

Subject: Allergy Immunotherapy	Current Effective Date: 08/11/2006
Policy#: MED.00001	Last Review Date: 03/23/2006
Status: Reviewed	

Description/Scope

Allergy immunotherapy is a treatment designed to prevent allergic reaction from occurring, thus treating the basic cause of the disease process. Immunotherapy involves giving gradually increasing doses of the substance, or allergen, to which the person is allergic. This causes the immune system to become less sensitive to the substance thereby reducing the symptoms of allergy when the substance is encountered in the future.

Policy Statement

Medically Necessary:

Allergy immunotherapy is considered **medically necessary** in individuals with a demonstrated hypersensitivity that cannot be managed by medications or avoidance and the specific type of immunotherapy is not identified below as investigational/not medically necessary.

Investigational/Not Medically Necessary:

Allergy immunotherapy is considered **investigational/not medically necessary** in all other cases where the hypersensitivity can be managed by medication or avoidance, and also for the specific types of immunotherapy listed below:

- Provocative and neutralization therapy for food allergies using sublingual, intradermal, and subcutaneous routes
- High dose (at least 20-375 times the cumulative subcutaneous dose) or low dose sublingual immunotherapy
- Oral immunotherapy (antigens in capsules that are swallowed immediately)
- Repository emulsion therapy
- Urine autoinjections and autogenous immunization therapy
- Rotational diets and multiple food elimination diets
- Enzyme potentiated desensitization (EPD)
- Acupuncture for allergies
- Allergoids (modification of allergens to reduce allergenicity)
- Ecology units/environmental chemical avoidance for multiple chemical sensitivity syndrome
- Homeopathy for allergies
- Idiopathic environmental intolerance (also known as multiple chemical sensitivity syndrome, clinical ecology, chemical AIDS, environmental/chemical hypersensitivity disease, total allergy syndrome, cerebral allergy, 20th-century disease)
- Photoinactivated extracts
- Polymerized extracts
- Poison ivy/poison oak extracts for immunotherapy in the prevention of toxicodendron (Rhus) dermatitis

Rationale

Based on available peer-reviewed medical literature, allergy immunotherapy has been demonstrated to be an effective therapy for the treatment of allergies when the conventional treatments of medication and avoidance have failed. In individuals with hypersensitivity, the goal of allergy immunotherapy is to prevent allergic reactions from occurring.

Subcutaneous immunotherapy (SCIT) is the current standard of care. It is established as effective for patients with allergic rhinitis and/or asthma, especially for allergies to grass pollen, ragweed pollen, birch pollen, mountain cedar pollen, house dust mite, cladosporium, alternaria, and cats. It is also effective for anaphylaxis to hymenoptera venom. Alternative routes of administration such as oral (OIT) and sublingual (SLIT) have been studied.

Since 1986, there have been at least 22 double blinded, placebo-controlled studies published in peer-reviewed journals assessing the effectiveness of sublingual immunotherapy (SLIT). The vast majority of these studies were conducted outside of the United States and with small sample sizes. In a review study published by Canonica and Passalacqua in 2003, analysis revealed that all but three of the studies confirmed the clinical efficacy of SLIT in rhinitis induced by common allergens (when compared to placebo). There have been no head-to-head studies comparing the effectiveness of SLIT to SCIT (the gold standard). Additionally, the allergen extracts that have been FDA approved for use in SCIT do not have a similar approval for use in SLIT and are used as an off-labeled indication. Additionally, it is uncertain exactly what dose of allergen extract is required when administered via the sublingual route. There is inadequate data to document the efficacy of immunotherapy for allergies to food, fungi, molds, yeasts, and other undefined allergens, or for the treatment of atopic dermatitis or eczema, angioedema, and urticaria.

Although the Allergic Rhinitis and its Impact on Asthma (ARIA) Workshop Report concluded, in collaboration with the World Health Organization (WHO), that high dose SLIT therapy was efficacious for treating allergies to pollen and dust mites, the fact that there have been no direct comparisons to the gold standard of SCIT and that there are no FDA approved allergen extracts for sublingual delivery make this form of immunotherapy investigational/not medically necessary at this time.

Lastly, there is no published data to support the clinical efficacy of oral immunotherapy.

