Allergy Immunotherapy

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DESCRIPTION

Note: *This policy will address allergy immunotherapy and rapid desensitization, for allergy testing see medical policy 02.02.02. For information regarding oral immunotherapy see the following pharmacy policies: Oralair, Ragwitk, and Odactra. For oral peanut immunotherapy see pharmacy policy: Palforzia.*

Allergy Immunotherapy

The treatment of allergy is approached 3 ways: avoidance therapy, pharmacologic therapy, and immunotherapy. Complete avoidance of the known allergen responsible for inducing the signs and symptoms of the allergy is the most effective treatment for any allergic condition and results in a cure. When avoidance of a specific allergen such as house dust, molds or pollens is impossible, pharmacologic therapy is used (e.g., antihistamines, adrenergic agonists, anticholinergics, beta-adrenergic agonists, corticosteroids, cromolyn sodium and methylxanthines). It has been advocated that the utilization of air cleaners, humidifiers, or dehumidifiers is helpful in reducing allergic irritant substances in the environment; however, research indicates that the use of these mechanical devices was ineffective in reducing clinical symptoms.

Allergy immunotherapy (also known as desensitization, hyposensitization, allergy injection therapy, or "allergy shots"), is indicated in patients whose triggering allergens are not readily avoidable, the allergy is IgE-mediated as documented by skin testing or RAST, the symptoms are not easily controlled with medication, the symptoms encompass more than one season, and the patients are likely to cooperate in the program. The severity, duration and frequency of episodes should be explored. Patients with life-threatening allergy (severe anaphylactic reaction) to hymenoptera (venom from bees, hornets, wasps or fire ants) have been shown to respond well to allergy immunotherapy, as well as patients with severe seasonal allergic rhinitis or conjunctivitis, perennial allergic rhinitis, allergic (extrinsic) asthma and mold induced allergic rhinitis. Allergy immunotherapy will help desensitize the patient to the effects of the allergen. The documented allergy should correspond to the allergen planned for immunotherapy. A trial of systemic medications or avoidance of the allergens should be attempted. Two or more medications (antihistamines, steroids, bronchodilators, intranasal cromolyn) if not contraindicated should have been prescribed during the past year or the patient should be currently receiving immunotherapy.

Allergy immunotherapy is defined as the repeated administration of specific allergens to patients with IgE-mediated conditions, for the purpose of providing protection against the allergic symptoms and inflammatory reactions associated with natural exposure to these allergens. The exact mechanism of action is not known but may involve an increase in allergen-specific IgG antibodies, a decrease in IgE synthesis, and alteration in T-lymphocyte activity. The principal and most effective route of allergen application is by subcutaneous injection. There are a great assortment of different allergen extracts available, but only standardized extracts should be used. In the United States, the Food and Drug Administration (FDA) determined that the intracutaneous technique should be used for assigning standardized unitage (i.e., bioequivalency allergy units [BAU]). Patients with allergic rhinitis and/or asthma from tree and grass pollens in the spring, ragweed pollen in the fall and year-round dust-mite sensitivity who have had inadequate response to acceptable symptomatic medication and allergen avoidance are excellent candidates for immunotherapy. Immunotherapy is recommended for patients with allergic asthma unresponsive to allergen avoidance, even when symptomatic relief can be achieved with drug therapy. Treatment plans vary, but generally follow an initial dosing of short intervals (2 to 7 days) and should be increased 1.5 to 2 times with each injection if no reaction occurs. This dosing is followed by a maintenance dosage regimen at 3- or 4-week intervals and is determined by patient tolerance and relief of symptoms. Length of therapy varies from 3 to 5 years. The progress of the patient should be reviewed at regular intervals by the physician. Progressive improvement may be observed over the first 2 -to- 3 years of treatment. Discontinuation of therapy may be considered any time after a 2-to-3-year trial. The risk of relapse must be weighed against patient preference for continuation of therapy. Examples of potential allergens for which immunotherapy is effective include animal dander, animal feathers, animal fur, dust, grasses, insects, mites, molds, mushrooms, orris root, plants, pyrethrum, seeds, trees, vegetable gums, weeds, hymenoptera or stinging insects (bees, hornets, wasps, fire ants).

