IMMUNOTHERAPY I (SUBLINGUAL / SLIT)

GENERAL INFORMATION ABOUT SUBLINGUAL IMMUNOTHERAPY (SLIT)

Sublingual immunotherapy (SLIT / Allergy Drops) is the name given to allergy vaccines that are administered orally. The vaccine, rather than being administered by an injection, is administered as oral allergy drops that are placed under the tongue ("sublingual"), held there for a short period of time, and then swallowed. Some medical authors call this route of administration the "sublingual-swallow mode" of immunotherapy. Sublingual immunotherapy is a unique immunotherapy modality that combines safety and convenience with excellent benefit. Popular in Europe for many years, sublingual immunotherapy is now being introduced into the United States and is gaining in popularity.

Advantages of sublingual immunotherapy include a safety profile that allows the treatment to be administered at home, saving the patient travel time and expense, as well as clinic visits. The lack of injections makes sublingual immunotherapy easier for children (and many adults) to tolerate the treatment. And, it is an ideal treatment for patients who travel frequently or who live a long distance from the allergist's office.

The primary disadvantages of sublingual immunotherapy center around two facts: (1) Although SLIT accounts for more than half of all allergen immunotherapy administered in Europe, it is currently considered "investigational" and "off-label" in the United States. Even though the allergen extracts that are used for subcutaneous (injection) immunotherapy (SCIT) and for sublingual immunotherapy (SLIT) are the same and are licensed for use in the United States for SCIT, the FDA has not yet approved the extracts for SLIT, and there is no current CPT billing code for the SLIT treatments. (2) Because of this "off-label" status for sublingual immunotherapy, insurance companies are not currently reimbursing this form of treatment, making the expense "out-of-pocket." Nevertheless, the overall cost of SLIT is significantly less than a lifetime of allergy medications and office visits for allergy-related illnesses and is comparable to the overall cost of receiving subcutaneous (injection) immunotherapy. We anticipate that this insurance reimbursement issue will improve in coming years, as the FDA is currently looking at several oral allergy vaccine products for potential approval.

Patients often ask if all allergy drop procedures are equal, and the answer is a definitive NO! There are many clinics in the U.S. that are offering oral immunotherapy as prescribed by "non-allergists" that are essentially placebo treatments. Our clinic offers targeted high-dose oral immunotherapy treatments, designed in accordance with well-established European protocols that have been shown to offer excellent benefit. The current studies still emphasize that injection immunotherapy may be the most efficacious for some types of allergies (e.g., venoms), but oral immunotherapy offers substantial benefits without many of the problems associated with injection immunotherapy and is rapidly becoming the preferential treatment for airborne allergies (pollen, mold, dust mites, and animal danders).

Once you have completed your allergy testing, Dr. Park will discuss the various immunotherapy protocols with you and help you decide which treatment procedure will best meet your needs.

Questions? **Please call us at** 269-415-7007.

IMMUNOTHERAPY II (SUBLINGUAL / SLIT)

QUESTIONS (*AND ANSWERS*) CONCERNING SUBLINGUAL IMMUNOTHERAPY (SLIT)

You or a family member may be starting treatment with oral allergy drops, also known as sublingual immunotherapy (SLIT). Recently, we have found that many people have similar questions concerning this treatment option, and this hand-out is designed to help answer many of those questions. Please feel free to speak with one of our staff members if your questions are not satisfactorily answered, or if new questions or problems arise. By working together on your treatment plan, we will have the best opportunity for good control of your allergy symptoms.

