BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Allergy Immunotherapy

Policy #: 081
Latest Review Date: March 2024
Category: Medical

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*

    - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
    - *Furnished in a setting appropriate to the patient's medical needs and condition;*
    - *Ordered and furnished by qualified personnel;*
    - *One that meets, but does not exceed, the patient's medical need; and*
    - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

Effective for dates of service on and after May 16, 2024:

Allergy Immunotherapy

Blue Advantage will treat **allergy immunotherapy** as a **covered benefit** for individuals with demonstrated hypersensitivity that cannot be managed by medications or avoidance when delivered based on ALL of the following guidelines:

- Maximum of 180 units for the first year of therapy during escalation, and
- Maximum of 120 units for yearly maintenance therapy thereafter, and
- Per unit reimbursement for allergy immunotherapy is based on the number of dosages prepared and intended for administration.

Blue Advantage will treat **the following treatments for allergies** as **non-covered benefits**:

- Provocative and neutralization therapy for food allergies, using oral, intradermal and subcutaneous routes.
- Urine auto-injections.
- Repository emulsion therapy.
- Tolerance Induction Program™ (TIP).

As of August 1, 2014, Sublingual Immunotherapy (SLIT), including FDA-approved tablets (Oralair®, Grastek® and Ragwitek®), is considered a prescription benefit, and coverage is dependent on the member's formulary and benefit plan design.

Non-FDA-approved SLIT therapy which is typically prepared and billed by an allergist is considered non-covered under the medical benefit.

Aspirin Desensitization

Blue Advantage will treat **aspirin (ASA) desensitization** as a **covered benefit** for individuals with aspirin-exacerbated respiratory disease (AERD) when one of the following criteria is met:

- Asthma or rhinosinusitis which is suboptimally controlled with inhaled corticosteroids and leukotriene-modifying drugs, OR
- Individuals who have required multiple polypectomies for nasal polyp control, OR
- Individuals who require anti-platelet therapy with cyclo-oxygenase-Y inhibitors.

The testing must be done in a hospital or physician's office with direct supervision by an eligible provider. The desensitization procedure should be followed by daily aspirin therapy.

Effective for dates of service prior to May 16, 2024

Allergy Immunotherapy

Blue Advantage will treat **allergy immunotherapy** as a **covered benefit** for individuals with demonstrated hypersensitivity that cannot be managed by medications or avoidance when delivered based on ALL of the following guidelines:

- Maximum of 180 units for the first year of therapy during escalation, and

- Maximum of 120 units for yearly maintenance therapy thereafter, and
- Per unit reimbursement for allergy immunotherapy is based on the number of dosages prepared and intended for administration.

Blue Advantage will treat **the following treatments for allergies** as **non-covered benefits**:

- Provocative and neutralization therapy for food allergies, using intradermal and subcutaneous routes.
- Urine auto-injections.
- Repository emulsion therapy.

As of August 1, 2014, Sublingual Immunotherapy (SLIT), including FDA approved tablets (Oralair®, Grastek® and Ragwitek®), is considered a prescription benefit and coverage is dependent on member's formulary and benefit plan design.

Non-FDA-approved SLIT therapy which is typically prepared and billed by an allergist is considered non-covered under the medical benefit.

Aspirin Desensitization

Blue Advantage will treat a**spirin (ASA) desensitization** as a **covered benefit** for individuals with aspirin-exacerbated respiratory disease (AERD) when one of the following criteria is met:

- Asthma or rhinosinusitis which is suboptimally controlled with inhaled corticosteroids and leukotriene-modifying drugs, OR
- Individuals who have required multiple polypectomies for nasal polyp control, OR
- Individuals who require anti-platelet therapy with cyclo-oxygenase-Y inhibitors.

The testing must be done in a hospital or physician's office with direct supervision by an eligible provider. The desensitization procedure should be followed by daily aspirin therapy.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

Allergy immunotherapy (a.k.a., desensitization, allergy injection therapy, or "allergy shots"), is an effective treatment for allergic rhinitis, allergic asthma, atopic dermatitis and Hymenoptera sensitivity. Immunotherapy is indicated in patients whose triggering allergens have been determined by appropriate skin or in vitro testing. The goal is to reduce the allergy patient's sensitivity when exposed to the offending allergen in the future. Treatment begins with low doses to prevent severe reactions. Gradually the doses are increased and are given once or twice a week until the body becomes tolerant of the allergen. After the maintenance dose is achieved, the interval between injections may range between two and six weeks. Immunotherapy may be administered continuously for several years.