Allergy Immunotherapy Administration Schedules

Injection Schedules	Description
There are two phase of allergy immunotherapy administration: • The initial build-up phase • The maintenance phase	Initial build-up phase: The dose and concentration of allergen immunotherapy extract are increased. Maintenance phase: the patient receives an effective therapeutic dose over a period of time. With the most common build-up phase schedule, injections are administered one to three times per week. With this schedule, patients usually reach a maintenance dose in three to six months, depending on the starting dilution and occurrence of reactions. If systemic reaction occurs, immunotherapy may be discontinued, or if continued, the dose is reduced. Immunotherapy schedules may need to be adjusted for a variety of reason, including missed visits, high pollen or mold seasons, addition of new allergen, or systemic reaction. One a patient reaches the maintenance phase, the interval between injections can be progressively increased as tolerated, to an interval of up to four weeks for inhalant allergens and up to eight weeks for venom. The effective therapeutic dose or maintenance dose is the dose that provides therapeutic efficacy without significant adverse local systemic reactions. Three to five years of maintenance therapy is generally considered optimal for maximum clinical benefit.
Accelerated immunotherapy schedules	Accelerated immunotherapy schedules include cluster immunotherapy and rush immunotherapy. Accelerated immunotherapy schedules may permit an

	individual to reach a maintenance dose sooner but are associated with a higher risk of systemic reactions for inhalant allergens, especially with high-risk patients (e.g., those with markedly positive prick/puncture or in vitro IgE test responses).
Cluster immunotherapy schedules	With cluster immunotherapy, several injections (usually two or three) are administered during each visit in order to achieve a maintenance dose more rapidly than conventional schedules. In cluster immunotherapy, several injections at increasing doses (generally 2–3 per visit) are administered sequentially in a single day of treatment on nonconsecutive days. The maintenance dose is usually achieved more rapidly that with a conventional (single injection per session) schedule. Cluster schedules usually include fewer total injections than are used with conventional schedules, and permit a patient to reach a maintenance dose sooner, usually in one to four weeks.
Rush immunotherapy schedules	With rush immunotherapy, incremental doses of allergen are administered at varying intervals between 15 and 60 minutes over one to three days until the target therapeutic dose is achieved. Rush immunotherapy for inhalant allergies may be associated with a significant risk of systemic reactions. Rush schedules for stinging Hymenoptera venom immunotherapy are not associated with an increased incidence of systemic reactions, however.

According to guidelines from the American Academy of Asthma, Allergy and Immunotherapy, allergen immunotherapy should be administered in a medical facility with trained staff and medical equipment capable of recognizing and treating anaphylaxis. There are a limited number of studies of home-based allergy immunotherapy.

There is no evidence that immunotherapy is beneficial for food allergy, migraine headaches, vasomotor rhinitis, intrinsic (non-allergic) asthma, or chronic urticaria. In addition, there is little evidence that immunotherapy benefits atopic dermatitis and angioedema. The major risk factor of allergy immunotherapy is anaphylaxis. Immunotherapy should be administered under the supervision of an appropriately trained physician who can recognize early signs and symptoms of anaphylaxis and administer emergency medications if needed.

Rapid Drug Desensitization for Immediate Hypersensitivity Reactions
Desensitization is a procedure that alters the immune response to the drug and results in temporary tolerance, allowing the patient with a drug hypersensitivity reaction to receive an uninterrupted course of the medication safely. Once the medication is discontinued or if treatment is interrupted for a sufficient period of time, the patient's hypersensitivity to the medication returns. Desensitization is only safe and effective for certain types of drug allergy.

Desensitization is usually performed by starting with a 1/1000th to 1/100th dilution of the drug, which is used to administer an initial **dose** that is 1/10,000th of the full dose (note the distinction between dilution and dose), typically over 15 minutes. In exquisitely sensitive patients, an even lower dilution that did **not** produce a positive reaction during skin testing can be used as a starting dilution instead (for patients who had positive results to lower concentrations on skin testing). Progressively greater doses of a drug are then administered in a stepwise manner until a full therapeutic dose has been delivered.

Desensitization can be performed by oral, intravenous (IV), intraperitoneal, or subcutaneous routes. The IV route is the most often used for IV medications, since it provides control of the rate and amount of drug infusion, which can be stopped at any time during the delivery of drug, in contrast to oral administration.

