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Overview of Allergen Immunotherapy Methods for Hay Fever (Allergic Rhinitis)

Introduction

Hay fever, or allergic rhinitis, is an IgE-mediated allergy affecting the nasal passages (often with eye symptoms, i.e., rhinoconjunctivitis). It is highly prevalent in Europe (affecting roughly 17–29% of adults) and significantly impacts quality of life [1]. Standard treatments (antihistamines, nasal corticosteroids) provide symptomatic relief, but allergen immunotherapy (AIT) is the only disease-modifying therapy. AIT involves regular exposure to specific allergens (e.g. pollen, dust mites) in controlled doses to induce long-term immune tolerance [2] [3]. In Europe (including the Netherlands), AIT is an established option for moderate-to-severe allergic rhinitis not controlled by medications [4]. This report provides a structured overview of major prescription AIT methods – **subcutaneous immunotherapy (SCIT)** and **sublingual immunotherapy (SLIT)** (including tablets and drops) – and emerging therapies. We compare their clinical effectiveness, side effect profiles, treatment regimens, and typical indications/contraindications to help readers determine which approach may be most appropriate.

(Note: All treatments discussed are those currently available or in development in Europe, with a focus on the Netherlands. In the Netherlands, both SCIT and SLIT are prescribed by allergists or trained GPs and are reimbursed by insurance when criteria are met [5].)

Subcutaneous Immunotherapy (SCIT) – "Allergy Shots"

Overview & Procedure: SCIT is the traditional form of allergen immunotherapy administered via injection. It has been used for over a century and remains a standard for inhalant allergies [6]. SCIT involves injecting small, increasing doses of allergen extract (e.g., grass pollen, tree pollen, house dust mite) into the subcutaneous tissue, typically in the upper arm. After a buildup phase of weekly injections reaching a maintenance dose, injections are given at regular maintenance intervals (usually monthly) for *3 to 5 years*. Each injection must be given under medical supervision with a post-injection observation period of ~30 minutes, due to the risk of systemic reactions [7] [8].

Clinical Effectiveness: SCIT has robust evidence for reducing hay fever symptoms and medication needs. Multiple randomized controlled trials (RCTs) and meta-analyses confirm that SCIT significantly improves seasonal allergic rhinitis symptoms compared to placebo [9]. For example, in seasonal allergies like grass pollen, SCIT led to ~26–36% reductions in nasal/eye symptom scores in large trials [10]. Long-term benefits are also well documented: a full 3-year course can induce sustained symptom improvement for at least 2–3 years after therapy completion [11]. SCIT can also help prevent progression of allergic rhinitis to asthma and new sensitizations [12]. Notably, SCIT's efficacy is strongest in seasonal allergic rhinitis; it is effective but relatively less so in perennial allergies (like dust mite) and in younger children [13]. Overall, both European and Dutch guidelines consider SCIT an effective, first-line AIT option for suitable patients with moderate to severe allergic rhinitis [14].

Side Effects and Safety: Because SCIT injections introduce allergens systemically, side effects range from mild local reactions to rare anaphylaxis. *Local reactions* at the injection site (redness, swelling, itching) are common but generally mild and not a major concern [15] [16]. *Systemic reactions*, however,

can occur in a small percentage of patients. Large surveys indicate any systemic allergic reaction occurs in about 0.025% of SCIT injections [17]. Serious anaphylactic reactions are very rare – roughly on the order of 5.4 per million injections (0.0005%) in seasonal allergy patients [17]. Nonetheless, because anaphylaxis, though *extremely rare*, is possible, patients must wait under observation after each injection and clinics must be equipped to manage emergencies [18] [19]. Reported severe reactions to SCIT include asthma exacerbations, generalized hives, or anaphylaxis; risk factors for these events include uncontrolled asthma, high allergen exposure period (e.g. peak pollen season), or improper dosing protocols [20] [21]. Modern allergen extracts (often aluminum-adsorbed or modified "allergoids") and adherence to build-up schedules have improved SCIT's safety, keeping serious reactions below 1% of patients [22] [19]. **In summary**, SCIT is considered safe and well-tolerated for most patients, but it carries a non-negligible risk of systemic allergic reactions, necessitating supervised administration [18] [8].

