

Allergy Immunotherapy Working Group Consensus Statement

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Among available treatments for allergic rhinitis, only allergy immunotherapy has the potential to alter the course of allergic disease. Unfortunately, there are significant barriers to the optimal use of allergy immunotherapy delivered subcutaneously (SCIT). In anticipation of the introduction of allergy immunotherapy delivered via the sublingual-oral route (SLIT) in the United States, a panel of experts in allergy immunotherapy were asked to develop consensus statements that could be used to guide health plans and payers as they consider coverage and reimbursement determinations for this new treatment. The consensus statements compiled by the Sublingual Allergy Immunotherapy Working Group include a recommendation that allergy immunotherapy be prepared and administered by specialists who collaborate with primary care physicians to promote appropriate referral of patients. Although plans and payers should be aware of the findings of recent reviews of SLIT, they should evaluate the efficacy and safety of SLIT products on an individual basis. Because of its similarity to SCIT, SLIT should be considered as a medical benefit with its own CPT code, advised the expert panel.

More than 50 million people in the United States are affected by allergies.¹ Allergic rhinitis (AR) is the most common allergic disease, with as many as 40% of US children and 20% of adults who have symptoms.² Symptoms of AR (sneezing; runny, stuffy or itchy nose; watery eyes; and cough) can be extremely debilitating, and most sufferers use both prescription and over-the-counter medications for symptom relief.³ The morbidity associated with allergic diseases in the United States in 2004 contributed to approximately 27 million office visits (16.7 million for AR and 10.4 million for asthma),⁴ 14.5 million lost workdays,⁴ 14 million

lost school days,⁴ and \$18 billion in health care expenditures (2000 data).¹

In the United States, currently available treatments for allergic disease include allergen avoidance, pharmacotherapy, and subcutaneous allergen immunotherapy (SCIT).⁵ Although pharmacotherapy temporarily relieves allergy symptoms, use of SCIT can alter the course of allergic disease, allowing for long-term benefit even after discontinuation of treatment, a reduction in risk of developing new-onset asthma, and a lower likelihood of developing new allergies. Because SCIT generally requires weekly to monthly visits to a physician's office over a period of 3 to 5

years, there are substantial barriers to access. It is therefore not surprising that currently only about 5% (3 to 5 million) of persons with AR and/or asthma in the United States receive SCIT.^{6,7}

In a number of European countries, allergen immunotherapy is routinely self-administered by patients at home via the sublingual-oral route (SLIT). Because clinical trials of SLIT are under way in the United States, a Sublingual Allergy Immunotherapy Working Group (SLIT Working Group) was recently convened to provide recommendations to plans and payers as they consider coverage and reimbursement determinations for SLIT. The SLIT Working Group members include a medical director (AL) and pharmacy directors (GE, DB) of health plans, allergists (LC, SA, authors of the related article, "Allergy Immunotherapy for Allergic Rhinitis and Asthma"), a specialist in coverage and reimbursement issues (MB), and a health economist (CH).

WORKING GROUP

CONSENSUS STATEMENT 1:

In contrast to pharmacotherapy, which only temporarily relieves allergy symptoms, allergen immunotherapy has the potential to alter the course of allergic disease, thereby reducing the need for long-term treatment, the progression of allergic rhinitis to asthma, and the development of new allergies.

Although allergy medications may temporarily ease symptoms of

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AR, allergen immunotherapy (IT) has the potential to modify the course of disease. Evidence indicates that IT can lead to long-lasting clinical remission following an appropriate course of treatment,⁸⁻¹² reduction of the risk for the future development of asthma in patients with AR,^{13,14} and prevention of the development of new allergen sensitivities in monosensitized patients.¹⁵⁻¹⁸ (See “Clinical Efficacy and Safety of Allergy Immunotherapy” for a detailed summary of research supporting the use of allergen IT as a disease-modifying treatment.)