Background/Overview

An allergy is an abnormal reaction or increased sensitivity to certain substances in the environment. The substances that cause this sensitivity or reaction are called allergens and can vary from naturally occurring materials, such as pollen and grass, to man-made materials including soaps or chemicals. According to the National Institute of Allergy and Infectious Diseases, about 20% of the general population experience allergic reactions triggered by harmless agents such as pollens, molds, and dust mites. First line treatment includes avoidance and minimization of exposure when possible. Medication, including antihistamines, bronchodilators, leucotriene inhibitors, and steroids (cortisone), may be used to reverse some of the symptoms of these allergic reactions.

Allergy immunotherapy is a form of treatment designed to prevent the allergic reaction from ever occurring, thus treating the basic cause of the disease process. Its mechanism of action is based upon the fact that the body produces different antibodies to the same antigen depending on how the antigen is introduced into the body. Allergy immunotherapy is typically used in patients where the use of conservative treatments, such as avoidance and medications, has been found to be inadequate. Allergy immunotherapy begins with exposing the patient to very low doses to prevent serious reactions, and progresses gradually to increased doses injected once or twice a week. This allows the body to slowly develop immunity to the antigen without the development of symptoms. After a period of time, a maximum dose of antigen is reached and injections are maintained at this dosage with the interval between injections changed to between two and six weeks. Immunotherapy may need to be administered continuously for several years. Immunotherapy does not cure allergies but rather makes the patient less sensitive to them. In some cases, allergic symptoms may be controlled to the point of disappearance, allowing a person to avoid allergen reactions.

Immunotherapy has been demonstrated to be effective in patients with allergic runny nose (rhinitis), allergic watery and red eyes (conjunctivitis), or extreme skin irritation to wasp stings. In some individuals, allergy immunotherapy may be effective in allergic asthma as well. Subcutaneous immunotherapy (SCIT) is the current standard of care and is the most common and effective route for administration of allergy immunotherapy. Sublingual immunotherapy (SLIT), generally performed as sublingual-swallow, has been suggested as an alternative route for administration of immunotherapy. Sublingual immunotherapy involves administration of antigen drops under the

tongue. The antigen drops are administered in gradually increasing doses in an effort to build up individual tolerance to the allergy-causing substance.

A reaction to allergy immunotherapy treatment can occur within the first 30 minutes following an injection, or it may be delayed for up to 12-24 hours. Most reactions are local, such as itching, pain and swelling when therapy is administered via injection. Occasionally, more severe reactions (such as hives or shock) may occur. The most severe reactions usually occur within the first 30 minutes after an injection; any reactions occurring after that time are generally mild. To monitor for these effects, treatment is given in a medical office. Environmental interventions, such as avoidance of allergens, and medications may be used in conjunction with allergy immunotherapy.

Definitions

Autogenous immunization therapy: a medical technique that involves the injection of a person's own sterilized urine for the purpose of treating allergies

Ecology units: a special section of a hospital or medical facility that is designed for the treatment of chemical sensitivity; these units are designed to minimize the presence of various chemicals in the environment

Enzyme potentiated desensitization (EPD): the combination of injections with an enzyme to improve the response to medical treatment for allergies

Multiple chemical avoidance: a treatment method that involves avoiding substances that cause allergic reactions

Photoinactivated extracts: a man-made form of any substance that causes allergic reactions, where the substance has been altered using strong light; the purpose of this light exposure is to decrease the substance's ability to cause an allergic reaction while maintaining its ability to build an immune resistance to it

Polymerized extracts: a man-made form of any substance that causes allergic reactions, where the individual molecules of the substance have been linked into a long chain; the purpose of this linking is to decrease the substance's ability to cause an allergic reaction while maintaining its ability to build an immune resistance to it

Provocative and neutralization therapy: a medical therapy that involves the injection under the skin of substances 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

Repository emulsion therapy: a form of therapy where certain materials are placed inside the body to improve allergies

Rotational diets: a type of diet that involves eating only limited foods or types of foods for a certain period of time on a cyclical basis to help identify foods that may cause allergic responses

Toxicodendron (Rhus) dermatitis: a form of allergic reaction caused by contact with a specific irritant from a plant, most commonly poison ivy, poison sumac, or poison oak

Coding

The following codes for treatments and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage or these services as it applies to an individual member.

