Medicare Medical Policy

Allergen Subcutaneous Immunotherapy (SCIT)

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INSTRUCTIONS FOR USE: Company Medicare Medical Policies serve as guidance for the administration of plan benefits and do not constitute medical advice nor a guarantee of coverage. Company Medicare Medical Policies are reviewed annually to guide the coverage or non-coverage decision-making process for services or procedures in accordance with member benefit contracts (otherwise known as Evidence of Coverage or EOCs) and Centers of Medicare and Medicaid Services (CMS) policies, manuals, and other CMS rules and regulations. In the absence of a CMS coverage determination or specific regulation for a requested service, item or procedure, Company policy criteria or applicable utilization management vendor criteria may be applied. These are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

The Company reserves the right to determine the application of Medicare Medical Policies and make revisions to these policies at any time. Any conflict or variance between the EOC and Company Medical Policy will be resolved in favor of the EOC.

SCOPE: Providence Health Plan, Providence Health Assurance, and Providence Plan Partners as applicable (referred to individually as “Company” and collectively as “Companies”).

PRODUCT AND BENEFIT APPLICATION

☒ Medicare Only

MEDICARE COVERAGE CRITERIA

IMPORTANT NOTE: More than one Centers for Medicare and Medicaid Services (CMS) reference may apply to the same health care service, such as when more than one coverage policy is available (e.g., both an NCD and LCD exist). All references listed should be considered for coverage decision-making. The Company uses the most current version of a Medicare reference available at the time of publication; however, these websites are not maintained by the Company, so Medicare references and their corresponding hyperlinks may change at any time. If there is a conflict between the Company Medicare Medical Policy and CMS guidance, the CMS guidance will govern.

Notes: This policy is specific to allergy immunotherapy injections (**subcutaneous** administration) **only** (aka, allergy shots). The policy **does not apply** to allergen immunotherapy by other modes of administration, including but not limited to, the following:

- Oral allergy immunotherapy, including sublingual (under the tongue) options, which may be considered **not medically necessary** by Medicare under National Coverage Determination (NCD) 110.9.
- The emergency treatment of allergic reactions, including anaphylaxis, using epinephrine nasal spray (e.g., Neffy®) or epinephrine auto-injectors, such as EpiPens.

Service	Medicare Guidelines
*Subcutaneous Neutralization Therapy for **Food** Allergies/Sensitivities*	**National Coverage Determination (NCD):** Food Allergy Testing and Treatment (110.11) *(LCDs L40050 & L36240 below also consider this a non-covered service.)*
*SCIT for **Aeroallergens - Build up and Maintenance Phases*** *The term "aeroallergens" refers to inhaled allergens, such as pollens, dust mites, animal dander.*	**Local Coverage Determination (LCD):** Allergen Immunotherapy (AIT) with Subcutaneous Immunotherapy (SCIT) (L40050) **NOTES:** • **Non-aeroallergen SCIT:** SCIT for ***other*** allergens, such as venoms, is **not** considered in this LCD, and other coverage criteria apply. • **Home SCIT:** While these LCDs, as well as the LCD L36240 below, all address patient self-administration at **home**, see the separate row below for more information. • **Frequency Utilization Guidelines:** For frequency utilization guidelines, see the internal Company policy criteria below.
Medicare Coverage Criteria: "MA organizations may create publicly accessible internal coverage criteria… when coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs." • **Medicare Coverage Manuals:** Medicare does not have fully established coverage criteria for allergy immunotherapy in a coverage manual.	

- **National Coverage Determination (NCD):** With the exception of the NCD identified above, Medicare does not have an NCD for allergy immunotherapy.
- **Noridian J-F Local Coverage Determination (LCD)/Local Coverage Article (LCA):** While four (4) Medicare Administrative Contractors (MACs) have LCDs for SCIT for other allergens (e.g., venom), the MAC for the Plan's service area (Noridian J-F) does **not** have an active LCD or LCA for SCIT for these **other allergens**.
- In this case, the Plan is in a jurisdiction without "not fully established" coverage criteria as defined under CFR § 422.101(b)(6)(i)(C) as there are no Medicare coverage criteria available. ***According to a CMS FAQ dated February 6, 2024, internal coverage criteria used by an MAO may include the use of LCD criteria from a geographic area that is not the MA plan's service area, as long as all requirements of § 422.101(b)(6) are satisfied.***
- For allergy immunotherapy, in the absence of established Medicare coverage criteria in a manual, NCD, LCD, or other regulatory guidance for the health plan's service area, **the plan is adopting published LCD criteria from the MAC, Novitas Solutions, Inc. (Novitas). By using the coverage criteria of a Medicare contractor, rather than other sources, criteria and evidence reviews are more likely to consider individuals associated with the Medicare-population.**
- See **Policy Guidelines** below for more information about CMS requirements for § 422.101(b)(6).

*SCIT for **Other Allergens - Build up and Maintenance Phases*** *Examples include, but may not be limited to, venom allergens.*	**Novitas Solutions, Inc. (Novitas) LCD:** Allergen Immunotherapy (L36240) **NOTES:** • See below for the Summary of Evidence and the sources (citations) used in the development of this LCD.

Medicare Coverage Criteria: "MA organizations may create publicly accessible internal coverage criteria… when coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs." *(§ 422.101(b)(6) – see Policy Guidelines below*)

- **Medicare Coverage Manuals:** Medicare does not have fully established criteria regarding medically reasonable and necessary frequency utilization standards for allergy SCIT in a coverage manual.
  - While Medicare may allow for a 12-month supply of antigens *(see Medicare Benefit Policy Manual, Chapter 15, §50.4.4.1 – Antigens and Chapter 16, §90 - Routine Services and Appliances, B. Antigens),* the MACs have determined home allergy SCIT is not medically reasonable and necessary except in rare situations, and therefore, the provision of a full year's worth of antigens at one time may not always be considered medically reasonable or necessary.
  - In addition, CMS states, "An MUE or the lack of an MUE, does not necessarily indicate coverage status of a HCPCS/CPT code. The NCCI program does not establish medical necessity or payment policy." *(NCCI Manual, Chapter 1)* Therefore, the presence of an MUE value does **not** mean CMS has determined that number of units will be considered medically reasonable and necessary for all patients.
  - These CMS sources are considered "not fully established" coverage criteria under CFR § 422.101(6)(i)(A) and additional criteria are needed to interpret or supplement these general coverage provisions in order to determine medical necessity consistently, in line with standard clinical benchmarks.

