmacologic therapy; AND
- Documentation must confirm individual's treatment plan, dosage and immunotherapy schedule, antigens to be administered, and target maintenance dose for allergy immunotherapy.

Harvard Pilgrim Health Care (HPHC) considers stinging insect immunotherapy as reasonable and medically necessary when administered under the supervision of an appropriately trained physician and when documentation confirms ALL the following:

- Diagnosis of anaphylaxis after an insect sting or hives alone in children under 16 years of age;
- Positive skin test or other documented IgE sensitivity to specific stinging insect venom

Harvard Pilgrim Health Care (HPHC) considers allergy immunotherapy as reasonable and medically necessary for individuals with ANY of the following:

- Animal dander sensitivity (epidermal) when documentation confirms antihistamines do not relieve symptoms
- Standardized dust mite extracts or perennials such as cat and dog danger and cockroach
- Delayed systemic reactions with symptoms of anaphylaxis with a positive skin test or presence of venom specific IgE
- Rapid desensitization for cases of allergy to insulin, penicillin, sulfonamides, cephalosporins and other commonly used drugs
- Seasonal pollinosis caused by trees, grasses and weeds with allergic rhinitis
- The treatment of mold-induced rhinitis

NOTE: Necessity of allergen immunotherapy depends on the following: degree to which symptoms can be reduced by medications, ability of the patient to tolerate possible side effects of the medication, amount, type and cost of the medications required to control symptoms, significant exposure to an allergen in which there is a significant level of sensitivity and the pattern of symptoms conform to the pattern of exposure, and whether conservative therapies (including avoidance) have failed to control the symptoms, or avoidance of the relevant antigen (e.g., dust mites, pollen, and mold) is impractical.

In Vivo Allergy Testing

Percutaneous Tests

Harvard Pilgrim Health Care (HPHC) considers percutaneous testing (scratch, puncture, prick) as reasonable and medically necessary for evaluation of immunoglobulin E (IgE) mediated hypersensitivity when documentation confirms testing is required for reactions to ANY of the following:

- Inhalants, OR
- Foods where individuals present signs or symptoms of urticarial, angioedema, eosinophilic esophagitis or anaphylaxis after ingestion of specific foods, OR
- Hymenoptera
- Specific drugs (e.g. penicillin, macromolecular agents, enzymes, egg-containing vaccines)

Intracutaneous/Intradermal Tests

Harvard Pilgrim Health Care (HPHC) considers intracutaneous/intradermal testing as reasonable and medically necessary when documentation confirms percutaneous tests are negative and there is suspected allergen sensitivity to ANY of the following:

- Inhalants

- Hymenoptera
- Specific drugs (e.g. penicillin, macromolecular agents)
- Vaccines

Patch Tests
Harvard Pilgrim Health Care (HPHC) considers patch testing as reasonable and medically necessary when documentation confirms test will be utilized to diagnose allergic contact dermatitis after ANY of the following exposures:

- Dermatitis due to detergents, OR
- Oils and greases, OR
- Solvents, drugs and medicines in contact with skin, OR
- Food in contact with skin, OR
- Plants, OR
- Cosmetics, OR
- Metals or rubber additives

Photo Patch Testing
Harvard Pilgrim Health Care (HPHC) considers photo patch testing as reasonable and medically necessary to diagnose suspected allergies resulting from light exposure (e.g. photo-allergic contact dermatitis).

Photo Tests
Harvard Pilgrim Health Care (HPHC) considers photo testing as reasonable and medically necessary to evaluate photo-sensitivity disorders.

Delayed Hypersensitivity Skin Testing
Harvard Pilgrim Health Care (HPHC) considers delayed hypersensitivity testing as reasonable and medically necessary for allergen testing, testing for infection with intracellular pathogens, or testing for sensitivity to contact allergens.