Why allergen immunotherapy?	Allergen immunotherapy is a type of preventative treatment for an allergic response to allergens such as pollen, mold, dust mites, and animal danders. *Allergen immunotherapy treats the underlying cause of the allergic reaction*, while medications such as antihistamines and nasal sprays only treat the symptoms. Immunotherapy involves administering gradually increasing doses of the "causative allergen" to the allergic patient. The gradual introduction of the allergen induces a natural immunity or tolerance to the allergen. This reduces the patient's allergic symptoms and lessons (and potentially eliminates) the need for medications.
Why sublingual immunotherapy (SLIT)?	Until recently, the only way to successfully administer allergen immunotherapy in the United States was by injections (allergy shots) at the doctor's office. Sublingual immunotherapy is now being introduced in the United States and is an injection-free procedure that offers patients the freedom to treat their allergies conveniently in their own home.
What are some advantages of sublingual immunotherapy compared to traditional allergy injections?	There are numerous advantages of sublingual immunotherapy: (1) The patient does not have to experience repeated injections or the potential for discomfort at the injection site. (2) There is less potential for a systemic anaphylactic reaction, and there have been no reported fatalities from sublingual immunotherapy. Consequently, sublingual immunotherapy may be administered in the privacy and convenience of the patient's home. (3) There is very little time commitment, as the treatment is administered once a day at home in a matter of minutes, eliminating the need for travel to the doctor's office and the 30 minute observation period that is required after allergy injections. (4) For patients living a great distance from the doctor's office or for patients who travel frequently, sublingual immunotherapy offers the convenience of being able to administer the treatment wherever the patient happens to be.

What are some disadvantages of sublingual immunotherapy compared to traditional allergy injections?	There are several distinct disadvantages of sublingual immunotherapy: (1) Although sublingual immunotherapy (SLIT) has been used in Europe for many years and currently accounts for more than half of all immunotherapy administered in the EU, it is still considered "investigational" and "off-label" in the United States and currently does not have FDA approval. (2) Although the extracts used for sublingual immunotherapy are the same as those used for injection immunotherapy, the sublingual administration is considered "off-label" and is currently not covered by insurance plans. Therefore, the cost of sublingual immunotherapy, although comparable to the cost of injection immunotherapy, is an entirely "out-of-pocket" expense, not reimbursable by insurance. (3) Although sublingual immunotherapy has been shown to be quite effective, it may not be as efficacious as the traditional injection protocols for some types of allergies (e.g., venom).
What conditions can be treated with sublingual immunotherapy?	Our clinic is currently using sublingual immunotherapy for the treatment of respiratory allergies secondary to airborne allergens such as trees, grasses, weeds, mold, dust mites, and animal danders. Although the drops are used in Europe for other types of allergic conditions (e.g., food allergies), we are currently recommending them primarily for allergic rhinitis and allergic asthma.
How quickly will I see relief of my allergy symptoms?	Although treatment success varies from patient to patient, we anticipate improvement within the first few months of treatment. Maximum benefit may not be noted until one year of therapy has been completed. Adjustments to your dosing may be made each time the extract vials are renewed, providing opportunity for increased efficacy. For that reason, it is important to keep Dr. Park informed about how you are responding to the treatment.
How do I get started on sublingual immunotherapy?	Dr. Park will take a medical history, complete a focused physical examination, and then order some specific allergy testing, usually in the form of allergy skin tests. Once the evaluation and testing are completed, he will discuss specific treatment options with you and guide you in your treatment decisions. If you choose to begin sublingual immunotherapy, your specific treatment kit will be prepared, usually within one week. You will come to the clinic and complete your consent form, then take the first oral dose in the clinic. You may then take your treatment vials with you for administration of daily doses at home. Dr. Park and the staff will provide you with complete dosing guidelines and renewal instructions. The staff will be available during routine office hours for phone advice concerning your sublingual immunotherapy. Dr. Park is available for emergency consultation 24-7 through our answering service.
Is there a minimum age for use of SLIT?	There are no age restrictions for sublingual immunotherapy, although it is rare to begin any form of immunotherapy prior to age two years.
How will the dosing proceed?	There is an initial "build-up phase" that involves once-a-day dosing, beginning with a few drops from a lower concentration and gradually increasing both the drop number and the vaccine concentration over a period of 30 days. At the 30-day point, you will begin a once-a-day dosing regimen with 5 drops as the standard maintenance dose. This 5 drop-per-day dose will be continued for control of your allergies. The usual treatment course is 3-5 years, at which time re-evaluation will be recommended. If you are doing well on maintenance immunotherapy, Dr. Park will want to see you in the clinic about every 6-12 months for a brief follow-up visit.