• **National Coverage Determination (NCD):** With the exception of the NCD noted above, Medicare does not have any other NCD for allergy treatment, nor does an NCD provide specific coverage criteria or guidance around utilization or frequency limitations. • **Noridian J-F Local Coverage Determination (LCD)/Local Coverage Article (LCA):** Neither of the LCDs noted above for allergy SCIT, including the Noridian J-F LCD, address frequency utilization. • Therefore, in the absence of **fully established** Medicare coverage criteria in a manual, NCD, LCD, or other regulatory guidance for the health plan's service area, Company criteria below are applied for medical necessity decision-making. In this case, Medicare coverage criteria are considered "not fully established" as defined under CFR § 422.101(6)(i)(B) as the available Medicare coverage policies provide flexibility for coverage decisions beyond the NCD and LCD. While they provide coverage guidance including **non-coverage** of home SCIT (except in rare situations), these sources do **not** provide guidelines around what is medically reasonable and necessary or medically unlikely. • ***NOTE:*** *The summary of evidence, as well as the list of citations/references used in the development of the Company's internal coverage criteria, are publicly available and can be found using the Company medical policy link below [CFR § 422.101(6)(ii)(A) and (B)].*	
Utilization and Frequency Limitations	Company medical policy for Allergen Subcutaneous Immunotherapy (SCIT) I. Supervision of preparation and provision of antigens for SCIT (CPT 95165) may be considered **medically necessary** up to the total limits found in the Company medical policy. II. Supervision of preparation and provision of antigens for SCIT are considered **not medically necessary** for Medicare members when medically reasonable and necessary quantity limits are exceeded. *See Policy Guidelines below.*
Home SCIT	For more information regarding clinical practice guidelines and Medicare coverage policy criteria and home SCIT, see *Policy Guidelines* below. I. Home administration of allergen immunotherapy may be considered **medically necessary** when the clinical documentation clearly states why it is being done by the patient in the home setting, and that the benefit of allergen immunotherapy clearly outweighs the risk of withholding immunotherapy (e.g., a patient with a history of venom-induced anaphylaxis living in a remote region) **and** that the individual administering the injection has been trained and is prepared to recognize and manage adverse reactions, particularly anaphylaxis. II. Because the option of home administration of allergen immunotherapy must be made on an individual patient basis, it is considered **not medically necessary** when Criterion I above is not met, including when utilized by an office as the standard or routine approach for all patients.

IMPORTANT NOTICE: While some services or items may appear medically indicated for an individual, they may also be a direct exclusion of Medicare or the member's benefit plan. Such excluded services or items by Medicare and member EOCs include, but are not limited to, services or procedures considered to be cosmetic, not medical in nature, or those considered not medically reasonable or necessary under *Title XVIII of the Social Security Act, §1862(a)(1)(A).* If there is uncertainty regarding coverage of a service or item, please review the member EOC or submit a pre-service organization determination request. Note that the Medicare Advance Beneficiary Notice of Noncoverage (ABN) form **cannot** be used for Medicare Advantage members. *(Medicare Advance Written Notices of Non-coverage. MLN006266 May 2021)*

POLICY CROSS REFERENCES

- Allergy Testing, MP152

The full Company portfolio of Medicare Medical Policies is available online and can be accessed here.

POLICY GUIDELINES

DOCUMENTATION REQUIREMENTS

In order to review for medical necessity, documentation requirements can be found in the billing and coding companion Novitas local coverage article (LCA) A56538.

DEFINITIONS

Allergen immunotherapy (AIT). AIT is "the repeated administration of specific allergens to individuals with IgE-mediated conditions to provide protection against allergic symptoms and inflammatory reactions associated with natural exposure to these allergens." ***(SOURCE: LCD L36240)***

VIT. Venom Immunotherapy

BACKGROUND

Allergy Immunotherapy (AIT)

Allergy Immunotherapy (AIT) 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. It may also be referred to as hyposensitization, allergen-specific desensitization, and the lay terms allergy shots or allergy injections.[1]

Preventive Allergy Immunotherapy

"The presence of IgE antibodies alone does not infer the need for immunotherapy; the presence of IgE antibodies to an allergen must correlate with the patient's history.1 For example, the presence of IgE antibodies to an allergen not locally found, with no history of exposure or expectation of exposure, would not be considered clinically relevant." *(Source: LCD L36240)*

Home Immunotherapy

"Home administration of allergen immunotherapy should only be considered in rare and exceptional cases when the benefits of immunotherapy clearly outweigh the risks. Frequent or routine home immunotherapy is not considered appropriate under any circumstances. If this method is utilized, informed consent should be attained from the patient and the individual administering the injection must be trained and equipped to recognize and manage immunotherapy reactions, particularly anaphylaxis." *(Source: LCD L36240)*

Provider Requirements

The Plan must follow Medicare rules. Medicare rules say that antigens must be prepared by a physician who is a doctor of medicine (MD) or osteopathy (DO). This rule can be found in the Medicare Benefit Policy Manual, Chapter 15, Section 50.4.4.1, and LCDs L40050 and L36240. Antigen preparation services provided by non-physician providers, including a nurse practitioner, are considered not medically necessary.

