# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Suprane Inhalation vapour, solution

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Desflurane 100% v/v

For a full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Inhalation vapour, solution.
A clear, colourless to practically odourless solution.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Desflurane is indicated as an inhalation agent for induction and maintenance of anaesthesia in adults.

Desflurane is indicated for maintenance of anaesthesia in intubated infants and children under 12 years.

Desflurane is not indicated for induction of anaesthesia in paediatric patients. (See Section 4.3)

Use of desflurane in dental anaesthesia should be restricted to hospitals and day care units only.

### 4.2 Posology and method of administration

Method of administration

Desflurane is administered by inhalation. The concentration of desflurane should be delivered from a vaporizer specifically designed and designated for use with desflurane.

Premedication
The premedication should be chosen to suit the individual requirements of the patient.

Studies to date have not shown an effect of premedication on respiratory tract reactions associated with inhalational induction of anaesthesia.

Individualization
The administration of general anaesthesia must be individualized based on the patient's response.

Effects on Concomitant Therapy
Opioids or benzodiazepines decrease the amount of desflurane required to produce anaesthesia.
Desflurane decreases the required doses of neuromuscular blocking agents (see Table 2, section 4.5). If added relaxation is required, supplemental doses of muscle relaxants may be used. (See section 4.5)

Dosage
The minimum alveolar concentration (MAC) of desflurane decreases with increasing patient age. The dose of desflurane should be adjusted accordingly. The MAC has been determined as listed in Table 1.

Table 1
MAC for desflurane according to patient age and inhalation mixture (Mean±SD)

| Age | N* | 100% Oxygen | N* | 60% Nitrous Oxide/40% Oxygen |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| 2 weeks | 6 | 9.2±0.0 | - | - |
| 10 weeks | 5 | 9.4±0.4 | - | - |
| 9 months | 4 | 10.0±0.7 | 5 | 7.5±0.8 |
| 2 years | 3 | 9.1±0.6 | - | - |
| 3 years | - | - | 5 | 6.4±0.4 |
| 4 years | 4 | 8.6±0.6 | - | - |
| 7 years | 5 | 8.1±0.6 | - | - |
| 25 years | 4 | 7.3±0.0 | 4 | 4.0±0.3 |
| 45 years | 4 | 6.0±0.3 | 6 | 2.8±0.6 |
| 70 years | 6 | 5.2±0.6 | 6 | 1.7 |

*N= number of crossover pairs (using up-and-down method of quantal response)

Induction of Anaesthesia in Adults

In adults, a starting concentration of 3% is recommended, increased in 0.5-1.0% increments every 2 to 3 breaths. Inspired concentrations of 4-11% of desflurane usually produce surgical anaesthesia in 2-4 minutes.Higher concentrations up to 15% may be used. Such concentrations of desflurane will proportionately dilute the concentration of oxygen and commencing administration of oxygen should be 30% or above. After induction in adults with an intravenous drug such as thiopental or propofol, desflurane can be started at approximately 0.5-1 MAC, whether the carrier gas is $O_2$ or $N_2O/O_2$.

Desflurane should be administered at 0.8 MAC or less, and in conjunction with a barbiturate induction and hyperventilation (hypocapnia) until cerebral decompression in patients with known or suspected increases in cerebrospinal fluid pressure. Appropriate attention must be paid to maintain cerebral perfusion pressure. (See section 4.4)

During induction in adults, the overall incidence of oxyhemoglobin desaturation ($SpO_2$ < 90%) was 6%. High concentrations of desflurane may induce upper airway adverse events. See section 4.8.

Induction of Anaesthesia in Children

Desflurane is not indicated for use as an inhalation induction agent in children and infants because of the frequent occurrence of cough, breath holding, apnoea, laryngospasm and increased secretions (see section 4.4)

Maintenance of Anaesthesia in Adults

Surgical levels of anaesthesia may be sustained with 2-6% concentration of desflurane when nitrous oxide is used concomitantly. Desflurane at 2.5-8.5 % may be required when administered using oxygen or oxygen enriched air. In adults, surgical levels of anaesthesia may be sustained at a reduced concentration of desflurane when nitrous oxide is used concomitantly.

