

# Immunotherapy, Subcutaneous

ACG: A-0429 (AC)

[Link to Codes](#)

- Clinical Indications for Procedure
- Alternatives to Procedure
- Evidence Summary
  - Background
  - Criteria
  - Inconclusive or Non-Supportive Evidence
- References
- Footnotes
- Codes

## Clinical Indications for Procedure

- Subcutaneous immunotherapy may be indicated for **1 or more** of the following<sup>[A]</sup>(1)(2)(3)(4)(5):
  - Allergic rhinitis or conjunctivitis and **ALL** of the following(23)(24)(25)(26)(27)(28):<sup>N</sup>
    - Age 2 years or older<sup>[B]</sup>(3)(31)
    - Initial or subsequent course of treatment, as indicated by **1 or more** of the following:
      - Initial course of treatment,<sup>[C]</sup> as indicated by **ALL** of the following:
        - Clinically complex allergic rhinitis, as indicated by **1 or more** of the following(19)(23)(26)(32)(33)(34):
          - Asthma exacerbations associated with allergic rhinitis(35)(36)
          - History of 2 or more seasons of allergy symptoms
          - Perennial allergy symptoms
        - Inadequate response to standard medical management interventions, including **ALL** of the following(19)(23)(26)(32)(33)(34):
          - Intranasal or oral antihistamine
          - Intranasal corticosteroid
        - Patient not pregnant at time of initiation of immunotherapy(37)
        - Positive skin test or quantitative allergen-specific IgE antibody assay to agents suspected as allergic triggers
        - Strong correlation between symptoms and suspected allergic triggers to **1 or more** of the following:
          - Animal allergens
          - Cockroaches
          - Dust mites
          - Grasses
          - Molds
          - Pollens
          - Trees
      - Subsequent course of treatment<sup>[D]</sup> is indicated if there has been favorable response to prior administration, as indicated by **1 or more** of the following(39):
        - Decrease in amount of medication required to control symptoms
        - Improvement in clinical symptom scores
    - No concomitant administration of beta-blockers(31)
    - No current significant cardiovascular disease (eg, recent myocardial infarction, unstable angina, significant arrhythmia) or compromised pulmonary function (eg, asthma exacerbation or poorly controlled chronic obstructive pulmonary disease)
  - Asthma and **ALL** of the following(41)(42)(43):<sup>N</sup>
    - Age 2 years or older<sup>[B]</sup>(3)(31)
    - Initial or subsequent course of treatment, as indicated by **1 or more** of the following:
      - Initial course of treatment,<sup>[C]</sup> as indicated by **ALL** of the following:
        - FEV<sub>1</sub> 70% or more of predicted(49)(50)
        - Inadequate response to standard medical management interventions, including **ALL** of the following(26)(42)(43)(51):
          - Avoidance of exposure to allergen triggers and irritants (eg, tobacco smoke)

- Controller medication (eg, inhaled corticosteroids, leukotrienes, long-acting beta-agonist with corticosteroid, tiotropium)
      - Rescue medication(52)
    - Patient not pregnant at time of initiation of immunotherapy(37)
    - Positive skin test or quantitative allergen-specific IgE antibody assay to agents suspected as allergic trigger
    - Strong correlation between symptoms and suspected allergic triggers to **1 or more** of the following:
      - Animal allergens
      - Cockroaches
      - Dust mites(47)(53)
      - Grasses
      - Molds
      - Pollens
      - Trees
  - Subsequent course of treatment[D] is indicated if there has been favorable response to prior administration, as indicated by **1 or more** of the following:
    - Decrease in amount of medication required to control symptoms and maintain peak flow rates or other measures of pulmonary function
    - Improvement in clinical symptom scores
  - No concomitant administration of beta-blockers(1)(31)
  - No current significant cardiovascular disease (eg, recent myocardial infarction, unstable angina, significant arrhythmia) or compromised pulmonary function (eg, asthma exacerbation or poorly controlled chronic obstructive pulmonary disease) (2)
- ☐ Stinging insect hypersensitivity and **ALL** of the following(54)(55)(56):<sup>[I]</sup>
- Age 2 years or older[B](3)(31)
  - Initial or subsequent course of treatment, as indicated by **1 or more** of the following:
    - Initial course of treatment,[E] as indicated by **ALL** of the following:
      - Appropriate diagnostic test results, as indicated by **1 or more** of the following:
        - Positive skin test
        - Positive venom-specific IgE antibody assay[F]
      - Patient not pregnant at time of initiation of immunotherapy(37)
      - Systemic reaction to sting, as indicated by **1 or more** of the following:
        - Patient older than 16 years and systemic reaction limited to cutaneous signs and symptoms (eg, urticaria, pruritus, flush)[G]
        - Patient with systemic reaction to sting that included respiratory symptoms, cardiovascular symptoms, or both
    - Subsequent course of treatment[H] is indicated if there has been favorable response to prior administration.
  - No current clinically significant cardiovascular disease (eg, recent myocardial infarction, unstable angina, significant arrhythmia) or compromised pulmonary function (eg, asthma exacerbation or poorly controlled chronic obstructive pulmonary disease)