MEDICARE AND MEDICAL NECESSITY

Medicare Advantage plans must follow Medicare rules. Medicare rules say items and services that are not medically necessary are not covered. Only medically reasonable and necessary services or items which treat illness or injury are eligible for Medicare coverage. This rule is found in *Title XVIII of the Social Security Act, §1862(a)(1)(A)*.

According to Medicare regulations:

> "MA organizations may create publicly accessible internal coverage criteria that are based on current evidence in widely used treatment guidelines or clinical literature when coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs. Current, widely-used treatment guidelines are those developed by organizations representing clinical medical specialties, and refers to guidelines for the treatment of specific diseases or conditions. Acceptable clinical literature includes large, randomized controlled trials or prospective cohort studies with clear results, published in a peer-reviewed journal, and specifically designed to answer the relevant clinical question, or large systematic reviews or meta-analyses summarizing the literature of the specific clinical question." *(§ 422.101(b)(6) and Medicare Managed Care Manual, Ch. 4, §90.5)*

When Medicare coverage criteria are considered "not fully established" as defined under CFR § 422.101(b)(6), including the absence of an LCD or LCA by the plan's service area MAC, then an MAO may elect to use their own internal coverage criteria, **or alternatively**, according to a *CMS FAQ dated February 6, 2024*, ***the MAO may use criteria from an LCD for a geographic area that is not the MA plan's service area, as long as all requirements of § 422.101(b)(6) are satisfied.***

The requirements of § 422.101(b)(6) are:

- Coverage criteria must be based on current evidence in widely used treatment guidelines or clinical literature.

- The coverage criteria can be used **only** when Medicare coverage criteria are not fully established for our service area (as described by § 422.101(b)(6)(i)(A)-(C)).
- The MAOs use of this criteria must be publicly accessible (as described by § 422.101(b)(6)(ii)(A)-(C)). This includes:
    - Publicly publish the internal coverage criteria used by the plan, accessible via a website (not behind a paywall or require a subscription for access) **and** must be available to **all** of the public (not just enrollees or contracted providers).
    - A summary of evidence.
    - Citations or sources of the evidence.
    - An explanation of the rationale for using the criteria that is in our policy.

According to the *Medicare Program Integrity Manual, Chapter 13 – Local Coverage Determinations, §13.1.1 - Local Coverage Determinations (LCD) Definition & Statutory Authority for LCDs*, these same elements are also required in LCDs. CMS states (bold added for emphasis):

> "The 2016 21st Century Cures Act included changes to the LCD process, adding language to 1862(l)(5)(D) of the SSA to describe the LCD process. Section 1862(l)(5)(D), of the SSA requires each MAC that develops an LCD to make available on the Internet website of such contractor and on the Medicare Internet website, at least 45 days before the effective date of such determination, the following information:
>
> (i) Such determination in its entirety.
> (ii) Where and when the proposed determination was first **made public**.
> (iii) Hyperlinks to the proposed determination and a response to comments submitted to the contractor with respect to such proposed determination.
> (iv) A **summary of evidence** that was considered by the contractor during the development of such determination and **a list of the sources of such evidence**.
> (v) **An explanation of the rationale that supports such determination.**"

Therefore, because Medicare coverage criteria are "not fully established" for allergy SCIT services for allergens **other than** aeroallergens in a manual, NCD, LCD, or other regulatory guidance for the health plan's service area, the plan has opted to adopt published LCD criteria from the MAC, Novitas Solutions, Inc. (Novitas) LCD L36240.

In addition, since there are not fully established coverage criteria for utilization frequency guidelines available in applicable Medicare statutes, regulations, NCDs or LCDs for the MAO service area, then Company medical policy criteria will be applied. See the Medicare Coverage Criteria table above for more information regarding the use of internal coverage criteria when Medicare coverage criteria are not fully established.

Finally, with regard to home allergen SCIT administration, the American Academy of Otolaryngic Allergy (AAOA) "**encourages the preferential practice of administering subcutaneous immunotherapy in a medical office setting with professionals trained in the recognition and management of anaphylactic reactions**."[2] In addition, the American Academy of Asthma, Allergy and Immunotherapy (AAAAI) advises that subcutaneous allergen immunotherapy should be administered in a clinical setting with trained staff and medical equipment capable of recognizing and treating anaphylaxis. **Under rare circumstances, when the benefit of allergen immunotherapy clearly outweighs the risk of withholding immunotherapy (e.g., individuals with a history of venom-induced anaphylaxis living in a remote**

region), at-home administration of allergen immunotherapy should be considered on an individual basis. Furthermore, AAAAI emphasizes that frequent or routine prescription of home immunotherapy is not appropriate under any circumstances.[3] *(Bold added for emphasis)*

According to LCD L40050, "It may be appropriate to permit patient self-administration at home for the patient with a history of life-threatening anaphylaxis who cannot receive immunotherapy in a health care facility. **This requires very careful consideration of potential benefits and risks and should be made on an individual patient basis** with appropriate informed consent." *(Bold added for emphasis)*

According to LCD L36240, "**Home administration of allergen immunotherapy should only be considered in rare and exceptional cases when the benefits of immunotherapy clearly outweigh the risks. Frequent or routine home immunotherapy is not considered appropriate under any circumstances.** If this method is utilized, informed consent should be attained from the patient and the individual administering the injection must be trained and equipped to recognize and manage immunotherapy reactions, particularly anaphylaxis." *(Bold added for emphasis)*

SUMMARY AND SOURCES OF EVIDENCE

For some services addressed by this policy, the plan has opted to adopt published LCD criteria from the MAC, Novitas Solutions, Inc. (Novitas) LCD L36240. This LCD is based on current evidence in widely used treatment guidelines or clinical literature, and it includes a systemic review of evidence-based guidelines and published literature, which were considered in the development of the LCD criteria. In addition, the summary of evidence, as well as the list of citations (bibliography list), that were used in the development of the LCD coverage criteria, are provided within the LCD, and are also publicly available. *[CFR § 422.101(b)(6)(ii)(A) and (B)]* As of the date of the most recent policy review, the summary of evidence and the sources of information used in the development of the Novitas LCD L36240 are as follows:

Summary of Evidence
A literature search was conducted using the following key words: allergens; allergen immunotherapy; practice guidelines; practice parameters; meta-analysis; systematic review; allergic rhinitis; seasonal allergic rhinitis; allergic conjunctivitis; allergic asthma; inhalant allergies; routes of immunotherapy administration; subcutaneous immunotherapy; allergen-specific immunotherapy, atopic dermatitis; acute and chronic urticaria; skin rash; food allergies; stinging insect allergy; Hymenoptera; anaphylaxis.