Maintenance of Anaesthesia in Children

Desflurane is indicated for maintenance of anaesthesia in intubated infants and children under 12 years of age. Surgical levels of anaesthesia may be maintained in children with end-tidal concentrations of 5.2 to 10% desflurane with or without the concomitant use of nitrous oxide. Although endtidal concentrations of up to 18% desflurane have been administered for short periods of time, if high concentrations are used with nitrous oxide it is important to ensure that the inspired mixture contains a minimum of 25% oxygen.

If added relaxation is required, supplemental doses of muscle relaxants may be used.

Due to limited data available, desflurane is not approved for maintenance of anaesthesia in children 12-18 years of age. (see Section 4.4)

Blood Pressure and Heart Rate During Maintenance

Blood pressure and heart rate should be monitored carefully during maintenance as part of the evaluation of depth of anaesthesia.

Dosage in Renal and Hepatic Impairment

Concentrations of 1-4% desflurane in nitrous oxide/ oxygen have been used in patients with chronic renal or hepatic impairment and during renal transplantation surgery.

Because of minimal metabolism, a need for dose adjustment in patients with renal and hepatic impairment is not to be expected.

**4.3 Contraindications**

Desflurane should not be used for patients in whom general anaesthesia is contraindicated.

Desflurane is also contraindicated:

- - in patients with known sensitivity to halogenated agents,
- - in patients with known or genetic susceptibility to malignant hyperthermia (see Section 4.4)
- - in all patients (adults and children) undergoing dental procedures outside a hospital or day care unit (see Section 4.1).

Desflurane should not be used in patients in whom liver dysfunction, jaundice, unexplained fever, leucocytosis or eosinophilia has occurred after a previous halogenated anaesthetic administration.

Myocardial ischaemia has occurred during induction with desflurane in a significant proportion of patients undergoing CABG. The product is not suitable for such use.

Desflurane is contraindicated for use as an inhalation induction agent in pediatric patients because of the frequent occurrence of cough, breath holding, apnea, laryngospasm and increased secretions. See also Section 4.4 - Paediatric Inhalation Induction.

**4.4 Special warnings and precautions for use**

Desflurane should only be administered by persons trained in the administration of general anaesthesia using a vaporizer specifically designed and designated for use with desflurane. All patients anaesthetised with desflurane should be constantly monitored, including ECG, BP, oxygen saturation and end-tidal $CO_2$, in a setting where full resuscitative equipment is available and with staff fully trained in resuscitative techniques.
The presence of additional risk factors should be taken into consideration (see also Section 4.8). Hypotension and respiratory depression increase as anaesthesia is deepened.

Use of desflurane in hypovolaemic, hypotensive and debilitated patients has not been extensively investigated. As with other potent inhaled anaesthetics, a lower concentration is recommended for use in these patients.

Desflurane should not be administered in patients who are prone to develop bronchoconstriction since bronchospasm can occur.

There is insufficient experience of use in repeated anaesthesia to make a definite recommendation in this regard. As with all halogenated anaesthetics repeat anaesthesia within a short period of time should be approached with caution.

This agent causes a rise in blood sugar levels during anaesthesia. The clinical significance of this is unknown.

As with other halogenated anaesthetics, desflurane has been reported to interact with dry carbon dioxide adsorbents during closed circuit anaesthesia, to form carbon monoxide. Inhalation of carbon monoxide may lead to formation of significant levels of carboxyhaemoglobin in exposed patients. In the event that a patient on closed circuit anaesthesia using desflurane develops oxygen desaturation which does not respond to the usual therapeutic corrective measures, direct measurement of carboxyhaemoglobin using reliable methods should be carried out. All necessary precautions should be taken to insure that carbon dioxide adsorbents are not allowed to dry out.