Rush immunotherapy (allergy shots) is a treatment that includes a fast increase in concentration and allergen extract doses. It was started to reduce hospital visits and the required hospital stay. This treatment delivers doses varying between 15 to 60 minutes over 1-3 days until the target therapeutic dose is achieved. Very sensitive individuals may experience various degrees of systemic reaction during this procedure. Therefore, physicians who use this method frequently pre-medicate individuals with both antihistamines and corticosteroids to minimize the risk of a systemic reaction. These forms of immunotherapy allow for faster advancement to maintenance.

The Joint Council of Allergy, Asthma and Immunology state that rush immunotherapy and cluster immunotherapy are forms of allergen immunotherapy in which incremental doses of allergen are administered at varying intervals, until the optimal effective dose is achieved. Cluster immunotherapy is an accelerated build-up schedule that entails administering several injections at increasing doses (generally 2-3 per visit) sequentially in a single day of treatment on non-consecutive days. The maintenance dose is generally achieved more rapidly than with a conventional (single injection per visit) build-up schedule (generally within 4-8 weeks).

Provocative and Neutralization Therapy

This procedure is purported to diagnose allergy to foods, chemicals, inhalant allergens, and endogenous hormones. Varying concentrations of test extracts of these substances are given to the patient by intracutaneous or subcutaneous injection or sublingually. The patient records all subjective sensations for 10 minutes afterward, and any reported sensation is taken as a positive test result for allergy. In the event of a positive test result, other doses of the same substance are given until the sensation has disappeared, at which point the action is said to be “neutralized.” Some proponents recommend measuring increase in the size of the injected wheal in the intracutaneous provocation procedure, but the primary indication of a positive result is the provocation and neutralization of symptoms.

Oral Immunotherapy (OIT) is an allergen-specific approach to the treatment of food allergy. Doctors prescribe and supervise a regimen of allergenic food, gradually increasing the dosage each day. This type of therapy will desensitize the food to the point where accidental ingestion of the allergenic food in a social setting would not cause anaphylaxis, and possibly intentionally eaten food can be added safely to a regular diet.

KEY POINTS:

The most recent literature review for this policy was performed March 27, 2024.

Summary of Evidence

For provocative and neutralization therapy for food allergies, urine auto-injections, and repository emulsion therapy, the evidence includes studies, and randomized controlled trials. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Oral immunotherapy for food is a major focus of investigation in the treatment of food allergy. However, studies have yet to demonstrate the ability to cure food allergy (and induce true tolerance). Furthermore, allergic reactions to OIT are common and occur at higher rates in patients on OIT than those avoiding the food. Many unanswered questions remain, and additional long-term follow-up data are needed to help determine in which patients the benefits may outweigh the risks.

Practice Guidelines and Position Statements

In 2013, the American Academy of Allergy, Asthma and Immunology and the European Academy of Allergy and Clinical Immunology published a consensus report on allergy immunotherapy. The report summarized the literature and current practices in the U.S. and Europe; it did not include clinical recommendations. The authors concluded, "AIT (allergy immunotherapy) is effective in reducing symptoms of allergic asthma and rhinitis, as well as venom-induced anaphylaxis. In addition, AIT modifies the underlying course of disease. However, AIT remains a niche treatment secondary to symptomatic drugs because of its cost, long duration of treatment and concerns regarding safety and effectiveness…"

In 2011, a joint task force of the American Academy of Allergy, Asthma and Immunology, the American College of Allergy, Asthma and Immunology, and the Joint Council of Allergy, Asthma and Immunology issued updated practice parameters for allergen immunotherapy. The document stated that RCTs of SLIT for individuals with allergic rhinitis and asthma have demonstrated significant improvement in symptoms. The authors note that there are no FDA-approved extract formulations for a non-injection route of immunotherapy.

U.S Preventive Services Task Force Recommendations

Not applicable.

KEY WORDS:

Allergy immunotherapy, IgE antibodies, allergen, antigen, immunotherapy, Rush immunotherapy, Rush schedules, sublingual immunotherapy, SLIT, acetylsalicylic acid (ASA), aspirin, asthma, desensitization, aspirin desensitization treatment, asthma-exacerbated respiratory disease (AERD), Allervision, cluster immunotherapy, Tolerance Induction Program, TIP, food allergy, oral immunotherapy, OIT

APPROVED BY GOVERNING BODIES:
Not applicable.