Bronchial Inhalation Challenges
Harvard Pilgrim Health Care (HPHC) considers bronchial inhalation challenge testing as reasonable and medically necessary when documentation confirms EITHER of the following:

- Inhalation bronchial challenge test is performed as dose-response assays where in provocation concentration thresholds can be determined on the basis of allergen concentration required to cause a significant decrease in measured pulmonary function, OR
- Inhalation bronchial challenge tests with occupational allergens are controlled by dosage and duration of exposure

Ingestion (Oral) Challenge Test
Harvard Pilgrim Health Care (HPHC) considers ingestion challenge testing as reasonable and medically necessary when documentation confirms ANY of the following:

- Food allergy dermatitis, OR
- Anaphylactic shock due to adverse food reaction, OR
- Allergy to medicinal agents, OR
- Allergy to foods, OR
- Allergy has resolved or has been disproven

When the criteria listed in this policy are met, allergy patch test for diagnosis of allergic contact dermatitis is limited to a maximum of 70 tests per year. Intradermal testing is limited to a maximum of 40 units per year. If additional tests are requested, medical documentation may be required.

Intracutaneous Testing (Delayed Reaction)
Harvard Pilgrim Health Care (HPHC) considers intracutaneous testing (delayed reaction) as reasonable and medically necessary on a case-by-case review for more than six tests.

Organ Challenge Testing
Harvard Pilgrim Health Care (HPHC) considers organ challenge testing as reasonable and medically necessary when documentation confirms testing is preceded by a control test with diluent.

In Vitro Allergy Testing
Harvard Pilgrim Health Care (HPHC) considers in vitro allergy testing as reasonable and medically necessary when skin testing is not possible and documentation confirms ANY of the following criteria:

- Individual has extensive dermatitis, severe dermatographism, ichthyosis or generalized eczema that will not make direct skin testing possible, OR
- Individual requires continued use of H-1 blockers (antihistamines), or in the rare patient with persistent unexplained negative histamine control, OR
- Individual cannot be safely withdrawn from medications that interfere with skin testing (e.g. long-acting antihistamines, tricyclic antidepressants, beta-blockers or medications that may put the individual at undue risk if they are discontinued), OR
- Individual is uncooperative due to mental or physical impairments, OR
- To evaluate cross-reactivity between insect venoms (e.g., fire ant, bee, wasp, yellow jacket, hornet), OR
- To utilize for adjunctive laboratory testing for disease activity of allergic bronchopulmonary aspergillosis and certain parasitic disease, OR
- To diagnose atopy in small children, OR
- Individual is at increased risk for anaphylactic response from skin testing based on clinical history (e.g., when an unusual allergen is not available as a licensed skin test extract), or who has a history of a previous systemic reaction to skin testing, OR
- Skin testing was inconclusive and in vitro testing is required as a confirmatory test.

Harvard Pilgrim Health Care (HPHC) considers total IgE testing as reasonable and medically necessary for follow-up of allergy bronchopulmonary aspergillosis (ABPA) and to help support a diagnose atopy in children and specifically hyperIgE syndrome and eosinophilic disorders.

When the criteria listed in this policy are met, in vitro testing is limited to a maximum of 30 allergens/beneficiary over a 12-month period when administered under the supervision of an appropriately trained physician. If additional tests are requested, medical documentation may be required.

Exclusions: Harvard Pilgrim Health Care (HPHC) considers allergen testing as not medically necessary for all other indications. In addition, HPHC does not cover:

- Serum IgG testing or IgG subclass testing for any specific allergens
- IgE testing at home
- Rapid desensitization for all other conditions not listed above
- Allergy immunotherapy for any of the following:
    - Therapy with allergoids or adjuvants

- Allergen immunotherapy for the management of skin and mucous membrane disease such as atopic dermatitis, and Candida vulvovaginitis
- Angioedema
- Chronic urticaria
- Desensitization for hymenoptera sensitivity using whole body extracts, with the exception of fire ant extracts
- Desensitization with bacterial vaccine (BAC: bacterial, antigen complex, streptococcus vaccine, staphylo-strepto vaccine, serobacterin, staphylococcus phage lysate)
- Desensitization with commercially available extracts of poison ivy, poison oak, or poison sumac
- Epicutaneous immunotherapy
- Food allergenic extracts immunotherapy
- Food allergy
- Intracutaneous desensitization (Rinkel Injection Therapy, RIT)
- Intracutaneous titration
- Intralymphactic immunotherapy
- Intranasal immunotherapy
- Intrinsic (non-allergic) asthma
- Migraine headaches
- Neutralization therapy (intradermal and subcutaneous)
- Non-allergic vasomotor rhinitis
- Oral or sublingual food immunotherapy
- Postmortem examination for IgE antibodies to identify allergens responsible for lethal anaphylaxis
- Repository emulsion therapy
- Sublingual desensitization
- Sublingual Immunotherapy (SLIT), delivered through drop formulation
- Sublingual provocative therapy
- Urine auto-injection (autogenous urine immunotherapy)