Warnings:

Malignant Hyperthermia (MH)
In susceptible individuals, potent inhalation anaesthetic agents may trigger a skeletal muscle hypermetabolic state leading to high oxygen demand and the clinical syndrome known as malignant hyperthermia. Desflurane was shown to be a potential trigger of malignant hyperthermia. The clinical syndrome is signaled by hypercapnia, and may include muscle rigidity, tachycardia, tachypnea, cyanosis, arrhythmias, and/or unstable blood pressure. Some of these non-specific signs may also appear during light anaesthesia: acute hypoxia, hypercapnia, and hypovolemia. Treatment of malignant hyperthermia includes discontinuation of triggering agents, administration of intravenous dantrolene sodium, and application of supportive therapy. Renal failure may appear later, and urine flow should be monitored and sustained if possible. Desflurane should not be used in subjects known to be susceptible to MH. Fatal outcome of malignant hyperthermia has been reported with desflurane.

Perioperative Hyperkalemia
Use of inhaled anaesthetic agents including desflurane, has been associated with rare increases in serum potassium levels that have resulted in cardiac arrhythmias, some fatal, in patients during the postoperative period. Patients with latent as well as overt muscular dystrophies, particularly Duchenne muscular dystrophy appear to be most vulnerable. Concomitant use of suxamethonium has been associated with most, but not all, of these cases. These patients also experienced significant elevations in serum creatinine kinase levels and, in some cases, changes in urine consistent with myoglobinuria. Despite the similarity in presentation to malignant hyperthermia, none of these patients exhibited signs or symptoms of muscle rigidity or hypermetabolic state.

Early and aggressive intervention to treat the hyperkalaemia and reistant arrhythmias is recommended, as is subsequent evaluation for latent neuromuscular disease.

Paediatric Inhalation Induction
Desflurane is not indicated for use as an inhalation induction agent in children and infants because of the frequent occurrence of cough, breath holding, apnoea, laryngospasm and increased secretions.

Use in Children with Bronchial Hyperreactivity
Desflurane should be used with caution in children with asthma or a history of recent upper airway infection due to the potential for airway narrowing and increases in airway resistance.

Maintenance of Anaesthesia in Children
Due to the limited data available, desflurane is not approved for maintenance of anaesthesia in children 12-18 years of age.

Due to the limited data available in non-intubated paediatric patients, desflurane is not approved for maintenance of anaesthesia in non-intubated children.

Caution should be exercised should desflurane be used for maintenance anaesthesia with laryngeal mask airway (LMA) in children, in particular for children 6 years old or younger, because of the increased potential for adverse respiratory reactions e.g. coughing and laryngospasm, especially with removal of the LMA under deep anaesthesia.

Emergence from anaesthesia in children may evoke a brief state of agitation that may hinder cooperation.

Obstetrics
Due to the limited number of patients studied, the safety of desflurane has not been established for use in obstetric procedures. Desflurane is a uterine-relaxant and reduces the uterine-placental blood-flow. (See section 4.6)

QT Prolongation
QT prolongation, very rarely associated with torsade de pointes, has been reported (see section 4.8). Caution should be exercised when administering desflurane to susceptible patients.

Precautions:
With the use of halogenated anaesthetics, disruption of hepatic function, icterus and fatal liver necrosis have been reported: such reactions appear to indicate hypersensitivity. As with other halogenated anaesthetic agents, desflurane may cause sensitivity hepatitis in patients who have been sensitized by previous exposure to halogenated anaesthetics. Cirrhosis, viral hepatitis or other pre-existing hepatic disease may be a reason to select an anaesthetic other than a halogenated anaesthetic.

Desflurane, as other volatile anaesthetics, may produce a dose-dependent increase in cerebrospinal fluid pressure (CSFP) when administered to patients with space occupying lesions. In such patients, desflurane should be administered at 0.8 MAC or less, and in conjunction with a barbiturate induction and hyperventilation (hypocapnia) until cerebral decompression in patients with known or suspected increases in CSFP. Appropriate attention must be paid to maintain cerebral perfusion pressure.

