SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sevon Liquid

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 250ml bottle contains:

Sevoflurane 100% w/w

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Inhalation vapour, liquid.

Sevoflurane is a clear, colourless, volatile liquid with a non-pungent, pleasant odour. It is non-flammable and non-explosive.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

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

4.2 Posology and Method of Administration

Route of administration: Inhalation via a calibrated vaporiser.

Premedication: Should be selected according to the individual patient's needs at the discretion of the anaesthetist.

Induction:

Adults: Inspired concentrations of up to 5% sevoflurane in oxygen or oxygen-nitrous oxide mixtures usually produce surgical anaesthesia in less than 2 minutes.

Children: Inspired concentrations of up to 7% sevoflurane usually produce surgical anaesthesia in less than 2 minutes. Alternatively, up to 8% may be used in unpremedicated patients.

Maintenance:

Surgical levels of anaesthesia may be sustained with concentrations of 0.5–3% sevoflurane with or without concomitant nitrous oxide.

Minimum Alveolar Concentration (MAC) Values:

Age of Patient	Sevoflurane in Oxygen	Sevoflurane in 65% N_2O/35% O_2
0–<1 month*	3.3%	2.0%**
1–<6 months	3.0%	—
6 months–<3 years	2.8%	—
3–12 years	2.5%	—
25 years	2.6%	1.4%
40 years	2.1%	1.1%

60 years	1.7%	0.9%
80 years	1.4%	0.7%

* Neonates are full term gestational age.

** In 1–<3 year old paediatric patients, 60% N_2O/40% O_2 was used.

Special Populations:

Older people: MAC decreases with age. The average concentration required in an 80-year-old is approximately 50% of that required in a 20-year-old.

Paediatric population: See MAC table above. Rapid emergence may be associated with agitation (in approximately 25% of cases); early post-operative pain relief may be required.

4.3 Contraindications

Known or suspected hypersensitivity to sevoflurane or other halogenated anaesthetics.

History of liver dysfunction, fever, or leucocytosis of unknown cause after anaesthesia with halogenated agents.

Known or suspected genetic susceptibility to malignant hyperthermia.

Patients in whom general anaesthesia is contraindicated.

4.4 Special Warnings and Precautions for Use

- Sevoflurane should be administered only by persons trained in general anaesthesia. Facilities for airway maintenance, artificial ventilation, oxygen enrichment, and circulatory resuscitation must be immediately available.
- Respiratory depression may occur and may be augmented by narcotic premedication.
- Only vaporisers specifically calibrated for sevoflurane must be used.
- Malignant hyperthermia: Potent inhalation anaesthetics may trigger this hypermetabolic syndrome in susceptible individuals (signs include hypercapnia, muscle rigidity, tachycardia, arrhythmias, unstable blood pressure). Some cases have been fatal.
- Perioperative hyperkalaemia: Rare increases in serum potassium have resulted in cardiac arrhythmias and death in paediatric patients post-operatively, particularly those with neuromuscular disease (e.g., Duchenne muscular dystrophy). Concomitant use of succinylcholine has been associated with most cases.
- Seizures: Rare cases reported, particularly in children and young adults from 2 months of age. Limit depth of anaesthesia in children at risk.
- Hepatic dysfunction: Very rare cases of post-operative hepatitis or hepatic failure. Use caution in patients with underlying hepatic conditions or repeated exposure to halogenated hydrocarbons within short intervals.
- Renal impairment: Use with caution; safety not fully established in patients with baseline serum creatinine >1.5 mg/dL.
- Neurosurgery: Use cautiously in patients at risk of elevated intracranial pressure; employ ICP-reducing manoeuvres.
- QT prolongation: Isolated reports, very rarely associated with torsade de pointes. Caution in susceptible patients.