Evidence-Based Guidelines

A Joint Task Force represented by the American Academy of Allergy, Asthma & Immunology (AAAAI); the American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy, Asthma & Immunology (JCAAI) has provided an updated practice parameter for allergen immunotherapy.1 Also, the European Academy of Allergy and Clinical Immunology (EAACI) and the AAAAI provided an updated, comprehensive consensus report which includes the mechanisms of allergy immunotherapy and its use in clinical practice.6 In addition, the AAAAI and the ACAAI have provided a practice parameter update for stinging insect hypersensitivity.2

Allergen immunotherapy is defined as the repeated administration of specific allergens to individuals with IgE-mediated conditions to provide protection against allergic symptoms and inflammatory reactions associated with natural exposure to these allergens. Immunotherapy is effective for pollen, animal allergens, dust mites, mold/fungi, and Hymenoptera hypersensitivity. Allergen immunotherapy should be considered for patients who have discernable evidence of specific IgE antibodies to these allergens.1

The decision to begin allergen immunotherapy may depend on a number of factors, including but not limited to, patient's preference/acceptability, adherence, medication requirements, response to avoidance methods, and the adverse effects of medications. The severity and duration of symptoms should also be considered when evaluating the need for allergen immunotherapy. Patient assessments should include a detailed clinical history, an applicable physical evaluation, and particular laboratory tests. Allergy testing results provide a conclusive diagnosis (e.g., immediate hypersensitivity skin tests, in vitro tests for serum specific IgE). When tests outcomes are positive for select IgE antibodies that align with likely triggers and patient exposure, immunotherapy is recommended; however, the manifestation of specific IgE antibodies alone does not infer the need for immunotherapy; the presence of IgE antibodies to an allergen must correlate with the patient’s history.1

Many well-designed controlled trials show that allergen immunotherapy is effective for individuals with symptoms of allergic rhinitis/conjunctivitis, allergic asthma and stinging insect hypersensitivity.2-9 Also, randomized trials demonstrate that allergen immunotherapy inhibits the development of asthma in individuals with allergic rhinitis.15 Several studies have also shown that aeroallergen immunotherapy may be beneficial for individuals with atopic dermatitis resulting from aeroallergen sensitization to dust mites.1,9-11

Venom immunotherapy (VIT) is recommended for individuals with a history of a systemic reaction to Hymenoptera stings who demonstrate Hymenoptera-specific IgE antibodies and exhibit large local reactions (LLRs). In this regard, measurements of serum tryptase levels are recommended in individuals with a history of moderate to severe anaphylactic reactions to stings. Studies have shown that greater serum tryptase levels are correlated with recurrent and severe systemic responses (including deadly reactions) to VIT injections, increased failure rates in VIT, and increased relapse rates with discontinuation of VIT. While venom extracts are available for honeybees, yellow jackets, white-faced hornets, yellow hornets, and wasps, there is currently no venom extract available for fire ants. However, literature supports the use of whole-body extract (WBE) to be used as a reagent for diagnostic testing and immunotherapy for fire ant sting allergy.1,2,9

The provider prescribing immunotherapy should be trained and experienced in prescribing and administering immunotherapy. The prescribing provider must choose the applicable allergen extracts based on the patient’s medical history, allergen exposure history, and the presence of specific IgE antibodies. The prescription must indicate the initial dose, the target maintenance dose, and the immunotherapy schedule.1,2

Immunotherapy treatments are generally separated into two phases; the build-up phase and the maintenance phase. The build-up phase (also referred to as updosing, induction, or dose-increase) involves gradually giving greater doses within 8-28 weeks. Usually a single dose increase is administered per visit and visits generally vary from 1-3 times per week. Accelerated timetables, also referred to as rush or cluster immunotherapy, involve giving several injections at increasing doses on a single visit. While accelerated timetables provide a means of reaching

the therapeutic dose sooner, a greater risk of a systemic reaction is possible in some individuals.1,9

The maintenance phase occurs when the effective therapeutic dose is reached. This dose provides therapeutic efficiency without significant adverse local or systemic consequences. This dose may not be the initial targeted concentration/dose. The maintenance immunotherapy schedule is generally every 4-8 weeks for venoms and every 2-4 weeks for inhalant allergens. Maintenance immunotherapy generally involves follow-up visits every 6-12 months. If clinical improvement is not achieved after one year of maintenance immunotherapy, potential reasons for lack of effectiveness should be investigated and if no reasons are discovered, cessation of immunotherapy should be contemplated and other therapy possibilities should be explored. For many patients, the recommended duration of immunotherapy is 3-5 years. However, the duration of immunotherapy should be personalized based on the benefits sustained from therapy, disease severity, immunotherapy reaction, patient preference, and certain antigens in the therapy.1,2,9

Generally, the initial dose is 1,000 to 10,000-fold less than the maintenance dose. The maintenance dose is usually 500-2,000 allergy units (AU) (e.g., for dust mites) or 1,000-4,000 bioequivalent allergy units (BAU) (e.g., for grass or cat) for standardized allergen extracts. For non-standardized extracts, a recommended dose is 3,000-5,000 protein nitrogen units (PNU) or 0.5 mL of a 1:100 or 1:200 weight/volume dilution of manufacturer's extract. If the main allergen concentration for the extract is available, a maintenance dose of 5-20 micrograms (µg) of the major allergen is recommended for inhalant allergens and 100 µg for Hymenoptera venoms.1,2

Desensitization involves the rapid administration of incremental doses of allergens or medications by which effector cells are rendered less reactive or nonreactive to an IgE-mediated immune response. Desensitization can involve IgE-mediated or other immune mechanisms. A positive skin test response to the allergens might lessen or actually convert to a negative response in some situations after desensitization. Tolerance to medications can be achieved through desensitization.

