

## **PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN**

### **Summary of risk management plan for SQ tree SLIT-tablet (Birch pollen extract)**

This is a summary of the risk management plan (RMP) for the SQ tree SLIT-tablet. The RMP details important risks of the SQ tree SLIT-tablet, and how more information will be obtained about the SQ tree SLIT-tablet's risks and uncertainties (missing information).

The SQ tree SLIT-tablet's summary of product characteristics (SmPC) and its package leaflet (PL) give essential information to healthcare professionals and patients on how the SQ tree SLIT-tablet should be used.

#### **I. The medicine and what it is used for**

The SQ tree SLIT-tablet is authorised for treatment of moderate-to-severe allergic rhinitis and/or conjunctivitis, induced by pollen from the birch homologous group (see SmPC for the full indication). It contains allergen extract from birch (*Betula verrucosa*) as the active substance and it is given by sublingual administration of a white to off-white freeze-dried debossed oral lyophilisate.

#### **II. Risks associated with the medicine and activities to minimise or further characterise the risks**

Important risks of the SQ tree SLIT-tablet, together with measures to minimise such risks and the proposed studies for learning more about the SQ tree SLIT-tablet's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals
- Important advice on the medicine's packaging
- The authorised package size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

##### **II.A List of important risks and missing information**

Important risks of the SQ tree SLIT-tablet are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of the SQ tree SLIT-tablet. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	<ul style="list-style-type: none"> <li>• None</li> </ul>
Important potential risks	<ul style="list-style-type: none"> <li>• Acute worsening of asthma symptoms</li> <li>• Eosinophilic esophagitis</li> </ul>
Missing information	<ul style="list-style-type: none"> <li>• None</li> </ul>

## II.B Summary of important risks

Important potential risk: Acute worsening of asthma symptoms	
<b>Evidence for linking the risk to the medicine</b>	Acute worsening of asthma is considered an important potential risk as it can lead to life threatening situations or even fatal outcomes for the patients in severe cases. In addition, asthma is a known risk factor for systemic allergic reactions ( <a href="#">Lieberman et al. 2010</a> ; <a href="#">Muraro et al. 2014</a> ; <a href="#">Simons et al. 2011</a> ) and has previously been known to constitute a risk in AIT although AIT has also been used to treat asthma ( <a href="#">GINA Executive Committee 2012</a> ). From the clinical development programme, it has not been possible to establish a clear causal relationship to treatment with the SQ tree SLIT-tablet, however the evidence from the literature and other SLIT-tablets provides evidence to suspect a causal relationship, thus a potential risk to the SQ tree SLIT-tablet.
<b>Risk factors and risk groups</b>	<ul style="list-style-type: none"> <li>• Impaired lung function/FEV<sub>1</sub>&lt;70% of predicted value at initiation of treatment</li> <li>• Severe asthma exacerbation within the last 3 months prior to initiation of treatment</li> <li>• Recent or ongoing upper respiratory tract infections</li> <li>• Pregnancy</li> </ul>
<b>Risk minimisation measures</b>	<p>Routine risk minimisation measures: <a href="#">SmPC section 4.2, 4.3 and 4.4</a> <a href="#">PL section 2, 3 and 4</a></p> <p>Additional risk minimisation measures: <i>None</i></p>

Important potential risk: Eosinophilic esophagitis	
<b>Evidence for linking the risk to the medicine</b>	Events of eosinophilic esophagitis (EoE) have occurred with the use of other SLIT-tablets ( <a href="#">Merck Sharp &amp; Dohme Corp 2014a</a> ; <a href="#">Merck Sharp &amp; Dohme Corp 2014b</a> ) but it is not yet confirmed that this association may be a class effect for SLIT. EoE is thus considered an important potential risk for the SQ tree SLIT-tablet.
<b>Risk factors and risk groups</b>	<ul style="list-style-type: none"> <li>• Male gender</li> <li>• Caucasian race</li> <li>• Atopy</li> </ul>

<b>Important potential risk: Eosinophilic esophagitis</b>	
	<ul style="list-style-type: none"><li>• Genetic predisposition</li><li>• Environmental factors including the timing and nature of food and aeroallergen exposure to the developing immune system may be important (<a href="#">Philpott et al. 2014</a>).</li></ul>
<b>Risk minimisation measures</b>	Routine risk minimisation measures: <a href="#">SmPC section 4.4</a> <a href="#">PL section 4</a>  Additional risk minimisation measures: <i>None</i>

## II.C Post-authorisation development plan

### II.C.1 Studies which are conditions of the marketing authorisation

Not applicable since the SQ tree SLIT-tablet has not yet obtained a marketing authorisation.

### II.C.2 Other studies in post-authorisation development plan

Not applicable since the SQ tree SLIT-tablet has not yet obtained a marketing authorisation.