- Desiccated CO_2 absorbents: Rare cases of extreme heat, smoke, and/or spontaneous fire in anaesthesia machines. Replace desiccated CO_2 absorbent before use. Avoid potassium hydroxide-containing absorbents (e.g., Baralyme®).
- Obstetric anaesthesia: Uterine relaxant effect may increase risk of uterine bleeding.
- Mitochondrial disorders: Caution advised.

4.5 Interaction with Other Medicinal Products

- Sympathomimetics: Beta-sympathomimetics (isoprenaline) and alpha-/beta-sympathomimetics (adrenaline, noradrenaline) — potential risk of ventricular arrhythmia.
- Non-selective MAO inhibitors: Risk of crisis during operation; discontinue 2 weeks prior to surgery.
- Calcium antagonists: Risk of marked hypotension and additive negative inotropic effects.
- Succinylcholine: Risk of hyperkalaemia and cardiac arrhythmias in paediatric patients.
- CYP2E1 inducers (e.g., isoniazid, alcohol): May increase metabolism and plasma fluoride concentrations; potentiate hepatotoxicity with isoniazid.
- St John's Wort: Severe hypotension and delayed emergence reported.
- Beta blockers: Increased negative inotropic, chronotropic, and dromotropic effects.
- Verapamil: Impairment of atrioventricular conduction.
- Benzodiazepines and opioids: Decrease MAC of sevoflurane; synergistic fall in heart rate, blood pressure, and respiratory rate with alfentanil/sufentanil.
- Nitrous oxide: Reduces MAC by approximately 50% in adults and 25% in paediatrics.
- Neuromuscular blocking agents: Potentiates non-depolarising blockers (pancuronium, vecuronium, atracurium). Dose reduction likely required during maintenance.

4.6 Fertility, Pregnancy and Lactation

- Pregnancy: No adequate and well-controlled studies in pregnant women. Animal studies have shown reproductive toxicity. Sevoflurane has a relaxant effect on the uterus which may increase uterine bleeding. Use during pregnancy only if clearly needed.
- Labour and delivery: Safety demonstrated for Caesarean section in one small study. Safety in labour and vaginal delivery not established.
- Breastfeeding: It is not known whether sevoflurane or its metabolites are excreted in human milk. Advise women to skip breastfeeding for 48 hours after administration and discard milk produced during this period.
- Fertility: No evidence of impaired fertility in animal studies.

4.7 Effects on Ability to Drive and Use Machines

Patients should be advised that performance of activities requiring mental alertness (e.g., driving, operating machinery) may be impaired for some time after general anaesthesia. Patients should not drive for a suitable period after sevoflurane anaesthesia.

4.8 Undesirable Effects

Summary of safety profile: Most adverse reactions are mild to moderate and transient. Nausea, vomiting, and delirium are commonly observed post-operatively.

Adverse reactions by frequency (Very common ≥1/10; Common ≥1/100 to <1/10; Uncommon ≥1/1,000 to <1/100; Rare ≥1/10,000 to <1/1,000; Very rare <1/10,000):

System Organ Class	Adverse Reaction	Frequency
Immune system disorders	Hypersensitivity (rash, dyspnoea, wheezing, anaphylactic reaction)	Rare
Metabolism and nutrition disorders	Perioperative hyperkalaemia	Rare
Psychiatric disorders	Agitation (children), delirium	Common
Nervous system disorders	Seizures, dystonic movements (children)	Rare
Cardiac disorders	Bradycardia, arrhythmias, cardiac arrest	Uncommon to Rare
Vascular disorders	Hypotension	Very common (adults)
Respiratory disorders	Cough, respiratory depression	Common
Gastrointestinal disorders	Nausea, vomiting	Very common (adults)
Hepatobiliary disorders	Hepatic dysfunction, hepatitis, hepatic failure	Very rare
Skin and subcutaneous tissue disorders	Contact dermatitis (occupational exposure)	Rare

Paediatric population: Seizures have occurred in children and young adults from 2 months of age, most without predisposing risk factors.

Observed post-marketing.

