**TABLE G31. SAFETY–SLIT– PEDIATRICS**

**SLIT LOCAL REACTIONS**

| **Study** | **SLIT Allergen** | **Number of Patients in Arm** | **Number of events and description** | **% of patients** | **Severity** |
| --- | --- | --- | --- | --- | --- |
| Pajno, 200018 | Dust mite | 12 | 2 patients presented local delayed reactions: one case of swelling of the mouth, lips, and face (at 2 h) and one case of itching of the mouth (at 3 h). Resolved spontaneously without drugs | 16% | Mild |
| Marogna, 200828 | Dust mite, Birch, Parietaria, Grass mix | 144 | 1 dropout because of oral itching | 0.6% | Unspecified |
| deBot201121 | Dust miteplacebo | 125126 | 14 patients reported oral pharyngeal irritation/swelling18 patients reported oral pharyngeal irritation/swelling | 11.2%14.3% | UnspecifiedUnspecified |
| Hirsch, 199729 | Dust mitePlacebo | 1515 | 5 patients reported local events. 1 patient required dose reduction.1 patient reported local events.Local events defined as swelling, reddening, and tingling of the tongue, buccal mucosa and/or gingiva within less than 30 minutes of application. | 33%6% | MildMild |
| Stelmach201127 | Grass mix (SLIT arms reported together)placebo | 4020 | 18 patients reported local reactions such as sublingual itching 3 patients reported local reactions such as sublingual itching  | 45%15% | UnspecifiedUnspecified |
| Novembre, 200425 | Grass mix | 54 | 1 patient had itching in the throat that resolved without requiring treatment discontinuation.  | 0.2% | Mild |
| Vourdas, 199834 | OlivePlacebo | 3432 | 8 patients presented local symptoms: 8 patients had buccal itching or oropharyngeal pruritus, 1 patient had labial swelling 2 patients presented buccal itching, labial swelling.  | 45%7% | MildMild |
| Valovirta, 200636Savolainen 200637 | Tree mix-high Tree mix-low Placebo | 323332 | Oral local reactions16 patients 12 patients 8 patients  | 50%36%25% | UnspecifiedUnspecifiedUnspecified |
| La Rosa, 199923Leonardi 200924 | ParietariaPlacebo | 2021 | 5 patients with local symptoms: 3 had oral itching, 2 had labial swelling4 patients with local symptoms: 2 had oral itching, 2 had labial swelling | 25%19% | UnspecifiedUnspecified |
| Roder200730 | Grass mixPlacebo | 10896 | 42 patients with oral pharyngeal irritation/swelling16 patients with oral pharyngeal irritation/swelling | 39%17% | UnspecifiedUnspecified |
| Pajno 200450 | Parietaria | 15 | 1 patient with itching in mouth and throat – maintenance dose decreased | 7% | Mild |
| Pajno2011 | Coseasonal grass mixContinuous grass mix | 4040 | Local side effects (itching/burning in mouth, gastrointestinal symptoms) were frequent. 5 patients with local symptoms led to discontinuation of SLIT. | At least 6% | Unspecified |

**SLIT Systemic Reactions: Upper respiratory events: Rhinitis/Nasal Reactions**

| **Study** | **SLIT Allergen** | **Number of Patients in Arm** | **Description** | **% of patients** | **Severity** |
| --- | --- | --- | --- | --- | --- |
| Tari, 199031 | Dust mite | 30 | 8 patients presented severe nasal symptoms | 25% | Severe-subjects exceeded max dose |
| deBot201121 | Dust miteplacebo | 125126 | 115 patients reported nasal complaints / rhinitis118 patients reported nasal complaints / rhinitis | 92%94% | UnspecifiedUnspecified |
| Valovirta, 200636Savolainen 200637 | Tree mix-high Tree mix-low Placebo | 323332 | - -1 patient Rhinitis 1 patient Rhinitis | \_\_3%3% | UnspecifiedUnspecified |
| La Rosa, 199923Leonardi 200924 | ParietariaPlacebo | 2021 | 1 patient: Rhinitis1 patient: Rhinitis | 5%5% | UnspecifiedUnspecified |
| Roder200730 | Grass mixPlacebo | 10896 | 89 patients with rhinitis76 patients with rhinitis | 82%79% | UnspecifiedUnspecified |