In patients with coronary artery disease, maintenance of normal hemodynamics is important to avoid myocardial ischemia. Marked increases in pulse rate, mean arterial pressure and levels of epinephrine and norepinephrine are associated with a rapid increase in desflurane concentrations. Desflurane should not be used as the sole agent for anesthetic induction in patients at risk of coronary artery disease or in patients where increases in heart rate or blood pressure are undesirable. It should be used with other medications, preferably intravenous opioids and hypnotics.

During maintenance of anaesthesia, increases in heart rate and blood pressure occurring after rapid incremental increases in end-tidal concentration of desflurane may not represent inadequate anaesthesia. The changes due to sympathetic activation resolve in approximately 4 minutes. Increases in heart rate and blood pressure occurring before or in the absence of a rapid increase in desflurane concentration may be interpreted as light anaesthesia.

Hypotension and respiratory depression increase as anaesthesia is deepened.

As with other rapid-acting anesthetic agents, rapid emergence with desflurane should be taken into account in cases where post-anaesthesia pain is anticipated. Care should be taken that appropriate analgesia has been administered to the patient at the end of the procedure or early in the post-anaesthesia care unit stay.

**4.5 Interaction with other medicinal products and other forms of interaction**

Concentration of other gases
The MAC for desflurane is reduced by concomitant N2O administration. (see Table 1)

Non-depolarizing and depolarizing muscle relaxants

Commonly used muscle relaxants are potentiated by desflurane.
Anaesthetic concentrations of desflurane at equilibrium reduce the ED95 of suxamethonium by approximately 30% and that of atracurium and pancuronium by approximately 50% compared to N2O/opioid anaesthesia. The doses of pancuronium, atracurium, suxamethonium and vecuronium needed to produce 95% (ED95) depression in neuromuscular transmission at different concentrations of desflurane are given in Table 2. With the exception of vecuronium, these doses are similar to isoflurane. The ED95 of vecuronium is 14% lower with desflurane than isoflurane. Additionally, recovery from neuromuscular blockade is longer with desflurane than with isoflurane.

**Table 2 - Dosage (mg/kg) of muscle relaxant causing 95% depression in neuromuscular transmission**

| **Desflurane Concentration** | **Pancuronium** | **Atracurium** | **Suxamethonium** | **Vecuronium** |
|---|---|---|---|---|
| 0.65 MAC/ 60%$N_2O/O_2$ | 0.026 | 0.133 | *NA | *NA |
| 1.25 MAC/ 60%$N_2O/O_2$ | 0.018 | 0.119 | *NA | *NA |
| 1.25 MAC/$O_2$ 100% $O_2$ | 0.022 | 0.120 | 0.360 | 0.019 |

*NA = not available

Pre-anaesthetic Drugs
No clinically significant adverse interactions with commonly used pre-anaesthetic drugs, or drugs used during anaesthesia (intravenous agents, and local anaesthetic agents) were reported in clinical trials. The effect of desflurane on the disposition of other drugs has not been determined.

Sedatives
Patients anaesthetised with different concentrations of desflurane who received increasing doses of fentanyl showed a marked reduction in the anaesthetic requirements or MAC. The administration of increasing doses of intravenous midazolam showed a small reduction in MAC. Results are reported in Table 3. These MAC reductions are similar to those observed with isoflurane. It is anticipated that there will be a similar influence on MAC with other opioid and sedative drugs.

Table 3: Effect of Fentanyl or Midazolam on Desflurane MAC

| *MAC (%) | %MAC | Reduction |
|---|---|---|
| No Fentanyl | 6.33 - 6.35 | - |
| Fentanyl (3 mcg/kg) | 3.12 - 3.46 | 46 - 51 |
| Fentanyl (6 mcg/kg) | 2.25 - 2.97 | 53 - 64 |
| No Midazolam | 5.85 - 6.86 | - |
| Midazolam (25 mcg/kg) | 4.93 | 15.7 |

| | | |
|---|---|---|
| Midazolam (50 mcg/kg) | 4.88 | 16.6 |

* Includes values for ages 18 - 65 years

**4.6 Fertility, pregnancy and lactation**

Due to the limited number of patients studied, the safety of desflurane has not been established for use in obstetric procedures. Desflurane is a uterine relaxant and reduces the uterine-placental blood-flow.