**WORKING GROUP
CONSENSUS STATEMENT 2:
The effective and safe
treatment of patients with
subcutaneous immunotherapy
requires particular expertise
in a variety of areas including
evaluation of appropriate
patients, allergy testing, allergen
preparation and administration,
monitoring of efficacy and
safety, and documentation
and record keeping. This
expertise typically resides
in the domain of the allergist
and otolaryngologist.**

Subcutaneous IT

The practice of SCIT requires expertise in evaluating patients for treatment and conducting allergy testing, allergen preparation and IT administration, monitoring of efficacy and safety, and documentation and record keeping. The SLIT Working Group noted that because of the complexity of SCIT and the specific expertise required, allergists or otolaryngologists (ear, nose, and throat specialists [ENTs]) should be responsible for the delivery of SCIT. Below, we summarize the main activities involved with the delivery of SCIT. For more detailed information, see Cox

and associates.⁵

Patient evaluation. Before administering SCIT, the allergist or ENT must evaluate whether a patient meets the core clinical indications for SCIT: symptoms of AR or asthma after exposure to aeroallergens and demonstrable evidence of clinically relevant specific IgE antibodies.⁵ Because no single diagnostic test can confirm AR, evaluation includes a physical examination, clinical history, assessment of the patient’s environment, and allergy testing.¹⁹

Allergy testing. A definitive diagnosis of AR or allergic asthma depends on the results of allergy testing (skin or in vitro tests for specific IgE antibodies).⁵ The skin prick/puncture test (also referred to as intradermal skin test) is generally the preferred method of testing for specific IgE antibodies, although in vitro testing for specific IgE antibodies is useful under certain circumstances.⁵ Before conducting the skin prick/puncture test, the patient must stop treatment with first-generation antihistamines at least 2 to 3 days before testing and second-generation drugs at least 3 to 10 days before testing.²⁰ In addition, patients should discontinue use of other medications with antihistaminic properties (such as anticholinergics and H₂-receptor antagonists).²⁰

To conduct the test, a drop of diluted antigen is placed on the skin, usually on the arm or back. The top-most layer of skin is lightly broken by pricking, puncturing, or scratching, allowing the extract to seep into the skin. A positive control (histamine) and negative control (diluent) as well as expertise are essential for proper interpretation of test results. Approximately 15 minutes after applying the antigen, the test site is examined for wheals surrounded by an inflamed red area (“flame”). By convention, a reaction is deemed posi-

tive when a flame appears and the wheal measures at least 3 mm greater in diameter than the negative-control response.²¹ A skin test panel typically tests for sensitivity to about 40 aeroallergens.²⁰

A blood test can be used to measure the specific level of IgE (specific IgE) that is produced when the body responds to allergens. This test is highly specific for diagnosing allergy (ie, useful for determining patients who *are not* allergic) but is less sensitive than skin testing (ie, not as useful for determining patients who *are* allergic).²⁰ IgE testing in lieu of skin prick/puncture testing is appropriate when histamine skin test controls are negative; the patient has a chronic skin condition that obscures skin test reading; the patient cannot discontinue medications that suppress skin test response; or there is concern regarding anaphylaxis triggered by the skin test.²⁰

Allergen preparation. Physicians select the appropriate patient-specific allergen(s) from more than 400 commercially available extracts. These extracts are purchased in high concentrations from allergen manufacturers and must be diluted according to each patient’s individual needs. Patients who are monosensitized will receive IT with only one allergen. Those with multiple sensitivities (the majority of patients) may receive IT as a mix of multiple allergens in one or more injections.

