Anesthesia Time Guidelines at 1 L fresh gas flow rate/min[1]

ULTANE sevoflurane

1/2 MAC ULTANE given for 4 hours =
1/4 MAC ULTANE given for 8 hours =
1 MAC ULTANE given for 2 hours =

2 MAC–hours

ULTANE exposure should not exceed 2 MAC-hours at flow rates of 1 to <2 L/min. Fresh gas flow rates <1 L/min are not recommended. There is a potential for renal injury when ULTANE is used at low flow rates.

- The concentration of ULTANE required for maintenance of general anesthesia is age dependent. In pediatric patients, the MAC equivalent dose of ULTANE should be reduced when used with nitrous oxide.
- MAC decreases with increasing age. The average concentration of ULTANE to achieve MAC in an 80-year-old is approximately 50% of that required in a 20-year-old.

Indication[1]

ULTANE® (sevoflurane) is indicated for induction and maintenance of general anesthesia in adult and pediatric patients for inpatient and outpatient surgery. ULTANE should be administered only by persons trained in the administration of general anesthesia. Facilities for maintenance of a patent airway, artificial ventilation, oxygen enrichment, and circulatory resuscitation must be immediately available. Since level of anesthesia may be altered rapidly, only vaporizers producing predictable concentrations of ULTANE should be used.

Safety Considerations

ULTANE **is contraindicated** in patients with known or suspected genetic susceptibility to malignant hyperthermia or known or suspected sensitivity to sevoflurane or to other halogenated inhalational anesthetics.

ULTANE minimum alveolar concentration (MAC) values by patient age[1]

Age	100% O_2	65% N_2O/35% O_2
0 to 1 month[a]	3.3%	–
1 to <6 months	3.0%	–
6 months to <3 years	2.8%	2.0%[b]
3 to 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%

[a] Neonates are full-term gestational age. MAC in premature infants has not been determined.
[b] In 1 to <3-year-old pediatric patients, 60% N_2O/40% O_2 was used.

Please see Important Safety Information on following page.
Please see accompanying full Prescribing Information or visit https://www.rxabbvie.com/pdf/ultanepi.pdf.

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Important Safety Information[1]

