# PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

## Summary of risk management plan for Aitmyte (Sublingual Tablet of House Dust Mite Allergen Extracts)

This is a summary of the risk management plan (RMP) for Aitmyte. The RMP details important risks of Aitmyte, how these risks can be minimised, and how more information will be obtained about Aitmyte's risks and uncertainties (missing information).

Aitmyte's Summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Aitmyte should be used.

Important new concerns or changes to the current ones will be included in updates of Aitmyte's RMP.

## I. THE MEDICINE AND WHAT IT IS USED FOR

Aitmyte is indicated in adolescents (12-17 years) and adults for treatment of moderate to severe house dust mite-induced allergic rhinitis or rhinoconjunctivitis diagnosed by clinical history and a positive test of house dust mite sensitisation (skin prick test and/or specific IgE). It contains "mixture of *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* house dust mite allergen extracts" as the active substance and it is given orally (sublingual tablet).

## II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Aitmyte, together with measures to minimise such risks and the proposed studies for learning more about Aitmyte 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 pack 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 minimize its risks.

Together, these measures constitute routine risk minimization measures.

If important information that may affect the safe use of Aitmyte is not yet available, it is listed under 'missing information' below.

## II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of Aitmyte 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 Aitmyte. 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

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| **Important Identified risks** | Severe laryngopharyngeal reactions<br><br>Anaphylactic reactions including anaphylactic shock<br><br>Eosinophilic oesophagitis (EoE) |
| **Important potential risk** | Autoimmune disorders |
| **Missing information** | Pregnancy and lactation |

## II.B SUMMARY OF IMPORTANT RISKS

| **Important Identified risk: Severe laryngopharyngeal reactions** | |
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| Evidence for linking the risk to the Medicine | The evidence is based on the data from clinical trials and the post-marketing experience. |
| Risk factors and risk groups | Administration in patients with severe, uncontrolled or unstable asthma and a history of severe reaction to previous AIT have been identified as a risk factors for severe AIT-induced laryngopharyngeal reactions [*Cox et al., 2011*]. |

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| Risk minimization measures | Routine risk minimisation measures<br><br>Routine risk communication<br>SmPC section 4.2, 4.4 and 4.8<br>PL section 1, 2, 3 and 4<br><br>Routine risk minimisation activities recommending specific clinical measures to address the risk<br><br>• Initiation of the treatment recommended under medical supervision and monitoring of the patient for 30 minutes (Section 4.2 of the SmPC and section 1 and 3 of the PL).<br><br>• Severe allergic reactions and their management by treatment discontinuation and seeking immediate medical care are included in the section 4.4 and 4.8 of the SmPC and in the section 2 and 4 of the PL.<br><br>Other routine risk minimisation measures beyond the Product Information:<br><br>Legal status: subject to restricted medical prescription by physicians experienced in the treatment of allergic diseases.<br><br>Additional risk minimization measures<br>None. |
| **Important Identified risk: Anaphylactic reactions including anaphylactic shock** | |
| Evidence for linking the risk to the Medicine | The evidence is based on the data from clinical trials and the post-marketing experience. |
| Risk factors and risk groups | Administration in patients with poorly controlled asthma has been identified as a risk factor for severe AIT-induced anaphylactic reaction. A high degree of hypersensitivity, or reaction to previous AIT were also identified as risk factors to develop severe anaphylactic reaction to AIT [*Cox et al., 2011*]. |

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| Risk minimisation measures | Routine risk minimisation measures<br><br>Routine risk communication<br>SmPC section 4.2, 4.4 and 4.8<br>PL section 1, 2, 3 and 4<br><br>Routine risk minimisation activities recommending specific clinical measures to address the risk<br><br>• Initiation of the treatment is recommended under medical supervision and surveillance of the patient for 30 minutes (Section 4.2 of the SmPC and section 1 and 3 of the PL).<br><br>• Severe allergic reactions and their management by treatment discontinuation and seeking immediate medical care are included in the section 4.4 and 4.8 of the SmPC and in the section 2 and 4 of the PL.<br><br>Other routine risk minimisation measures beyond the Product Information:<br><br>Legal status: subject to restricted medical prescription by physicians experienced in the treatment of allergic diseases.<br><br>Additional risk minimisation measures<br>None |
| **Important Identified risk: eosinophilic oesophagitis (EoE)** | |
| Evidence for linking the risk to the Medicine | The evidence is based on the data from clinical trials and post-marketing experience. |
| Risk factors and risk groups | The aetiologies of EoE are not fully identified, but an association between EoE and food allergies is recognised, suggesting that food antigens may represent a possible cause [*Philpott et al., 2014*]. Environmental allergens have also been implicated as possible contributors in the evolution of the disease, as described in a published case of an EoE exacerbation during pollen season [*Fogg et al., 2003*]. It is noteworthy that most patients developing EoE have underlying allergic disease suggesting a strong allergic component of this disease. |

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| Risk minimisation measures | Routine risk minimisation measures<br><br>Routine risk communication<br>SmPC section 4.4 and 4.8<br>PL section 3 and 4<br><br>Routine risk minimisation activities recommending specific clinical measures to address the risk<br><br>Eosinophilic oesophagitis and its management by treatment interruption and physician consultation is mentioned in the section 4.4 and 4.8 of the SmPC and the section 4 of the PL.<br><br>Other routine risk minimisation measures beyond the Product Information:<br><br>Legal status: subject to restricted medical prescription by physicians experienced in the treatment of allergic diseases.<br><br>Additional risk minimisation measures<br>None |
| **Important potential risk: autoimmune disorders** | |
| Evidence for linking the risk to the Medicine | The analysis of clinical development as well as post-marketing data. |
| Risk factors and risk groups | Autoimmune diseases are multifactorial pathologies, resulting from a complex interaction between genetic predispositions and environmental triggers factors. |
| Risk minimisation measures | Routine risk minimisation measures<br>Routine risk communication:<br>SmPC section 4.3 and 4.4<br>PL section 2<br><br>Other routine risk minimisation measures beyond the Product Information<br>Legal status: subject to restricted medical prescription by physicians experienced in the treatment of allergic diseases.<br><br>Additional risk minimisation measures<br>None |

| **Missing information: pregnancy and lactation** | |
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| Evidence for linking the risk to the Medicine | Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. Contraception was a clinical trial requirement. In addition, pregnant and lactating women were excluded from enrolment in clinical studies with sublingual tablet of Aitmyte. There are insufficient post-marketing data available on the use of Aitmyte in pregnant and lactating women.<br>It is unknown whether HDM allergen extracts are excreted in human breast milk. |
| Risk minimisation measures | <u>Routine risk minimisation measures</u><br><br>Routine risk communication<br>SmPC section 4.6<br>PL section 2<br><br><u>Other routine risk minimisation measures beyond the Product Information:</u><br><br>Legal status: subject to restricted medical prescription by physicians experienced in the treatment of allergic diseases.<br><br><u>Additional risk minimisation measures</u><br>None |