There are several important considerations when mixing allergens. First, the cross reactivity of allergens must be considered: when one allergen elicits the same immunologic response as another, it is not necessary or advisable to include both in the same mixture.⁵ Second, to avoid allergen interactions, extracts with higher proteolytic enzyme activity should not be mixed with those that have lower proteolytic enzyme activity.⁵ For example, dust mite allergen

should not be mixed with grass or tree pollen allergen. Third, as multiple allergens are mixed, the concentration of each is decreased and appropriate corrections should be made to ensure that the optimal dose of each constituent is included in the mixture.⁵ Fourth, diluted ITs are less stable than highly concentrated ITs with loss of potency occurring within days at temperatures higher than 4°C.⁵ Given these complex considerations, the Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI), recommends that IT extract preparation be performed by persons experienced and trained in handling allergenic products.⁵

IT administration. Before the administration of IT, the patient should be questioned about increased manifestations of asthma or allergy symptoms, β -blocker use, change in health status (including pregnancy and recent infections), or an adverse reaction to a previous injection (including delayed large local reactions persisting through the next day). Persons with significant systemic illness generally should not receive an injection.⁵ According to the Joint Task Force, the preferred location for administration of SCIT is the office of the physician who prepared the IT extract.⁵ SCIT is administered using a 1-mL syringe with a 26- or 27-gauge half-inch non-removable needle. The injection is usually given in the posterior of the middle third of the upper arm. If blood is aspirated before the injection, IT should not be administered and another dose should be drawn into a new syringe and administered at a different site. The plunger should be depressed at a rate that does not result in wheal formation or excessive pain. Following injection, mild pressure

is applied to the injection site for 1 minute.⁵

Dose and schedule. IT is administered in 2 phases, commonly referred to as the buildup (also the “up-dosing,” “induction,” or “dose-increase”) phase and the maintenance phase.⁵ In general, the starting dose in the buildup phase is 1000-fold to 10,000-fold less than in the maintenance phase. During the buildup phase, gradually increasing doses are administered until the maintenance dose (the dose that provides therapeutic efficacy without significant adverse local or systemic reactions) is reached. Typically, a single-dose increase is administered on each visit, and visit frequency can range from 1 to 3 times weekly over 3 to 6 months. Less conventional, accelerated buildup schedules include “rush” IT (incremental doses are administered at intervals varying between 15 and 60 minutes over 1 to 3 days) or “cluster” IT (2 or more injections are administered per visit on nonconsecutive days 1 to 2 times per week). These accelerated schedules offer the advantage of more rapidly reaching the maintenance dose, but may increase the risk of systemic reaction among some patients.⁵

The maintenance dose is the dose that provides therapeutic efficacy without significant adverse local or systemic reactions. Once patients reach the maintenance phase, the interval between injections often can be progressively increased as tolerated up to about 4 weeks for persons with AR. Patients receiving maintenance IT generally should have follow-up visits at least every 6 to 12 months, during which allergy symptoms and medication use are reassessed, medical history is updated, and clinical response to IT, adverse reactions, and adherence are evaluated and the IT schedule and dose are adjusted as required.⁵

Duration of treatment. The decision to discontinue IT should be individualized, taking into account severity of the patient’s illness at treatment initiation, the treatment benefit sustained, frequency or severity of systemic reactions to IT, the inconvenience of IT borne by the patient, and the potential effect of a clinical relapse on the patient.⁵ Although the duration of IT efficacy for AR has not been as extensively studied, some research suggests that a 3- to 5-year treatment duration is sufficient.⁵ There are no specific markers that will predict who will remain in clinical remission after discontinuing effective IT.

Monitoring of efficacy and safety. Whether IT is effective can be determined by measuring objective and subjective parameters. Non-quantitative skin testing or in vitro IgE antibody testing of patients during IT is not recommended because it has not been demonstrated that skin test reactivity (to a single dilution) or specific IgE antibody levels correlate closely with a patient’s clinical response.⁵ Instead, allergists commonly rely on subjective assessments, such as a patient’s report that he or she is feeling better during a season previously causing symptoms, which can be influenced by patient and physician expectations.⁵ A more objective means for determining efficacy as validated in controlled clinical studies is the use of clinical symptom scores and the amount of medication required to control symptoms and maintain peak flow rates or pulmonary function tests within acceptable limits. Sequential measurement of disease-specific quality of life also might be helpful.⁵

