APPROVED PROFESSIONAL INFORMATION FOR SEVONU

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

SEVONU liquid

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

SEVONU liquid contains sevoflurane 100,0 % v/v.

SEVONU is comprised only of the active ingredient with no additives.

3. PHARMACEUTICAL FORM

A clear, colourless, volatile liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

SEVONU is indicated for induction and maintenance of general anaesthesia in adult and paediatric patients for inpatient and outpatient surgery.

4.2 Posology and method of administration

Surgical-anaesthesia:

The concentration of **SEVONU** being delivered from a vaporiser during anaesthesia should be known. This may be accomplished by using a vaporiser calibrated specifically for **SEVONU**.

Induction:

Dosage should be individualised and titrated to the desired effect according to the patient's age and clinical status. A short acting intravenous induction medicine may be administered, followed by

inhalation of **SEVONU**. Induction with **SEVONU** may be achieved in oxygen or in combination with oxygen-nitrous oxide mixtures.

Inspired concentrations of up to 8 % **SEVONU** usually produce surgical anaesthesia in less than 2 minutes in both adults and children.

Maintenance:

Surgical levels of anaesthesia may be sustained with concentrations of 0,5 - 3 % **SEVONU** with or without the concomitant use of nitrous oxide.

<table>
<tr><th colspan="3">MAC values in Adults and Paediatric Patients According to Age</th></tr>
<tr><td>Age of patient (years):</td><td>Sevoflurane in oxygen:</td><td>Sevoflurane in
65 % N_2O/ 35 % O_2:</td></tr>
<tr><td>0 – 1 month*</td><td>3,3 %</td><td rowspan="4">2,0 %**</td></tr>
<tr><td>1 month – < 6 months</td><td>3,0 %</td></tr>
<tr><td>6 months – < 3 years</td><td>2,8 %</td></tr>
<tr><td>3 – 12</td><td>2,5 %</td></tr>
<tr><td>25</td><td>2,6 %</td><td>1,4 %</td></tr>
<tr><td>40</td><td>2,1 %</td><td>1,1 %</td></tr>
<tr><td>60</td><td>1,7 %</td><td>0,9 %</td></tr>
<tr><td>80</td><td>1,4 %</td><td>0,7 %</td></tr>
<tr><td colspan="3">* Neonates are full-term gestational age. MAC in premature infants has not been determined.
** In 3 – < 5 year old paediatric patients, 60 % N_2O/40 % O_2 was used.</td></tr>
</table>

Emergence:

Emergence times are generally short following **SEVONU** anaesthesia. Therefore, patients may require postoperative pain relief earlier.

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Special populations

Elderly population:

Lesser concentrations of **SEVONU** are normally required to maintain surgical anaesthesia.

Paediatric population:

Refer to Table above for MAC values for paediatric patients according to age.

4.3 Contraindications

- **SEVONU** should not be used in patients with known or suspected hypersensitivity to sevoflurane or other halogenated medicines (e.g. history of hepatotoxicity, usually including elevated liver enzymes,fever, leukocytosis and/or eosinophilia temporally related to anaesthesia with one of the medicines).
- **SEVONU** should not be used in patients with known of suspected genetic susceptibility to malignant hyperthermia (see section 4.4).
- **SEVONU** should not be used in patients with latent as well as overt neuro-muscular disease, particularly Duchenne muscular dystrophy (see section 4.4).

4.4 Special warnings and precautions for use

Sevoflurane may cause respiratory depression, which may be augmented by narcotic premedication or other medicines causing respiratory depression.

Respiration should be supervised and if necessary, assisted. **SEVONU** should be administered only by persons trained in the administration of general anaesthesia. Facilities for maintenance of a patent airway, artificial ventilation and oxygen enrichment and circulatory resuscitation must be immediately available.

The concentration of sevoflurane being delivered from a vaporiser must be known exactly.

Since levels of anaesthesia may be altered easily and rapidly, only vaporisers specifically calibrated for **SEVONU** should be used. The administration of general anaesthesia must be individualised based on the patient's response. Hypotension and respiratory depression increase as anaesthesia is deepened.