When services are Medically Necessary:

CPT

95130-95134	Professional services for allergen immunotherapy in prescribing physician's office or institution, including provision of allergenic extract; stinging insect venom(s)
95145-95149	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy; stinging insect venom(s)
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

ICD-9 Diagnosis

All applicable diagnoses

When services are also Medically Necessary:

CPT

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; two or more injections
95120	Professional services for allergen immunotherapy in prescribing physician's office or institution, including provision of allergenic extract; single injection
95125	Professional services for allergen immunotherapy in prescribing physician's office or institution, including provision of allergenic extract; two or more injections
95144	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy, single dose vial(s)
95165	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy; single or multiple antigens

ICD-9 Procedure

99.12	Immunization for allergy; desensitization
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ICD-9 Diagnosis

All applicable diagnoses not listed as investigational

When Services are Investigational/Not Medically Necessary:

For the procedure codes listed above with the following diagnosis codes, or when the code describes a procedure indicated in the Policy section as Investigational/Not Medically Necessary

ICD-9 Diagnosis

477.1	Allergic rhinitis, due to food
693.1	Dermatitis, due to food
V15.01-V15.05	Allergy, other than to medicinal agents (peanuts, milk, eggs, seafood, other foods)

When services are also Investigational/Not Medically Necessary:

CPT

97780	Acupuncture, one or more needles, without electrical stimulation (deleted 01/01/2005)
97781	Acupuncture, one or more needles, with electrical stimulation (deleted 01/01/2005)
97810-97814	Acupuncture

ICD-9 Procedure

99.92	Other acupuncture
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ICD-9 Diagnosis

477.0-477.9	Allergic rhinitis
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692.0-692.9	Contact dermatitis and other eczema
693.0-693.9	Dermatitis due to substances taken internally
V14.0-V14.9	Personal history of allergy to medicinal agents
V15.01-V15.09	Personal history of allergy, other than to medicinal agents

References

Peer Reviewed Publications:

1. Akdis CA, Blaser K. Immunologic mechanisms of allergen-specific immunotherapy. *Adv Exp Med Biol.* 2001; 495:247-59.
2. ARIA Workshop Group. Allergic rhinitis and its impact on asthma. *Journal of Allergy and Clinical Immunology.* Nov 2001; 108(5): S220-S255.
3. Bousquet J, et al. Sublingual-swallow immunotherapy (SLIT) in patients with asthma due to housedust mites: a double-blind, placebo-controlled study. *Allergy.* 1999; 54(3): 249-260.
4. Broide D, Malling HJ. Immunologic treatment of allergic diseases. *Curr Opin Allergy Clin Immunol.* 2001;1(6):541-3.
5. Canonica G, Passalacqua G. Non-injection routes for immunotherapy. *Journal of Allergy and Clinical Immunology.* 2003 March; 111(3).
6. Casale TBB. Status of immunotherapy: current and future. *Journal of Allergy and Clinical Immunotherapy.* 2004 June; 113(6):1036-9.
7. Esch RE, Portnoy J. Allergen immunotherapy. *Curr Allergy Asthma Rep.* 2001; 1(6):491-7.
8. Frew AJ, Smith HE. Sublingual immunotherapy. *Journal of Allergy and Clinical Immunology.* March 2001; 107(3): 441-444.
9. Frew AJ. Assessment and modulation of the immune response. *Journal of Allergy and Clinical Immunology.* 2003 Feb; 111(2).
10. Kagi MK, Wuthrich B. Different methods of local allergen-specific immunotherapy. *Allergy.* 2002; 57(5):379-88.
11. Li JT, Lockley RF, Bernstein IL, et al. Allergen immunotherapy: a practice parameter. *American Academy of Allergy, Asthma and Immunotherapy. American College of Allergy, Asthma and Immunology. Ann Allergy Asthma Immunol.* 2003; 90(Suppl 1):1-40.
12. Li XM, Sampson HA. Novel approaches for the treatment of food allergy. *Curr Opin Allergy Clin Immunol.* 2002; 2(3):273-8.
13. Lima MT, Wilson D, Pitkin L, et al. Grass pollen sublingual immunotherapy for seasonal rhinoconjunctivitis: a randomized controlled trial. *Clin Exp Allergy.* 2002; 32(4):507-14.
14. Lockey RF. ARIA: Global policies and new forms of allergen immunotherapy. *Journal of Allergy and Clinical Immunology.* 2001; 108(4):497-499.
15. Lombardi C, Gargioni S, Melchiorre A, et al. Safety of sublingual immunotherapy with monomeric allergoid in adults: multicenter post-marketing surveillance study. *Allergy.* 2001; 56(10):989-92.
16. Malling HJ. Allergen-specific immunotherapy in allergic rhinitis. *Curr Opin Allergy Clin Immunol.* 2001 1(1):43-6.
17. Mungan D, Misirligil Z, and Gurbuz L. Comparison of the efficacy of subcutaneous and sublingual immunotherapy in mite-sensitive patients with rhinitis and asthma - a placebo controlled study. *Annals of Allergy, Asthma and Immunology.* May 1999; 82(5): 485-490.
18. Nelson HS. Advances in upper airway diseases and allergen immunotherapy. *Journal of Allergy and Clinical Immunotherapy.* April 2004; 113(4): 635-42.
19. Passalacqua G, Lombardi C, Canonica GW. Sublingual immunotherapy: an update. *Curr Opin Allergy Clin Immunol.* 2004; 4(1):31-6.
20. Patriarca G, Nucera E, Pollastrini E, et al. Sublingual desensitization: a new approach to latex allergy problem. *Anesth Analg.* 2002; 95(4):956-60.
21. Pawankar R, Fokkens W. Evidence-based treatment of allergic rhinitis. *Curr Allergy Asthma Rep.* 2001; 1(3):218-26.
22. Rakoski J, Wessner D. A short assessment of sublingual immunotherapy. *Int Arch Allergy Immunol.* 2001; 126(3):185-7.