The route of desensitization does not need to be the same as the route of administration. As an example, IV desensitization may be used even if subsequent therapy will be oral. Once the patient is successfully desensitized to a given dose, that dose can be administered by any route.

Typically for IV desensitization, the dose is doubled at each step. Increasing the dose faster than doubling is not recommended.

- In IV desensitization for immediate reactions, is delivered with each step over 15 minutes by continuous infusion. The dose is determined by the concentration of the solution and the rate at which the infusion pump is set. If there is no adverse reaction, proceed immediately to the next step.
- For oral desensitization, longer intervals may be required to assure complete absorption before increasing the dose but excessively long periods between doses may allow the cellular effects to be reversed. It is suggest allowing 20 to 30 minutes between steps.

The main risk during a desensitization procedure is that of a recurrent immediate reaction. The risk of this in any individual patient depends upon the drug in question and the sensitivity of the patient. Most breakthrough reactions are mild and less severe than the patient's initial hypersensitivity reaction. However, clinical judgement and experience is invaluable in determining how to adjust a desensitization procedure if the patient does have breakthrough symptoms and in knowing when to abort a procedure.

Risk Stratification

- Grade 1 reactions: Skin only
- Grade 2 reactions: Two organ systems involved (e.g., skin and respiratory tract)
- Grade 3 reactions: Includes changes in vital signs with one or more organ systems involved

Desensitization is usually performed in patients with past grade 1 or 2 reactions in the outpatient setting under close observation.

Allergists should be available within several minutes of the location where the desensitization is being performed. One-to-one nursing is provided with a nurse who has been specifically trained to monitor desensitization protocols and recognize and treat allergic reactions during the first desensitization, and one-to-two nursing for subsequent desensitization's. This nurse has been trained and preauthorized to administer any medications that may be required to treat an allergic reaction, including intramuscular epinephrine for anaphylaxis, so that there will be no delay in treatment if the supervising clinician is not at the bedside when the symptoms begin.

Complications include breakthrough allergic reactions, anaphylaxis, and rare immunologic sequelae.

The overall success rate of desensitization depends upon the protocol used, the sensitivity of the patient, and the mix of IgE-mediated and other immediate reactions. Another important factor is the expertise of the supervising clinician in managing any symptoms that occur and adjusting the procedure accordingly.

IgE-mediated reactions, such as those to beta-lactam antibiotics and platinum-based chemotherapy agents, have very high rates of success. In experienced hands, virtually all of these desensitization's are successful.

After a patient has been desensitized, the drug is given normally at the usual intervals, if doses are at least daily. If the drug is stopped, allergic sensitivity will return shortly after the medication is cleared from the bloodstream.

Maintaining the desensitized state is dependent upon the continuous presence of the drug in the patient's system. Accordingly, it is important to give doses regularly and on time so that there is no interruption in exposure.

The success rate of drug desensitization is very high when performed by experienced drug allergy experts. Patients may experience mild breakthrough reactions during as many as 20 percent of desensitization's, and the clinician's experience in managing these is critical. Breakthrough symptoms are managed by stopping the infusion temporarily, administering specific treatments, and restarting the protocol again at the step that elicited symptoms. The protocol should be adjusted to advance through the problematic step more gradually if it is to be performed again in the same patient. The patient must be counseled that desensitization is not a permanent cure for allergy to the drug in question. The sensitivity returns once the drug is cleared from the bloodstream, and the patient should continue to report an allergy to that agent in the future.

Alternative Allergy Treatment Methods

Numerous alternative allergy treatment methods have been identified in the professional society guidelines and literature. These allergy treatment methods remain unproven at this time due to a lack of supporting evidence published in the peer-reviewed scientific literature. The role of these techniques in the management of allergic disease has not yet been established. Some of the alternative allergy treatment methods utilize extracts that are not U.S. Food and Drug Administration (FDA)-approved.

Allergoids

Allergoids are formalin treated allergens which have been shown to be as effective as conventional aqueous extracts and superior to placebo in terms of reduction of symptom medication scores, production of an increase in ragweed IgG levels, and a decrease in seasonal rise in ragweed IgE levels. Allergoids are licensed and manufactured for general distribution in Europe, but not yet in the United States.