Reporting of suspected adverse reactions If you experience any side effects, talk to your doctor or pharmacist. By reporting side effects, you can help provide more information on the safety of this product. Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

Symptoms include respiratory depression and circulatory insufficiency.

Management: Stop drug administration, establish a clear airway, initiate assisted or controlled ventilation with pure oxygen, and maintain adequate cardiovascular function.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: General anaesthetics, halogenated hydrocarbons

ATC code: N01AB08

Sevoflurane is a halogenated methyl isopropyl ether inhalational anaesthetic. Changes in clinical effects rapidly follow changes in inspired concentration. It produces loss of consciousness, reversible abolition of pain and motor activity, diminution of autonomic reflexes, and dose-dependent respiratory and cardiovascular depression.

MAC (Minimum Alveolar Concentration): Age-specific; see section 4.2.

Cardiovascular effects: Dose-related depression of cardiovascular function; decreases mean arterial pressure without significant change in heart rate.

Nervous system effects: Minimal effect on intracranial pressure in normocapnic patients; preserves CO_2 responsiveness. No significant effect on cerebral blood flow.

5.2 Pharmacokinetic Properties

Sevoflurane has low blood solubility (blood/gas partition coefficient 0.63–0.69 at 37°C), resulting in rapid induction and emergence.

Metabolism: Less than 5% of absorbed sevoflurane is metabolised via cytochrome P450 (CYP2E1) to hexafluoroisopropanol (HFIP) and inorganic fluoride. HFIP is rapidly conjugated with glucuronic acid and excreted in urine.

Elimination: Primarily via pulmonary exhalation. Inorganic fluoride concentrations peak within 2 hours post-anaesthesia and return to pre-operative levels within 48 hours.

5.3 Preclinical Safety Data

Animal studies demonstrate that hepatic and renal circulation are well maintained with sevoflurane. Sevoflurane decreases cerebral metabolic rate for oxygen ($CMRO_2$) by approximately 50% at 2.0 MAC. No significant effect on cerebral blood flow.

Reproductive toxicity: Animal studies at doses up to 1 MAC have not shown impaired fertility or harm to the fetus.

Carcinogenicity: No carcinogenicity studies have been performed. No mutagenic effect in Ames test; no chromosomal aberrations in mammalian cells.

Nephrotoxicity: Nephrotoxicity observed in rats exposed to Compound A levels exceeding those in routine clinical practice. Relevance to humans has not been established.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

None.

6.2 Incompatibilities

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

Chemical degradation can occur upon exposure to CO_2 absorbents within the anaesthesia machine. Degradation is enhanced by:

- Desiccated CO_2 absorbent (especially potassium hydroxide-containing, e.g., Baralyme®)
- Increased absorbent temperature
- Increased sevoflurane concentration
- Decreased fresh gas flow

Degradants include Compound A (pentafluoroisopropenyl fluoromethyl ether), formaldehyde, methanol, and carbon monoxide under extreme conditions.

6.3 Shelf Life

Unopened: 24 months

After first opening: Use immediately. Do not store for later use.

6.4 Special Precautions for Storage

Store below 30°C.

Do not freeze.

Store in the original container protected from light.

6.5 Nature and Contents of Container

Amber glass bottle with aluminium cap and fluoropolymer-lined seal.

Pack size: 250 ml

6.6 Special Precautions for Disposal and Other Handling

Any unused product or waste material should be disposed of in accordance with local requirements for hazardous pharmaceutical waste.

Avoid contact with desiccated CO_2 absorbents. Replace CO_2 absorbent routinely regardless of colour indicator status.

7. MARKETING AUTHORISATION HOLDER

Crown healthcare Limited CrownPlex, Mombasa Rd, Opp. JKIA Flyover, P.O. Box 40449-00100, Nairobi, Kenya

8. MARKETING AUTHORISATION NUMBER

CTD6282

9. DATE OF FIRST AUTHORISATION/RENEWAL

11th January 2022

10. DATE OF REVISION OF THE TEXT

11th January 2022