---

## Alternatives to Procedure

- Alternatives include:
  - For allergic asthma: inhaled beta-adrenergic agonists, inhaled or oral corticosteroids, leukotriene receptor antagonists, tiotropium, theophylline, and omalizumab(42)(51)(60)
  - For allergic rhinitis: antihistamines, nasal cromolyn, and intranasal corticosteroids(23)(24)(61)
  - Sublingual immunotherapy. See Immunotherapy, Sublingual <sup>[J]</sup> AC for further information.

---

## Evidence Summary

### Background

Subcutaneous immunotherapy is a desensitization procedure that uses controlled exposure to known allergens to reduce the severity of subsequent allergic reactions associated with natural exposures to these allergens.(1)(5)(6) (**EG 2**) The most serious complication of subcutaneous immunotherapy is anaphylaxis; most serious systemic reactions occur within 30 minutes of injection.(1)(7)(8)(9) (**EG 2**) Epicutaneous immunotherapy, which utilizes a patch to apply allergens to the skin, is currently being investigated as an alternative to subcutaneous immunotherapy.(10) (**EG 1**)

### Criteria

For allergic rhinitis or conjunctivitis, evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** A systematic review of 61 randomized controlled trials (6379 patients) evaluating the efficacy of allergen immunotherapy for allergic rhinitis found high-quality evidence that subcutaneous immunotherapy is associated with improvements in symptom scores and rhinitis/rhinoconjunctivitis medication usage.(27) **(EG 1)** A systematic review and meta-analysis including 46 randomized controlled trials compared (via adjusted indirect comparison) the effectiveness of either subcutaneous or sublingual immunotherapy for the treatment of adults with pharmacotherapy refractory allergic rhinitis or rhinoconjunctivitis with or without asthma and found that both subcutaneous and sublingual immunotherapy were associated with improvements in symptom severity, allergy/asthma rescue medication usage, and quality of life (measured by the Rhinoconjunctivitis Quality of Life Questionnaire); no significant differences were found between the 2 immunotherapy modalities. The authors noted that the analysis was limited by the heterogeneity in reported outcome measures in the included studies and the lack of randomized controlled trials that directly compared subcutaneous to sublingual immunotherapy; future studies were recommended.(29) **(EG 1)** A specialty society guideline recommends allergen immunotherapy in pediatric patients with severe allergic rhinitis and grass or birch pollen allergy who are not adequately controlled with medical therapy as it may prevent the onset of asthma in the short term, in addition to improving allergic rhinitis symptoms and decreasing medication use. However, the guideline was unable to make a recommendation for or against the use of allergen immunotherapy for preventing asthma in the long term in patients with allergic rhinitis, for preventing asthma in adults with allergic rhinitis, or for patients with allergic rhinitis and allergy to allergens other than grass or birch pollen.(22) **(EG 2)** A specialty society guideline conditionally recommends subcutaneous allergen immunotherapy in patients with moderate to severe allergic rhinitis in whom the allergen trigger has been identified when symptoms are not controlled with allergen avoidance and pharmacotherapy or who prefer immunotherapy (eg, to avoid long-term use of pharmacotherapy), as well as in patients with coexisting controlled asthma and allergic rhinitis.(19) **(EG 2)**

For asthma, evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** A systematic review of allergen immunotherapy for asthma which included 54 double-blind randomized controlled trials (2305 patients) of subcutaneous immunotherapy for asthma reported that subcutaneous immunotherapy is associated with improvements in asthma symptom scores in the short term, asthma medication use, and disease-specific quality of life.(44) **(EG 1)** A systematic review of subcutaneous immunotherapy identified 38 randomized controlled trials addressing asthma (with and without concomitant rhinitis/rhinoconjunctivitis) and found high-grade evidence that immunotherapy reduces asthma symptoms and medication use.(41) **(EG 1)** A systematic review of immunotherapy for asthma evaluated data from 6 randomized controlled trials (404 patients) and reported that subcutaneous immunotherapy reduces the use of control medication over the long term; other randomized controlled trials provided lower-quality support for a beneficial impact on asthma-specific quality of life, rescue medication use, systemic corticosteroid use, and pulmonary function (ie, FEV<sub>1</sub>). (45) **(EG 1)** A systematic review of 25 studies (17 randomized controlled trials) of subcutaneous immunotherapy for allergic asthma in pediatric patients reported moderate-strength evidence that subcutaneous immunotherapy improves long-term inhaled corticosteroid use.(46) **(EG 1)** A specialty society guideline recommends house dust mite subcutaneous immunotherapy for children and adults with controlled house dust mite-driven allergic asthma in addition to standard therapy, but notes that the available evidence is limited by heterogeneity in immunotherapy products and a lack of studies evaluating reduced asthma exacerbations or improved asthma control as primary outcomes.(47) **(EG 2)** An expert consensus guideline recommends the use of subcutaneous immunotherapy as an adjunct to standard therapy for individuals 5 years and older with mild or moderate controlled allergic asthma.(43) **(EG 2)** A review article noted that severe or poorly controlled asthma is considered a contraindication for subcutaneous immunotherapy.(48) **(EG 2)**