Malignant hyperthermia:

In susceptible individuals **SEVONU** may trigger a skeletal muscle hypermetabolic state leading to high oxygen demand and the clinical syndrome known as malignant hyperthermia (see section 4.8). The clinical syndrome is signalled by hypercapnia, and may include muscle rigidity, tachycardia, tachypnoea, cyanosis, dysrhythmias, and/or unstable blood pressure. Some of these non-specific signs may also appear during light anaesthesia, acute hypoxia, hypercapnia and hypovolaemia. Fatalities have occurred.

Treatment of malignant hyperthermia includes discontinuation of **SEVONU** administration of intravenous dantrolene sodium and application of supportive therapy. Such therapy includes vigorous efforts to restore body temperature to normal, respiratory and circulatory support as indicated, and management of electrolyte-fluid-acid-base abnormalities. Renal failure may appear later, and urine flow should be monitored and sustained if possible.

Peri-operative Hyperkalaemia:

Use of inhaled anaesthetic medicines, including **SEVONU**, has been associated with increases in serum potassium levels that have resulted in cardiac dysrhythmias and death in paediatric patients during the peri-operative period. Patients with latent as well as overt neuromuscular disease, particularly Duchenne muscular dystrophy, appear to be most vulnerable (see section 4.3). Concomitant use of succinylcholine has been associated with most, but not all, of these cases. These patients also experienced significant elevations in serum creatine phosphokinase 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 resistant dysrhythmias is recommended, as is subsequent evaluation for latent neuromuscular disease.

Reports of QT prolongation, associated with Torsades de Pointes (in exceptional cases, fatal), have been received. Caution should be exercised when administering **SEVONU** to susceptible patients.

Isolated cases of ventricular dysrhythmia were reported in paediatric patients with Pompe's disease.

Caution should be exercised in administering general anaesthesia, including **SEVONU**, to patients with mitochondrial disorders.

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Hepatic:

Cases of mild, moderate and severe post-operative hepatic dysfunction or hepatitis with or without jaundice have been reported.

In addition, there have been reports of hepatic failure and hepatic necrosis associated with the use of potent volatile anaesthetic agents, including sevoflurane.

However, the actual incidence and relationship of sevoflurane to these events cannot be established with certainty (see section 4.8).

Caution should be exercised when **SEVONU** is used in patients with underlying hepatic conditions or under treatment with medicines known to cause hepatic dysfunction (see section 4.8).

It has been reported that previous exposure to halogenated hydrocarbon anaesthetics may increase the potential for hepatic injury.

General:

During maintenance of anaesthesia, increasing the concentrations of **SEVONU** produces dose-dependent decreases in blood pressure. Excessive decrease in blood pressure may be related to depth of anaesthesia and in such instances may be corrected by decreasing the inspired concentration of **SEVONU**.

Particular care must be taken when selecting the dosage for patients who are hypovolaemic, hypotensive, or otherwise hemodynamically compromised, e.g.,due to concomitant medications.

Maintenance of haemodynamic stability is important to the avoidance of myocardial ischaemia in patients with coronary artery disease.

Caution should be observed when using **SEVONU** during obstetric anaesthesia because the relaxant effect on the uterus could increase the risk of uterine bleeding (see section 4.6).

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The recovery from general anaesthesia should be assessed carefully before patients are discharged from the post-anaesthesia care unit.

Rapid emergence from anaesthesia is generally seen with sevoflurane so early relief of postoperative pain may be required.

Although recovery of consciousness following **SEVONU** administration generally occurs within minutes, the impact on intellectual function for two or three days following anaesthesia has not been studied. As with other anaesthetics, small changes in mood may persist for several days following administration (see section4.7). Rapid emergence in children may be associated with agitation and lack of co-operation (in about 25 % of cases).

Replacement of Desiccated CO_2 Absorbents:

Cases of extreme heat, smoke and/or spontaneous fire in the anaesthesia machine have been reported during **SEVONU** use in conjunction with the use of desiccated CO_2 absorbent, specifically those containing potassium hydroxide (e.g. Baralyme).

An unusually delayed rise or unexpected decline of inspired **SEVONU** concentration compared to the vaporiser setting may be associated with excessive heating of the CO_2 canister.