There are no adequate data from the use of desflurane in pregnant or lactating women, therefore desflurane is not indicated for use during pregnancy and lactation. (see section 5.3).

**4.7 Effects on ability to drive and use machines**

There is no information on the effects of desflurane on the ability to drive or operate machinery. However, patients should be advised that the ability to perform tasks such as driving or operation of machinery may be impaired after general anaesthesia, and it is advisable to avoid such tasks for a period of 24 hours.

**4.8 Undesirable effects**

As with all potent inhaled anaesthetics desflurane may cause dose-dependent cardio-respiratory depression. Most other adverse events are mild and transient. Nausea and vomiting have been observed in the postoperative period, common sequelae of surgery and general anaesthesia, which may be due to inhalational anaesthetic, other agents administered intraoperatively or post- operatively and to the patient's response to the surgical procedure.

ADR frequency is based upon the following scale:
Very Common (≥1/10);
Common (≥1/100 - <1/10),
Uncommon (≥1/1,000 - <1/100),
Rare (≥1/10,000 - <1/1,000),
Very Rare (<1/10,000),
Unknown (adverse reactions reported in the post-marketing experience)

| | **Adverse Reactions** | |
|---|---|---|
| **System Organ Class (SOC)** | **Preferred MedDRA Term** | **Frequency** |
| **INFECTIONS AND INFESTATIONS** | **Pharyngitis** | Comm on |
| **BLOOD AND THE LYMPHATIC SYSTEM DISORDERS** | **Coagulopathy** | Unknown |
| **METABOLISM AND NUTRITION DISORDERS** | **Hyperkalemia** | Unknown |
| | **Hypokalemia** | Unknown |
| | **Metabolic acidosis** | Unknown |
| **PSYCHIATRIC DISORDERS** | **Breath holding**[+] | Common |
| | **Agitation** | Uncommon |
| | **Delirium** | Unknown |
| **NERVOUS SYSTEM DISORDERS** | **Headache** | Common |
| | **Dizz iness** | Uncommon |
| | **Convulsions** | Unknown |
| **EYE DISORDERS** | **Conjunctivitis** | Comm on |
| | **Ocular icterus** | Unknown |
| **CARDIAC DISORDERS** | **Nodal arrhythmia** | Comm on |
| | **Bradycardia** | Comm on |
| | **Tachycardia** | Comm on |
| | **Hypertension** | Comm on |
| | **Myocardial infarction** | Uncomm on |
| | **Myocardial ischemia** | Uncomm on |
| | **Arrthymia** | Uncomm on |
| | **Cardiac arrest** | Unknown |
| | **Torsade de pointes** | Unknown |
| | **Ventricular failure** | Unknown |