- ULTANE **is contraindicated** in patients with known or suspected genetic susceptibility to malignant hyperthermia or known or suspected sensitivity to sevoflurane or to other halogenated inhalational anesthetics..
- In susceptible individuals, volatile anesthetic agents, including sevoflurane, may trigger malignant hyperthermia. Fatal outcomes of malignant hyperthermia have been reported. The risk of developing malignant hyperthermia increases with the concomitant administration of succinylcholine and volatile anesthetic agents. Successful treatment depends on early recognition of the clinical signs. If malignant hyperthermia is suspected, discontinue all triggering agents, administer intravenous dantrolene sodium, and initiate supportive therapies.
- Sevoflurane may cause respiratory depression, which may be augmented by opioid premedication or other agents causing respiratory depression. Monitor respiration and, if necessary, assist with ventilation.
- Due to ULTANE's insolubility in blood, hemodynamic changes may occur more rapidly than with other volatile anesthetics. Excessive decreases in blood pressure or respiratory depression may be related to depth of anesthesia and may be corrected by decreasing the inspired concentration of ULTANE.
- Seizures have been reported in association with ULTANE use, the majority of which have occurred in children and young adults, most of whom had no predisposing risk factors. Clinical judgment should be exercised when using ULTANE in patients who may be at risk for seizures.
- Rare increases in serum potassium resulting in cardiac arrhythmias and death have been noted in pediatric patients during the postoperative period following the use of inhaled anesthetic agents. Contributing risk factors appear to be latent or overt neuromuscular disease, particularly Duchenne muscular dystrophy. Concomitant use of succinylcholine has been associated with most, but not all, of these cases. Early, aggressive intervention to treat both hyperkalemia and resistant arrhythmias, and subsequent evaluation for latent neuromuscular disease, is recommended.
- Reports of QT prolongation, associated with torsade de pointes (in exceptional cases, fatal), have been received. Caution should be exercised when administering ULTANE to susceptible patients (eg, patients with congenital long QT syndrome or patients taking drugs that can prolong the QT interval).
- Studies conducted in young animals and children suggest repeated or prolonged use of general anesthetic or sedation drugs in the third trimester of gestation through the first three years of age may result in adverse cognitive or behavioral effects on their developing brains. The studies in children have substantial limitations, and it is not clear if the observed effects are due to the anesthetic/sedation drug administration or other factors, such as the surgery or underlying illness. Anesthetic and sedation drugs are a necessary part of the care of children when needed, and no specific medications have been shown to be safer than any other. Decisions regarding the timing of any elective procedures requiring anesthesia should take into consideration the benefits of the procedure weighed against the potential risks.
- Episodes of severe bradycardia and cardiac arrest have been reported postmarketing during anesthesia induction in pediatric patients with Down syndrome. Closely monitor heart rate during induction.
- Risk of renal toxicity: Findings taken from patient and animal studies suggest that there is a potential for renal injury when ULTANE is used at low flow rates, which is presumed due to compound A. ULTANE may be associated with glycosuria and proteinuria when used for long procedures at low flow rates. The level of compound A exposure at which clinical nephrotoxicity might be expected to occur has not been established. To minimize exposure to compound A, ULTANE exposure should not exceed 2 MAC-hours at flow rates of 1 to <2 L/min. Fresh gas flow rates <1 L/min are not recommended. Because clinical experience in administering ULTANE to patients with renal insufficiency (creatinine >1.5 mg/dL) is limited, its safety in these patients has not been established.
- Performance of activities requiring mental alertness, such as driving or operating machinery, may be impaired after sevoflurane anesthesia.
- Cases of mild, moderate, and severe hepatic dysfunction or hepatitis (eg, jaundice associated with fever and/or eosinophilia) after anesthesia with sevoflurane have been reported. In addition, postmarketing reports of hepatic failure and hepatic necrosis have associated the conditions with the use of ULTANE. Clinical judgment should be used in patients with underlying hepatic conditions or who are under treatment with drugs known to cause hepatic dysfunction. It has been reported that previous exposure to halogenated hydrocarbon anesthetics may increase the potential for hepatic injury.
- Drug interactions: Epinephrine administered with sevoflurane may increase risk of ventricular arrhythmias. Monitor electrocardiogram and blood pressure and ensure availability of emergency medications. Sevoflurane may lead to marked hypotension in patients treated with calcium antagonists. Monitor blood pressure and ensure availability of emergency medications in these patients. Concomitant use of MAO inhibitors and inhalational anesthetics may increase risk of hemodynamic instability. Benzodiazepines and opioids would be expected to decrease the MAC of ULTANE. The anesthetic requirement for ULTANE is decreased when administered in combination with nitrous oxide. ULTANE increases both the intensity and duration of neuromuscular blockade induced by nondepolarizing muscle relaxants.
- Adverse events reported by ≥5% of the surgical patients receiving ULTANE during clinical trials during induction included: bradycardia, tachycardia, agitation, laryngospasm, airway obstruction, breathholding, and increased cough; during maintenance and emergence: shivering, hypotension, bradycardia, somnolence, agitation, nausea, vomiting, and increased cough were reported.
- KOH containing CO_2 absorbents are not recommended for use with ULTANE. An exothermic reaction occurs when ULTANE is exposed to CO_2 absorbents. This reaction is increased when the absorbent becomes desiccated. Rare cases of extreme heat, smoke, and/or spontaneous fire have been reported during ULTANE use in conjunction with the use of desiccated CO_2 absorbent, specifically those containing potassium hydroxide (eg, Baralyme).

Reference: 1. ULTANE [package insert]. North Chicago, IL: AbbVie Inc.

Please see Indication on page one.

Please see accompanying full Prescribing Information or visit https://www.rxabbvie.com/pdf/ultanepi.pdf.

ULTANE® sevoflurane

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