**SLIT Systemic Reactions: Lower Respiratory Reactions**

| **Study** | **SLIT Allergen** | **Number of Patients in Arm** | **Description** | **% of patients** | **Severity** |
| --- | --- | --- | --- | --- | --- |
| Tari, 199031 | Dust mite | 32 | 8 patients had mild asthma 3 patients presented severe asthma | 25%9% | MildSevere: patients exceeded max dose |
| deBot201121 | Dust miteplacebo | 125126 | 84 patients reported shortness of breath / cough87 patients reported shortness of breath / cough | 67%69% | UnspecifiedUnspecified |
| Marogna, 200828 | Birch and Grass mix | 144 | 1 dropouts due to asthma | 0.6 | Unspecified |
| La Rosa, 199923Leonardi 200924 | ParietariaPlacebo | 2021 | 0 patients2 patients: 1 mild asthma attack, 1 severe asthma attack | 0%10% | Mild; severe |
| Roder200730 | Grass mixPlacebo | 10896 | 29 patients with shortness of breath/cough28 patients with shortness of breath/cough | 27%29% | UnspecifiedUnspecified |

**SLIT Systemic Reactions: Cutaneous: (rash/urticaria/angioedema )**

| **Study** | **SLIT Allergen** | **Number of Patients in Arm** | **Description**  | **% of patients** | **Severity** |
| --- | --- | --- | --- | --- | --- |
| Tari, 199031 | Dust mite | 30 | 3 patients presented urticaria.  | 10% | Unspecified |
| deBot201121 | Dust miteplacebo | 125126 | 71 patients reported cutaneous adverse events82 patients reported cutaneous adverse eventsCutaneous events : Eczema, itch, rash | 57%65% | UnspecifiedUnspecified |
| Novembre, 200425 | Grass mixPlacebo | 5459 | 1 patient with cutaneous rash, which spontaneously resolved without any intervention. 1 patient had cutaneous rash  | 2%2% | MildMild |
| Marogna, 200828 | Birch and Grass mix | 130 | 1 patient reported 1 episode of generalized itching (without skin lesions) within 30 minutes of taking the dose. This adverse event appeared during the maintenance phase, self-resolved without therapy | 0.7% | Mild |
| Roder200730 | Grass mixPlacebo | 10896 | 42 patients with eczema/itch/rash34 patients with eczema/itch/rash | 39%35% | UnspecifiedUnspecified |

**SLIT Systemic Reactions: Gastrointestinal (nausea/pain/diarrhea)**

| **Study** | **SLIT Allergen** | **Number of Patients in Arm** | **Description** | **% of patients** | **Severity** |
| --- | --- | --- | --- | --- | --- |
| Tari, 199031 | Dust mite | 32 | 4 patients with GI symptoms: abdominal swelling and/or pain, and/or diarrhea | 12% | Unspecified |
| Novembre, 200425 | Grass mix | 54 | 1 patient experienced mild gastrointestinal complaints that spontaneously resolved without requiring treatment  | 2% | Mild |
| Valovirta, 200636Savolainen 200637 | Tree mix-high Tree mix-low Placebo | 323332 | Abdominal pain1 patient 2 patient -- | 3%6%-- | UnspecifiedUnspecified |
| La Rosa 199923Leonardi 200924 | ParietariaPlacebo | 2021 | 19 patients (12 in the active group and 7 in the placebo group) had gastrointestinal complaints. These complaints led to withdrawal from the trial in 4 cases in the active group and in 1 case in the placebo group.  | 60%33% | UnspecifiedUnspecified |
| Marogna, 200828 | Birch, Grass mix | 144 | 1 dropout due to abdominal pain.  | 0.7% | Unspecified |
| Stelmach201127 | Dust mite (arm 1 + 2 reported together)placebo | 4020 | Stomach aches in the first year of immunotherapy, 3.5% vs. %0.5% and 6% vs. 5.6% in the second year of immunotherapy. | NC | UnspecifiedUnspecified |
| Roder200730 | Grass mixPlacebo | 10896 | 80 patients with gastrointestinal complaints70 patients with gastrointestinal complaints | 74%73% | UnspecifiedUnspecified |
| deBot201121 | Dust mitePlacebo | 125126 | 85 patients with gastrointestinal complaints76 patients with gastrointestinal complaints | 68%60.3% | UnspecifiedUnspecified |