For stinging insect hypersensitivity, evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** Venom immunotherapy is strongly recommended for patients who have had systemic reactions to Hymenoptera stings, especially when associated with respiratory or cardiovascular symptoms, accompanied by positive skin tests or evidence of specific IgE antibodies.(38) (55) **(EG 2)** An evidence-based specialty society guideline notes that patients 16 years or younger who present only with systemic cutaneous reactions without other manifestations to Hymenoptera or imported fire ants usually do not require venom immunotherapy. Some reports note that patients who have negative venom skin test results and negative venom-specific IgE test results have had subsequent systemic reactions to stinging insects. When patients experience a large local reaction, their risk of systemic reaction is 4% to 10%. In adults with systemic cutaneous reactions without other manifestations, venom immunotherapy is considered optional rather than mandatory, and may be especially helpful in those patients who face unavoidable exposure, have comorbid conditions that increase their risk, or have impaired quality of life as a result of their venom sensitivity.(54) **(EG 2)** Another evidence-based specialty society guideline notes that venom immunotherapy for adults with generalized cutaneous reactions leads to significant improvements in quality of life as compared with adults who rely on epinephrine administration in response to insect sting.(55) **(EG 2)** Regarding a subsequent course of venom immunotherapy treatment, long-term follow-up studies suggest that a 5-year course appears to be better than 3 years, especially in patients at high risk (eg, frequent exposure, honeybee allergy, severe anaphylaxis).(54) **(EG 2)** However, treatment may be appropriately continued indefinitely in patients with a history of extreme or near-fatal anaphylaxis to a sting, or with honeybee allergy.(54)(55)(57) **(EG 2)** A systematic review of randomized controlled trials concluded that venom immunotherapy is effective for the prevention of additional allergic reactions due to insect stings, with a small but significant risk of adverse systemic reaction.(58) **(EG 1)** A retrospective cohort study of 1532 patients who underwent sting challenge to evaluate the effectiveness of venom immunotherapy reported that predictors of treatment failure included allergy to honeybee venom, use of ACE inhibitor medication during sting challenge, high risk for systemic mastocytosis, and systemic allergic reactions during the buildup or maintenance phase of immunotherapy; chances of failure decreased with longer duration of immunotherapy.(59) **(EG 2)** However, the evidence evaluating the impact of ACE inhibitor medication is inconsistent, especially in patients who experience anaphylaxis and have comorbidities (eg, cardiovascular disease), as the benefits of venom immunotherapy may outweigh the risks.(54)(55) **(EG 2)**

## Inconclusive or Non-Supportive Evidence

For atopic dermatitis, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A systematic review and meta-analysis evaluating the efficacy of specific allergen immunotherapy for atopic eczema that identified 6 randomized controlled trials of subcutaneous immunotherapy concluded that immunotherapy could not be recommended for the treatment of atopic eczema due to the low quality of evidence; the authors recommended future large blinded randomized controlled trials to clarify the role of allergen immunotherapy for this disorder.(11) **(EG 1)** Although some studies indicate that immunotherapy can be effective for atopic dermatitis (eczema) when this condition is associated with aeroallergen sensitivity, the studies involve a small number of patients.(1)(12) **(EG 2)** A specialty society guideline recommends against the use of subcutaneous immunotherapy to treat atopic dermatitis.(13) **(EG 2)**

For chronic urticaria or angioedema, evidence demonstrates a lack of net benefit; additional research is recommended. **(RG C1)** Clinical studies do not support the use of allergen immunotherapy for chronic urticaria or angioedema.(1)(3) **(EG 2)**