BENEFIT APPLICATION:
Coverage is subject to member's specific benefits. Group-specific policy will supersede this policy when applicable.

CURRENT CODING:
CPT 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
95120	Professional services for allergen immunotherapy in the office of the prescribing physician or other qualified health care professional, including provision of allergenic extract; single injection
95125	Professional services for allergen immunotherapy in the office or institution of the prescribing physician or other qualified health care professional, including provision of allergenic extract; 2 or more injections
95130	Professional services for allergen immunotherapy in the office or institution of the prescribing physician or other qualified health care professional, including provision of allergenic extract; single stinging insect venom
95131	Professional services for allergen immunotherapy in the office or institution of the prescribing physician or other qualified health care professional, including provision of allergenic extract; 2 stinging insect venoms
95132	Professional services for allergen immunotherapy in the office or institution of the prescribing physician or other qualified health care professional, including provision of allergenic extract; 3 stinging insect venoms
95133	Professional services for allergen immunotherapy in the office or institution of the prescribing physician or other qualified health care professional, including provision of allergenic extract; 4 stinging insect venoms

95134	Professional services for allergen immunotherapy in the office or institution of the prescribing physician or other qualified health care professional, including provision of allergenic extract; 5 stinging insect venoms
95144	Professional services for the supervision of preparation of antigens for allergen immunotherapy, single does vials (specify number of vials)
95145	Professional services for the supervision and provision of antigens for allergen immunotherapy (specify the 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)
95199	Unlisted allergy/clinical immunologic service or procedure

REFERENCES:

1. American Academy of Allergy Asthma Immunology, American College of Allergy Asthma Immunology, Joint Council of Allergy Asthma Immunology. Allergen immunotherapy: a practice parameter third update. 2011. Available online at: www.guideline.gov.
2. Bahceciler NN, Galip N. Comparing subcutaneous and sublingual immunotherapy: what do we know? Curr Opin Allergy Clin Immunol 2012; 12(6):640-7.

3. Berges-Gimeno MP, et al. Long-term treatment with aspirin desensitization in asthmatic patients with aspirin-exacerbated respiratory disease. Journal of Allergy and Immunology, January 2003, Vol. 111, No. 1.
4. Bernstein IL, Li JT, Bernstein DI, et al. Allergy diagnostic testing: an updated practice parameter. Annals of Allergy, Asthma and Immunology, March 2008, Vol, 100.
5. Bikhazi NB. Contemporary management of nasal polyps. Otolaryngologic Clinics of North America, April 2004, Vol. 37, No. 2.
6. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Sublingual immunotherapy for allergies. TEC Assessments 2003; Volume 18, Tab 4.
7. Burks AW, Calderon MA, Casale T et al. Update on allergy immunotherapy: American Academy of Allergy, Asthma & Immunology/European Academy of Allergy and Clinical Immunology/PRACTALL consensus report. J Allergy Clin Immunol, May 2013; 131(5):1288-96.
8. Calamita Z, Saconato H, Pela AB and Atallah AN. Efficacy of sublingual immunotherapy in asthma: Systematic review of randomized-clinical trials using the Cochrane Collaboration method. Allergy, October 2006; 61(10): 1162-1172.
9. Calderon MA, Penagos M, Sheikh A et al. Sublingual immunotherapy for treating allergic conjunctivitis. Cochrane Database Syst Rev 2011; (7):CD007685.
10. Compalati E, Penagos M, Tarantini F et al. Specific immunotherapy for respiratory allergy: state of the art according to current meta-analyses. Ann Allergy Asthma Immunol 2009; 102(1-Jan):22-8.
11. Covar RA, et al. Medications as asthma triggers. Immunology and Allergy Clinics of North America, February 2005, Vol. 25, No. 1.
12. Cox L, et al. Allergen immunotherapy: A practice parameter third update. Journal of Allergy and Clinical Immunology 2011; 127(1):S1-S55.
13. Cox LS, Linnemann DL, Nolte H, et al. Sublingual immunotherapy: a comprehensive review. J Allergy Clin Immunol, May 2006; 117(5): 1021-1035.
14. De Bot C. M., Moed H, Berger MY et al. Sublingual immunotherapy in children with allergic rhinitis: quality of systematic reviews. Pediatr Allergy Immunol 2011; 22(6):548-58.
15. Di Bona D, Plaia A, Scafidi V et al. Efficacy of sublingual immunotherapy with grass allergens for seasonal allergic rhinitis: a systematic review and meta-analysis. J Allergy Clin Immunol 2010; 126(3) 558-66.
16. Dretzke J, Meadows A, Novielli N et al. Subcutaneous and sublingual immunotherapy for seasonal allergic rhinitis: A systematic review and indirect comparison. J Allergy Clin Immunol. May 2013; 131(5):1361-6.
17. Durham SR, Yang WH, et al. Sublingual immunotherapy with once-daily grass allergen tablets: a randomized controlled trial in seasonal allergic rhinoconjunctivitis. J Allergy Clin Immunol, April 2006; 117(4): 802-809.
18. Dykewicz MS, Fineman S, Skoner DP. Joint Task Force summary statements on Diagnosis and Management of Rhinitis. Ann Allergy Asthma Immunol. 1998 Nov;81(5 Pt 2):474-477.
19. Eifan AO, Akkoc T, Yildiz A et al. Clinical efficacy and immunological mechanisms of sublingual and subcutaneous immunotherapy in asthmatic/rhinitis children sensitized to