The most common adverse event following SCIT is an injection site reaction (eg, pain, swelling, redness). Large local reactions associated with allergen IT are fairly com-

mon, with a frequency ranging from 26% to 86% of injections.⁵ Although there is a low risk of severe systemic reactions with appropriately administered allergen IT, life-threatening and fatal reactions do occur. Per injection rates of systemic reactions (eg, pruritus, rhinitis, urticaria, angioedema, wheezing, bronchospasm, and anaphylaxis with hypotension) to SCIT typically vary from 0.03% to 0.6%.^{22,23} Severe systemic adverse reactions to SCIT are rare, with one near-fatal reaction occurring every 1 million injections²⁴ and one fatality every 2.5 million injections.²⁵

An assessment of the patient's health status should be made before administration of the allergen injection to determine whether there were any recent health changes that might require modifying or withholding a patient's IT treatment.⁵ Risk factors for severe IT reactions include symptomatic asthma and injections administered during periods of symptom exacerbation. Before the administration of the allergen injection, the patient should be evaluated for the presence of asthma or allergy symptom exacerbation. The physician might also consider an objective measure of airway function (eg, peak flow) for the asthmatic patient before allergen injections. Because most systemic reactions that result from allergen IT occur within 30 minutes, patients should remain in the physician's office at least 30 minutes after an injection. Allergen IT should be administered in a setting where procedures are in place that can reduce the risk of anaphylaxis and where the prompt recognition and treatment of anaphylaxis is ensured.⁵

Documentation and record keeping. Careful documentation must be employed for the welfare of the patient. Documentation includes informed consent for IT; an IT pre-

scription form (documents the name of each allergen and diluent included in the mixture, the concentration and type of manufacturer's extract, name of extract manufacturer, lot number, and expiration date to ensure precise duplication); IT extract contents (labeling of each patient-specific vial to allow easy identification); and administration procedures (detailed documentation of IT administration procedures and patient reactions to reduce errors in subsequent administration).⁵ Sample forms can be found online at www.aaaai.org.

WORKING GROUP

CONSENSUS STATEMENT 3:

There are substantial barriers to allergy immunotherapy in the United States, which may be ameliorated by the introduction of sublingual-oral immunotherapy and improved communication between allergists/otolaryngologists and primary care physicians. Allergists and otolaryngologists must assume a leadership role in collaborating with primary care physicians to educate them regarding the benefits and risks of immunotherapy and appropriate referral of patients with allergic rhinitis to allergy or otolaryngology specialists.

In the United States, patients face barriers to receiving a complete course of SCIT, including lack of access to treatment and poor coordination of care. Currently, SCIT is received by 5% or fewer patients with AR and/or asthma in the United States.^{6,7} As previously noted, SCIT typically requires weekly to monthly visits to the physician's office over a period of 3 to 5 years; this time-consuming and demanding treatment regimen is challenging for patients, requiring considerable commitment

over a prolonged period. Consequently, rates of treatment persistence are low and patients may be at risk for potential medical consequences of AR, including increased risk of developing asthma and protracted use of pharmacotherapy for symptomatic relief. Studies have reported that most patients fail to complete the desired course of treatment.^{6,7,26-30} In addition, 21% of persons report being fearful of the sight of blood or having injections,³¹ which may prevent patients from seeking SCIT.

The SLIT Working Group suggested that primary care physicians may not be sufficiently knowledgeable about when to refer patients for IT. In a survey, the most commonly endorsed reason for referring allergic patients to a specialist was patient request rather than a specific clinical indication.³² Only 38% of generalists reported that they "always" referred asthma patients to allergists for allergen IT; 14% "occasionally" and 32% "rarely" or "never" referred these patients to allergists.³² Even patients with severe allergy symptoms often were not referred to specialists: 40% of physicians reported that they "occasionally" or "rarely" referred patients with uncontrolled asthma to an allergist and 80% of patients who received more than 2 courses of systemic corticosteroids in the past 12 months were only "occasionally," "rarely," or "never" referred.³² There is some indication that educating generalists about allergy may improve referral patterns. A survey of internal medicine and pediatric physicians and residents revealed that those who had not received specialized training in allergy/immunology (75% of the sample) were 66% less likely to have referred a patient to an allergist than physicians who received training in allergy/immunology.³³

WORKING GROUP

CONSENSUS STATEMENT 4:

Plans and other health care payers should be aware of the technology reviews that have been conducted to date regarding sublingual immunotherapy. However, because dosage, preparation, and administration of sublingual immunotherapy extracts to be used in the United States will substantially vary by manufacturer, when considering the safety and efficacy of sublingual immunotherapy, payers should individually evaluate the safety and efficacy of each manufacturer's products independent of other manufacturers' products.