Government Agency, Medical Society, and Other Authoritative Publications:

1. American College of Physicians. *Clinical Ecology.* *Ann Intern Med* 1989; 111(2):168-78.

2. Blue Cross Blue Shield Assoc. Sublingual immunotherapy for allergies. Technology Evaluation Center. Volume 18, No 4 June 2003.
3. Diagnosis and management of rhinitis. Ann Allergy Asthma Immunol. 1998 Nov; 81(5 Pt 2):478-518.

Web Sites for Additional Information

1. American Academy of Allergy, Asthma, and Immunology (AAAAI) Board of Directors. Idiopathic Environmental Intolerances Position Statement. Available at: http://www.aaaai.org/media/resources/academy_statements/position_statements/ps35.asp. Accessed: January 10, 2006.
2. American Academy of Asthma, Allergy and Immunology (AAAAI). Available at <http://www.aaaai.org/patients/publicedmat/tips/whatareallergyshots.stm> Accessed January 10, 2006.
3. American College of Occupational and Environmental Medicine. (ACOEM) Position Statement on Multiple chemical sensitivities: idiopathic environmental intolerance available at: <http://www.acoem.org/policys/article.asp?ID=46J>. Accessed: January 10, 2006.
4. National Institute of Allergy and Infectious Diseases. Available at: www.niaid.nih.gov January 10, 2006.

Index

- Allergy Immunotherapy
- Desensitization
- Neutralization Therapy
- Provocative Therapy
- Repository Emulsion Therapy
- Rinkel Method of Allergy Immunotherapy
- Sublingual
- Urine, Autoinjection

Policy History

Status	Date	Action	
Reviewed	03/23/2006	Medical Policy & Technology Assessment Committee (MPTAC) review.	
Revised	04/28/2005	MPTAC review. Revision based on Policy Harmonization: Pre-merger Anthem and Pre-merger WellPoint. Updated coding; Noted deleted CPT codes 97780 and 97781 (effective 01/01/2005); added new CPT code range 97810-97814 (effective 01/01/2005)	
Pre-Merger Organizations	Last Review Date	Policy Number	Title
Anthem, Inc.	03/21/2003	MED.00001	Allergy Immunotherapy
WellPoint Health Networks, Inc.	12/02/2004	8.12.02	Sublingual and Oral Immunotherapy
	12/02/2004	2.01.20	Diagnosis and Management of Idiopathic Environmental Intolerance (Clinical Ecology)

Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member's contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

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