For food allergy or hypersensitivity, evidence demonstrates a lack of net benefit; additional research is recommended. **(RG C1)** The primary treatments for food allergy include an avoidance diet as well as education about emergency measures to be taken in case of accidental food allergen ingestion.(14) **(EG 2)** Subcutaneous immunotherapy is contraindicated for food allergy due to the risk of anaphylaxis.(14)(15) **(EG 2)** A phase III randomized, double-blind, controlled trial of 356 children age 4 to 11 years with peanut allergy comparing an epicutaneous patch with 250 micrograms of peanut protein with placebo reported a statistically significant between-group difference in the proportion of patients who tolerated a double-blind placebo-controlled food challenge (35.3% vs 13.6%, respectively); however, the treatment effect was not considered clinically significant. The authors noted that the study excluded patients with a history of severe reactions (eg, anaphylaxis) to peanuts, which may have impacted the study results; further long-term studies are recommended.(16) **(EG 1)**

For latex allergy, evidence demonstrates a lack of net benefit; additional research is recommended. **(RG C1)** A review article identified only 3 randomized trials (64 patients) studying the use of subcutaneous immunotherapy for latex allergy, of which only one trial demonstrated improvement in symptoms; however, patients in all 3 trials experienced systemic reactions, with an incidence ranging from 47% to 82%. The authors noted that published guidelines do not support the use of subcutaneous immunotherapy for latex allergy.(17) **(EG 2)**

For local allergic rhinitis, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** Local allergic rhinitis is defined as chronic rhinitis associated with a positive nasal allergen provocation test and local nasal mucosa production of allergen-specific IgE without markers of systemic atopy (ie, negative skin prick test and negative serum allergen-specific IgE).(18)(19) **(EG 2)** A systematic review and meta-analysis including 4 randomized controlled trials (134 patients) evaluated the effectiveness of either subcutaneous immunotherapy or placebo for the treatment of local allergic rhinitis and found that subcutaneous immunotherapy was associated with a reduction in rescue medication use and improvements in allergic symptoms, quality of life (measured by the Rhinoconjunctivitis Quality of Life Questionnaire), and allergen tolerance compared to placebo. However, the authors noted that the analysis was limited by the small sample size and high variability in allergen dosing, treatment schedules, and scoring algorithms used in the included studies; larger, multi-centered, longer-term randomized controlled trials were recommended.(20) **(EG 1)**

For prevention of new allergen sensitization, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A systematic review assessing the efficacy of allergen immunotherapy in preventing the onset of new allergen sensitizations in patients with allergic rhinitis or asthma identified 12 studies (10,022 patients) that evaluated subcutaneous immunotherapy. Although there was low-quality evidence supporting allergen immunotherapy, the authors cautioned that the findings are limited by bias and that further randomized controlled studies with longer follow-up are needed.(21) **(EG 1)** A specialty society guideline was unable to make a recommendation for or against the use of allergen immunotherapy for preventing later allergic manifestations in children with atopic dermatitis and other early atopic manifestations.(22) **(EG 2)**

---

## References

1. Cox L, et al. Allergen immunotherapy: a practice parameter third update. *Journal of Allergy and Clinical Immunology* 2011;127(1 Suppl):S1-S55. DOI: 10.1016/j.jaci.2010.09.034. (Reaffirmed 2022 May) [ Context Link 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 ] View abstract...
2. Krishna MT, Huissoon AP. Clinical immunology review series: an approach to desensitization. *Clinical and Experimental Immunology* 2011;163(2):131-146. DOI: 10.1111/j.1365-2249.2010.04296.x. [ Context Link 1, 2, 3 ] View abstract...
3. Halken S, Lau S, Valovirta E. New visions in specific immunotherapy in children: an iPAC summary and future trends. *Pediatric Allergy and Immunology* 2008;19 Suppl 19:60-70. DOI: 10.1111/j.1399-3038.2008.00768.x. [ Context Link 1, 2, 3, 4, 5 ] View abstract...
4. Jutel M, et al. International consensus on allergy immunotherapy. *Journal of Allergy and Clinical Immunology* 2015;136(3):556-568. DOI: 10.1016/j.jaci.2015.04.047. [ Context Link 1, 2, 3 ] View abstract...
5. Roche AM, Wise SK. Subcutaneous immunotherapy. *International Forum of Allergy and Rhinology* 2014;4 Suppl 2:S51-S54. DOI: 10.1002/alr.21382. [ Context Link 1, 2 ] View abstract...
6. Lei DK, Saltoun C. Allergen immunotherapy: definition, indications, and reactions. *Allergy and Asthma Proceedings* 2019;40(6):369-371. DOI: 10.2500/aap.2019.40.4249. [ Context Link 1 ] View abstract...
7. Rodriguez Del Rio P, et al. The European Survey on Adverse Systemic Reactions in Allergen Immunotherapy (EASSI): A paediatric assessment. *Pediatric Allergy and Immunology* 2017;28(1):60-70. DOI: 10.1111/pai.12660. [ Context Link 1 ] View abstract...

