Sublingual Immunotherapy for Seasonal Allergies

The FDA has recently approved 3 allergen extracts for administration under the tongue (sublingual immunotherapy or SLIT) for seasonal allergies or allergic rhinitis that has been confirmed by positive skin test or pollen specific IgE antibody blood test [(Oralair, a mixture of 5 grass pollens, indicated for patients 5 through 65 with spring grass allergies; Ragwitek (ragweed pollen) indicated for patients 18 through 65 with fall ragweed allergies, and Grastek (timothy pollen) indicated for patients 5 through 65 who are allergic to grass pollen in the spring.] Sublingual allergy tablets have been used for treatment for seasonal allergies for many years in Europe. For the 3 recently approved products, studies have shown that treatment with sublingual tablets started 3 to 4 months before the pollen season and taken daily throughout the season can reduce symptom scores and other medication use by 20-40%. In one long-term 5-year study with Grastek given for 3 consecutive years, symptom relief was sustained after sublingual immunotherapy was stopped after 1 year but symptoms returned following the second year off of sublingual immunotherapy. A long-term study using Oralair for 3 consecutive grass pollen seasons and then discontinuing therapy did not demonstrate continued efficacy 1 or 2 years after discontinuation of Oralair.

For over 100 years, subcutaneous allergen-specific immunotherapy ("allergy shots" or "allergy injections" or SCIT) for allergic rhinitis has been a significant treatment remedy for patients who have upper respiratory allergies of the nose, sinuses and eyes, asthma, bee sting allergy, and in some cases of atopic dermatitis, allergic fungal sinusitis and allergic candida vaginitis. Allergy injections over the years have proven to be efficacious in up to 85% of treated patients who are compliant with therapy and those injection benefits may be sustained for years after injections are discontinued. Complications from allergy injections relate to local or systemic adverse reactions including rare anaphylactic reactions requiring patients to remain in the office for 30 minutes after injection and to personally carry an epinephrine autoinjector pen on shot days. In our experience, the incidence of severe systemic reactions is very low and it is unlikely that someone actually uses his/her epinephrine injection outside of our office. The most recent published study of reactions from allergy shots from 2008 – 2012 has shown 1 fatality among over 23 million injection visits, the last occurring in 2009. Nonfatal systemic reactions occur 0.1% of the time.

ADVERSE TO SLIT:

Local reactions to SLIT are common after the first dose as well as sometimes after subsequent doses with all 3 allergen extracts. Itchy mouth and throat irritation are common in 25% of patients. Other local symptoms may include tongue itching, swelling, and mouth swelling. Our practice reported the first case of anaphylaxis experienced with sublingual immunotherapy in the United States and the risks of anaphylaxis continues with oral sublingual immunotherapy such that the FDA requires that auto-injectable epinephrine always be available. (Parenthetically, although we ask patients on allergy injections to carry an epinephrine auto-injectable on their person only on the day of shots for safety concerns, the FDA does not mandate this.) SLIT extracts have not been studied in patients with unstable or severe asthma and are contraindicated in such patients having exacerbations and not been sufficiently studied in mild to moderate asthmatic patients who require daily medications. Oralair and Grastek are classified as category B drugs (no evidence of risk in animals but no human studies in pregnant women are available) and Ragwitek is a category C drug (animal studies have shown adverse reactions on the fetus; risk cannot be ruled out for use during pregnancy since no human studies in pregnant women are available). Neither sublingual nor subcutaneous immunotherapy should be initiated during pregnancy.

DRUG INTERACTIONS WITH SLIT:

In regard to all 3 allergy extracts, sublingual tablets should be used with caution for patients who are taking the following medications: beta-adrenergic blockers (i.e. Tenormin, metoprolol, propanol, Lopressor, Inderal); alpha-adrenergic blockers (i.e. Prazosin, Minipress, Hytrin, Cardura, terazosin); ergot alkaloid (tricyclic) anti-depressants (i.e. amitriptyline, doxepin, nortriptyline, Pamelor); monoamine oxidase inhibitors (i.e. Marplan, isocarboxazid, Nardil, phenelzine, Parnate, tranylcypromine); and thyroid medication like levothyroxine. These drugs can either potentiate or inhibit the effect of epinephrine needed to treat an allergic reaction.