| | | |
|---|---|---|
| | **Ventricular hypokinesia** | Unknown |
| | **Atrial Fibrillation** | Unknown |
| | **Electrocardiogram QT prolonged** | Unknown |
| **VASCULAR DISORDERS** | **Vasodilation** | Uncomm on |
| | **Malignant hypertension** | Unknown |
| | **Hemorrhage** | Unknown |
| | **Hypotension** | Unknown |
| | **Shock** | Unknown |
| **RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS** | **Apnea**[+] | Comm on |
| | **Cough**[+] | Comm on |
| | **Laryngospasm*** | Comm on |
| | **Hypoxia**[+] | Uncomm on |
| | **Respiratory arrest** | Unknown |
| | **Respiratory failure** | Unknown |
| | **Respiratory distress** | Unknown |
| | **Bronchospasm** | Unknown |
| | **Hemoptysis** | Unknown |
| **GASTROINTESTINAL DISORDERS** | **Vomiting**[+] | Very Comm on |
| | **Nausea**[+] | Very Comm on |
| | **Salivary hypersecretion**[+] | Comm on |
| | **Pancreatitis acute** | Unknown |
| | **Abdominal pain** | Unknown |
| **HEPATOBILIARY DISORDERS** | **Hepatic failure** | Unknown |
| | **Hepatic necrosis** | Unknown |
| | **Hepatitis** | Unknown |
| | **Cytolytic hepatitis** | Unknown |
| | **Cholestasis** | Unknown |
| | **Jaundice** | Unknown |
| | **Hepatic function abnormal** | Unknown |
| | **Liver disorder** | Unknown |
| **SKIN AND SUBCUTANEOUS TISSUE DISORDER** | **Urticaria** | Unknown |
| | **Erythema** | Unknown |
| **MUSCULOSKELETAL, CONNECTIVE TISSUE AND BONE DISORDERS** | **Myalgia** | Uncomm on |
| | **Rhabdomyolysis** | Unknown |
| **GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS** | **Hyperthermia malignant** | Unknown |
| | **Asthenia** | Unknown |
| | **Malaise** | Unknown |
| **INVESTIGATIONS** | **Increased creatinine phosphokinase** | Comm on |
| | **ECG abnormal** | Comm on |
| | **Electrocardiogram ST-T change** | Unknown |
| | **Electrocardiogram T w ave inversion** | Unknown |
| | **Transaminases increased** | |
| | **Alanine aminotransferase increased** | Unknown |
| | **Aspartate aminotransferase increased** | Unknown |
| | **Blood bilirubin increased** | Unknown |
| | **Coagulation test abnormal** | Unknown |
| | **Ammonia increased** | Unknown |
| | **Increased blood glucose levels** | Unknown |
| | | Unknown |
| **INJURY, POISONING, AND PROCEDURAL COMPLICATIONS** | **Agitation postoperative** | Unknown |
| | **Dizz iness** | Unknown |
| | **Migraine** | Unknown |
| | **Tachyarrhythmia** | Unknown |
| | **Palpitations** | Unknown |
| | **Eye burns** | Unknown |
| | **Blindness transient** | Unknown |
| | **Encephalopathy** | Unknown |
| | **Ulcerative keratitis** | Unknown |
| | **Ocular hyperemia** | Unknown |

| | | |
|---|---|---|
| | **Visual acuity reduced** | Unknown |
| | **Eye irritation** | Unknown |
| | **Eye pain** | Unknown |
| | **Fatigue** | Unknown |
| | **Accidental exposure** | Unknown |
| | **Skin burning sensation** | Unknown |
| | **Drug administration error** | Unknown |

* reported during induction with desflurane
+ reported during induction and maintenance with desflurane
§ All of reactions categorized within this SOC were accidental exposures to non-patients

*Reporting of suspected adverse reactions*
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via
**Ireland**
HPRA Pharmacovigilance
Website : www.hpra.ie

**4.9 Overdose**

Symptoms and treatment of overdosage

The symptoms of overdosage of desflurane can present as a deepening of anesthesia, cardiac and/or respiratory depression in spontaneously breathing patients, and cardiac depression in ventilated patients in whom hypercapnia and hypoxia may occur only at a late stage.

In the event of overdosage or what may appear to be overdosage, the following actions should be taken:

1. Discontinue or minimize exposure to desflurane
2. Establish an airway and initiate assisted or controlled ventilation with 100% oxygen.
3. Support and maintain adequate hemodynamics

**5 PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Desflurane is one of a family of halogenated methylethylethers which are administered by inhalation producing a dose-related, reversible loss of consciousness and of pain sensations, suppression of voluntary motor activity, modification of autonomic reflexes and sedation of respiration and the cardiovascular system. Other members of the series include enflurane and its structural isomer isoflurane which are halogenated with chlorine as well as fluorine.