The exothermic reaction that occurs with **SEVONU** and CO_2 absorbents is increased when the CO_2 absorbent becomes desiccated, such as after an extended period of dry gas flow through the CO_2 absorbent canisters. **SEVONU** degradants (methanol, formaldehyde, carbon monoxide and Compounds A, B, C and D) were observed in the respiratory circuit of an experimental anaesthesia machine using desiccated CO_2 absorbents and maximum **SEVONU** concentrations (8 %) for extended periods of time (≥ 2 hours). (*Compound A is pentafluoroisopropanyl fluoromethyl ether, Compound B is the methoxy addition product formed after reaction of Compound A with methanol, and Compound B can undergo further HF elimination to form Compounds C, D and E*). Concentrations of formaldehyde observed at the anaesthesia respiratory circuit (using sodium hydroxide containing absorbents) were consistent with levels known to cause mild respiratory irritation.

The clinical relevance of the degradants observed under this extreme experimental model is unknown.

When a health care professional suspects that the CO_2 absorbent may be desiccated, it should be replaced before administration of **SEVONU**. The colour indicator of most CO_2 absorbents does not

necessarily change as a result of desiccation. Therefore, the lack of significant colour change should not be taken as an assurance of adequate hydration. CO_2 absorbents should be replaced routinely regardless of the state of the colour indicator.

Renal Impairment:

Because of the small number of patients with renal insufficiency studied (baseline serum creatinine greater than 15 mg/L (133 µmol/L), the safety of **SEVONU** administration in this group has not yet been fully established. Therefore, **SEVONU** should be used with caution in patients with renal insufficiency.

Neurosurgery & Neuromuscular Impairment:

In patients at risk for an increase in intracranial pressure, **SEVONU** should be administered cautiously in conjunction with measures to reduce intracranial pressure (such as hyperventilation).

Seizures:

Cases of seizures have been reported in association with **SEVONU** use (see section 4.8).

Use of sevoflurane, as in **SEVONU**, has been associated with seizures occurring in children and young adults as well as older adults with and without predisposing risk factors. Clinical judgment is necessary before sevoflurane is used in patients at risk of seizures. In children the depth of anaesthesia should be limited. EEG may permit the optimization of **SEVONU** dose and help avoid the development of seizure activity in patients with a predisposition for seizures (see section Paediatric use, below).

Paediatric use:

The use of **SEVONU** has been associated with seizures. Many of these have occurred in children and young adults starting from 2 months of age, most of whom had no predisposing factors. Clinical judgement should be exercised when using **SEVONU** in patients who may be at risk for seizures.

Dystonic movements in children have been observed (see section 4.8).

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Hypersensitivity:

Reports of hypersensitivity (including contact dermatitis, rash, dyspnoea, wheezing, chest discomfort, swelling face or anaphylactic reaction) have been received, including cases of association with long-term occupational exposure to **SEVONU**.

4.5 Interaction with other medicines and other forms of interaction

Beta-sympathomimetic medicines like isoprenaline and alpha- and beta- sympathomimetic medicines like adrenaline and noradrenaline should be used with caution during sevoflurane narcosis, due to a potential risk of ventricular dysrhythmia.

Epinephrine/Adrenaline:

Sevoflurane is similar to isoflurane in the sensitisation of the myocardium to the arrhythmogenic effect of exogenously administered adrenaline.

Indirect-acting Sympathomimetics:

There is a risk of acute hypertensive episode with the concomitant use of sevoflurane and indirect-acting sympathomimetics products (amphetamines, ephedrine).

Non-selective MAO-inhibitors:

Risk of crisis during the operation. It is generally recommended that treatment should be stopped 2 weeks prior to surgery.

Sevoflurane may lead to marked hypotension in patients treated with calcium antagonists, in particular dihydropyridine derivates.

Caution should be exercised when calcium antagonists are used concomitantly with inhalation anaesthetics due to the risk of additive negative inotropic effect.

Concomitant use of succinylcholine with inhaled anaesthetic medicines has been associated with rare increases in serum potassium levels that have resulted in cardiac dysrhythmias and death in paediatric patients during the post-operative period.

Sevoflurane has been shown to be safe and effective when administered concurrently with a wide variety of medicines commonly encountered in surgical situations such as central nervous system medicines, autonomic medicines, skeletal muscle relaxants, anti-infective medicines including aminoglycosides, hormones and synthetic substitutes, blood derivatives and cardiovascular medicines, including epinephrine.

Beta blockers:

Sevoflurane may increase the negative inotropic, chronotropic and dromotropic effects of beta blockers (by blocking cardiovascular compensatory mechanisms).

Verapamil:

Impairment of atrioventricular conduction was observed when verapamil and sevoflurane were administered at the same time.