**SLIT Systemic Reactions: Cardiovascular**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study** | **SLIT Allergen** | **Number of Patients in Arm** | **Description** | **% of patients** | **Severity** |
| NO study described any cardiovascular reaction |

**SLIT Systemic Reactions: Ocular Reactions**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study** | **SLIT Allergen** | **Number of Patients in Arm** | **Description** | **% of patients** | **Severity** |
| Vourdas, 199834 | Olive | 34 | 1 patient presented conjunctivitis symptoms | 3% | Mild |
| La Rosa, 199923Leonardi 200924 | ParietariaPlacebo | 2021 | 1 patient with conjunctivitis1 patient with conjunctivitis | 5%5% | UnspecifiedUnspecified |
| Roder200730 | Grass mixPlacebo | 10896 | 53 patients with conjunctivitis54 patients with conjunctivitis | 49%56% | UnspecifiedUnspecified |
| Tari, 199031 | Dust mite | 30 | 6 patients with severe eye symptoms | 20% | Severe |
| deBot201121 | Dust mitePlacebo | 125126 | 69 patients with conjunctivitis82 patients with conjunctivitis | 55%65% | Unspecified Unspecified |

**SLIT Systemic Reactions: General symptoms**

| **Study** | **SLIT Allergen** | **Number of Patients in Arm** | **Description** | **% of patients** | **Severity** |
| --- | --- | --- | --- | --- | --- |
| Pajno, 200018 | Dust mitePlacebo | 1212 | 4 patients : reported tiredness1 patient : reported tiredness These side-effects resolved spontaneously without drugs | 30%8% | UnspecifiedUnspecified |
| Hirsch, 199729 | Dust mite | 15 | 1 patient dropped out after 8 weeks of therapy (14 years old), complaining of local swelling under the tongue and a subjective feeling of weakness after having reached the maintenance dose. | 7% | Unspecified |
| Valovirta 200636Savolainen 200637 | Tree mix-high  | 32 | 1 patient had flushing, 2 patients had allergic reaction | 9% | Unspecified |
| Stelmach201127 | Dust mite (arm 1 + 2 reported together)placebo | 4020 | Headaches in first year of immunotherapy, 4.1% vs 4% and 0 vs .2% in the second year of immunotherapy | NC | UnspecifiedUnspecified |
| Roder200730 | Grass mixPlacebo | 10896 | 10 patients with allergy (not specified)9 patients with allergy (not specified) | 9%9% | UnspecifiedUnspecified |
| Pajno 200450 | ParietariaPlacebo | 1515 | 3 patients with tiredness after drop ingestion- 1 dropout due to abdominal pain, shortness of breath, and wheezing 20 mins after drops ingestion2 patients with tiredness after drop ingestion | 27%13% | MildMild |
| deBot201121 | Dust mitePlacebo | 125126 | 75 patients with allergy (not specified)84 patients with allergy (not specified) | 60%67% | UnspecifiedUnspecified |
| Tseng 200822 | Dust mitePlacebo | 3033 | 19 patients with side effects including tongue numbness, as most common AE, and epistaxis, mouth ulceration, asthma attacks 7 patients with side effects including tongue numbness, as most common AE, and epistaxis, mouth ulceration, asthma attacks  | 63%21% | MildMild |
| Niu 2006  | Dust mite | 56 | 5 patients with 10 incidences of mild-moderate local reactions (tongue disorder, vomiting, abdominal pain, circumoral paresthesia) | 9% | Mild-moderate |

NC not calculated

**SLIT ANAPHYLACTIC Reactions**

| **Study** | **SLIT Allergen** | **Number of Patients in Arm** | **Description** | **% of patients** | **Severity** |
| --- | --- | --- | --- | --- | --- |
| NO study described any anaphylactic reaction |