Desflurane is halogenated exclusively with fluorine. As suggested by its structure, the low blood/gas partition coefficient of desflurane (0.42) is lower than that of other potent inhaled anaesthetics such as isoflurane (1.4) and even lower than that of nitrous oxide (0.46). These data explain the rapid recovery from desflurane anaesthesia. Animal studies showed a more rapid induction and recovery from anaesthesia than for isoflurane, with a similar cardiorespiratory profile.

Clinical studies, however, could not uniformly confirm these data on more rapid recovery with desflurane. There were no signs of epileptogenic or other untoward effects on EEG, and adjuvant drugs produced no unanticipated or toxic EEG responses during anaesthesia with desflurane.

Studies in pigs bred to be susceptible to malignant hyperthermia (MH) indicated that desflurane is a potential trigger for MH.

The pharmacological effect is proportional to the inspired concentration of desflurane. The main adverse effects are extensions of the pharmacological action.

**5.2 Pharmacokinetic properties**

a. General characteristics

As predicted from its physicochemical profile, pharmacokinetic studies in animals as in man indicate that desflurane washes into the body more rapidly than other volatile anaesthetic agents, suggesting a more rapid induction of anaesthesia. It also washes out of the body more rapidly, allowing quick recovery and flexibility in adjustment of the depth of anaesthesia. Desflurane is eliminated via the lungs, undergoing only minimal metabolism (0.02%).

b. Characteristics in patients

MAC decreases with increasing age. A reduction of dosage is recommended in hypovolaemic, hypotensive and debilitated patients, as discussed under Special Warnings and Special Precautions (4.4).

**5.3 Preclinical safety data**

In swine, desflurane does not sensitize the myocardium to exogenously administered adrenaline. Desflurane appears to produce coronary vasodilation at arteriolar level in selected animal models, in a similar fashion to that of isoflurane. In an animal model simulating coronary artery disease with conscious, chronically instrumented dogs, desflurane does not appear to divert blood from collateral dependent myocardium to normally perfused areas ("coronary steal"). Clinical studies to date evaluating myocardial ischaemia, infarction and death as outcome parameters have not established that the coronary arteriolar property of Suprane (desflurane) is associated with coronary steal or myocardial ischaemia in patients with coronary artery disease.

Published studies in animals (including primates) at doses resulting in light to moderate anaesthesia demonstrate that the use of anaesthetic agents during the period of rapid brain growth or synaptogenesis results in cell loss in the developing brain that can be associated with prolonged cognitive deficiencies. The clinical significance of these nonclinical findings in not known.
A detailed experimental program including in vivo and in vitro studies, did not result in any indication of mutagenic properties of desflurane.

No teratogenic effect was observed in rats or rabbits at approximately 10 and 13 cumulative MAC hour desflurane exposures during organogenesis. Embryo-toxicity, probably due to the pharmacological effect of desflurane on the dams, was seen at maternally toxic exposures.

**6 PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

None.

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

Three years.

**6.4 Special precautions for storage**

Store in upright position with cap firmly in place.

This medicinal product does not require any special temperature storage conditions.

**6.5 Nature and contents of container**

Suprane is presented in glass or aluminium bottles.

o Glass bottles: Type III amber glass bottles with a protective PVC coating, containing 240ml of desflurane.

oAluminium bottles: an aluminium bottle that is internally coated with an epoxyphenolic resin, containing 240ml of desflurane.

The bottle is closed with a crimped-on valve directly compatible with the filling port of the desflurane vaporizer and cap.

**6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

See under section 4.2, Posology and Method of Administration.

Any discarded anaesthetic should be collected in a glass or plastic container, which can be sealed and disposed of through the hospital's waste disposal service.

**7 MARKETING AUTHORISATION HOLDER**

Baxter Holding B.V.
Kobaltweg 49
3542CE Utrecht
Netherlands

**8 MARKETING AUTHORISATION NUMBER**

PA2299/023/001

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 16 December 1999
Date of last renewal: 16 December 2009

**10 DATE OF REVISION OF THE TEXT**

March 2024