# PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

## Summary of risk management plan for Suprane (desflurane)

This is a summary of the risk management plan (RMP) for Suprane. The RMP provides details on the important risks of Suprane, how these risks can be minimized, and how more information will be obtained about the risks and uncertainties (missing information) for Suprane. The summary of product characteristics (SmPC) and package leaflet (PL) for Suprane provide essential information to healthcare professionals and patients on how Suprane should be used.

This summary of the RMP for Suprane should be read in the context of all other related information, including the assessment report of the evaluation and its plain-language summary, all of which are part of the European Public Assessment Report (EPAR).

Important new safety concerns and/or changes to the current safety concerns will be included in future updates of the RMP.

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

Suprane is indicated as an inhalation agent for induction and/or maintenance of anesthesia for inpatient and outpatient surgery in adults and for maintenance of anesthesia for inpatient and outpatient surgery in intubated infants and children; refer to the SmPC for complete indication wording. It contains desflurane 100% as the active substance, and it is given by inhalation.

## II. Risks associated with the medicine and activities to minimize or further characterize the risks

The important risks of Suprane, together with measures to minimize such risks, are outlined below.

Measures to minimize 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 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.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

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

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

The important risks of Suprane are risks that need special risk management activities to further investigate or minimize 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 Suprane. 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). The important risks and missing information for Suprane are listed in the table below.

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| **Important identified risks** | Hepatic dysfunction |
| | Malignant hyperthermia |
| | Perioperative hyperkalemia |
| | Cardiac arrhythmias |
| | Myocardial ischemia in patients with a history of coronary artery disease |
| | Laryngospasm during induction and maintenance of anesthesia in non-intubated children |
| **Important potential risks** | Increased intracranial pressure in patients with space occupying lesions |
| **Missing information** | Use in pregnant and lactating women and during labor and vaginal delivery |

## *II.B Summary of important risks and missing information*

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| **Important identified risk: Hepatic dysfunction** | |
| **Evidence for linking the risk to the medicine** | Hepatic injury, and immune-mediated hepatitis, has been associated with use of halogenated anesthetics, including Suprane. Cases of mild, moderate, and severe post-operative hepatic dysfunction or hepatitis with or without jaundice, including hepatic necrosis, and hepatic failure, have been reported with Suprane in clinical trials and with post-market use. |
| **Risk factors and risk groups** | Patients with a history of hepatic dysfunction or confirmed or suspected hepatitis following administration of halogenated anesthetics in the past. |
| **Risk minimization measures** | **Routine risk minimization measures:**<br>Discussed in SmPC sections 4.2, 4.3, and 4.4.<br>Adverse reactions representing hepatic dysfunction are included in SmPC section 4.8.<br>Discussed in PL sections 2 and 4.<br>**Additional risk minimization measures:**<br>None proposed. |
| **Additional pharmacovigilance activities** | None proposed. |
| **Important identified risk: Malignant hyperthermia** | |
| **Evidence for linking the risk to the medicine** | Malignant hyperthermia is a severe potentially fatal complex hypermetabolic reaction which can be triggered by Suprane. Cases of malignant hyperthermia have been reported with Suprane in clinical trials and with post-market use. |
| **Risk factors and risk groups** | Patients with a history or family history of malignant hyperthermia or with established or genetic risk factors for malignant hyperthermia. |
| **Risk minimization measures** | **Routine risk minimization measures:**<br>Discussed in SmPC sections 4.3 and 4.4.<br>Malignant hyperthermia is included in SmPC section 4.8.<br>Discussed in PL section 2.<br>**Additional risk minimization measures:**<br>None proposed. |
| **Additional pharmacovigilance activities** | None proposed. |
| **Important identified risk: Perioperative hyperkalemia** | |
| **Evidence for linking the risk to the medicine** | Use of inhaled anesthetics, including Suprane, has been associated with rare increases in serum potassium levels that have resulted in cardiac arrhythmias in the post-operative period, some of which had fatal outcomes. |