Treatment Duration & Adherence: A typical SCIT course lasts *3 years* (sometimes up to 5 years) of continuous treatment [14]. Patients must adhere to frequent injection visits, especially in the initial months. During the build-up phase, weekly appointments are required for 3–6 months until maintenance dosing is reached; thereafter, maintenance injections are usually every 4 weeks [23]. This schedule demands significant commitment. Adherence in real-world practice can be challenging, yet studies show that if patients commit, many do complete the recommended duration. In the Netherlands, historical analyses (1990s–2000s) found that only ~23% of SCIT patients persisted for the full 3-year course [24]. However, more recent data suggest improved adherence: for example, in a Danish cohort, about 57% of SCIT patients were still on treatment at 3 years [25]. Factors influencing SCIT adherence include the inconvenience of clinic visits, injection discomfort, and early symptom improvement leading patients to stop early. On the other hand, some patients prefer the monthly supervised injections over daily self-medication (as with SLIT) – thus adherence can vary by individual preference [23] [26]. To maximize SCIT success, patients and providers must plan for the long haul; completing ~3 years is essential to achieve long-term disease modification [14].

Indications: SCIT is generally indicated for patients with **moderate-to-severe allergic rhinitis** (with or without conjunctivitis) attributable to specific allergens, especially when symptoms are not adequately controlled by medications or when patients seek a long-term solution [2] [3]. Common allergens treated with SCIT in Europe include grass and tree pollens (for seasonal hay fever), house dust mite (for perennial rhinitis), and animal dander (e.g. cat) if these cause significant rhinitis. SCIT is suitable for adults and also used in children (typically age $\geq$5; younger ages may be considered on a case-by-case basis by specialists) [27]. In practice, Dutch guidelines require a confirmed IgE sensitization (positive skin prick test or specific IgE) to relevant allergens and persistent significant symptoms despite optimal medication before starting SCIT [4]. SCIT can be particularly beneficial if a patient has multiple allergies – injection mixtures can include 2–3 allergens in one regimen (though mixing too many allergens can dilute efficacy) [28] [29].

Contraindications/Cautions: Absolute contraindications for SCIT include patients with **uncontrolled asthma** or active, severe asthma symptoms – poor lung control greatly increases the risk of life-threatening reactions [21]. Significant cardiovascular disease or use of beta-blocker medications are relative contraindications, because they could complicate treatment of anaphylaxis. Patients with certain immune system disorders (autoimmune diseases, immune deficiencies) or those on immunosuppressants are usually not candidates, as effectiveness and safety haven't been established. SCIT is generally not initiated during pregnancy; if a patient becomes pregnant while on maintenance doses, continuation might be considered with caution, but starting immunotherapy while pregnant is discouraged due to the risk of systemic reactions. Young children (<5 years) are often steered towards alternative therapies mainly due to difficulty with injections and communication of symptoms, though this is not a strict contraindication if an allergist deems it necessary. Finally, patients who cannot reliably

adhere to frequent clinic visits or who have a strong needle phobia may not be good candidates for SCIT.

Sublingual Immunotherapy (SLIT) – Tablets and Drops

Overview & Forms: SLIT is a newer, needle-free immunotherapy route where allergens are administered under the tongue (sublingually) and absorbed through oral mucosa. Developed in the 1990s as an alternative to injections, SLIT has become a standard immunotherapy approach, especially in Europe [30] [31]. There are two prescription forms: **SLIT tablets** (sublingual dissolvable tablets) and **SLIT drops** (allergy drops). SLIT tablets are approved, standardized products for specific allergens – for example, grass pollen tablets, ragweed pollen tablets, and house dust mite tablets are available in the EU (the Dutch authorities approved a dust mite SLIT tablet in 2016) [32] [33]. SLIT drops are liquid allergen extracts, often provided in dropper bottles; some are licensed products in certain countries or prepared by specialist pharmacies. Patients self-administer SLIT at home by placing the tablet or measured drops under the tongue daily (usually once daily). The allergen is held under the tongue for 1–2 minutes before swallowing [30]. The first dose of SLIT is typically given under medical supervision (to monitor for any reaction), but subsequent doses are taken at home without direct supervision [27]. Treatment usually continues daily for **3 years** (for perennial allergies) or in annual pre-seasonal courses for seasonal allergies (e.g. starting a few months before pollen season each year for 3 years, depending on product recommendations).