Enzyme Potential Desensitization (EPD)

Enzyme potentiated desensitization is patented in Europe under the brand name of Epidyme. This immunotherapy consists of a mixture of allergens to molds, grass, weeds, trees, dust mites, dog and cat dander, and house dust. These allergens are administered in the doctor's office. While this is common practice in Europe, it is not on the United States market or regulated/approved by the U.S. FDA. The FDA has banned importation of EPD. There is a lack of clinical trials supporting the efficacy of this product.

A variant of enzyme potentiated desensitization is ultra-low dose enzyme activated immunotherapy (also known as low dose allergens or LDA), which has been described as a method of immunotherapy enhanced by a minute dose of the enzyme, beta glucuronidase. According to proponents, the beta glucuronidase activates extremely miniscule doses of various allergens and stimulates the production of T-suppressor cells. The T-suppressor cells, in turn, down regulate the T-helper cells that are causing allergic symptoms by misidentifying normal substances in the body as allergens. LDA uses the same active components as EPD, but utilizes more pollens, foods and other allergens.

Photo-Inactivation
Photo-inactivation of an antigen with ultraviolet may allow larger doses of antigen to be administered with fewer adverse effects. Currently, these preparations are used for research purposes only and not in clinical practice.

Polymerized Ragweed Extract
Polymerized ragweed extract has been employed for treatment of ragweed hay fever in placebo-controlled trials and has been shown to produce a significant decrease in symptoms and medication scores. However, polymerized ragweed extracts have not yet been licensed or manufactured for general distribution in the United States.

Intranasal Immunotherapy
Treatment with intranasal immunotherapy has been proposed as a treatment for allergic rhinitis. Local adverse reactions are common with this approach and are the most frequent reason for discontinuing treatment. This allergy treatment method remains unproven due to a lack of supporting evidence published in the peer-reviewed scientific literature.

Rhinophototherapy
Rhinophototherapy uses UV-B, UV-A, and visible light to treat allergic rhinitis. This allergy treatment method remains unproven due to a lack of supporting evidence published in the peer-reviewed scientific literature.

Helminth Trichuris Suis Therapy
Treatment with helminth trichuris suis has been proposed as a treatment for allergic rhinitis. A therapeutic approach has been suggested in different experimental models of allergic disease showing that live ova from trichuris suis, an intestinal helminth of pigs, can protect against allergic reactivity by helminth-induced regulatory T cells and cytokines. This allergy treatment method remains unproven due to a lack of supporting evidence published in the peer-reviewed scientific literature.

Urine Auto-Injection
The practice of injection of an extract of the patient's own urine for diagnosis and treatment of allergy is clearly unacceptable and must be discouraged. It is not based on rational theory, and there have been no scientific investigations of efficacy and safety. There is a potential danger for autoimmune nephritis with this procedure.

Multiple Chemical Sensitivity Syndrome
Multiple chemical sensitivity (MCS) (also known as 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) has been used to describe a condition whereby an individual becomes chronically ill from exposure to chemicals in foods and the environment at doses far below the levels normally considered safe. Resulting “allergies” to these chemicals have been postulated to cause a number of troubling symptoms (e.g., fatigue,

irritability, behavior problems, depression, confusion, and nervous tension in children) in the absence of objective physical findings. The existence of such a syndrome has been based on anecdotal reports and uncontrolled studies. Several well-designed investigations suggest that most people diagnosed with MCS have a medical or psychosomatic disorder that they cannot accept, preferring instead to interpret their symptoms as environmental sensitivities. If this is true, the diagnosis of MCS may delay proper medical and psychiatric care.

The theories and practices involving environmental allergies of this type have been severely criticized by the American Medical Association, the American College of Physicians, the Canadian Psychiatric Association, the International Society of Regulatory Toxicology and Pharmacology, the American Academy of Allergy, Asthma and Immunology (AAAAI), and several scientific panels that have investigated them. Based on the reports in the peer-reviewed scientific literature, the American Medical Association's Council on Scientific Affairs stated that "there are no well controlled studies establishing a clear mechanism or cause for multiple chemical sensitivity syndrome." The AAAAI reviewed the evidence again and concluded, "Rigorously controlled studies to verify the patient's reported subjective sensitivity to specific environmental chemicals have yet to be done. Moreover, there is no evidence that these patients have any immunologic or neurologic abnormalities. In addition, no form of therapy has yet been shown to alter the patient's illness in a favorable way."