8. Sanchez-Borges M, Bernstein DI, Calabria C. Subcutaneous immunotherapy safety: incidence per surveys and risk factors. *Immunology and Allergy Clinics of North America* 2020;40(1):25-39. DOI: 10.1016/j.iac.2019.09.001. [ Context Link 1 ] View abstract...
9. Bernstein DI, Epstein TEG. Safety of allergen immunotherapy in North America from 2008-2017: Lessons learned from the ACAAI/AAAAI National Surveillance Study of adverse reactions to allergen immunotherapy. *Allergy and Asthma Proceedings* 2020;41(2):108-111. DOI: 10.2500/aap.2020.41.200001. [ Context Link 1 ] View abstract...
10. Xiong L, Lin J, Luo Y, Chen W, Dai J. The efficacy and safety of epicutaneous immunotherapy for allergic diseases: a systematic review and meta-analysis. *International Archives of Allergy and Immunology* 2020;181(3):170-182. DOI: 10.1159/000504366. [ Context Link 1 ] View abstract...
11. Tam H, et al. Specific allergen immunotherapy for the treatment of atopic eczema. *Cochrane Database of Systematic Reviews* 2016, Issue 2. Art. No.: CD008774. DOI: 10.1002/14651858.CD008774.pub2. [ Context Link 1 ] View abstract...
12. Ridolo E, Martignago I, Riario-Sforza GG, Incorvaia C. Allergen immunotherapy in atopic dermatitis. *Expert Review of Clinical Immunology* 2018;14(1):61-68. DOI: 10.1080/1744666X.2018.1401469. [ Context Link 1 ] View abstract...
13. Sidbury R, et al. Guidelines of care for the management of atopic dermatitis: Section 4. Prevention of disease flares and use of adjunctive therapies and approaches. *Journal of the American Academy of Dermatology* 2014;71(6):1218-1233. DOI: 10.1016/j.jaad.2014.08.038. (Reaffirmed 2021 Jul) [ Context Link 1 ] View abstract...
14. Boyce JA, et al. Guidelines for the diagnosis and management of food allergy in the United States: summary of the NIAID-sponsored expert panel report. *Journal of Allergy and Clinical Immunology* 2010;126(6):1105-1118. DOI: 10.1016/j.jaci.2010.10.008. (Reaffirmed 2022 May) [ Context Link 1, 2 ] View abstract...
15. Muraro A, et al. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. *Allergy* 2014;69(8):1008-1025. DOI: 10.1111/all.12429. (Reaffirmed 2022 Jul) [ Context Link 1 ] View abstract...
16. Fleischer DM, et al. Effect of epicutaneous immunotherapy vs placebo on reaction to peanut protein ingestion among children with peanut allergy: the PEPITES randomized clinical trial. *Journal of the American Medical Association* 2019;321(10):946-955. DOI: 10.1001/jama.2019.1113. [ Context Link 1 ] View abstract...
17. Nettis E, et al. Latex immunotherapy: state of the art. *Annals of Allergy, Asthma, & Immunology* 2012;109(3):160-165. DOI: 10.1016/j.anai.2012.07.004. [ Context Link 1 ] View abstract...
18. Terada T, Kawata R. Diagnosis and treatment of local allergic rhinitis. *Pathogens (Basel, Switzerland)* 2022;11(1):80. DOI: 10.3390/pathogens11010080. [ Context Link 1 ] View abstract...
19. Dykewicz MS, et al. Rhinitis 2020: A practice parameter update. *Journal of Allergy and Clinical Immunology* 2020;146(4):721-767. DOI: 10.1016/j.jaci.2020.07.007. (Reaffirmed 2022 Jul) [ Context Link 1, 2, 3, 4 ] View abstract...
20. Zhu W, Gao P, Zhang Q, Chen J. Efficacy and safety of subcutaneous immunotherapy for local allergic rhinitis: a meta-analysis of randomized controlled trials. *American Journal of Rhinology and Allergy* 2022;36(2):245-252. DOI: 10.1177/19458924211050547. [ Context Link 1 ] View abstract...
21. Di Bona D, Plaia A, Leto-Barone MS, La Piana S, Macchia L, Di Lorenzo G. Efficacy of allergen immunotherapy in reducing the likelihood of developing new allergen sensitizations: a systematic review. *Allergy* 2017;72(5):691-704. DOI: 10.1111/all.13104. [ Context Link 1 ] View abstract...
22. Halcken S, et al. EAACI guidelines on allergen immunotherapy: Prevention of allergy. *Pediatric Allergy and Immunology* 2017;28(8):728-745. DOI: 10.1111/pai.12807. [ Context Link 1, 2 ] View abstract...
23. Seidman MD, et al. Clinical practice guideline: allergic rhinitis. *Otolaryngology Head and Neck Surgery* 2015;152(1 Suppl):S1-S43. DOI: 10.1177/0194599814561600. (Reaffirmed 2022 Jul) [ Context Link 1, 2, 3, 4 ] View abstract...
24. Wheatley LM, Togias A. Clinical practice. Allergic rhinitis. *New England Journal of Medicine* 2015;372(5):456-463. DOI: 10.1056/NEJMcp1412282. [ Context Link 1, 2 ] View abstract...
25. Scadding GK, et al. BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis (Revised Edition 2017; First edition 2007). *Clinical and Experimental Allergy* 2017;47(7):856-889. DOI: 10.1111/cea.12953. [ Context Link 1 ] View abstract...
26. Wise SK, et al. International consensus statement on allergy and rhinology: allergic rhinitis. *International Forum of Allergy and Rhinology* 2018;8(2):108-352. DOI: 10.1002/alar.22073. [ Context Link 1, 2, 3, 4 ] View abstract...
27. Dhami S, et al. Allergen immunotherapy for allergic rhinoconjunctivitis: A systematic review and meta-analysis. *Allergy* 2017;72(11):1597-1631. DOI: 10.1111/all.13201. [ Context Link 1, 2 ] View abstract...
28. Bousquet J, et al. 2019 ARIA Care pathways for allergen immunotherapy. *Allergy* 2019;74(11):2087-2102. DOI: 10.1111/all.13805. [ Context Link 1 ] View abstract...
29. Tie K, Miller C, Zanation AM, Ebert CS. Subcutaneous versus sublingual immunotherapy for adults with allergic rhinitis: a systematic review with meta-analyses. *Laryngoscope* 2022;132(3):499-508. DOI: 10.1002/lary.29586. [ Context Link 1 ] View abstract...
30. Alvaro-Lozano M, et al. EAACI allergen immunotherapy user's guide. *Pediatric Allergy and Immunology* 2020;31 Suppl 25:1-101. DOI: 10.1111/pai.13189. [ Context Link 1, 2 ] View abstract...
31. Pitsios C, et al. Clinical contraindications to allergen immunotherapy: an EAACI position paper. *Allergy* 2015;70(8):897-909. DOI: 10.1111/all.12638. [ Context Link 1, 2, 3, 4, 5 ] View abstract...
32. Dykewicz MS, et al. Treatment of seasonal allergic rhinitis: An evidence-based focused 2017 guideline update. *Annals of Allergy, Asthma, & Immunology* 2017;119(6):489-511. DOI: 10.1016/j.anai.2017.08.012. (Reaffirmed 2022 Jul) [ Context Link 1, 2 ] View abstract...
33. Wallace DV, Dykewicz MS, Oppenheimer J, Portnoy JM, Lang DM. Pharmacologic treatment of seasonal allergic rhinitis: synopsis of guidance from the 2017 Joint Task Force on Practice Parameters. *Annals of Internal Medicine* 2017;167(12):876-881. DOI: 10.7326/M17-2203. (Reaffirmed 2022 Jul) [ Context Link 1, 2 ] View abstract...

