PACKAGE LEAFLET: INFORMATION FOR THE USER

SEVOFLURANE®

250 ml Inhalation Anaesthetic
Sevoflurane

IMPORTANT INFORMATION
Read all of this leaflet carefully before you receive Sevoflurane.

- Keep this leaflet as you may need to read it again.
- This leaf let provides a summary of the information currently available on Sevoflurane.
- For further information or advice, ask your ward doctor or anaesthetist.
- Tell your ward doctor or anaesthetist if you experience any side effects.

In this leaflet:

1. What is Sevoflurane and what does it do?

Sevoflurane belongs to a group of medicines called general anaesthetics. These work by temporarily reducing the activity of the body's central nervous system. This causes a complete loss of sensation in the body, including loss of consciousness allowing surgery to be carried out without pain or distress. Sevoflurane is a clear colourless liquid, that when put into a special anaesthetic machine (vaporiser) becomes a gas. This mixes with the oxygen you will be breathing in. Once breathed in (inhaled), Sevoflurane will induce and maintain a deep, pain-free sleep (general anaesthesia) in adults and children.

2. What should you know before receiving Sevoflurane?

TELL YOUR WARD DOCTOR, SURGEON OR ANAESTHETIST if:

- You have been told previously that you should not receive general anaesthesia.
- You have been told that you are sensitive or have an allergy to Sevoflurane or any other anaesthetic.
- You or any member of your family has had a condition called malignant hyperthermia (rapid increase in body temperature and severe muscle contractions) during an operation.
- You have liver problems or if you have previously had general anaesthetics, particularly if repeated over a short period of time. Some anaesthetics can occasionally cause problems in the liver, which can cause yellowing of the skin and eyes (jaundice).
- You are prone to or at risk for seizures (fits).
- You have ever had QT prolongation (prolongation of a specific time interval in an ECG) or torsade de pointes (a specific type of heart rhythm), which may also be associated with QT prolongation. Sevoflurane has sometimes been known to cause these.
- You have a mitochondrial disease.

In addition to the above, if Sevoflurane is to be administered to your child, please tell their ward doctor, surgeon or anaesthetist if they:

- Have seizures or seizure disorder (fits), as Sevoflurane may increase the risk of seizures
- Have Pompe's disease (a metabolic disorder). Sevoflurane may produce abnormal heart rhythms, which may be severe in some cases
- Have a severe muscle disorder such as Duchenne muscular dystrophy
- have a mitochondrial disorder, which is a disorder that people may be born with and may affect special cells of the heart, brain, and kidney.

As with all drugs, it is important that you tell your ward doctor or anaesthetist which medications you are taking. This is particularly important if you are taking the following drugs:

- Amphetamines (stimulants)
- Beta blockers, calcium antagonists or a drug called verapamil (used to treat high blood pressure and certain heart conditions)
- Isoniazid (an antibiotic used to treat tuberculosis)
- St John's Wort (a herbal remedy used to help with depression)
- Decongestants (ephedrine).
- Non-selective monoamine oxidase (MAO) inhibitors (a type of antidepressants)
- Calcium antangonists

PREGNANCY AND BREAST FEEDING

Tell your ward doctor, surgeon or anaesthetist if you are pregnant, could be pregnant or are breast feeding. It is not known whether Sevoflurane or its by-products are transferred into human milk. It is advisable to stop breast-feeding for 48 hours after Sevoflurane administration and discard any milk that is produced during this period.

DRIVING & USING MACHINERY

You should NOT drive or operate machinery after your operation or procedure, for which the anaesthetic has been administered, until your ward doctor advises that you may do so. Your ability to drive or operate machinery may be impaired for some time.

3. How will you receive Sevoflurane?

Sevoflurane will ALWAYS be administered to you by an anaesthetist. They will decide on the dose you will receive, depending on your age, weight and the type of operation you are having. Sevoflurane will send you to sleep quickly and smoothly. It also has a pleasant smell.

Inducing sleep at the start of anaesthesia

To send you to sleep, you may be asked to breathe in Sevoflurane through a mask. However on most occasions you will be given an injection of another anaesthetic to make you go to sleep before receiving Sevoflurane.

Maintaining sleep during anaesthesia

Under the observation of the anaesthetist you will continue to breathe in Sevoflurane during the operation via a mask.

Waking-up after anaesthesia

Once the anaesthetist stops you from inhaling Sevoflurane you will wake up within a few minutes.

4. What will happen after receiving Sevoflurane?

As with all anaesthetics, Sevoflurane can cause side effects. These can occur both during and after your operation. The frequency of side effects is classified as follows:

Very common: more than 1 out of 10 persons treated;

Common: less than 1 out of 10, but more than 1 out of 100 persons treated;

Uncommon: less than 1 out of 100, but more than 1 out of 1,000 persons treated;

Rare: less than 1 out of 1,000, but more than 1 out of 10,000 persons treated.