How will the drops be administered?	The allergen extract is provided in convenient amber-glass bottles with a dropper mechanism that allows easy dosing under the tongue. Dosing should be done in the morning. Drops are placed under the tongue and held there for one (ı) minute, then swallowed. We recommend no food or water for a period of 5 minutes after dosing. After that, there are no restrictions for eating or drinking. Also, there are no restrictions for eating or drinking prior to taking the drops.
Do the drops have any taste?	Due to the glycerin additive mixed with the extract, there is a slight sweet taste. However, since there are no taste buds under the tongue, most patients experience very little taste sensation.
How often do I take the drops?	The drops are taken once a day, every day, for 3-5 years. Treatment duration varies from patient to patient, depending on the response to treatment and the need for continued symptom control.
What if I forget to take the drops one day?	There is a dose adjustment schedule on the dosing record. In general, there will be no problem if you miss a day or two periodically. However, the best relief for your allergies will be experienced if you are taking the treatment each and every day. As with any preventative treatment, compliance is critical for success. The appropriate cumulative therapeutic doses are achieved only if daily therapy is maintained.
How long will a treatment set last?	The initial "build-up" treatment set will consist of three concentrations (3 or 6 vials, depending on your particular prescription) and last approximately 7 weeks. Thereafter, the maintenance treatment sets will consist of one concentration. Renewal prescriptions will be prepared and are designed to last approximately 2 months (2 vials if you are on a "single kit" and 4 vials if you are on a "double kit.").
How do I re-order my treatment set?	As you complete the second week in your final vial(s), you will complete the renewal form and send it back to Dr. Park along with payment information. The renewal treatment sets will be sent to you within 2 weeks of receipt of the order.
Do I need to keep the vials refrigerated?	The treatment vials contain a glycerin preservative, which helps maintain stability even at room temperature, probably for a period of weeks. You may keep the vial(s) you are currently using at room temperature, in a convenient location for dosing; however, it is best to keep the other vials refrigerated to insure maximum potency.
Are there any medications that could interfere with my sublingual immunotherapy?	As with subcutaneous (injection) immunotherapy, we do not recommend that you receive sublingual immunotherapy if you are taking a beta-blocker medication (usually used for high blood pressure or glaucoma). If you are started on any new medication by a doctor and you are not sure what the medication is, please call our office and discuss this with one of the nurses before taking any more sublingual immunotherapy.
What are the potential side effects of sublingual immunotherapy?	Reported reactions to sublingual immunotherapy include itching of the tongue or lips (the most common reaction), gastrointestinal symptoms such as nausea and cramping, skin rashes including hives, and very rarely headaches. Systemic reactions (anaphylaxis) have been reported and may include symptoms such as throat tightness, wheezing, and a drop in blood pressure. These systemic reactions are extremely rare; there has never been a reported incidence of a fatal reaction to sublingual immunotherapy. However, we recommend that you always have an oral antihistamine available for mild local reactions, as well as an epinephrine auto-injector (Epi-Pen, Auvi-Q) available for systemic reactions. These precautionary measures will be discussed with you at the time sublingual immunotherapy is initiated.

How will I receive my renewal vials?	Once the renewal order and payment have been received in our clinic, you may pick up the renewal prescription at the designated time or we can ship it to your home.
How do I pay for the treatments?	Patients may pay using cash, check, or credit card (Visa, MasterCard, or Discover).