Sublingual IT

Several recent reviews examining clinical evidence for the safety and efficacy of SLIT have been completed.^{5,34-37} All of these noted that there are few head-to-head comparisons of SCIT versus SLIT. The findings of these reviews, as well as case reports of anaphylaxis associated with SLIT and European postmarketing data, are summarized below. Although systematic literature reviews and meta-analyses are useful in establishing the overall efficacy and safety of SLIT, decisions regarding the value of each SLIT product must be made individually as the studies included in these reviews varied considerably by manufacturer.

The Joint Task Force on Practice Parameters. A Joint Task Force of the AAAAI and the ACAAI developed the allergen IT practice parameters, which were updated in 2007.⁵ These practice guidelines noted that SLIT has been found to be effective in many cases of adults and children with AR and asthma, but a consistent relationship among dose, duration of treatment, and clinical efficacy has not been established. Based on this limitation and the lack of FDA-approved formulations for

SLIT, the Joint Task Force concluded that this treatment "should be considered investigational at this time." Given this conclusion, the endorsement of SLIT by the medical community will be critical to its use. Because the next update of the practice parameters will not be published until 2009, an interim summary statement was prepared by an expert panel to summarize the role and supporting evidence for SLIT.

SLIT Task Force. In 2006, the SLIT Task Force reviewed 47 randomized controlled trials that evaluated the clinical efficacy of SLIT and 3 studies that compared the efficacy of SLIT with SCIT.³⁴ Although most SLIT studies demonstrated some evidence of clinical efficacy, approximately one third of selected trials failed to show a significant reduction in either symptom or medication scores. Moreover, a consistent relationship among allergen dose, treatment duration, and clinical efficacy could not be established. With regard to safety, the majority of adverse reactions associated with SLIT were local reactions (oral mucosal pruritus, burning, and lip swelling); uncommon adverse reactions included abdominal complaints, urticaria, and asthma. Few studies reported use of SLIT in patients with severe asthma, and no studies examining multiple-allergen SLIT met inclusion criteria. Because of the paucity of available data, investigators concluded that use in young children requires further study.

Several studies assessed adherence to SLIT. In a multicenter observational study, 86 persons treated with a monomeric allergoid for AR and/or asthma reported consuming 97% of SLIT tablets after 1 year of treatment for dust mite allergy and a mean 18 weeks of treatment for pollen allergy.³⁸ In a 4-year randomized controlled study of 511 patients (319 of whom received SLIT), adher-

ence over 3 years of treatment was assessed by measuring the remaining volume in returned SLIT vials.¹⁷ Seventy-two percent of patients showed excellent adherence (greater than 80% of SLIT consumed), 18% showed good adherence (60% to 80% of SLIT consumed), and 10% showed poor adherence (less than 60% of SLIT consumed). In an open-label study of children who received SCIT (n = 1886), SLIT (n = 806), or local nasal IT (n = 82) for at least 1 year, 10.9% of SCIT patients versus 21.5% of SLIT patients ($P < .0005$) stopped treatment without authorization from the prescribing physician.³⁹ In a study of 433 adult and adolescent patients with AR and/or asthma, adherence to SLIT assessed by self-reported pill count was greater than 90% in 76.3% of patients at 3 months and in 74.8% of patients at 6 months.⁴⁰