- In vivo and In vitro allergy testing for any of the following:
  - Ingestion (oral) challenge food testing, when performed in home setting
  - Provocative testing
  - Neutralization testing/therapy (Rinkel Test) of food allergies (sublingual, intracutaneous and subcutaneous)
  - IgG and IgG subclass antibody tests
  - Antigens
  - Radioallergosorbent test (RAST), fluoroallergosorbent test (FAST), and multiple antigen simultaneous
  - test (MAST)
  - ELISA (enzyme-linked immunoaorbent assay) test
  - Ophthalmic Mucous Membrane Test/ Direct Nasal Mucous Test
  - Quantitative multi-allergen screen
  - Cytotoxic leukocyte tests
  - Sublingual intracutaneous and subcutaneous provocative and neutralization testing and neutralization therapy for food allergies
  - Antigen leukocyte cellular antibody (ALCAT) automated food allergy testing
  - Applied kinesiology or Nambudripad's allergy elimination test (NAET (i.e., muscle strength testing or measurement after allergen ingestion)
  - Anti-Fc epsilon receptor antibodies testing

- Anti-IgE receptor antibody testing
- Blood, urine, or stool micro-nutrient assessments
- Candidiasis test
- Chemical analysis of body tissues (e.g. hair)
- Chlorinated pesticides (serum)
- Chronic urticarial index testing
- Clifford materials reactivity testing
- Complement (total or components)
- Complement antigen testing
- C-reactive protein
- Cytokine and cytokine receptor assay
- Cytotoxic testing for environmental or clinical ecological allergy testing (Bryans Test, ACT)
- Electrodermal testing or electro-acupuncture
- Electromagnetic sensitivity syndrome/disorder (allergy to electricity, electro-sensitivity, electrohypersensitivity, and hypersensitivity to electricity).
- Environmental cultures and chemicals
- Eosinophil cationic protein (ECP) test
- Food immune complex assay (FICA) or food allergenic extract immunotherapy
- General immune system assessments
- Immune complex assay
- Immunoglobulin G (IgG) testing for allergy
- Iridology
- Leukocyte antibodies testing
- Leukocyte histamine release test (LHRT)/basophil histamine release test
- Lymphocytes (B or T subsets)
- Lymphocyte function assay
- Mediator release test (MRT) or the LEAP program
- Metabolic assessments
- Multiple chemical sensitivity syndrome (a.k.a., idiopathic environmental intolerance (IEI), clinical ecological illness, clinical ecology, environmental illness, chemical AIDS, environmental/chemical hypersensitivity disease, total allergy syndrome, cerebral allergy, 20th century disease)
- Prausnitz-Kustner or P-K testing - passive cutaneous transfer test
- Pulse response test
- Qualification of nutritional assessments
- Rebuck skin window test
- Secretory IgA (salvia)
- Sage Complement Antigen Test
- Specific Immunoglobulin (IgG) (e.g., by Radioallergosorbent (RAST) or Enzyme-linked immunosorbent assay (ELISA)
- Sublingual provocative neutralization testing and treatment with hormones.
- Total serum IgG, immunoglobulin A (IgA) and immunoglobulin M (IgM
- Venom blocking antibodies
- Volatile chemical panels (blood testing for chemicals)
- Live Cell Analysis
- Passive Transfer
- Cytotoxic Food Testing

Supporting Information:

Allergy immunotherapy (also known as desensitization, hyposensitization, allergy injection therapy, or allergy shots), is well established indicated in patients with unavoidable allergen triggers and the allergy is IgE-mediated as documented by skin testing or RAST. Allergy immunotherapy is appropriate in patients with symptoms not well controlled by medication and the allergy is not season-specific. Patients with life-threatening allergy, such as severe anaphylactic reaction, to hymenoptera (venom from bees, hornets, wasps or fire ants) typically respond well to allergy immunotherapy, as well as patients with severe seasonal allergic rhinitis or conjunctivitis, perennial allergic rhinitis, and allergic asthma. Allergen extracts can be administered through several routes in addition to the subcutaneous (injection) route.