Clinical Effectiveness: SLIT has been shown to significantly reduce allergic rhinitis symptoms and medication needs, in both adults and children [27]. In clinical trials for seasonal allergic rhinitis, SLIT (both tablets and drops) produced improvements in symptom scores on the order of 20–40%, similar to SCIT in comparable studies [10]. For example, one large trial of grass pollen SLIT tablets reported about a 30% reduction in symptoms versus placebo, comparable to the benefit seen with grass SCIT injections [10]. Long-term efficacy is also achievable: like SCIT, a full 3-year SLIT course can confer sustained relief for at least 2–3 years after stopping therapy [34] [35]. SLIT is effective for seasonal pollens (grass, tree) and there is evidence it can improve perennial rhinitis from dust mite allergy as well [36]. (Notably, a SLIT tablet for house dust mite allergic rhinitis/asthma has shown significant symptom and medication score improvements in trials [37] [38].) Some studies in children with dust mite allergy are less conclusive, but overall SLIT is considered beneficial across age groups [13]. In summary, **SLIT provides clinical efficacy comparable to SCIT for many patients** [39]. Both routes reduce hay fever symptoms and can modify the course of disease; neither is universally “more effective,” and head-to-head trials have generally found no major outcome differences or only modest advantages to one route [40] [41]. (Indeed, indirect comparisons are mixed: a few meta-analyses suggest slightly greater symptom relief with SCIT, while others find them equivalent [40] [41].) In practice, the choice often comes down to practical considerations and patient preference rather than efficacy.

Side Effects and Safety: SLIT’s safety profile is favorable, especially compared to SCIT. Because the allergen exposure is mostly localized to the oral mucosa, **side effects are usually local and mild**. The most common SLIT reactions are *oral/throat symptoms*: itching or tingling under the tongue, mouth or tongue swelling, throat irritation, and sometimes mild gastrointestinal discomfort [42]. In clinical trials of SLIT for pollen, up to ~40–50% of patients experienced mild oral itching or irritation, and minor swelling of lips or mouth occurred in a smaller subset [10]. These symptoms typically arise in the first days or weeks of treatment and often subside with continued dosing. They usually do not require medication and rarely cause patients to discontinue therapy [43]. For example, one large trial reported oral pruritus in 46% of SLIT patients and lip swelling in 18%, but only 4% withdrew due to side effects [10]. Gastrointestinal symptoms (nausea, stomach ache) or mild wheezing can occur uncommonly. Crucially, *serious systemic allergic reactions (anaphylaxis)* with SLIT are exceedingly rare – far rarer than with SCIT [20] [44]. No fatal anaphylaxis from SLIT has been reported, and estimated frequency of

anaphylaxis is on the order of 1 in 100 million SLIT doses [20] [45]. A review of over 1 million SLIT doses found systemic reactions in only ~0.05% of doses, and severe systemic reactions in ~0.001% [20]. In real-world post-marketing surveillance, SLIT self-administration has proven very safe, with anaphylaxis extremely rare and no fatalities [46] [47]. Thus, unlike SCIT, routine SLIT does **not** require patients to stay in a medical office after dosing – after the first supervised dose, patients take SLIT at home with an epinephrine auto-injector prescribed as a precaution, though needing to use it is exceptionally uncommon. Overall, **SLIT is considered safer and more tolerable than SCIT** [46]. Patients must be counseled on the possibility of oral itch or discomfort, but these side effects are generally manageable and transient. Adherence to daily dosing can actually improve tolerability over time, as studies note local reactions tend to decrease after the first few months of therapy [48] [49].