house dust mite: an open randomized controlled trial. Clin Exp Allergy 2010; 40(6):922-32.
20. Feuille E, Nowak-Wegrzyn A. Allergen-Specific Immunotherapies for Food Allergy. Allergy Asthma Immunol Res 2018; 10:189.
21. Food Allergy Institute. Tolerance Induction Program (TIP)™Guide. 2024. foodallergyinstitute.com/resources/tip-program-guide/.
22. Food Allergy Resource Alliance. Are There Any Treatment Options? 2022. www.foodallergyresourcealliance.com/treatment-options.
23. Fritzsching, B., Contoli, M., Porsbjerg, C., Buchs, S., Larsen, J. R., Elliott, L., Rodriguez, M. R., & Freemantle, N. (2021). Long-term real-world effectiveness of allergy immunotherapy in patients with allergic rhinitis and asthma: Results from the REACT study, a retrospective cohort study. The Lancet regional health. Europe, 13, 100275.
24. Greenhawt M, et al. Sublingual immunotherapy: a focused allergen immunotherapy practice parameter updaate. Annuals of Allergy, Asthma, & Immunology. 2017:118:276-282.
25. IOM (Institute of Medicine). 2011. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press.
26. Joint Task Force on Practice Parameters, American Academy of Allergy, Asthma and Immunology, American College of Allergy, Asthma and Immunology, Joint Council of Allergy, Asthma and Immunology. Allergen immunotherapy: a practice parameter second update. J Allergy Clin Immunol 2007; 120(3 Suppl):S25-85.
27. Keles S, Karokov-Aydiner E, Ozen A et al. A novel approach in allergen-specific immunotherapy: combination of sublingual and subcutaneous routes. J Allergy Clin Immunol 2011; 128(4):808-15.
28. Lee JH, Choi JH, Jeong KB, Lee SJ, Lee MK, Lee WY, Yong SJ, Kim SH. Safety and Utility of Rush Immunotherapy with Aqueous Allergen Extracts for Treatment of Respiratory Allergies. J Korean Med Sci. 2021 Jan 18;36(3):e18.
29. Li JT, Lockey RF, et al. Allergen immunotherapy: a practice parameter. Annals of Allergy, Asthma, & Immunology. January 2003, Vol. 90.
30. Lin SY, Erekosima N, Kim JM et al. Sublingual immunotherapy for the treatment of allergic rhinoconjunctivitis and asthma: a systematic review. JAMA 2013; 309(12):1278-88.
31. Lin SY, Erekosima N, Suarez-Cuervo C et al. Allergen-specific immunotherapy for the treatment of allergic rhinoconjunctivitis and/or asthma: comparative effectiveness review No. 111. (Prepared by the Johns Hopkins University Evidence-based Practice Center under Contract No. 290-2007-10061-I.) AHRQ Publication No. 13-EHC061-EF. 2013. Available online at: www.effectivehealthcare.ahrq.gov/reports/final.cfm.
32. Macy E, Bernstein JA, Castells MC, et al. Aspirin challenge and desensitization for aspirin-exacerbated respiratory disease: a practice paper. Annals of Allergy, Asthma and Immunology, February 2007, Vol. 98, pp. 172-174.
33. Mauro M, Russello M, et al. Comparison of efficacy, safety and immunologic effects of subcutaneous and sublingual immunotherapy in birch pollinosis: A randomized study. Allerg Immunol 2007; 39(4): 119-122.