Confinement in an environmental control unit or facility (ecology unit), which has been used as a treatment for environmental illnesses and hypersensitivities, has not been established as an effective or appropriate treatment.

Electromagnetic Sensitivity Syndrome

A number of people who suffer from non-specific health symptoms (e.g., allergies, headache, fatigue, skin symptoms, anginal-like complaints, difficulties in concentrating, mood and sleep disturbances) have claimed that they are sensitive to electromagnetic waves and electromagnetic pollution from antennas, cell phones, computers, electrical appliances, video display units, and overhead power lines, etc. The term "electromagnetic sensitivity (also known as allergy to electricity, electro-sensitivity, electrohypersensitivity, and hypersensitivity to electricity) has been used to describe these individuals. However, it is not an established disease. There is no reliable clinical data to support the theory that low level electromagnetic waves cause these symptoms. There are no accepted diagnostic criteria or procedures for the diagnosis and treatment of electromagnetic sensitivity. Furthermore, no direct cause-effect relationship between electromagnetic sensitivity symptoms and electromagnetic fields has been proven.

A number of controlled studies have found no effect of exposure to electromagnetic fields on symptoms or signs.

Detoxification
Detoxification is a method used by individuals who believe that an allergic state can be induced by toxic damage to the immune system from exposure to environmental chemicals. It is believed that certain lipid-soluble chemicals may be stored in body fat for long periods. Detoxification consists of sauna and exercise. The individual ingests high-dose niacin to induce erythema. Body fluids are replenished with water and electrolytes and certain essential oils are consumed, presumably to help replace fat-soluble chemical contaminants. This procedure takes approximately five hours and is repeated daily for 20–30 days. This form of therapy has not been well-studied and is unproven.

Homeopathic Remedies
A homeopathic remedy administers a causative agent of a disease and is administered therapeutically in small amounts. There is no scientific evidence to support homeopathic practice as a method for treating allergies.

Injection of Food Extracts
An injection of food extracts consists of a combination of foods based on skin test results or a patient's report of intolerance to foods. There is a lack of clinical trials support this treatment.

Rotational and Multiple Food Elimination Diets
Proponents of the concept of multiple food allergies sometimes recommend a "rotary diversified diet," in which the patient rotates foods so that the same food is eaten only once every 4–5 days to help identify foods that may cause allergic responses. This allergy treatment method remains unproven due to a lack of supporting evidence published in the peer-reviewed scientific literature.

Low-Dose Immunotherapy or Ultra-Low dose Enzyme Activated Immunotherapy/Low Dose Allergens (LDA)
Both of these methods involve the use of extremely low doses of antigens alone or in conjunction with beta-glucuronidase in an attempt to down regulate an inappropriate immune response. These allergy treatment methods remain unproven due to a lack of supporting evidence published in the peer-reviewed scientific literature.

Intralymphatic Immunotherapy (ILIT)
Intralymphatic immunotherapy is a new process of administering immunotherapy that is thought to increase the safety and convenience of prolonged immunotherapy. Allergen extract is injected into a lymph node under ultrasound guidance. Therapy is reported to be completed after 3 injections given on a monthly basis. This method of immunotherapy is currently being studied in clinical trials. The reason that ILIT appears to be effective in some studies but did not show efficacy in others might be related to the different outcome parameters. The parameters that signify efficacy are not straightforward.

Epicutaneous Immunotherapy (EPIT)
Epicutaneous immunotherapy involves the use of patches as a dosage form for allergen specific immunotherapy. An adverse effect of this therapy is patch-induced eczema at the patch site. This allergy treatment method remains unproven due to a lack of supporting evidence published in the peer-reviewed scientific literature.

Peptide Therapy
The concept that the clinical response to allergen immunotherapy probably reflects the induction of nonresponsiveness in Th2 lymphocytes led to the concept of immunotherapy with allergen-derived peptides representing T cell activating epitopes that do not react with IgE antibodies. This allergy treatment method remains unproven due to a lack of supporting evidence published in the peer-reviewed scientific literature.