Questions? **Please call us at** 269-415-7007

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IMMUNOTHERAPY III (SUBLINGUAL / SLIT)

MEDICATIONS TO BE AVOIDED WHILE ON IMMUNOTHERAPY (SLIT)

NOTE: The use of beta blocker medications (*which may be prescribed for high blood pressure, cardiac conditions, glaucoma, etc.*) may hinder the effectiveness of treating systemic reactions to immunotherapy. **Immunotherapy should not be administered while a patient is taking a beta blocker.** A list of the more commonly prescribed beta blocker medications is below. **(*Please note: This may not be an all-inclusive list. Please advise the nurses of any new medication started since your last visit with Dr. Park.*)**

BETA ADRENERGIC BLOCKING AGENTS:

Betapace Tablets (Sotalol)	Kerlone Tablets (Betaxolol)
Blocadren Tablets (Timolol)	Levatol Tablets (Penbutalol)
Brevibloc Injection (Esmolol)	Nadolol Tablets (Nadolol)
Bystolic (Nebivolol)	Normadyne (Labetalol)
Cartrol Filmtab Tablets (Carteolol)	Sectral Capsules (Acebutolol)
Coreg Tablets (Carvedilol)	Tenormin Tablets / Injectable (Atenolol)
Corgard (Nadolol)	Toprol-XL Tablets (Metoprolol)
Inderal Tabs/Caps/Injectable (Propranolol)	Trandate (Labetalol)
InnoPran XL Capsules (Propranolol)	Visken (Pindolol)
Lopressor (Metoprolol)	Zebeta Tablets (Bisoprolol)

BETA ADRENERGIC BLOCKING AGENTS WITH DIURETICS:

Corzide 40/5 Tablets (Nadolol)	Lopressor HCT (Metoprolol)
Corzide 80/5 Tablets (Nadolol)	Tenoretic Tablets (Atenolol/HCTZ)
Inderide LA Capsules (Propranolol)	Timolide Tablets (Timolol/HCTZ)
Inderide Tablets (Propranolol)	Ziac Tablets (Bisoprolol/HCTZ)

BETA ADRENERGIC OPHTHALMIC PREPARATIONS:

AK Beta (Levobunolol)	Optipranolol (Metipranolol)
Betagan (Levobunolol)	Ocupress (Carteolol)
Betimol Ophthalmic Solution (Timolol)	Timoptoc in Ocudose (Timolol)
Betoptic S Ophthalmic Suspension (Betaxolol)	Timoptic Sterile Ophthalmic Solution (Timolol)
Combigan (Timolol)	Timoptic-XE Sterile Ophthalmic Gel (Timolol)
Cosopt Sterile Ophthalmic Solution (Timolol)	

NOTE: Patients taking a Monoamine Oxidase Inhibitor (MAO Inhibitor) cannot be given adrenalin (epinephrine) because this may provoke a severe hypertensive crisis (very high blood pressure). If it is necessary to take these medications, allergen immunotherapy will need to be discontinued.

MONOAMINE OXIDASE INHIBITORS (MAO INHIBITORS):

Azilect (Rasagiline)	Marsilid (Iproniazid)
Aurorix (Moclobemide)	Nardil (Phenelzine)
Eldepryl (Selegiline)	Parnate (Tranylcypromine)
Marplan (Isocarboxazid)	Zyvox (Linezolid)

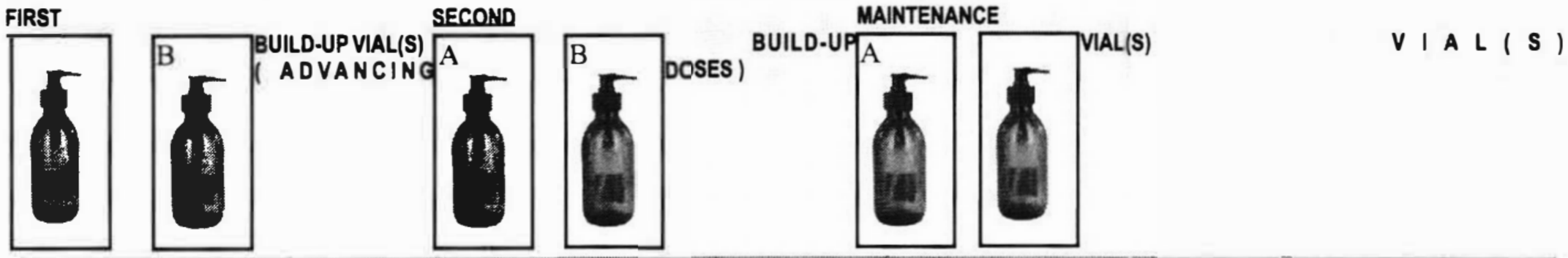
All of the above medications need to be avoided if a patient is taking specific allergen immunotherapy. Review your current medication list and contact Dr. Park immediately if you find that you are taking any of these medications.