34. Brown T. Diagnosis and management of allergic rhinitis in children. *Pediatric Annals* 2019;48(12):e485-e488. DOI: 10.3928/19382359-20191111-01. [ Context Link 1, 2 ] View abstract...
35. Agache I, Laculiceanu A, Cojanu C, Spanu D, Rogozea L. Advances in allergen immunotherapy for asthma. *Current Opinion in Allergy and Clinical Immunology* 2020;20(6):602-608. DOI: 10.1097/ACI.0000000000000686. [ Context Link 1 ] View abstract...
36. Bousquet J, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy* 2008;63 Suppl 86:8-160. DOI: 10.1111/j.1398-9995.2007.01620.x. [ Context Link 1 ] View abstract...
37. Schatz M, Chambers C, Macy E, Zeiger RS. Asthma and allergic diseases during pregnancy. In: Burks AW, et al., editors. *Middleton's Allergy: Principles and Practice*. 9th ed. Elsevier; 2020:919-939.e1. [ Context Link 1, 2, 3 ]
38. Frew AJ. Allergen immunotherapy. *Journal of Allergy and Clinical Immunology* 2010;125(2 Suppl 2):S306-S313. DOI: 10.1016/j.jaci.2009.10.064. [ Context Link 1, 2, 3, 4 ] View abstract...
39. Penagos M, Durham SR. Allergen immunotherapy for long-term tolerance and prevention. *Journal of Allergy and Clinical Immunology* 2022;Online. DOI: 10.1016/j.jaci.2022.01.007. [ Context Link 1, 2 ] View abstract...
40. Arroabarren E, Tabar AI, Echechipia S, Cambra K, Garcia BE, Alvarez-Puebla MJ. Optimal duration of allergen immunotherapy in children with dust mite respiratory allergy. *Pediatric Allergy and Immunology* 2015;26(1):34-41. DOI: 10.1111/pai.12296. [ Context Link 1 ] View abstract...
41. Erekosima N, et al. Effectiveness of subcutaneous immunotherapy for allergic rhinoconjunctivitis and asthma: a systematic review. *Laryngoscope* 2014;124(3):616-627. DOI: 10.1002/lary.24295. [ Context Link 1, 2 ] View abstract...
42. Global Initiative for Asthma. *Global Strategy for Asthma Management and Prevention* [Internet] Global Initiative for Asthma Management and Prevention (GINA). 2022 Jun Accessed at: <https://www.ginasthma.org/>. [accessed 2022 Jul 21] [ Context Link 1, 2, 3 ]
43. 2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group. NIH Publication No. 29-HL-8140 [Internet] National Heart, Lung, and Blood Institute. 2020 Dec Accessed at: <https://www.nhlbi.nih.gov/health-topics/asthma>. [accessed 2022 Oct 20] [ Context Link 1, 2, 3 ]
44. Dhami S, et al. Allergen immunotherapy for allergic asthma: A systematic review and meta-analysis. *Allergy* 2017;72(12):1825-1848. DOI: 10.1111/all.13208. [ Context Link 1 ] View abstract...
45. Lin SY, et al. The Role of Immunotherapy in the Treatment of Asthma. Comparative Effectiveness Review #196 AHRQ Publication No. 17(18)-EHC029-EF [Internet] Agency for Healthcare Research and Quality (AHRQ). 2018 Mar Accessed at: <https://www.effectivehealthcare.ahrq.gov/>. [accessed 2022 Oct 16] DOI: 10.23970/AHRQEPCCER196. [ Context Link 1 ] View abstract...
46. Rice JL, et al. Allergen-specific immunotherapy in the treatment of pediatric asthma: a systematic review. *Pediatrics* 2018;141(5):e20173833. DOI: 10.1542/peds.2017-3833. [ Context Link 1 ] View abstract...
47. Agache I, et al. EAACI Guidelines on Allergen Immunotherapy: House dust mite-driven allergic asthma. *Allergy* 2019;74(5):855-873. DOI: 10.1111/all.13749. (Reaffirmed 2022 Jul) [ Context Link 1, 2 ] View abstract...