Treatment Duration & Adherence: Like SCIT, SLIT is recommended as a **3-year course** for long-term benefit [14]. SLIT dosing is *daily* (or in some cases, three times per week for certain drop preparations) throughout this period. The daily self-administration places a different kind of commitment on patients – one of consistent at-home adherence rather than frequent clinic visits. Adherence in SLIT has been a known challenge: some patients find it hard to remember or continue daily treatment for years, especially once symptoms improve. Indeed, early real-world studies in the Netherlands (when SLIT drops were commonly used) showed a high dropout rate – only about 7% of SLIT patients made it to 3 years in one analysis (median SLIT duration ~7 months) [50] [51]. That study found SLIT users were more likely to discontinue than SCIT users, possibly due to the burden of daily treatment or differences in patient follow-up [52] [53]. However, more recent data – particularly with the newer SLIT tablet formulations – suggest better persistence. In Denmark, for example, ~53% of SLIT patients were still adherent at 3 years, nearly comparable to SCIT patients (57%) [25]. Likewise, a Dutch clinical practice study of dust mite SLIT-tablets reported that 74.5% of patients were compliant (took ≥80% of doses) over the first year [54] [55]. Key factors to support SLIT adherence include patient education, symptom tracking to reinforce benefits, and managing side effects early on. Convenience is a plus: no clinic visits are needed beyond periodic check-ins, and patients can take the medication at home or even while traveling (tablets are portable). In contrast, the *daily* nature of SLIT can be a downside for those who prefer not to take medication every day. Therefore, choosing SLIT versus SCIT often involves considering *which regimen the patient is more likely to stick with*: daily self-therapy or monthly injections [23] [26]. Overall, when properly motivated and supported, many patients can successfully complete SLIT. As with SCIT, the full course is important – studies show that completing ~3 years of SLIT yields sustained tolerance even after stopping [34].

Indications: SLIT is indicated for largely the **same patient profile as SCIT** – individuals with significant allergic rhinitis (with or without conjunctivitis) due to confirmed allergen sensitization, who desire a long-term solution and are good candidates for immunotherapy. In Europe, SLIT is widely used for *pollen allergies* (e.g. grass, birch, ragweed depending on region) and *house dust mite* allergy. For instance, in the Netherlands common SLIT prescriptions include grass pollen tablets (for hay fever) and dust mite tablets (for perennial symptoms) [32] [33]. SLIT is approved for children in many cases; some products (like grass pollen tablets) are indicated down to age 5, and clinical experience shows SLIT drops have been used even in young children with encouraging results [27]. SLIT can be a preferred option for patients who cannot easily attend frequent appointments or who are needle-averse. Many patients opt for SLIT due to its at-home convenience and lower risk profile. In Europe, allergists often discuss both SCIT and SLIT with eligible patients so that the chosen method aligns with the patient's lifestyle and preferences. It's worth noting that SLIT tablets are **allergen-specific** – each tablet targets one allergen (e.g., only grass or only dust mite). If a patient is allergic to multiple pollens, they may require multiple SLIT products or a strategic choice of the dominant allergen to treat. SLIT liquid drops can sometimes be mixed to cover multiple allergens, but such mixtures are used carefully and evidence mainly supports single-allergen efficacy [29]. Overall, a patient with one or multiple hay fever triggers can still be a candidate for SLIT; the allergist will tailor the prescription accordingly.

Contraindications/Cautions: SLIT shares many of the **general contraindications** of SCIT, but some are more relaxed given the safety profile. Uncontrolled or severe asthma is still a precaution – while SLIT has very low risk of anaphylaxis, patients with poorly controlled asthma could have difficulty if any systemic reaction occurs [21]. Therefore, asthma should be reasonably controlled before starting SLIT, though well-controlled mild-to-moderate asthmatics often do fine (and may even see asthma improvement with SLIT). Unlike SCIT, use of beta-blocker medications or cardiovascular disease is not an absolute contraindication for SLIT (since systemic reactions are so rare), but many guidelines still advise caution. Active autoimmune diseases or immune deficiencies are generally listed as contraindications for any allergen immunotherapy due to uncertain efficacy and safety. SLIT is typically avoided in patients with active oral inflammation or wounds (e.g. oral ulcers, severe gingivitis) at the time of dosing, because mucosal disruption could increase systemic absorption – patients are usually advised not to take SLIT on days of major dental work, for example. As with SCIT, starting SLIT during pregnancy is not recommended (due to inability to easily treat a rare reaction); however, if a patient becomes pregnant after months on SLIT, some physicians continue it with careful monitoring since the risk of a reaction is low. Finally, patient reliability is a consideration: those who cannot commit to daily therapy or who have conditions making self-administration difficult (e.g. severe cognitive impairment) might not be ideal SLIT candidates. In summary, SLIT's contraindication profile is slightly more permissive than SCIT's, but the decision is individualized, ensuring the patient's underlying health status allows for safe immunotherapy.