Barbiturates:

SEVONU administration is compatible with barbiturates as commonly used in surgical practice.

Benzodiazepines and Opioids:

Benzodiazepines and opioids decrease the MAC of **SEVONU**. **SEVONU** administration is compatible with benzodiazepines and opioids as commonly used in surgical practice.

Inducers of CYP2E1:

Medicines and compounds that increase the activity of cytochrome P450 isoenzyme CYP2E1, such as isoniazid and alcohol, may increase the metabolism of **SEVONU** and lead to significant increases in plasma fluoride concentrations. Concomitant use of sevoflurane, as in **SEVONU**, and isoniazid can potentiate the hepatotoxic effects of isoniazid.

As with other medicines, lesser concentrations of sevoflurane may be required following use of an intravenous anaesthetic e.g. propofol.

Significant increases in plasma fluoride concentrations have been observed following the increased activity of CYP2E1.

St John's Wort:

Severe hypotension and delayed emergence from anaesthesia with halogenated inhalational anaesthetics have been reported in patients treated long-term with St John's Wort.

Nitrous oxide:

The MAC of **SEVONU** is decreased when administered in combination with nitrous oxide. The MAC equivalent is reduced approximately 50 % in adult and approximately 25 % in paediatric patients. Altitude may affect the effects of nitrous oxide.

Neuromuscular blocking medicines:

SEVONU affects both the intensity and duration of neuromuscular blockade by non-depolarising muscle relaxants. When used to supplement alfentanil-N_20 anaesthesia, **SEVONU** potentiates neuromuscular block induced with pancuronium, vecuronium or atracurium. The dosage adjustments for these muscle relaxants when administered with sevoflurane are similar to those required with isoflurane.

The effect of **SEVONU** on succinylcholine and the duration of depolarising neuromuscular blockade has not been studied.

Dosage reduction of neuromuscular blocking medicines during induction of anaesthesia may result in delayed onset of conditions suitable for endotracheal intubation or inadequate muscle relaxation because potentiation of neuromuscular blocking medicines is observed a few minutes after the beginning of **SEVONU** administration.

Among non-depolarising medicines, vecuronium, pancuronium and atracurium interactions have been studied. In the absence of specific guidelines: (1) for endotracheal intubation, do not reduce the dose of non-depolarising muscle relaxants, (2) during maintenance of anaesthesia, the dose of non-depolarising muscle relaxants is likely to be reduced compared to that during N_20/opioid anaesthesia. Administration of supplemental doses of muscle relaxants should be guided by the response to nerve stimulation.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Safety in pregnancy or lactation has not been established. The safety of **SEVONU** in labour and delivery has not been demonstrated. **SEVONU** may be used for anaesthesia during Caesarean section.

Published animal studies of some anaesthetic/sedation medicines have reported adverse effects on brain development in early life.

SEVONU has relaxant effects on the uterus with the potential risk for uterine bleeding. Caution should be observed when using **SEVONU** during obstetric anaesthesia.

Breastfeeding:

It is not known whether **SEVONU** is excreted in human milk. Caution should be exercised when **SEVONU** is administered to a breastfeeding woman.

Women should be advised to skip breast-feeding for 48 hours after administration of sevoflurane and discard milk produced during this period.

Fertility:

A fertility study in rats has revealed no evidence of impaired fertility due to sevoflurane.

4.7 Effects on ability to drive and use machines

Patients should be advised that performance of activities requiring mental alertness, such as decision making or operating a motor vehicle or hazardous machinery, may be impaired for some time after general anaesthesia.

Patients should not be allowed to drive for a suitable period after sevoflurane anaesthesia.

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4.8 Undesirable effects

Summary of the safety profile:

As with all potent inhaled anaesthetics, sevoflurane may cause dose-dependent cardio-respiratory depression. Most adverse reactions are mild to moderate in severity and are transient in duration.

Nausea, vomiting, and delirium have been observed in the postoperative period, common sequelae of surgery and general anaesthesia, which may be due to inhalational anaesthetic, other medicines administered intra-operatively or post-operatively, and to the patient's response to the surgical procedure.

The most frequently reported adverse reactions were as follows:

In adult patients: hypotension, nausea and vomiting;

In elderly patients: bradycardia, hypotension and nausea; and

In paediatric patients: agitation, cough, vomiting and nausea.