Provocation-Neutralization Therapy
This treatment involves the injection of substances under the skin that are suspected of triggering an allergic reaction in sufficient quantity to cause symptoms similar to the patient's complaints. This is then followed by an immediate injection of a weaker or stronger dilution of the same antigen to relieve the symptoms. This allergy treatment method remains unproven due to a lack of supporting evidence published in the peer-reviewed scientific literature.

Practice Guidelines and Position Statements

Guidelines Task Force: American Academy of Allergy, Asthma & Immunology (AAAAI); the American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy Asthma & Immunology
Immunotherapy is effective for the treatment of allergic rhinitis, allergic conjunctivitis, allergic asthma, and stinging insect hypersensitivity. Clinical trials do not support the use of subcutaneous immunotherapy for food hypersensitivity. Oral immunotherapy and SLIT (sublingual immunotherapy) for food hypersensitivity/food allergies are considered investigational. Immunotherapy is not currently approved by the Food and Drug Administration for use to treat food allergy.

American Academy of Allergy, Asthma & Immunology (AAAAI)
The preferred location for receiving shots is your prescribing allergist’s office. Injections can sometimes be given at another facility where the physician and staff are trained to recognize and treat reactions and have received instructions by your prescribing allergist.

The European Academy of Allergy and Clinical Immunology (EAACI)
The risk of adverse reactions, including anaphylaxis. EAACI guidelines do not recommend food immunotherapy for routine clinical use. The conclusions of the position statement: Immunotherapy is effective in reducing symptoms of allergic asthma and rhinitis and potentially modifies the underlying course of disease. Studies on AIT in the treatment of AD and food allergy could broaden the indications. However, AIT remains underused because of a lack of awareness, limited access to specialist care, the

reimbursement policy, long duration, and concerns regarding safety and effectiveness. The major barrier for the further development of immunotherapy, especially for the new technologies, is the capacity to perform 1 or more phase 3 confirmatory double-blind, placebo-controlled trials per allergen source.

PRIOR APPROVAL

Not applicable.

POLICY

See Related Medical Policies

- 02.02.02 Allergy Testing
- For information regarding oral immunotherapy see the following Pharmacy Policies:
    - Oralair
    - Ragwitk,
    - Odactra
- For oral peanut immunotherapy see Pharmacy Policy: Palforzia

Allergy immunotherapy administered in a medical facility may be considered **medically necessary** for the treatment of the following IgE-mediated allergies:

- Allergic (extrinsic) asthma
- Dust mite atopic dermatitis
- Hymenoptera (bees, hornets, wasps, fire ants) sensitive individuals
- Mold-induced allergic rhinitis
- Perennial rhinitis
- Seasonal allergic rhinitis or conjunctivitis;

When the following conditions are met

- The individual has severe, seasonal, or perennial IgE-dependent symptoms of allergic rhinoconjunctivitis or asthma after natural exposure to the allergen and both of the following criteria are met:
    - The individual has skin test and/or serological evidence of IgE-mediated antibody to a potent extract of the allergen; **and**
    - Avoidance or pharmacologic therapy cannot control allergic symptoms or member has unaccepted side effects with pharmacologic therapy; **or**

- The individual has a life-threatening IgE mediated allergy to insect stings (bees, hornets, wasps, and fire ants); **or**
- The individual has hypersensitivity to allergens that cannot be managed by medication or avoidance.

Allergy immunotherapy is considered **investigational** for all other indications, including but not limited to:

- Angioedema
- Atopic dermatitis (cover for dust mite atopic dermatitis)
- Chronic urticaria
- Food allergies,
- Intrinsic (non-allergic) asthma
- Migraine headaches
- Nasal polyposis
- Non-allergic vasomotor rhinitis

Home administration of allergy immunotherapy is considered **investigational,** according to guidelines from the American Academy of Asthma, Allergy, and Immunotherapy (AAAAI), allergen immunotherapy should be administered in a medical facility with trained staff and medical equipment capable of recognizing and treating anaphylaxis. There are a limited number of studies regarding home-based allergy immunotherapy. The evidence is insufficient in determining the technology results in improved net health outcomes.