Subcutaneous immunotherapy (SCIT) is proven treatment for patients with certain allergies. According to current clinical guidelines from Cox et al. (2011), SCIT is appropriate for allergic rhinitis, allergic asthma, and stinging insect hypersensitivity. In a summary statement, Cox et al. noted "Immunotherapy is effective for the treatment of allergic rhinitis, allergic conjunctivitis, allergic asthma, and stinging insect hypersensitivity. Therefore, immunotherapy merits consideration in patients with these disorders as a possible treatment option."

In vivo and in vitro allergy testing may be used to determine and diagnosis immunoglobulin E (IgE)-mediated allergic disorders. In vivo allergy testing involves skin tests that introduce antigens into the skin to confirm IgE-mediated diseases. In vitro allergy testing detects hypersensitivity by measuring allergen specific IgE in the blood serum.

Extensive clinical trials and studies have established the safety and efficacy of SCIT for the treatment of allergic rhinitis, allergic asthma, stinging insect allergy, allergic conjunctivitis, and atopic dermatitis. Leading professional societies also recognize SCIT as an effective treatment option for these conditions.

Insect venom-specific IgG testing has been investigated to correlate the efficacy of venom immunotherapy. In practice, clinicians may use the testing to assess patients who have failed venom immunotherapy. However, the utility of the testing remains unclear. Wilson, et al. (1994) found absolute levels of IgG subclass anti-venom antibodies are not reliably indicative of clinical responsiveness. Reisman (1992) reviewed evidence investigating whether routine, venom-specific IgG testing should be standard of practice in patients receiving venom immunotherapy. The review concluded, "although the accurate measurement of serum venom-specific IgG is an important research tool and has clarified many aspects of the insect sting allergy field, no current clinical indication exists for its assay as part of the routine assessment of patients with insect sting allergy."

A 2008 Practice Parameter on Allergy Testing from the American Academy of Allergy Asthma and Immunology (AAAAI) on Allergy Testing states: "IgG and IgG subclasses can be measured using immunoassays similar to those used for allergen specific IgE. Controversy exists regarding whether increases of IgG4 are valid harbingers of either diagnosis or clinical efficacy after immunotherapy. Specific IgG/IgG4 results do not correlate with oral food challenges and are not recommended for the diagnosis of food allergy."

Brown et al. (2004) conducted a double-blind randomized placebo-controlled crossover trial of venom-specific tests with ant venom immunotherapy. The tests were performed and completed prior to a diagnostic sting challenge. IgE RAST and histamine release test (HRT), along with the intradermal venom skin testing (VST) and basophil activation test (BAT) were also performed. Results showed that VST and HRT were the only tests that identified those at risk of sting anaphylaxis in the placebo group. The authors concluded that HRT permits further assessment for diagnosis of venom allergy based on its efficacy.

Simola et al. (2000) measured the nasal responsiveness to histamine in a series of 73 individuals with long-continuing allergic rhinitis and to compare the measurements with skin test responses. Tests showed that skin prick with common allergens were performed and presence of nasal allergy was confirmed by allergen provocation. Non-specific nasal hyper-reactivity was determined with nasal histamine. The authors also concluded that milder non-specific nasal hyper-activity was due to the lack of reactivity in skin prick tests and nasal allergen challenge. Individuals with allergic rhinitis had reactivity to histamine which was linked to changes in skin and nasal mucosal reactivity in allergens.

