Indication and Important Safety Information you should know about Sevoflurane

Indication

- Sevoflurane is indicated for induction and maintenance of general anesthesia in adult and pediatric patients for inpatient and outpatient surgery. Sevoflurane 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 Sevoflurane should be used.

Important Safety Information

- Sevoflurane can cause malignant hyperthermia. Postmarketing reports of malignant hyperthermia, some of which have been fatal, have occurred. Sevoflurane should not be used in patients with known sensitivity to Sevoflurane or to other halogenated agents, or in patients with known or suspected susceptibility to malignant hyperthermia.

- Findings taken from patient and animal studies suggest that there is a potential for renal injury when Sevoflurane is used at low flow rates, which is presumed due to Compound A. 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, Sevoflurane 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 Sevoflurane to patients with renal insufficiency (creatinine >1.5 mg/dL) is limited, its safety in these patients has not been established.

- Sevoflurane may be associated with glycosuria and proteinuria when used for long procedures at low flow rates.

- KOH containing CO_2 absorbents are not recommended for use with Sevoflurane. An exothermic reaction occurs when Sevoflurane 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 Sevoflurane use in conjunction with the use of desiccated CO_2 absorbent, specifically those containing potassium hydroxide (e.g., Baralyme).

- Reports of QT prolongation, associated with torsade de pointes (in exceptional cases, fatal), have been received. Caution should be exercised when administering Sevoflurane to susceptible patients (e.g. patients with congenital Long QT Syndrome or patients taking drugs that can prolong the QT interval).

- 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.

- During the maintenance of anesthesia, increasing the concentration of Sevoflurane produces dose-dependent decreases in blood pressure. Due to Sevoflurane'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 Sevoflurane.

- Seizures have been reported in association with Sevoflurane 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 Sevoflurane in patients who may be at risk for seizures.

- Drug interactions: Benzodiazepines and opioids would be expected to decrease the MAC of Sevoflurane. The anesthetic requirement for Sevoflurane is decreased when administered in combination with nitrous oxide. Sevoflurane increases both the intensity and duration of neuromuscular blockade induced by nondepolarizing muscle relaxants.

- Very rare cases of mild, moderate, and severe postoperative hepatic dysfunction or hepatitis with or without jaundice have been reported from postmarketing experiences. In addition, rare postmarketing reports of hepatic failure and hepatic necrosis have been associated with the use of Sevoflurane. 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.

- Adverse events reported by ≥5% of the surgical patients receiving Sevoflurane 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.

Sevoflurane, USP [Package insert, October 2015].

CONTRAINDICATIONS:

Sevoflurane can cause malignant hyperthermia. It should not be used in patients with known sensitivity to sevoflurane or to other halogenated agents nor in patients with known or suspected susceptibility to malignant hyperthermia.

WARNINGS:

Although data from controlled clinical studies at low flow rates are limited, findings taken from patient and animal studies suggest that there is a potential for renal injury which is presumed due to Compound A. Animal and human studies demonstrate that sevoflurane administered for more than 2 MAC·hours and at fresh gas flow rates of <2 L/min may be associated with proteinuria and glycosuria.

While a level of Compound A exposure at which clinical nephrotoxicity might be expected to occur has not been established, it is prudent to consider all of the factors leading to Compound A exposure in humans, especially duration of exposure, fresh gas flow rate, and concentration of sevoflurane. During sevoflurane anesthesia the clinician should adjust inspired concentration and fresh gas flow rate to minimize exposure to Compound A. To minimize exposure to Compound A, sevoflurane 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 sevoflurane to patients with renal insufficiency (creatinine>1.5 mg/dL) is limited, its safety in these patients has not been established.

Sevoflurane may be associated with glycosuria and proteinuria when used for long procedures at low flow rates. The safety of low flow sevoflurane on renal function was evaluated in patients with normal preoperative renal function. One study compared sevoflurane (N = 98) to an active control (N = 90) administered for ≥2 hours at fresh gas flow rate of ≤1 Liter/minute. Per study defined criteria (Hou et al.) one patient in the sevoflurane group developed elevations of creatinine, in addition to glycosuria and proteinuria. This patient received sevoflurane at fresh gas flow rates of ≤800 mL/minute. Using these same criteria, there were no patients in the active control group who developed treatment emergent elevations in serum creatinine.

Sevoflurane may present an increased risk in patients with known sensitivity to volatile halogenated anesthetic agents. KOH containing CO_2 absorbents are not recommended for use with sevoflurane.

Reports of QT prolongation, associated with torsade de pointes (in exceptional cases, fatal), have been received. Caution should be exercised when administering sevoflurane to susceptible patients (e.g. patients with congenital Long QT Syndrome or patients taking drugs that can prolong the QT interval).

Malignant Hyperthermia:

In susceptible individuals, potent inhalation anesthetic agents, including sevoflurane, may trigger a skeletal muscle hypermetabolic state leading to high oxygen demand and the clinical syndrome known as malignant hyperthermia. Sevoflurane can induce malignant hyperthermia in genetically susceptible individuals, such as those with certain inherited ryanodine receptor mutations. The clinical syndrome is signaled by hypercapnia, and may include muscle rigidity, tachycardia, tachypnea, cyanosis, arrhythmias, and/or unstable blood pressure. Some of these nonspecific signs may also appear during light anesthesia, acute hypoxia, hypercapnia, and hypovolemia.

In clinical trials, one case of malignant hyperthermia was reported. In addition, there have been postmarketing reports of malignant hyperthermia. Some of these cases have been fatal.

Treatment of malignant hyperthermia includes discontinuation of triggering agents (e.g., sevoflurane), administration of intravenous dantrolene sodium (consult prescribing information for intravenous dantrolene sodium for additional information on patient management), and application of supportive therapy. Supportive therapy may include efforts to restore body temperature, 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.

Perioperative Hyperkalemia:

Use of inhaled anesthetic agents has been associated with rare increases in serum potassium levels that have resulted in cardiac arrhythmias and death in pediatric patients during the postoperative period. Patients with latent as well as overt neuromuscular disease, particularly Duchenne muscular dystrophy, appear to be most vulnerable. Concomitant use of succinylcholine 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 hyperkalemia and resistant arrhythmias is recommended; as is subsequent evaluation for latent neuromuscular disease.