Cochrane SLIT reviews. In 2003, the Cochrane Collaboration reviewed 22 randomized controlled trials of SLIT, involving 979 patients with AR, and found a significant reduction in both symptoms (standardized mean difference [SMD] -0.42; 95% confidence interval [CI], -0.69 to -0.15; $P = .002$) and medication requirements (SMD, -0.43; 95% CI, -0.63 to -0.23; $P = .00003$) following SLIT.³⁵ A subanalysis of studies of children had insufficient power to determine the effect of SLIT in this subgroup. The authors concluded that "SLIT is a safe treatment which significantly reduces symptoms and medication requirements in AR. The size of this benefit compared with that of other available therapies, particularly injection immunotherapy, is not clear, having been assessed directly in very few studies. Further research is required concentrating on optimizing allergen dosage and patient selection."³⁵

In 2006, the Cochrane Collaboration published a review of 25 ran-

domized controlled studies of SLIT in 1706 patients with allergic asthma.³⁶ A combined analysis of change in asthma symptoms, need for symptom relief medication, respiratory function test, and lung hyper-reactivity revealed a significant improvement across studies (relative risk, 0.48; 95% CI, 0.40 to 0.57). Results indicated that 3.7 patients must be treated with SLIT to avoid leaving one patient unimproved or worse. In studies reporting asthma symptoms and medications combined with other allergic symptoms (eg, rhinitis, conjunctivitis) and medications, there was a significant reduction of symptoms (SMD, -1.18; 95% CI, -1.93 to -0.43) and medication use (SMD, -0.82; 95% CI, -1.25 to -0.39) following SLIT. Respiratory function improved following SLIT as indicated by a greater percentage of patients experiencing an improvement in forced expiratory volume (FEV) in 1 second (SMD, 1.48; 95% CI, 0.13 to 2.82) and speed (FEV_{25%-75%}; SMD, 1.06; 95% CI, 0.40 to 1.71). The authors concluded that although the evidence was “not very strong, the results from analyzing all the parameters together (asthmatic symptoms, respiratory function tests, relief medication, and lung hyperreactivity) suggest that SLIT reduces asthma expression.”

SLIT TEC assessment. A 2003 Technology Evaluation Center (TEC) assessment reviewed 21 randomized, placebo-controlled trials of SLIT involving 1116 patients.³⁷ The preponderance of evidence suggested that when prepared in potencies similar to those used in available studies and compared with placebo, use of SLIT significantly reduced one or more symptoms or symptom groups in persons with pollen or dust mite allergies. However, it could not be determined whether the reduction was sufficient to result in a clinically meaningful benefit to patients. Evi-

dence was conflicting about whether SLIT reduced medication use. Few patients experienced adverse effects from SLIT, and such effects were nearly always mild, brief, and local. Systemic adverse effects (non-life-threatening) were reported in only 1 trial. Authors concluded that “whether SLIT improves health outcomes when compared with injection allergen-specific immunotherapy has not yet been demonstrated in the investigational setting. It is uncertain whether FDA-licensed allergen preparations manufactured for allergy testing and injection ASIT are suitable for sublingual administration. Based on the above, use of SLIT for patients with allergies does not meet the TEC criteria.”

Life-threatening reactions to SLIT. The reviews summarized above noted the absence of SLIT-induced life-threatening reactions and anaphylaxis. However, since these reports were published, 3 cases of anaphylaxis (no fatalities) have been reported: one in a patient receiving rush SLIT for latex allergy,⁴¹ a second in a patient receiving a mixture of 6 standardized and unstandardized SLIT extracts,⁴² and a third in an 11-year-old girl with AR and asthma who received high-dose multi-pollen and house-dust-mite SLIT.⁴³