34. Penagos M, Passalacqua G, Compalati E, et al. Metaanalysis of the efficacy of sublingual immunotherapy in the treatment of allergic asthma in pediatric patients, 3 to 18 years of age. Chest, March 2008; 133(3): 599-609.
35. Pipet A, Botturi K, Pinot D et al. Allergen-specific immunotherapy in allergic rhinitis and asthma: mechanisms and proof of efficacy. Respir Med 2009; 103(6):800-12.
36. Radulovic S, Wilson D, Calderon M et al. Systematic reviews of sublingual immunotherapy (SLIT). Allergy 2011; 66(6):740-52.
37. Shaker M, Lobb A, Jenkins P, et al. An economic analysis of aspirin desensitization in aspirin-exacerbated respiratory disease. J Allergy Clin Immunol. January 2008Vol. 121, No. 1, pp. 81-86.
38. Sieber J, Shah-Hosseini K, Mosges R. Specific immunotherapy for allergic rhinitis to grass and tree pollens in daily medical practice- symptom load with sublingual immunotherapy compared to subcutaneous immunotherapy. Ann Med 2011; 43(6):418-24.
39. Slavin RG, et al. The diagnosis and management of sinusitis: a practice parameter update. Journal of Allergy and Clinical Immunology. December 2005, Vol. 116, No. 6 (Suppl).
40. Stevenson DD, et al. Aspirin desensitization treatment of aspirin-sensitive patients with rhinosinusitis-asthma: long-term outcomes. Journal of Allergy and Clinical Immunology. October 1996, Vol. 98, No. 4.
41. Stevenson DD. Aspirin and NSAID sensitivity. Immunology and Allergy Clinics of North America, August 2004, Vol. 24, No. 3.
42. Szczeklik A, Stevenson DD, et al. Aspirin-induced asthma: advances in pathogenesis, diagnosis, and management. Journal of Allergy and Clinical Immunology. 2003 May;111(5):913-921.
43. Vickery BP, Burks AW. Immunotherapy in the treatment of food allergy: focus on oral tolerance. Curr Opin Allergy Clin Immunol 2009; 9:364.
44. Wise SK, Schlosser RJ. Evidence-based practice: sublingual immunotherapy for allergic rhinitis. Otolaryngol Clin North Am 2012; 45(5):1045-54.
45. Yepes-Nuñez J, et al. Allergen immunotherapy for atopic dermatitis: Systematic review and meta-analysis of benefits and harms. J Allergy Clin Immunol. 2023 Jan;15(1):147-158.
46. Yukselen A, Kendirli SG, Yilmaz MEoo-ys et al. Int Arch Allergy Immunol 2011; 157(3-Jan):288-98.
47. Zacharek MA, et al. The office management of recalcitrant rhinosinusitis. Otolaryngologic Clinics of North America, April 2004, Vol. 37, No. 2.

POLICY HISTORY:

Adopted for Blue Advantage, March 2009
Available for comment March 17-April 30, 2009
Medical Policy Group, April 2010
Medical Policy Group, March 2011
Medical Policy Group, March 2012
Medical Policy Group, December 2012
Medical Policy Group, November 2013

Medical Policy Group, August 2014
Available for comment July 29 through September 11, 2014
Medical Policy Group, June 2015
Medical Policy Group. October 2016
Available for comment October 19 through December 2, 2016
Medical Policy Group, March 2017
Medical Policy Group, October 2020
Medical Policy Group, November 2020
Medical Policy Group, January 2022
Medical Policy Group, January 2023
UM Committee, December 2023: Policy approved by UM Committee for use for Blue Advantage business.
Medical Policy Group, February 2024: Reviewed by consensus. No new published peer-reviewed literature is available that would alter the coverage statement in this policy update.
Medical Policy Group, March 2024: Available for comment April 5, 2024, through May 15, 2024. Policy statement updated to include oral provocative and neutralization therapy and tolerance induction program for food allergies as non-covered benefits.
UM Committee, April 2024: Policy annual review updates approved by UM Committee

---