Tabulated summary of adverse reactions:

System Organ Class:	**Frequency:**	**Side effects:**
Blood and the lymphatic system disorders	Less frequent	Leukopenia, leukocytosis
Immune system disorders	Frequency unknown	Anaphylactic reaction, anaphylactoid reaction, hypersensitivity
Psychiatric disorders	Frequent Less frequent	Agitation Confusional state
Nervous system disorders	Frequent	Somnolence, dizziness, headache

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	Frequency unknown	Convulsion, dystonia
Cardiac disorders	Frequent	Bradycardia, tachycardia
	Less frequent	Atrioventricular block complete, atrial fibrillation, dysrhythmia, ventricular extrasystoles, supraventricular extrasystoles, extrasystoles
	Frequency unknown	QT prolongation associated with Torsade, cardiac arrest
Vascular disorders	Frequent	Hypotension, hypertension
Respiratory, thoracic and mediastinal disorders	Frequent	Cough, respiratory disorder, laryngospasm
	Less frequent	Apnoea, hypoxia, asthma
	Frequency unknown	Bronchospasm, dyspnoea, wheezing, pulmonary oedema
Gastrointestinal disorders	Frequent	Nausea, vomiting, salivary hypersecretion
Hepato-biliary disorders	Frequency unknown	Hepatitis, hepatic failure, hepatic necrosis
Skin and subcutaneous tissue disorders	Frequency unknown	Pruritus, rash, urticaria, contact dermatitis, face swelling

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Musculoskeletal, and connective tissue disorders	Frequency unknown	Muscle twitching
Renal and urinary disorders	Less frequent Frequency unknown	Urinary retention, glycosuria Acute renal failure
General disorders and administration site conditions	Frequent Frequency unknown	Chills, pyrexia Malignant hyperthermia, chest discomfort
Investigations	Frequent Less frequent	Increased blood glucose, abnormal liver function test, increased white blood cell count, increased fluoride*, increased aspartate aminotransferase Increased alanine aminotransferase, increased blood creatinine, increased blood lactate dehydrogenase
Injury, poisoning and procedural complications	Frequent	Hypothermia

*Increases in serum inorganic fluoride levels may occur during and after **SEVONU** anaesthesia. Concentrations of inorganic fluoride generally peak within two hours of the end of **SEVONU** anaesthesia and return within 48 hours to pre-operative levels.

In clinical trials, elevated fluoride levels were not associated with impairment of renal function.

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Reporting of suspected adverse reactions:

Reporting of suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

In the event of apparent overdosage, the following action should be taken:

Discontinue administration of **SEVONU**, maintain a patent airway, initiate assisted or controlled ventilation with oxygen and maintain adequate cardiovascular function.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

A 2. 1 - Anaesthetics

Pharmaco-therapeutic group: Anaesthetics, general -ATC code: N01A

Sevoflurane is a halogenated anaesthetic given by inhalation. Sevoflurane depresses respiratory function and blood pressure in a dose-related manner.

Sevoflurane is a dose-related cardiac depressant. Sevoflurane does not produce increases in heart rate at doses less than 2 minimum alveolar concentration (MAC).

A study investigating the epinephrine (adrenaline) induced prodysrhythmogenic effect of sevoflurane in adult patients undergoing transsphenoidal hypophysectomy demonstrated that the threshold dose of epinephrine (i.e. the dose at which the first sign of dysrhythmia was observed) producing multiple ventricular dysrhythmias was 5 micrograms/kg.

Sevoflurane has minimal effect on neurodynamics or ICP (intracranial pressure) and preserves CO_2 responsiveness.

Sevoflurane does not affect renal concentrating ability.

Minimum alveolar concentration (MAC):

The minimum alveolar concentration (MAC) is the concentration at which 50 % of the population tested does not move in response to a single stimulus of skin incision.

For MAC equivalents for sevoflurane for various age groups (see section 4.2).

The MAC of sevoflurane in oxygen was determined to be 2, 05 % for a 40 year old adult. MAC decreases with age and with the addition of nitrous oxide.

Tracheobronchial tree secretions are mildly stimulated.

5.2 Pharmacokinetic Properties

Solubility:

The low solubility of sevoflurane in blood results in a rapid increase in the alveolar concentrations upon induction and a rapid decrease upon cessation of the inhaled medicine. In a clinical study the F_A/F_1 (wash-in) value at 30 minutes for sevoflurane was 0,85. The F_A/F_{AO} (wash-out) value at 5 minutes was 0,15.