Immunotherapy may have severe unpredictable systemic and local reactions within the first 30 minutes following the injection. It is recommended that immunotherapy be administered in a setting that permits the prompt recognition and management of adverse reactions.6 The preferred location for such administration is the prescribing physician's office. However, patients can receive immunotherapy at another health care facility if the physician and staff at that location are trained and equipped to recognize and manage immunotherapy reactions, particularly anaphylaxis. It is recommended that patients wait at the physician's office/medical clinic for at least 30 minutes after the immunotherapy injection. Regardless of the location, allergen immunotherapy should be administered under the direct supervision of an appropriately trained physician, qualified nurse practitioner or physician assistant in a facility with the proper equipment, medications, and personnel to treat anaphylaxis.1,9

The risk of severe systemic reactions is low with allergen immunotherapy that is administered appropriately; however, life-threatening and fatal reactions do happen. Studies have shown that severe responses following allergen immunotherapy occur in less than 1% of patients receiving conventional immunotherapy, but occur in about 34% of patients receiving rush (e.g., accelerated timetable) immunotherapy.1

Limitations for Immunotherapy

Immunotherapy injections should be withheld if the patient presents with an acute asthma exacerbation; allergen immunotherapy should not be initiated unless the patient's asthma is stable with pharmacotherapy as patients with severe or uncontrolled asthma are at a greater risk for systemic reactions to immunotherapy injections. Regarding inhalant and venom allergen immunotherapy, individual evaluations of risk versus benefit must be made for individuals on beta-blockers and ACE inhibitor medications.1,2,9

Home administration of allergen immunotherapy should only be considered in rare and exceptional cases when the benefits of immunotherapy clearly outweigh the risks. Frequent or routine home immunotherapy is not considered appropriate under any circumstances. If this method is utilized, informed consent should be attained from the patient and the individual administering the injection must be trained and equipped to recognize and manage immunotherapy reactions, particularly anaphylaxis.1

Methods of Immunotherapy not Supported in the Literature

In addition to the subcutaneous route, allergen extracts can be given by various methods. However, there are currently no FDA-approved formulations for a non-injection immunotherapy extract. In this regard, the quality of evidence in the literature does not support the following methods of immunotherapy: Oral and sublingual immunotherapy for food hypersensitivity, neutralization-provocation therapy, low-dose subcutaneous therapy based on the Rinkel method, intranasal, intra-bronchial, intralymphatic, and epicutaneous. Further research is needed to clarify the utility and efficacy of these methods.1,6,12,13

Conditions not Supported in the Literature for Immunotherapy

The quality of evidence in the literature is lacking in support of allergen immunotherapy for food hypersensitivity, cockroach hypersensitivity, chronic urticaria and/or angioedema, and therefore, is not recommended.1,12,13 The use of therapy formulations, such as allergoids and adjuvants is also not supported in the literature.1

Evidence Submitted for Reconsideration

Cox et al1 provides a practice parameter (third update) for allergen immunotherapy. This guideline indicates that few studies have examined the effectiveness of multiallergen subcutaneous immunotherapy. These studies have conflicting outcomes, with some showing substantial clinical improvement compared with placebo and others demonstrating no benefit over optimal pharmacotherapy and environmental control measures. While it is important to treat patients with relevant allergens, the multiallergen studies have shown effectiveness overall, although some did not provide outcomes specific to the multiallergens. Furthermore, this practice is commonly utilized by U.S. allergists.

Nelson16 provides a review of the literature regarding differences in the method of providing subcutaneous allergy immunotherapy in patients with multiple allergies for European and U.S. allergists. This is considered a significant issue as evidence shows that polysensitization is more common than monosensitization.

In the U.S., the above referenced practice parameter (third update), published in 2011 by Cox et al1, for allergen immunotherapy is the most current guideline for multiallergen subcutaneous immunotherapy. This guideline recommends providing subcutaneous allergy immunotherapy

“with a mixture consisting of all the allergen extracts to which the patient has evident clinical sensitivity.”16(p583)

In 2018, the EAACI Taskforce provided a guideline on allergen immunotherapy for allergic rhinoconjunctivitis. This guideline includes a recommendation “that a polyallergic patient whose sensitivities are to homologous or related allergens (such as northern grasses or birch/alder/hazel) be given a single representative extract or a mixture of two of the related extracts. Where the extracts are not homologous, they recommend separate allergen immunotherapy preparations for the one or at the most two of the clinically most important allergens with, if two, doses be given 30 – 60 minutes apart in separate locations.”16(p583)

The literature indicates that methods of providing allergy immunotherapy in polyallergic patients are different in the U.S. and Europe. “The U.S. practice parameter’s recommendation that only clinically relevant allergen extracts be included in a multiallergen subcutaneous immunotherapy mixture probably represents the consensus of most practicing U.S. allergists.”16(p584) Allergists in the U.S. seem satisfied with the multiallergen approach, "because empirically it appears to be working well.”16(p588)

Nelson17 provides a review of the literature regarding multiallergen immunotherapy for allergic rhinitis and asthma. Literature was reviewed for studies concurrently using two or more different allergen extracts in subcutaneous or sublingual immunotherapy (this summary focuses on subcutaneous administration). The author concludes, “The findings of the current review strongly suggest that the simultaneous delivery of multiple unrelated allergens can be clinically effective with the proper identification of relevant allergens, and treatment with adequate doses for a sufficient period of time is essential.”17(p768)

Burks et al6 provides a consensus report from the EAACI and the AAAAI for allergy immunotherapy. This consensus report represents a comprehensive review of the literature for allergy immunotherapy and includes the mechanisms of allergy immunotherapy and the utilization of this therapy in clinical practice, variations in methods between Europe and the U.S., and addresses specific unmet clinical needs in allergy immunotherapy with select therapeutic approaches.