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| **Risk factors and risk groups** | Patients with a history of myopathy or history of Duchenne Muscular Dystrophy may be more susceptible. Patients receiving concomitant succinylcholine may also be susceptible. |
| **Risk minimization measures** | **Routine risk minimization measures:**<br>Discussed in SmPC section 4.4.<br>Hyperkalemia is included in SmPC section 4.8.<br>Discussed in PL sections 2 and 4.<br>**Additional risk minimization measures:**<br>None proposed. |
| **Additional pharmacovigilance activities** | None proposed. |
| **Important identified risk: Cardiac arrhythmias** | |
| **Evidence for linking the risk to the medicine** | Use of inhaled anesthetics, including Suprane, has been associated with cardiac arrhythmias in the post-operative period.<br>Cardiac arrhythmias including tachycardia, bradycardia, nodal arrhythmias, ECG abnormalities (i.e., bigeminy, supraventricular tachycardia, and atrial fibrillation) have occurred in clinical trials with Suprane.<br>Torsade de pointes (potentially resulting from QT prolongation) has been reported with Suprane in clinical trials and with post-market use. |
| **Risk factors and risk groups** | Patients with latent as well as overt muscular dystrophies, particularly Duchenne Muscular Dystrophy, appear to be most vulnerable to increases in serum potassium resulting in cardiac arrhythmias. Patients receiving concomitant succinylcholine may also be susceptible.<br>Patients with coronary artery disease may be more susceptible to increases in heart rate.<br>Patients with congenital long QT syndrome or patients taking drugs that can prolong the QT interval may be more susceptible to QT prolongation and thereby torsade de pointes. |
| **Risk minimization measures** | **Routine risk minimization measures:**<br>Discussed in SmPC section 4.4.<br>Adverse reactions representing cardiac arrhythmias are included in SmPC section 4.8.<br>Discussed in PL sections 2 and 4.<br>**Additional risk minimization measures:**<br>None proposed. |
| **Additional pharmacovigilance activities** | None proposed. |
| **Important identified risk: Myocardial ischemia in patients with a history of coronary artery disease** | |
| **Evidence for linking the risk to the medicine** | Dose related changes in hemodynamic parameters have been observed with Suprane administration. In patients with pre-existing coronary artery disease, these changes may lead to decreased blood flow to the heart, or myocardial ischemia. |

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| | Myocardial ischemia has been described in both in clinical trials and with post-market use of Suprane. |
| **Risk factors and risk groups** | Patients with coronary artery disease may be more susceptible to dose related changes in hemodynamic parameters and thereby myocardial ischemia, especially when Suprane is the only anesthetic used. |
| **Risk minimization measures** | **Routine risk minimization measures:**<br>Discussed in SmPC section 4.4.<br>Myocardial ischemia is included in SmPC section 4.8.<br>Discussed in PL section 2.<br>**Additional risk minimization measures:**<br>None proposed. |
| **Additional pharmacovigilance activities** | **Additional pharmacovigilance activities:**<br>None proposed. |
| **Important identified risk: Laryngospasm during induction and maintenance of anesthesia in non-intubated children** | |
| **Evidence for linking the risk to the medicine** | Off-label use of Suprane for induction of anesthesia may result in airway irritation (which can result in coughing, laryngospasm, and a decrease in oxygen saturation) in children.<br>Use of Suprane for maintenance anesthesia with LMA in children, in particular for children 6 years old or younger, may result in an increased potential for adverse respiratory reactions, e.g., coughing and laryngospasm, especially with removal of the LMA under deep anesthesia.<br>Laryngospasm has been described in both in clinical trials and with post-market use of Suprane. |
| **Risk factors and risk groups** | Pediatric patients receiving Suprane off-label for induction anesthesia. Non-intubated pediatric patients receiving Suprane for maintenance anesthesia, in particular those children six years old or younger. |
| **Risk minimization measures** | **Routine risk minimization measures:**<br>Discussed in SmPC sections 4.3 and 4.4.<br>Laryngospasm is included in SmPC section 4.8.<br>Discussed in PL sections 2 and 4.<br>**Additional risk minimization measures:**<br>None proposed. |
| **Additional pharmacovigilance activities** | **Additional pharmacovigilance activities:**<br>None proposed. |
| **Important identified risk: Increased intracranial pressure in patients with space occupying lesions** | |
| **Evidence for linking the risk to the medicine** | Patients with decreased intracranial compliance due to head injury or caused by space occupying lesions may be at risk for cerebral hyperemia and further increases in intracranial pressure if administered a volatile anesthetic (such as Suprane) at high concentrations and/or as the sole anesthetic agent. |

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| **Risk factors and risk groups** | Patients with known or suspected increases in cerebrospinal fluid pressure or intra-cranial space occupying lesions. |
| **Risk minimization measures** | **Routine risk minimization measures:**<br>Discussed in SmPC section 4.4.<br>Discussed in PL section 2.<br>**Additional risk minimization measures:**<br>None proposed. |
| **Additional pharmacovigilance activities** | None proposed. |
| **Missing information: Use in pregnant and lactating women and during labor and vaginal delivery** | |
| **Risk minimization measures** | **Routine risk minimization measures:**<br>Discussed in SmPC sections 4.4, 4.6, and 5.3.<br>Discussed in PL section 2.<br>**Additional risk minimization measures:**<br>None proposed. |
| **Additional pharmacovigilance activities** | None proposed. |

## *II.C Post-authorization development plan*

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

There are no studies which are conditions of the marketing authorization or specific obligations of Suprane.

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

There are no studies required for Suprane.