Other and Emerging Immunotherapy Approaches

Beyond the established SCIT and SLIT modalities, various **emerging immunotherapy methods** are being explored to improve convenience, safety, or efficacy. While these are not yet mainstream, a brief overview is provided:

- **Intralymphatic Immunotherapy (ILIT):** ILIT is an experimental technique where a few high-concentration allergen injections are delivered directly into a lymph node (usually in the groin) rather than under the skin. The rationale is that by targeting lymph nodes, which are rich in immune cells, one might induce tolerance with far fewer doses. Small studies for cat dander and grass pollen allergies have shown ILIT can significantly reduce rhinitis symptoms with as few as *three injections* (typically given one month apart) [56] [57]. Remarkably, ILIT trials (three injections of allergen) have reported clinical improvements comparable to multi-year SCIT, at least in the short term [56]. Another advantage is safety: ILIT appears to have a low incidence of systemic reactions – one head-to-head study found ILIT caused fewer adverse events than SCIT during the buildup period, with no anaphylaxis observed in ILIT patients [58] [59]. The concept of ILIT is very appealing (a "3-shot cure" for hay fever), but it is still under research. No standardized ILIT product is approved yet in Europe, and protocols are confined to clinical trials or a few specialized centers. If ongoing research confirms its efficacy and long-term benefit, ILIT may become a future alternative for patients unable to commit to years of treatment.

- **Epicutaneous (Transdermal) Immunotherapy:** This approach uses patches applied to the skin, containing allergen that diffuses through the skin to immune cells. It's being studied more in food allergy (e.g., peanut patch) but a small study with grass pollen patches applied for days showed some symptom reduction in hay fever [60] [61]. The appeal is a completely needle-free, at-home method with potentially fewer systemic effects (since allergen uptake is slow). However, data on epicutaneous AIT for inhalant allergies are still preliminary [62]. As of 2025, no epicutaneous product for allergic rhinitis is on the market in Europe; this remains a research avenue.

- **Intranasal Immunotherapy:** Instead of oral or injections, intranasal immunotherapy involves spraying or dropping allergen extracts directly into the nose regularly. Some early studies (mostly in past decades) showed that localized nasal administration can improve rhinitis symptoms [63]. However, intranasal AIT never became widely adopted, partly due to irritation side effects and dosing difficulties. Currently, it is not a commonly available therapy in Europe, but historically it demonstrated proof-of-concept that local mucosal tolerance can be induced.

- **Oral Administration:** Interestingly, simply swallowing allergen (as opposed to holding under the tongue) was tried for respiratory allergies but found ineffective [60]. Orally ingested allergen tends to be destroyed by digestion, and no benefit for hay fever was seen [60]. (Oral immunotherapy is effective for food allergies, but that is a different context.)

- **Modified Allergens and Adjuvants:** Another frontier in AIT is using recombinant allergens, peptide fragments, or adding immune adjuvants to improve safety and efficacy. For example, "allergoids" (chemically modified allergen extracts with reduced IgE reactivity) are already used in some SCIT formulations to lower side-effect risk while maintaining efficacy [30] [64]. Adjuvants like MPL (Monophosphoryl lipid A) have been combined with allergens to enhance immune tolerance induction. Short synthetic peptides representing allergenic epitopes are also being studied – these aim to induce tolerance without triggering IgE-mediated reactions. These strategies remain in research or specialized use, but they underline ongoing efforts to create faster, safer immunotherapy.

In summary, **SCIT and SLIT remain the only widely approved immunotherapies for hay fever in Europe as of 2025** [56] [65]**.** Emerging methods like ILIT or epicutaneous patches may expand future options, but for now they are not routine. Patients should be cautious of any "too good to be true" quick fixes, since the 3-5 year SCIT/SLIT paradigm is still the proven route to long-term allergic rhinitis relief.