The report indicates that European practices generally provide single-allergen subcutaneous immunotherapy. Though, subcutaneous immunotherapy is commonly provided with multiple allergens in the U.S., which is supported by some older studies.6

Wise et al18 provides an international consensus statement on allergy and rhinology for allergic rhinitis based on a review of the literature. Regarding single-allergen versus multiple-allergen allergen immunotherapy, the authors state, “It is the common practice among U.S. allergists to include in their treatment multiple allergen extracts to which the patient is sensitized.”18(p128) Whereas, “European guidelines recommend treating with the single most troublesome allergen identified clinically, or if more than 1 extract is to be given they should be given at separate sites with at least 30 minutes in between administration.”18(p128)

Wood et al19 provides a report of four pilot studies: “(1) an open-label study to assess the safety of cockroach sublingual immunotherapy (SLIT) in adults and children; (2) a randomized, double-blind biomarker study of cockroach SLIT versus placebo in adults; (3) a randomized, double-blind biomarker study of 2 doses of cockroach SLIT versus placebo in children; and (4) an open-label safety and biomarker study of cockroach subcutaneous immunotherapy (SCIT) in adults.”19(p2) (This summary will focus on the study for subcutaneous immunotherapy as SLIT is

nationally non-covered by Medicare; antigens must be administered by injection to be considered for coverage).

An open-label, pilot study was conducted utilizing German cockroach allergen extract administered by subcutaneous injection to evaluate the safety of this therapy in cockroach-sensitive individuals. “The objective of this protocol was to assess whether treatment with cockroach SCIT using the per-protocol allergen extract doses is safe. The primary outcome measure was the rate of related adverse events and serious adverse events in the course of treatment.”19(p9) The study included ten study participants (average age of 37.5 years) with cockroach sensitivity. Seven of the participants had asthma and six had allergic rhinitis.

The study participants were given increased doses of subcutaneous cockroach extract twice per week for 11 weeks until they reached the maintenance dose of 0.6 mL of a 1:20 concentration of extract. Study participants were then monitored for 15 weeks as they were given weekly injections at the maintenance dose. Blood was collected each month for evaluation of cockroach-specific IgE levels and other biomarkers of allergen immunotherapy.19

The average cockroach skin prick test wheal was 6.75 mm (range, 3–9 mm), and the average cockroach IgE level was 3.8 kU/L (range, 0.9–24.9 kU/L). Three adverse events occurred for localized injection-site reactions and were considered moderate in severity. An additional 147 adverse events occurred for minor injection-site reactions or symptoms that were consistent with the study participants’ underlying allergic rhinitis and were considered mild in severity and likely related to the treatment. Study results showed that changes from baseline in cockroach-specific IgE levels (1.78-fold increase, P=.02), IgG4 levels (12.95-fold increase, P<.001), and facilitated allergen binding activity (43% inhibition of B-cell binding, P<.001) were detected. Five study participants showed at least a 3-fold increase in cockroach IgE levels, while all of the study participants had at least a 2-fold increase in cockroach IgG4 levels.19

The authors stated that “The SCIT trial was designed as an early safety study but also as a proof of concept that consistent, allergen immunotherapy-related immunologic changes can be induced with German cockroach extract. Findings with regard to safety were reassuring because no severe reactions were seen. Mild reactions to SCIT were common, but they did not affect dosing.”19(p6)

The quality of evidence provided is insufficient to support allergen immunotherapy for cockroach hypersensitivity. Further research is needed to clarify the utility and efficacy of allergen immunotherapy for cockroach sensitivity.

Evidence Submitted During Comment Period

Rudman Spergel et al performed a study to identify a range of German cockroach extract doses that cause nasal symptoms and to examine the safety of a cockroach nasal allergen challenge test in children with asthma. However, this report does not present any data regarding treatment effectiveness. It only suggests that the data presented may be useful in the future development of immunotherapy.20

Analysis of Evidence (Rationale for Determination)
Allergen immunotherapy, also known as allergy shots involves the repeated administration of allergen extracts to individuals with IgE-mediated conditions to decrease symptoms and improve quality of life during subsequent natural allergen exposure. Allergen immunotherapy

consists of administering increasingly greater doses of specific allergens to individuals who have shown immunologic sensitivity or reaction to a particular allergen through allergy testing.

Multiple evidence-based practice guidelines and appropriate use criteria are available for allergen immunotherapy. Many well-designed controlled studies have shown that immunotherapy is effective for pollen, animal allergens, dust mites, mold/fungi, and Hymenoptera hypersensitivity. Also, aeroallergen immunotherapy is recommended for individuals with atopic dermatitis resulting from aeroallergen sensitization to dust mites. In addition, VIT is recommended for individuals with a history of a systemic reaction to Hymenoptera stings who demonstrate Hymenoptera-specific IgE antibodies and exhibit LLRs. Measurements of serum tryptase levels are also recommended for these individuals as increased serum tryptase levels are correlated with recurrent and severe systemic responses (including deadly reactions) to VIT injections, increased failure rates in VIT, and increased relapse rates with discontinuation of VIT. Also, the use of WBE is recommended for fire ant sting allergy as venom extracts are not currently available for fire ants.