Other Treatments

Rapid desensitization (also known as rush, cluster, or acute desensitization) may be considered **medically necessary** with any of the following conditions:

- Allergy to a particular drug that cannot be treated effectively with alternative medications; **or**
- Insect sting (e.g., wasps, hornets, bees, fire ants) hypersensitivity (hymenoptera); **or**
- Members with moderate to severe allergic rhinitis who need treatment during or immediately before the season of the affecting allergy.

Notes:

- *Allergens should be individually prepared for the individual and the allergen content should be based on appropriate skin testing or appropriate in vitro testing.*
- *If a woman is contemplating pregnancy and requires initiation of allergy immunotherapy and/or it is anticipated that she will require allergy medications that may increase risk to her or the fetus, rapid desensitization is an acceptable approach.*

Rapid desensitization is considered **investigational** for all other indications, because they have not been proven to be effective. The evidence is its effectiveness for indications other than the ones listed above has not been established.

Immunotherapy treatments including but not limited to the following are considered **investigational** because they have not been proven to be effective. The evidence is insufficient in determining the technology results in improved net health outcomes:

- Allergoids (modification of allergens to reduce allergenicity)
- Autogenous urine immunization (urine auto injection)
- Detoxification for allergies
- Epicutaneous immunotherapy
- Enzyme potentiated desensitization (EPD)
- Helminth Trichuris suis therapy for allergic rhinitis
- Homeopathic remedies for allergies
- Injection of food extracts
- Intranasal immunotherapy
- Low does immunotherapy
- Multiple chemical sensitivity syndrome (environmental chemical avoidance for idiopathic environmental intolerances)
- Peptide therapy
- Provocation – neutralization therapy
- Rhinophototherapy
- Rotational and multiple food elimination diets (e.g., rotary diversified diet)

Non-Covered

Allergen-proof supplies, such as mattresses, pillows, and casings, etc., are considered personal convenience items and are therefore considered a non -covered benefit, refer to the member's plan document.

Policy Guidelines

Required Documentation

The member's medical record must contain documentation that fully supports the medical necessity for services included within this medical policy. This documentation includes, but is not limited to, relevant medical history, physical examination and results of pertinent diagnostic tests or procedures.

- Include the following information:
    - Medical history, examination, and results of diagnostic testing (including allergy testing) upon which the need for the treatment is based.
    - Plan of treatment and dosage regimen must be documented in the member's medical record. The record should be prepared so that data regarding injection and responses can be appreciated in a logical and sequential sense.
    - When an evaluation and management service is billed on the same day as allergen immunotherapy (by the same physician) a separately identifiable service must be documented in the medical record.
    - Documentation must support the use of the code (e.g., number of venoms, number of vials).

Immunotherapy Serum Coding

- Per unit reimbursement for allergy immunotherapy is based on the number of dosages prepared and intended for administration. When billing, providers should report the number of units representing the number of 1cc doses being prepared. A maximum of 10 doses per vial is allowed.
- Allergy immunotherapy, including insect immunotherapy, is limited to 120 units annually (this would equate to 12 pure allergen vial preparations that are then diluted and used for therapy) for the first year of therapy during escalation, and 90 units (which equates to 9 pure allergen vials) for yearly maintenance therapy thereafter.

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- 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

- 95180 Rapid desensitization procedure, each hour (e.g. insulin, penicillin, equine serum)
- 95199 Unlisted allergy/clinical immunologic service or procedure (e.g., sublingual immunotherapy)
- K1026 Mechanical allergen particle barrier/inhalation filter, cream, nasal, topical

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POLICY HISTORY

Date	Reason	Action
February 2022	Annual Review	Policy Renewed
November 2021	Interim Review	Policy Revised

February 2021	Annual Review	Policy Revised
February 2020	Annual Review	Policy Revised
February 2019	Annual Review	Policy Revised
February 2018	Annual Review	Policy Revised
February 2017	Annual Review	Policy Revised
April 2016	Annual Review	Policy Revised
January 2016	Interim Review	Policy Revised
May 2015	Annual Review	Policy Revised
May 2014	Annual Review	Policy Revised
July 2013	Annual Review	Policy Revised
September 2012	Annual Review	Policy Revised
September 2011	Annual Review	Policy Revised

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
PO Box 9232
Des Moines, IA 50306-9232

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