48. Slovick A, Durham SR, Till SJ. Grass pollen immunotherapy for treatment of allergic rhinitis. *British Medical Journal* 2014;349:g6586. [ Context Link 1 ] View abstract...
49. Nakagome K, Nagata M. Allergen immunotherapy in asthma. *Pathogens (Basel, Switzerland)* 2021;10(11):Online. DOI: 10.3390/pathogens10111406. [ Context Link 1 ] View abstract...
50. Nelson HS. Injection immunotherapy for inhalant allergens. In: Burks AW, et al., editors. *Middleton's Allergy: Principles and Practice*. 9th ed. Elsevier; 2020:1401-1419.e1. [ Context Link 1 ]
51. Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma. [Internet] National Heart Lung and Blood Institute. 2007 Accessed at: <https://www.nhlbi.nih.gov/health-pro/guidelines/current>. [accessed 2022 Mar 25] [ Context Link 1, 2 ]
52. Crossingham I, et al. Combination fixed-dose beta agonist and steroid inhaler as required for adults or children with mild asthma. *Cochrane Database of Systematic Reviews* 2021, Issue 5. Art. No.: CD013518. DOI: 10.1002/14651858.CD013518.pub2. [ Context Link 1 ] View abstract...
53. Stelmach I, Sobocinska A, Majak P, Smejda K, Jerzynska J, Stelmach W. Comparison of the long-term efficacy of 3- and 5-year house dust mite allergen immunotherapy. *Annals of Allergy, Asthma, & Immunology* 2012;109(4):274-278. DOI: 10.1016/j.anai.2012.07.015. [ Context Link 1 ] View abstract...
54. Golden DB, et al. Stinging insect hypersensitivity: A practice parameter update 2016. *Annals of Allergy, Asthma, & Immunology* 2017;118(1):28-54. DOI: 10.1016/j.anai.2016.10.031. (Reaffirmed 2022 Jul) [ Context Link 1, 2, 3, 4, 5, 6, 7, 8 ] View abstract...
55. Muraro A, Roberts G. Allergen Immunotherapy Guidelines Part 2: Recommendations. [Internet] European Academy of Allergy and Clinical Immunology. 2017 Accessed at: <https://www.eaaci.org/>. [accessed 2022 Oct 16] [ Context Link 1, 2, 3, 4, 5 ]
56. Cardona V, et al. World Allergy Organization anaphylaxis guidance 2020. *World Allergy Organization Journal* 2020;13(10):100472. DOI: 10.1016/j.waojou.2020.100472. (Reaffirmed 2022 Aug) [ Context Link 1 ] View abstract...
57. Golden DBK. Venom immunotherapy: questions and controversies. *Immunology and Allergy Clinics of North America* 2020;40(1):59-68. DOI: 10.1016/j.iac.2019.09.002. [ Context Link 1 ] View abstract...
58. Boyle RJ, et al. Venom immunotherapy for preventing allergic reactions to insect stings. *Cochrane Database of Systematic Reviews* 2012, Issue 10. Art. No.: CD008838. DOI: 10.1002/14651858.CD008838.pub2. [ Context Link 1 ] View abstract...
59. Rueff F, et al. Predictors of clinical effectiveness of Hymenoptera venom immunotherapy. *Clinical and Experimental Allergy* 2014;44(5):736-746. DOI: 10.1111/cea.12275. [ Context Link 1 ] View abstract...
60. Papathanassiou E, Loukides S, Bakakos P. Severe asthma: anti-IgE or anti-IL-5? *European Clinical Respiratory Journal* 2016;3:31813. [ Context Link 1 ] View abstract...
61. Scadding GK. Optimal management of allergic rhinitis. *Archives of Disease in Childhood* 2015;100(6):576-582. DOI: 10.1136/archdischild-2014-306300. [ Context Link 1 ] View abstract...