Metabolism:

The rapid pulmonary elimination of sevoflurane minimises the amount of anaesthetic available for metabolism. In humans < 5 % sevoflurane absorbed is metabolised to hexafluoroisopropanol (HFIP), with release of inorganic fluoride and carbon dioxide (or a one carbon fragment). Once formed HFIP

is rapidly conjugated with glucuronic acid and eliminated. No other metabolic pathways for sevoflurane have been identified.

Fluoride Ion:

The defluorination of sevoflurane is not inducible by barbiturates. Fluoride ion concentrations are influenced by the duration of anaesthesia, the concentration of sevoflurane administered, and the composition of the anaesthetic gas mixture (see section 4.8).

Serum inorganic fluoride concentrations after sevoflurane anaesthesia have been reported to be dose dependent and reach about 10 to 20 µmol/L (after 1 to 2 MAC hours), 20 to 40 µmol/L (after 2 to 7 MAC hours) and may be as high as 20 to 90 µmol/L with prolonged exposure.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

SEVONU contains no additives.

6.2 Incompatibilities

Sevoflurane Degradation:

SEVONU is stable when stored under normal room lighting conditions. No discernible degradation of sevoflurane occurs in the presence of strong acids or heat. Sevoflurane is not corrosive to stainless steel, brass, aluminium, nickel-plated brass, chrome-plated brass, or copper beryllium alloy.

Chemical degradation can occur upon exposure of inhaled anaesthetics to CO_2 absorbent within the anaesthesia machine. When used as directed with fresh absorbents, degradation of sevoflurane is minimal, and degradants are undetectable or non-toxic. Sevoflurane degradation and subsequent degradant formation are enhanced by increasing absorbent temperature, desiccated CO_2 absorbent increased sevoflurane concentration and decreased fresh gas flow.

Sevoflurane can undergo alkaline degradation by two pathways. The first results from the loss of hydrogen fluoride with the formation of pentafluoroisopropanyl fluoromethyl ether (PIFE or more

commonly known as Compound A). The second pathway for degradation of sevoflurane occurs only in the presence of desiccated CO_2 absorbents and leads to the dissociation of sevoflurane into hexafluoroisopropanol (HFIP) and formaldehyde. HFIP is inactive, nongenotoxic, rapidly glucoronidated, cleared, and has toxicity comparable to sevoflurane.

Formaldehyde is present during normal metabolic processes. Upon exposure to a highly desiccated absorbent, formaldehyde can further degrade into methanol and formate. Formate can contribute to the formation of carbon monoxide, in the presence of high temperature. Methanol can react with Compound A to form the methoxy addition product Compound B. Compound B can undergo further HF elimination to form Compounds C, D, and E. With highly desiccated absorbents, especially those containing potassium hydroxide (e.g. Baralyme), the formation of formaldehyde, methanol, carbon monoxide, Compound A and perhaps some of its degradants, Compounds B, C, and D may occur.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

SEVONU is packed in 250 mL Type III amber glass bottles with a collar on the neck, sealed with a poly-seal cap, and secured with PET film.

Pack size: 1 x 250 mL bottle.

6.6 Special precautions for disposal and other handling

Sevoflurane should be administered via a vaporiser calibrated specifically for sevoflurane using a key filling system designed for sevoflurane specific vaporisers or other appropriate sevoflurane specific vaporiser filling systems. Carbon dioxide absorbents should not be allowed to dry out when inhalational anaesthetics are being administered. Some halogenated anaesthetics have been reported to interact with dry carbon dioxide absorbent to form carbon monoxide. However, in order to minimise the risk of formation of carbon monoxide in re-breathing circuits and the possibility of

elevated carboxyhaemoglobin levels, CO_2 absorbents should not be allowed to dry out. There have been cases of excessive heat production, smoke and fire in the anaesthetic machine when sevoflurane has been used in conjunction with a desiccated (dried out) CO_2 absorbent. If the CO_2 absorbent is suspected to be desiccated it should be replaced.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Lamar International (Pty) Ltd

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Waterford Place

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Cape Town, South Africa

8. REGISTRATION NUMBER

51/21/0228

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 24 January 2021

10. DATE OF REVISION OF THE TEXT

06 June 2022