The decision to begin allergen immunotherapy may depend on a number of factors, including but not limited to, patient's preference/acceptability, adherence, medication requirements, response to avoidance methods, and the adverse effects of medications. The severity and duration of symptoms should also be considered when evaluating the need for allergen immunotherapy. Patient assessments should include a detailed clinical history, an applicable physical evaluation, and particular laboratory tests. Evidence-based guidelines recommend immunotherapy when allergy testing results are positive for select IgE antibodies that align with likely triggers and patient exposure. The presence of IgE antibodies alone does not infer the need for immunotherapy; the presence of IgE antibodies to an allergen must correlate with the patient’s history.

Per evidence-based guidelines, the provider prescribing immunotherapy should be trained and experienced in prescribing and administering immunotherapy. The prescribing provider must choose the applicable allergen extracts based on the patient’s medical history, allergen exposure history, and the presence of specific IgE antibodies. The prescription must indicate the initial dose, the target maintenance dose, and the immunotherapy schedule.

Evidence-based guidelines recommend that immunotherapy be administered in a setting that permits the prompt recognition and management of adverse reaction. The preferred location for such administration is the prescribing physician's office. However, patients can receive immunotherapy at another health care facility if the physician and staff at that location are trained and equipped to recognize and manage immunotherapy reactions, particularly anaphylaxis. It is recommended that patients wait at the physician's office/medical clinic for at least 30 minutes after the immunotherapy injection as immunotherapy may have severe unpredictable systemic and local reactions within the first 30 minutes following the injection. Regardless of the location, allergen immunotherapy should be administered under the direct supervision of an appropriately trained physician, qualified nurse practitioner or physician assistant in a facility with the proper equipment, medications, and personnel to treat anaphylaxis.

Evidence-based guidelines support the following limitations for allergen immunotherapy: 1) Patients should not have substantial comorbid conditions that could increase immunotherapy risk (e.g., severe asthma uncontrolled by pharmacotherapy, significant cardiovascular disease); 2) Patients on beta-blockers and/or ACE inhibitor medications must have individualized assessments of risk versus benefit prior to receiving inhalant or venom allergen immunotherapy;

3) Patients should be able to cooperate during therapy; and 4) Home administration of allergen immunotherapy should only be considered in rare and exceptional cases when the benefits of immunotherapy clearly outweigh the risks. Frequent or routine home immunotherapy is not considered appropriate under any circumstances.

The quality of evidence in the literature does not support the following methods of immunotherapy: 1) oral and sublingual immunotherapy for food hypersensitivity; 2) neutralization-provocation therapy; 3) low-dose subcutaneous therapy based on the Rinkel method; 4) intranasal; 5) intra-bronchial; 6) intralymphatic; and 7) epicutaneous. Further research is needed to clarify the utility and efficacy of these methods. Also, the quality of evidence in the literature is lacking in support of allergen immunotherapy for the following conditions: a) food hypersensitivity; b) cockroach hypersensitivity; and c) chronic urticaria and/or angioedema. In addition, the use of therapy formulations, such as allergoids and adjuvants is also not supported in the literature.

SOURCES OF EVIDENCE

Sources of Information

N/A

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Details regarding the review of this literature can be found in the LCD directly.

REGULATORY STATUS

U.S. FOOD & DRUG ADMINISTRATION (FDA)

While clearance by the Food and Drug Administration (FDA) is a prerequisite for Medicare coverage, the 510(k) premarket clearance process does not in itself establish medical necessity. Medicare payment policy is determined by the interaction of numerous requirements, including but not limited to, the availability of a Medicare benefit category and other statutory requirements, coding and pricing guidelines, as well as national and local coverage determinations and clinical evidence.

BILLING GUIDELINES AND CODING

GENERAL

See associated local coverage articles (LCAs) for related billing and coding guidance, as well as additional coverage and non-coverage scenarios and frequency utilization allowances and limitations:

- LCA: Billing and Coding: Allergen Immunotherapy (AIT) with Subcutaneous Immunotherapy (SCIT) (A56538)

Utilization Guidelines

As with all medically necessary services, allergy immunotherapy is expected to be performed at frequencies as indicated by current medical literature and/or standards of practice. All units reported on any claim must be justified, and documentation must support the units of services rendered, that the services have been coded correctly, and that the services were medically reasonable and necessary for the individual. Units should be billed on the preparation date and not split over subsequent days.

General Coding

Prior to January 1981, Medicare only allowed reimbursement to a physician for the preparation of an antigen **only if** that physician also administered the antigen to the patient.

Starting January 1, 1981, Medicare changed this rule, allowing reimbursement for a reasonable supply of antigens prepared for a patient, even if those antigens were administered by a *different* physician, as long as both of the following are met:

- the antigens are prepared by a physician who is a doctor of medicine (MD) or osteopathy (DO), **and**
- the physician who prepared the antigens has examined the patient and has determined a plan of treatment and a dosage regimen.[4]

Allergen immunotherapy is divided into categories of codes, which are described in Table 1 below.[5]

Table 1: Allergen Immunotherapy Coding

CATEGORY	CODES	NOTES
Complete service	CPT 95120-95134	• Represent services that include the injection service (administration), the antigen and its preparation.
Injection only	CPT 95115 & 95117	• Used for the professional administration (injection) of the allergenic extract. They do **not** include the provision or preparation of the extract. • *Example: An allergist provides a patient with an allergenic extract, and the patient brings the extract to a family or primary care practitioner who administers the injection(s). These codes would be used by the family or primary care provider.* • These codes should **not** be used if the antigen is self-administered by the member.

Antigen provision & preparation only	CPT 95144-95170	• Used when injection will be performed by a different physician, **or** will be self-administered by the member.
		• Used to report the antigen/antigen preparation service (professional services) when this is the **only** service rendered by the physician.
		• The code selected is based on the specific type of antigen provided:
		  ○ CPT codes 95145-95149 and 95170 are used to report ***stinging insect venoms***.
		  ○ CPT 95144 - used to report antigens, ***other than*** stinging insect.
		  ○ CPT 95165 - used to report multiple dose vials of ***non-venom*** antigens.
		• Considered single dose codes. This means providers must specify the number of doses provided.