IMMUNOTHERAPY IV (SUBLINGUAL / SLIT)

INITIAL IMMUNOTHERAPY DOSING SCHEDULE (SLIT)

When beginning sublingual immunotherapy...

The initial prescription will consist of three advancement concentrations, each one progressively stronger. There will be three "A" vials and three "B" vials for the advancement or "build-up" phase. Once maintenance doses are achieved, renewals will consist of "maintenance" vials (stable doses), labeled "A" and "B". An outline of the "build-up" phase is below:



Dose from each vial:		Dose from each vial:		Dose from each vial:		MAINTENANCE
1	1 drop	11	1 drop	21	1 drop	From this point forward, you will continue taking 5 drops per day from each maintenance vial. *(Unless instructed otherwise by Dr. Park.)*
2	1 drop	12	1 drop	22	1 drop	
3	2 drops	13	2 drops	23	2 drops	
4	2 drops	14	2 drops	24	2 drops	
5	3 drops	15	3 drops	25	3 drops	
6	3 drops	16	3 drops	26	3 drops	
7	4 drops	17	4 drops	27	4 drops	
8	4 drops	18	4 drops	28	4 drops	
9	5 drops	19	5 drops	29	5 drops	
10	5 drops	20	5 drops	30	5 drops	

Once you have reached the anticipated maintenance dose of 5 drops from each "maintenance" vial, you will be instructed to schedule a follow-up visit with Dr. Park to review your course of treatment prior to preparation of renewal maintenance vials. Thereafter, you should plan on a follow-up visit with Dr. Park every 6-12 months to review your treatment plan and to make any necessary adjustments in your maintenance dose. Of course, if there are problems with the treatment during the advancement phase, an earlier follow-up appointment with Dr. Park can be arranged.

As advancement progresses through the initial "build-up" vials of extract, it may be necessary to repeat a given dose, depending upon any reaction to the last dose or any lengthy interval of time since the last dose. There should be sufficient extract in the initial two "build-up" vials to allow for repeat doses. If the advancement proceeds as outlined above, there will be some unused extract remaining in the initial "build-up" vials. All of the extract in the "maintenance" vials will be utilized. Renewal extract vials will need to be re-ordered two weeks prior to completing the maintenance vials.

After completion of the initial advancement phase and determination of the appropriate maintenance dose, renewal prescriptions will consist of the MAINTENANCE vials only, ... and you will remain on this maintenance concentrate for the duration of treatment.

Questions? **Please call us at** 269-415-7007.

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■ PRACTICAL INFORMATION REGARDING ADMINISTRATION OF ALLERGY DROPS:

ADMINISTRATION OF SUBLINGUAL DROPS:

1. Dosing should be done at the same time each day, preferably in the morning.
2. Record all doses on the attached Treatment Record (Pages 3 and 4).
3. Record the date of dosing.
4. Prior to dosing, review the Health Screen and, if applicable, check your Peak Flow reading. If the Health Screen questions are answered "no" and if your Peak Flow is in the green zone, check the Health Screen box and proceed with dosing. If not, call our office and ask to speak with one of the nurses.
5. Drops should be placed under the tongue and held there for one minute, then swallowed. For multiple vial sets, drops from each vial may be added together under the tongue all at once. If local mouth itching occurs and is uncomfortable, then spit out the dose and do not swallow.
6. If local mouth itching persists beyond 5 minutes after dosing, take an oral antihistamine. If local mouth itching persists beyond 30 minutes after taking the antihistamine, call our office.
7. If any suspected systemic allergy symptoms occur, follow the instructions outlined below.
8. When dosing is completed, check the appropriate boxes on the Treatment Record.
9. Any adverse events associated with the dosing should be recorded in the "Remarks" section (and continued on the back of the sheet if necessary).
10. If you are unsure of any dosing, please call our office for advice.