Very rare: less than 1 out of 10,000 persons treated.

Unknown: when an estimation of frequency is not possible.

The following side effects with Sevoflurane are serious and will be managed by your surgeon or anaesthetist, as necessary, during the operation. If you experience any of these side effects after your operation **get medical help immediately.**

Those occurring with unknown frequency:

- Allergic reactions with symptoms such as rash, swelling of the face, wheezing
- Rapid rise in body temperature (malignant hyperthermia)
- Slow heart rate (bradycardia)
- Wheezing and breathlessness
- Heart disorders (AV block), which will be closely monitored by your anaesthetist during your operation and may be recognized by dizziness after your operation.

Those occurring very commonly:

- Throat spasm

The frequency of other side effects observed following the use of Sevoflurane are:

Very common frequency:

- agitation

4 There have been very rare postmarketing reports of cardiac arrest in the setting of Sevoflurane use.
5 Occasional cases of transient changes in hepatic function tests were reported with Sevoflurane and reference agents.
6 Transient increases in serum inorganic fluoride levels may occur during and after Sevoflurane anaesthesia. See **Description of selected adverse reactions** below.

Description of selected adverse reactions

Transient increases in serum inorganic fluoride levels may occur during and after Sevoflurane anaesthesia. Concentrations of inorganic fluoride generally peak within two hours of the end of Sevoflurane anaesthesia and return within 48 hours to pre-operative levels. In clinical trials, elevated fluoride concentrations were not associated with impairment of renal function.

Rare reports of post-operative hepatitis exist. In addition, there have been rare post-marketing 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 **Warnings and Precautions**).

Rare reports of hypersensitivity (including contact dermatitis, rash, dyspnoea, wheezing, chest discomfort, swelling face, or anaphylactic reaction) have been received, particularly in association with long-term occupational exposure to inhaled anaesthetic agents, including Sevoflurane.

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 (see **Warnings and Precautions**).

Paediatric population

The use of Sevoflurane 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 risk factors. Clinical judgment should be exercised when using Sevoflurane in patients who may be at risk for seizures (see Warnings and Precautions).

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 the local reporting system.

To report any side effect(s):

In Bahrain, United Arab Emirates, Yemen, Kuwait, Oman, and Qatar:

- Hotline: +971 56 413 5746
- Email: pv.gulf@abbvie.com

In Iraq, Jordan, Lebanon, Syria, and Iran:

- Hotline: +961 70122946
- Email: Pharmacovigilance_levant@abbvie.com

Overdosage: In the event of overdosage, the following action should be taken: Stop drug administration, establish a clear airway and initiate assisted or controlled ventilation with pure oxygen and maintain adequate cardiovascular function.

Pharmaceutical precautions:

Sevoflurane 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 CO2 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 CO2 absorbent (especially potassium hydroxide-containing, e.g. BaralymeR), 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 pentafluoroisopropenyl fluoromethyl ether (PIFE or more commonly known as Compound A). The second pathway for degradation of Sevoflurane occurs only in the presence of desiccated CO2 absorbents and leads to the dissociation of Sevoflurane into hexafluoroisopropanol (HFIP) and formaldehyde. HFIP is inactive, non-genotoxic, 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. BaralymeR) the formation of formaldehyde, methanol, carbon monoxide, Compound A and perhaps some of its degradants, Compounds B, C and D may occur.

Package quantities: 100ml and 250ml amber polyethylene napthalate (PEN) bottles.

Not all pack sizes may be marketed.

Further information: The low solubility of Sevoflurane in blood should result in alveolar concentrations which rapidly increase upon induction and rapidly decrease upon cessation of the inhaled agent.

In humans <5% of the absorbed Sevoflurane is metabolised. The rapid and extensive pulmonary elimination of Sevoflurane minimises the amount of anaesthetic available for metabolism. Sevoflurane is defluorinated via cytochrome p450 (CYP)2E1 resulting in the production of hexafluoroisopropanol (HFIP) with release of inorganic fluoride and carbon dioxide (or a one carbon fragment). HFIP is then rapidly conjugated with glucuronic acid and excreted in the urine.

The metabolism of Sevoflurane may be increased by known inducers of CYP2E1 (e.g. isoniazid and alcohol), but it is not inducible by barbiturates.

Transient increases in serum inorganic fluoride levels may occur during and after Sevoflurane anaesthesia. Generally, concentrations of inorganic fluoride peak within 2 hours of the end of Sevoflurane anaesthesia and return within 48 hours to pre-operative levels.

Special Precautions for Storage: Do not store above 25°C. Do not refrigerate. Keep cap tightly closed.

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