---

## Footnotes

[A] Subcutaneous immunotherapy is associated with a small risk of serious systemic reaction, including anaphylaxis; most reactions occur within 30 minutes of injection. Patients should be observed in a healthcare setting for at least 30 minutes after an immunotherapy injection. Subcutaneous immunotherapy should be delivered in a setting with appropriate clinical staff and equipment to provide emergency treatment if needed.(1) [ A in Context Link 1 ]

[B] Specialty society guidelines state that allergen immunotherapy may be considered as a treatment option for selected children age 2 to 5 years.(1)(30) However, most studies evaluating allergen immunotherapy in children were conducted in patients 5 years and older, and administration of subcutaneous immunotherapy may be distressing for very young children.(30) [ B in Context Link 1, 2, 3 ]

[C] The duration of this buildup phase for inhalant allergens generally ranges from 3 months (2 injections per week) to 6 months (1 injection per week).(1) With an accelerated schedule, the therapeutic dose may be achieved sooner but with increased risk of systemic reaction for some patients.(1)(2)(4) [ C in Context Link 1, 2 ]

[D] Once a patient reaches a maintenance dose, maintenance injections are then usually given at 4-week to 6-week intervals.(38) Discontinuation of inhalant allergen immunotherapy should be considered after 3 to 5 years of ongoing treatment.(1)(4)(38)(39)(40) [ D in Context Link 1, 2 ]

[E] The duration of this buildup phase for stinging insect hypersensitivity to maintenance dose and clinical protection can routinely be achieved with 8 weekly treatments.(1) With an accelerated schedule, the therapeutic dose may be achieved sooner without the high incidence of systemic reactions seen in accelerated inhalant allergen schedules despite the more severe nature of reaction to natural exposure to stinging insects.(1) [ E in Context Link 1 ]

[F] Approximately 5% to 10% of patients with negative venom skin test results with a history of systemic reactions have a positive venom-specific serum IgE test result.(54) [ F in Context Link 1 ]

[G] In adults with systemic cutaneous reactions without other manifestations, venom immunotherapy is considered optional rather than mandatory, and may be especially helpful in those patients who face unavoidable exposure, have comorbid conditions that increase their risk, or have impaired quality of life as a result of their venom sensitivity.(54) [ G in Context Link 1 ]

[H] Once a patient reaches a maintenance dose, venom immunotherapy maintenance injections are then usually given at 4-week to 8-week intervals.(38)(54) [ H in Context Link 1 ]

---

## Codes

**CPT®: 95115, 95117, 95120, 95125, 95130, 95131, 95132, 95133, 95134, 95144, 95145, 95146, 95147, 95148, 95149, 95165, 95170** [Hide]

**HCPCS: G0069**

*CPT copyright 2022 American Medical Association. All rights reserved.*

---

MCG Health  
Ambulatory Care 27th Edition  
Copyright © 2023 MCG Health, LLC  
All Rights Reserved

Last Update: 9/21/2023 5:09:08 AM  
Build Number: 27.2.2023092114759.013030