PRECAUTIONS:

1. Always be certain that your oral antihistamines and your Epinephrine Auto-injector are available at the time of dosing.
2. Prescription vials should be kept refrigerated for optimum maintenance of potency. However, studies have shown that the extracts are stable at room temperatures for 30 days. Avoid extreme heat or freezing of the extract vials.
3. Always check the vial labels before dosing, to be certain that you have the correct vial.
4. Do not take drops if you are running fever > 99.5, if you are wheezing or have a Peak Flow reading less than 80% of your personal best, or if you have any open sores or wounds in the mouth.
5. Do not dose on days of dental procedures.
6. Dose adjustments based on missed days or adverse reactions are outlined below.
7. Do not take allergy drops if you are also taking a prescription beta blocker medication.
8. For women of child-bearing age, notify our office if you become pregnant.

■ DOSAGE ADJUSTMENTS BASED ON INTERVAL BETWEEN TREATMENTS / LOCAL ADVERSE REACTIONS:

MISSED DAYS: ⇨⇨		DOSAGE ADJUSTMENT:
a.	1-7 days ⇨	a. Continue advancement or repeat the maintenance dose.
b.	8-14 days ⇨	b. Resume a 10-day advancement from the vial(s) most recently used.: Days 1 and 2 – take 1 drop Days 3 and 4 – take 2 drops Days 5 & 6 – take 3 drops Days 7 & 8 – take 4 drops Days 9 & 10 – take 5 drops, then resume scheduled dosing
c.	> 14-days ⇨	c. Call our office for instructions

LOCAL REACTION: ⇨⇨		RESPONSE:
a.	No reaction ⇨	a. ↑ dose according to schedule or continue maintenance dosing.
b.	Itching of mouth ⇨	b. Take an oral antihistamine as needed.
c.	Swelling of lips / tongue ⇨	c. Take an oral antihistamine as needed; ↓ to last tolerated dose, repeat x 2; then continue advancement.
d.	Nausea or cramping ⇨	d. Take an oral antihistamine. If symptoms persist, use EPI and call 911. Call our office before taking further doses.
e.	Hives ⇨	e. Take an oral antihistamine. If symptoms persist, use EPI and call 911. Call our office before taking further doses.
f.	Throat tightness / wheeze ⇨	f. Take oral antihistamine, use EPI and call 911. Call our office and arrange a follow-up visit before further dosing.

■ TREATMENT OF SYSTEMIC ADVERSE REACTIONS TO ALLERGEN IMMUNOTHERAPY:

There is always the possibility of a systemic allergic reaction (anaphylaxis) to one of the doses, even though the same dose may have been previously well tolerated. Anaphylactic symptoms may include progressive itching (nose, throat, eyes, skin, palms of hands, soles of feet, groin, etc.), sneezing, coughing, nasal congestion / drainage, throat tightness, wheezing, asthma, nausea, vomiting, abdominal cramping, diarrhea, generalized hives. Rarely, hypotension and fainting may occur.

At the first signs of any systemic reaction, give at once **0.15 – 0.30 cc of 1:1000 aqueous epinephrine intramuscularly**. ***CALL 911.*** Depending on the nature and severity of the reaction, this dose of epinephrine may be repeated at 5-10 minute intervals. A short-acting antihistamine should also be given by mouth.

PLEASE NOTE: IF ANY SYSTEMIC REACTION OCCURS, YOU MUST RETURN TO OUR OFFICE FOR FURTHER INSTRUCTIONS PRIOR TO TAKING ANY MORE SUBLINGUAL IMMUNOTHERAPY.

Questions? **Please call us at 269-415-7007.**