DOSING ADMINISTRATION OF SLIT:

Sublingual immunotherapy should begin at least 12 weeks (16 weeks for Oralair) before the beginning of the allergy season and should be continued for the duration of the season. This tablet should be stored in a dry place at room temperature in the original package. Take the tablet from the booster pak removing it carefully with dry hands, place the tablet under the middle of the tongue, allow to remain there until it is completely dissolved, and not swallow for at least 1 minute and do not take water or food for the following 5 minutes. Wash hands after use.

WHAT ARE THE DIFFERENCES BETWEEN SUBLINGUAL IMMUNOTHERAPY (ORAL TABLETS) AND TRADITIONAL SUBCUTANEOUS IMMUNOTHERAPY (ALLERGY INJECTIONS)?

Sublingual immunotherapy is specific for only grass or ragweed allergy. If someone is sensitized to other important allergens, their other allergies would not be treated (i.e. tree pollen, mold, cat & dog dander). So for the individual who is polysensitized with multiple allergic sensitivities, sublingual immunotherapy may require multiple tablets that still may not cover the full spectrum of their allergic sensitivities. In regard to adherence to treatment, studies have shown that although it is more convenient to take sublingual immunotherapy at home, this convenience is not associated with more compliance compared to receiving office based injection therapy. Studies have shown that 55-85% of patients abandon SLIT before completing the recommended course of therapy. The safety of sublingual immunotherapy may be marginally better regarding systemic reactions; however, there is a much larger reaction rate locally with sublingual immunotherapy (25%). Furthermore, patients are still subject to the risk of anaphylactic reactions and therefore require epinephrine on their person at all times compared to the patients on injection therapy who require epinephrine availability only on the day of their injections. Subcutaneous immunotherapy is one of the recognized treatments for all stages of asthma whether intermittent or persistent-mild, moderate or severe. Sublingual immunotherapy, however, is contraindicated in patients with severe or uncontrolled asthma of any severity, and has not been studied in patients who have moderate to severe asthma on daily controller therapy. The completion of a 3-5 year course of subcutaneous immunotherapy has been shown to provide sustained symptom relief for years beyond treatment compared to 3 years of SLIT treatment where return of symptoms starts 1 year after discontinuation. SCIT has been shown to improve other forms of respiratory disease like sinusitis, eustachian tube dysfunction, allergic fungal sinusitis, allergic candida vaginitis and some cases of atopic dermatitis. Improvement of similar disease states outside of upper respiratory allergies of the nose, eyes, and asthma for SLIT has not been confirmed. Comparing the cost of SLIT vs SCIT over a 3 year period of continuous treatment, allergy treatment with grass extracts given as SLIT was 2 – 4 times more expensive than grass extracts given as SCIT treatment.

Because of the potential for anaphylaxis and throat swelling, the first dose of SLIT should be administered in the physician's office. The patient should remain for at least 30 minutes after the first dose. Subsequent doses can be administered at home but the patient must always have an auto-injectable epinephrine available. Prior skin testing to excipients in SLIT like mannitol and gelatin may be performed at the time of initial dosing to rule out a potential reaction to one of the inactive ingredients.

SLIT extracts are not medications given for immediate relief of symptoms of seasonal allergy. They should not be given to individuals having a seasonal exacerbation of asthma or having severe allergic reactions, having difficulty breathing, swallowing disorders, individuals diagnosed with eosinophilic esophagitis, individuals allergic to any of its excipients, individuals who had recent mouth surgery procedures such as tooth removal or individuals with acute mouth infection, ulcer, or cuts in mouth or throat or have a history of recurrent aphthous ulcers.