Postmarketing data. Several postmarketing surveillance studies have evaluated the long-term safety of SLIT in adults and children.⁴⁴⁻⁴⁷ A study of 268 children who received SLIT for 3 months to 7 years (mean, 36 months) reported 8 adverse effects (7 mild and 1 controlled with treatment) in 3% of patients and 0.083 per 1000 doses; the clinical outcome was judged good or excellent in 80% of patients.⁴⁴ In a post-marketing safety study of 198 SLIT patients aged 15 to 51 years, 17 adverse effects corresponding to 7.5% of patients and 0.52 per 1000 doses were reported over 3 years.⁴⁵ Medical in-

tervention was needed in just 6 patients over a 3-year period. A 1-year postmarketing surveillance study of 159 children and adults receiving SLIT revealed that medication requirements were significantly reduced compared with the year before treatment ($P = .023$) and 6.3% experienced adverse events (none serious or severe).⁴⁶ Finally, in a post-marketing safety study of 126 children aged 5 years or younger who received SLIT, 9 adverse effects (2 local, 7 systemic) were reported in 7 children, corresponding to 5.6% of patients and 0.2% of 1000 doses administered.⁴⁷

Differences across SLIT studies.

The SLIT Working Group noted a wide variation in treatments in studies of SLIT, including different manufacturers, dosage (strength and purity of extract), extract preparation (single or mixed extracts), and administration (drops held under tongue or dissolvable oral tablets). Given that the dosage, preparation, and administration of SLIT extracts to be used in the United States will vary by manufacturer, the SLIT Working Group recommends that payers evaluate each manufacturer’s clinical trial results of safety and efficacy.

WORKING GROUP

CONSENSUS STATEMENT 5:
Given that treatment of sublingual immunotherapy and subcutaneous immunotherapy only differ in the route of administration, and sublingual immunotherapy requires the same physician expertise in the patient-specific, customized selection and mixing of allergen extracts, the working group recommends that sublingual immunotherapy, like subcutaneous immunotherapy, be considered as a procedure under the medical benefit. It is further recommended that a separate current procedural terminology or CPT be assigned to facilitate internal tracking of sublingual and subcutaneous procedures.

As noted above, SLIT differs from SCIT only in the route of administration, and requires physician expertise in the patient-specific, customized selection, and mixing of allergen extracts. The SLIT Working Group recommends that SLIT be considered as a procedure under the medical benefit and that a separate CPT code be requested so as to allow payers to individually track SLIT and SCIT utilization. Based on the more than 600 commercially available allergen extracts and need for each patient's allergen mix to be individualized, the SLIT Working Group recognizes that it would be impractical for allergen extracts to be provided to the physician from any source other than the manufacturer. The SLIT Working Group also notes that because SLIT is administered at home with no direct medical supervision, prescribing physicians must provide patients with specific instructions on how to manage adverse reactions, unplanned treatment interruptions, situations in which the dose should be withheld, and dosing adjustments for any or all of these situations. In addition to assessing the patient's likely adherence to SLIT, physicians should consider the patient's ability to follow these instructions before prescribing this treatment.

Conclusion

AR is a highly prevalent chronic condition associated with significant morbidity if not adequately controlled. Both pharmacotherapy and IT are effective treatments for AR (and can be supplemented by allergen avoidance measures), but IT has the potential to change the course of disease such that patients may eventually discontinue treatment without relapse, avoid progression from AR to asthma, and reduce the likelihood of developing new allergies. Currently, SCIT is used by only a small

minority of patients in the United States because of barriers to treatment access, including the need for frequent office visits to receive treatment, the painful and intrusive nature of treatment, and failure by generalists to refer patients to allergists and ENTs. Because of the complexity involved in prescribing IT (ie, evaluation of patients, selection and preparation of allergen extracts, administration of IT, and patient monitoring), this treatment is most appropriately offered by allergists and ENTs. To increase referrals of appropriate patients for IT, these specialists must educate and collaborate with generalists.

Because SLIT can be self-administered at home, is painless, and does not involve injections, its impending introduction in the United States promises to improve patient adherence to treatment and ameliorate some barriers to access. Payers should familiarize themselves with current technology reviews of SLIT and also should evaluate the efficacy and safety of individual SLIT products, which may vary by manufacturer. Because SLIT is very similar to SCIT up to the point of administration and requires physician expertise in the patient-specific, customized selection, and mixing of allergen extracts, SLIT, like SCIT, should be considered a procedure under the medical benefit. ■

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