Comparative Summary of SCIT vs. SLIT

Both SCIT and SLIT are effective prescription therapies for allergic rhinitis, each with its own pros and cons. The table below summarizes key comparisons to aid decision-making:

Aspect	Subcutaneous Immunotherapy (SCIT)	Sublingual Immunotherapy (SLIT)
Administration	Regular **injections** by healthcare provider. Initial weekly shots, then monthly maintenance [23]. Requires 15–30 min observation after each injection [7] [8].	Daily **sublingual doses** self-administered at home (tablet dissolved or drops) [31] [27]. First dose under medical supervision, subsequent dosing without clinic visits [27].
Treatment Duration	Typically **3–5 years** of injections for lasting effect [14]. Full course needed for sustained tolerance (≥2–3 years benefit post-therapy) [11].	Typically **3 years** of daily dosing [14]. Full course yields sustained benefits for ~2–3 years post-therapy [34] [35]. (Some seasonal SLIT protocols are preseasonal each year for 3 years.)

Aspect	Subcutaneous Immunotherapy (SCIT)	Sublingual Immunotherapy (SLIT)
Efficacy	Proven effective in reducing symptoms and medication use in allergic rhinitis [9]. Some data suggest **slightly higher efficacy** (greater symptom relief) in certain cases [40], especially for seasonal pollen allergies [13]. Long-term disease modification (prevention of new allergies, asthma) documented [12].	Proven effective and **comparable efficacy** to SCIT in most studies [10] [41]. Highly effective for seasonal allergies; evidence for perennial (dust mite) also positive, including in adult asthmatics [36]. Long-term benefits and some preventative effect (e.g. reducing asthma development) noted, though research is ongoing.
Onset of Relief	Noticeable symptom improvement often in the first year (after build-up), with further improvement in years 2–3. Some patients report benefits even during the build-up season.	Similarly, improvement can be seen in the first year (sometimes as early as the first pollen season on therapy). Maximal benefit typically by the second year of continuous SLIT. SLIT-tablets for grass have shown significant relief in the first treated season in trials.
Common Side Effects	*Local:* Injection-site redness, swelling or itch is common [15] [16], usually mild. *Mild systemic:* may experience temporary hay fever-like symptoms (sneezing, mild asthmatic symptoms) after injections occasionally. These are generally manageable.	*Local:* Oral itching or tingling is very common (up to ~50% patients) [10]; also throat irritation, mild tongue or lip swelling [10]. *GI:* sometimes mild nausea or abdominal discomfort. These typically lessen over time [48] [49]. Local reactions are the predominant side effect category for SLIT [43].
Serious Risks	*Anaphylaxis risk:* Present but **very low** per injection (on the order of 1 in 50,000 injections for any systemic reaction; fatality exceptionally rare) [17]. Requires medical setting and availability of emergency treatment [7]. Risk is highest during buildup and if asthma is uncontrolled [21].	*Anaphylaxis risk:* **Extremely low**. Anaphylactic reactions to SLIT are exceedingly rare (estimated ~1 per 100 million doses) and no known fatalities [20] [45]. Systemic reactions are very uncommon (<<1% of doses) [20]. Thus, SLIT is considered a safer modality – can be taken at home with rare emergency issues [46].
Monitoring	Requires in-clinic administration with post-shot observation each time. Patients need ready access to medical care during therapy visits.	Only first dose is monitored; thereafter no routine clinic visits for dosing. Patients typically carry an epinephrine autoinjector as a precaution but self-treatment is the norm.