Guidelines:

The American Academy of Allergy, Asthma and Immunology (AAAAI, 2019) indicates two phases of immunotherapy: a build-up phase and a maintenance phase. The build-up phase usually involves an individual receiving increasing amounts of allergen injections about one to two times per week. This generally ranges from three to six months and depends on the frequency of the injections. The maintenance phase beings once the effective dosage is reached and the success of this phase is dependent on the level of allergen sensitivity and the individual's response to the build-up phase. During this stage, treatments are administered between longer periods of time, extending from two to four weeks. AAAAI indicates individuals may notice a decrease in symptoms during the build-up phase, but it may take as long as 12 months on the maintenance dosage to notice progress.

The 2015 American Academy of Otolaryngic Allergy (AAOA) guidelines supports the use of in vitro testing as a diagnostic option and recommends the use of this test for individuals who have severe or poorly controlled asthmatics, severe to anaphylactic reactions to food or venom, widespread dermatologic conditions or for those who use or are unable to discontinue medications that may hinder the cutaneous response or may make anaphylaxis more problematic to treat.

The 2002 American Academy of Family Physician (AFP) guidelines support percutaneous and intradermal skin tests of specific IgE antibodies and deems these tests as useful for allergy management. Major indications for allergy testing include rhinitis, asthma, suspected food, drug or insect sting allergy.

Coding:

Codes are listed below for informational purposes only, and do not guarantee member coverage or provider reimbursement. The list may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible.

Allergy Testing Codes

CPT® Codes	Description
82785	Gammaglobulin (immunoglobulin); IgE
86003	Allergen specific IgE; quantitative or semiquantitative, crude allergen extract, each
86008	Allergen specific IgE; quantitative or semiquantitative, recombinant or purified component, each
95004	Percutaneous tests (scratch, puncture, prick) with allergenic extracts, immediate type reaction, including test interpretation and report, specify number of tests
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
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
95044	Patch or application test(s) (specify number of tests)
95052	Photo patch test(s) (specify number of tests)
95056	Photo tests
95060	Ophthalmic mucous membrane tests
95065	Direct nasal mucous membrane test
95070	Inhalation bronchial challenge testing (not including necessary pulmonary function tests); with histamine, methacholine, or similar compounds
95076	Ingestion challenge test (sequential and incremental ingestion of test items, e.g., food, drug or other substance); initial 120 minutes of testing
95079	Ingestion challenge test (sequential and incremental ingestion of test items, e.g., food, drug or other substance); each additional 60 minutes of testing

Allergy Immunotherapy Codes

CPT® Codes	Description
95115	Professional services for allergen immunotherapy not including provision of allergenic extracts; single injection
95117	Professional services for allergen immunotherapy not including provision of allergenic extracts; 2 or more injections
95144	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy, single dose vial(s) (specify number of vials)
95145	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); single stinging insect venom
95146	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); 2 single stinging insect venoms
95147	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); 3 single stinging insect venoms
95148	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); 4 single stinging insect venoms
95149	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); 5 single stinging insect venoms
95165	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy; single or multiple antigens (specify number of doses)
95170	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy; whole body extract of biting insect or other arthropod (specify number of doses)
95180	Rapid desensitization procedure, each hour (e.g., insulin, penicillin, equine serum)

Non-covered Allergy Testing Codes

CPT® Codes	Description
86001	Allergen specific IgG quantitative or semi-quantitative, each allergen
86005	Allergen specific IgE; qualitative, multiallergen screen (e.g., disk, sponge, card)

List of Medically Necessary ICD-10 Codes

Billing Guidelines:

Member's medical records must document that services are medically necessary for the care provided. Harvard Pilgrim Health Care maintains the right to audit the services provided to our members, regardless of the participation status of the provider. All documentation must be available to HPHC upon request. Failure to produce the requested information may result in denial or retraction of payment.

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Summary of Changes:

Date	Changes
8/21	Coding updated
5/21	Criteria and coding updated
3/21	Background updated
10/20	Criteria and coding updated
9/20	Coding updated
3/20	Policy coverage criteria, coding, references and supporting information updated
12/19	Annual review; no changes
10/17	Background and references updated; criteria refined
4/17	Removed benchmarks and ICD 9 references

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