The Medicare *National Physician Fee Schedule Relative Value File (NPFSRVF)*[6] indicates CPT codes 95120-95134 have been assigned a Status Indicator of "I," which is defined as "Not valid for Medicare purposes." While Original Medicare doesn't recognize codes 95120-95134, as a Medicare Advantage plan, these codes may be accepted by the Plan.

Providers may use either complete service codes (95120-95134) **OR** a combination of injection (95115, 95117) and antigen (95144-95170) codes. Regardless of what methodology is used, coding must accurately represent the service(s) rendered to the patient **and** be supported by the medical record.

According to correct coding guidelines, component services deny as bundled to the comprehensive services when they are reported together. Therefore, CPT codes 95115-95117 and 95144-95170 deny as bundled when reported with CPT codes 95120-95134.

If no specific CPT or HCPCS code is available, then an unlisted code may be used. Note that unlisted codes may be reviewed for medical necessity, correct coding, and pricing at the claim level. Thus, if an unlisted code is billed related to a non-covered service addressed in this policy, it will be denied as not covered.

CPT 95165

The number of units is not based on the estimated number of injections. Rather, it is based on the number of 1-cc doses in the vial, and Medicare defines a dose as a "1-cc aliquot from a single multidose vial."[5]

Allergen Immunotherapy in the Home

While home allergen immunotherapy should **not** be used as standard care, for patients who receive allergy immunotherapy in the home and when such is supported by the clinical documentation, the supplying physician can bill for the **preparation and provision** of the immunotherapy antigens, but no provider is able to submit claims for the **administration**, since patient is performing the administration on themselves.

Frequency Limits

In the event home immunotherapy has been approved as medically necessary, a reasonable supply of antigens is considered to be not more than a 12-month supply of antigens that has been prepared for a particular patient at any one time.[7,8] The purpose of the reasonable supply limitation is to assure that the antigens retain their potency and effectiveness over the period in which they are to be administered to the patient.[7,8] This guideline serves as a benchmark for antigen services only; it does **not** guarantee that number of units is always going to be considered medically reasonable and necessary for all patients since it is not expected that all patients will have the same medical need. In addition, label instructions for shelf life and storage to optimize potency must also be considered, which may vary by product.

CMS has established medically unlikely edits (MUEs) for many of the services addressed by this medical policy. MUEs represent the maximum number of units for a service that would reasonably be reported for a service by the same provider, for the same member, on the same date of service. However, MUEs do not guarantee that those number of units are always going to be considered medically necessary. It is not expected that all patients will have the same medical need for this maximum number of units at every visit, or even collectively over the course of an entire year.

It should also be noted according to CMS, "An MUE or the lack of an MUE, does not necessarily indicate coverage status of a HCPCS/CPT code. The NCCI program does not establish medical necessity or payment policy." Therefore, the presence of an MUE value does not mean CMS has determined that number of units will be considered medically necessary for all individuals.[9]

All units for a service reported on any claim must be justified, meaning documentation must support the units of services rendered, that the services have been coded correctly, that the services were medically reasonable and necessary for the individual, and that the date of service on the claim aligns with the date the services were rendered to the patient. **The date of service reported on a claim must match the actual date the services were rendered and be supported by the medical record. Units should be billed on the preparation date and not split over subsequent days. Reporting services provided on a single date across multiple claims using different service dates constitutes incorrect billing and is not appropriate.**

CODES*		
Injection Only – Not Including Preparation or Antigen Provision		
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; 2 or more injections
Combined Preparation, Supply and Injection		
	95120	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 injection *(CMS-assigned Status "I" code – See above billing guidelines)*
	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 *(CMS-assigned Status "I" code – See above billing guidelines)*
	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 *(CMS-assigned Status "I" code – See above billing guidelines)*
	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 *(CMS-assigned Status "I" code – See above billing guidelines)*
	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 *(CMS-assigned Status "I" code – See above billing guidelines)*
	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 *(CMS-assigned Status "I" code – See above billing guidelines)*
	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 *(Not allowed by Medicare)*
Antigen and Preparation Only – Not Including Injection		
	95144	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy, single dose vial(s) (specify number of vials)
	95145	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); single stinging insect venom
	95146	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); 2 single stinging insect venoms
	95147	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); 3 single stinging insect venoms
	95148	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); 4 single stinging insect venoms
	95149	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy (specify number of doses); 5 single stinging insect venoms
	95165	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy; single or multiple antigens (specify number of doses)
	95170	Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy; whole body extract of biting insect or other arthropod (specify number of doses)
Miscellaneous		
	95180	Rapid desensitization procedure, each hour (eg, insulin, penicillin, equine serum)
	95199	Unlisted allergy/clinical immunologic service or procedure
HCPCS	None	

***Coding Notes:**

- The code list above is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit. According to Medicare, "presence of a payment amount in the MPFS and the Medicare physician fee schedule database (MPFSDB) does not imply that CMS has determined that the service may be covered by Medicare." The issuance of a CPT or HCPCS code or the provision of a payment or fee amount by Medicare does **not** make a procedure medically reasonable or necessary or a covered benefit by Medicare. *(Medicare Claims Processing Manual, Chapter 23 - Fee Schedule Administration and Coding Requirements, §30 - Services Paid Under the Medicare Physician's Fee Schedule, A. Physician's Services)*
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- **See the non-covered and prior authorization lists on the Company Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website for additional information.**
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as "medically unlikely edits" (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

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POLICY REVISION HISTORY

DATE	REVISION SUMMARY
1/2026	New Medicare Advantage medical policy
11/2026	Annual review; no changes