Aspect	Subcutaneous Immunotherapy (SCIT)	Sublingual Immunotherapy (SLIT)
Patient Burden	**Logistics:** Weekly to monthly clinic visits for years. Time commitment and travel can be burdensome. **Discomfort:** Needle injections (may deter needle-phobic patients). **Cost:** In the Netherlands and most of Europe, cost is covered by insurance if criteria met [5], but indirect costs (time off work, travel) exist.	**Logistics:** Daily home dosing (requires patient to remember and adhere). Minimal clinic visits (only periodic follow-ups). **Discomfort:** Oral itch can be bothersome initially; no needles involved, which is preferable for many. **Cost:** Also usually reimbursed; medication delivered via pharmacy for at-home use [5]. Requires patient discipline to maintain daily routine.
Adherence Patterns	Historically higher completion rates than SLIT in some studies – e.g. more patients persist to 3 years with SCIT than with SLIT in older real-world data [24]. Some patients find the structured appointments help them stay on track. But drop-out still occurs due to duration and travel demands (in one Dutch study, only ~23% persisted 3 years) [24].	Convenience of home dosing is a plus, but daily regimen can lead to forgetfulness or fatigue over time. Older studies showed poor SLIT persistence (~7% at 3 years) [24], but newer data with tablets show improvement (over 50% completion in recent cohorts) [25]. Adherence is crucial; missed doses can be common if not motivated. Overall, no injections and flexible dosing timing can improve willingness for some patients.
Indications	Moderate-to-severe allergic rhinitis (seasonal or perennial) with confirmed IgE sensitization, in patients who can comply with injection therapy. Often favored if multiple allergens need to be treated simultaneously (since different extracts can be mixed/administered in one visit) [28]. Indicated for both adults and children (commonly down to age ~5). Also indicated in some allergic asthma patients (under careful supervision) to improve asthma control.	Same spectrum of allergic rhinitis indications. Particularly suitable for needle-averse individuals or those without easy access to specialist clinics. Approved for children (often age 5 and up for tablets). Each SLIT product is allergen-specific, so best suited when one or two allergens are the main culprits (or sequential treatment of each allergen). Patients with mild asthma can use SLIT; SLIT-tablets are even indicated for allergic rhinitis with co-morbid asthma in some cases [37].

Aspect	Subcutaneous Immunotherapy (SCIT)	Sublingual Immunotherapy (SLIT)
Contraindications	Uncontrolled asthma; severe asthma (FEV_1 below safety threshold). Active systemic illnesses like severe immunological disorders. Use of beta-blockers (relative contra – increases risk in anaphylaxis management) [66] [67]. Significant cardiovascular disease (relative, due to epinephrine risk). Pregnancy (do not start; if already on SCIT and stable, may continue cautiously). Inability to adhere to schedule or history of severe reactions to immunotherapy in past.	Largely overlapping with SCIT: uncontrolled asthma is a precaution (though SLIT reactions are rare, an asthmatic in crisis should not introduce allergens). Active autoimmune diseases or cancers are usually exclusions. Relative contra: patients with conditions that would complicate even rare anaphylaxis (though rare, still caution). Oral inflammation can necessitate delaying doses. Pregnancy (do not initiate anew). Not recommended in patients who cannot understand or follow the daily regimen. Overall fewer strict contraindications given safer profile, but careful patient selection remains important [21].

Table: Comparison of SCIT vs. SLIT for allergic rhinitis (hay fever) in key domains of use, efficacy, and safety.

Choosing the Appropriate Approach

Both SCIT and SLIT are effective treatments for hay fever with proven long-term benefits, so the choice between them often hinges on practical considerations and patient-specific factors. Here are some guidance points to help decide:

- **Efficacy and Long-Term Outcome:** If maximal efficacy is the sole priority, some evidence suggests SCIT might have a slight edge for certain patients (e.g., slightly greater symptom score improvements in some studies) [40]. However, the difference is not dramatic; both methods, when properly administered for 3 years, substantially improve symptoms and can induce lasting tolerance [41]. The decision should not be based purely on efficacy, as both will likely help a suitable patient. Notably, **both SCIT and SLIT require a multi-year commitment** to achieve disease modification – there is no "quick fix" short of experimental options.

- **Safety Considerations:** For patients with high anxiety about allergic reactions or those with risk factors (such as mild unstable asthma or distant travel to clinic), SLIT may be preferable due to its superior safety profile (virtually no anaphylaxis in record) [44] [46]. SLIT's side effects are mostly nuisance-level (local mouth symptoms), whereas SCIT carries a very small but present risk of severe reaction requiring emergency care [20] [45]. For example, an older patient with cardiac issues or someone on a beta-blocker (who might have trouble with epinephrine) would likely be steered towards SLIT or careful consideration before SCIT. On the other hand, SCIT can be done very safely in most healthy individuals with proper precautions, and clinics are equipped to handle reactions. In a supervised environment, even higher-risk patients have completed SCIT safely, but the comfort margin is undeniably higher with SLIT.

- **Lifestyle and Adherence:** This is often the **deciding factor**. SCIT demands frequent clinic visits especially in the first year – feasible for those who have easy access to an allergist and can take time for appointments. Patients who prefer a set routine under medical supervision might do well with SCIT. Meanwhile, SLIT offers freedom from clinic visits after initiation; it suits independent self-disciplined patients or those living far from specialists. However, SLIT requires daily action from the patient. A forgetful person or someone who dislikes daily meds might inadvertently miss doses, jeopardizing efficacy. Some patients know they're more likely to stick with a monthly injection than a daily pill, and vice versa. Data shows no clear winner in real-world persistence – when supported, many patients can adhere to either (about half or more in 3 years) [25]. Thus, the best method is the one the patient feels they can consistently follow through. Shared decision-making is key: discussing the logistics openly often clarifies which approach is more suitable for an individual's routine and personality.

- **Age and Patient Preferences:** Children and adolescents might lean towards SLIT since it spares them injections (and indeed pediatric use of SLIT is common). Parents might favor SLIT for a child to avoid injection trauma, provided the child can cooperate with daily dosing. Adults who travel frequently or have variable schedules might also prefer SLIT (no need to find clinics while traveling). Conversely, some patients strongly prefer an injection they "don't have to think about every day." Needle phobic patients almost always choose SLIT if available. In the Netherlands, both methods are offered widely; GPs and allergists can guide patients in making this personal choice, and insurance coverage is similar for both when indicated [5].

- **Allergen Profile:** If a patient is allergic to multiple allergens (e.g., several pollens plus dust mite), SCIT might treat them more efficiently by mixing extracts (up to 2-3 allergens in one regimen) [28]. SLIT tablets treat one allergen each; doing multiple SLIT concurrently can be complex and sometimes not possible if products for certain allergens aren't available. For instance, a patient allergic to grass, tree, and dust mite could get a combined injection schedule for all three, whereas with SLIT, there are tablets for grass and dust mite, but perhaps not for the specific tree pollen (some regions have a birch pollen SLIT tablet, but not all). In such cases, SCIT might be recommended to cover all sensitivities at once. If the patient's allergy is mainly to one allergen (like solely grass pollen), SLIT tablet for grass is a convenient targeted solution. Thus, the allergen sensitization pattern influences the decision.

- **Medical Contraindications:** As noted, severe uncontrolled asthma would usually disqualify a patient from SCIT until asthma is improved; SLIT might be considered safer in milder asthmatics, but if asthma is very severe even SLIT might be postponed (pharmacotherapy optimized first). If a patient is on beta-blockers for heart conditions, many allergists avoid SCIT due to the anaphylaxis concern and might choose SLIT instead [66] [67]. Pregnancy status or planned pregnancy in the near future might lean towards SLIT as well (or deferring immunotherapy entirely until after pregnancy), to avoid the scenario of managing injection reactions during pregnancy. These medical factors must be reviewed case by case.

In conclusion, **there is no one-size-fits-all answer** to which immunotherapy method is "better" – both SCIT and SLIT are effective and accepted in Europe for treating hay fever. Patients in the Netherlands benefit from a healthcare system where AIT (in either form) is accessible through specialists or trained GPs and is reimbursed when appropriate [5]. The choice should be individualized, considering the patient's allergy profile, risk factors, and ability to adhere to the regimen. For many, the convenience and safety of SLIT make it an attractive first choice. For others, the structured and potentially more customizable approach of SCIT is preferred. What's important is that the patient is well-informed of the commitments and expectations. With either method, committing to the full course is crucial – those

who persevere through the years of therapy often enjoy significant relief from seasonal sneezes and sniffles for years to come, finally getting lasting control over their hay fever [11] [68].

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