Indication and Important Safety information you should know about Isoflurane

Isoflurane, USP

Liquid for Inhalation
Rx only

DESCRIPTION: Isoflurane, USP, a nonflammable liquid administered by vaporizing, is a general inhalation anesthetic drug. It is 1-chloro-2,2,2- trifluoroethyl difluoromethyl ether and is a clear, colorless, stable liquid containing no additives or chemical stabilizers. Isoflurane has a mildly pungent, musty, ethereal odor. Samples stored in indirect sunlight in clear, colorless glass for five years, as well as samples directly exposed for 30 hours to a 2 amp, 115 volt, 60 cycle long wave U.V. light were unchanged in composition as determined by gas chromatography.

INDICATIONS AND USAGE
Isoflurane, USP may be used for induction and maintenance of general anesthesia. There are no adequate data to establish its use in obstetrical anesthesia.

CONTRAINDICATIONS
Known sensitivity to Isoflurane, USP or to other halogenated agents. Known or suspected genetic susceptibility to malignant hyperthermia.

WARNINGS
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 of these cases. Early and aggressive intervention to treat the hyperkalemia and resistant arrhythmias is recommended, as is subsequent evaluation for latent neuromuscular disease.

Malignant Hyperthermia
In susceptible individuals, isoflurane anesthesia may trigger a skeletal muscle hypermetabolic state and the clinical syndrome known as malignant hyperthermia. Treatment includes discontinuance of isoflurane, 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 derangements. (Consult prescribing information for dantrolene sodium intravenous for additional information). Renal failure may appear later, and urine flow should be sustained if possible.

Since levels of anesthesia may be altered easily and rapidly, only vaporizers producing predictable concentrations should be used. Hypotension and respiratory depression increase as anesthesia is deepened.

Increased blood loss comparable to that seen with halothane has been observed in patients undergoing abortions.

Isoflurane, USP markedly increases cerebral blood flow at deeper levels of anesthesia. There may be a transient rise in cerebral spinal fluid pressure, which is fully reversible with hyperventilation.

PRECAUTIONS
General

As with any potent general anesthetic, Isoflurane, USP should only be administered in an adequately equipped anesthetizing environment and by appropriately qualified and experienced staff.

Regardless of the anesthetics employed, maintenance of normal hemodynamics is important to the avoidance of myocardial ischemia in patients with coronary artery disease.

Isoflurane, USP, can react with desiccated carbon dioxide (CO_2) absorbents to produce carbon monoxide, which may result in elevated levels of carboxyhemoglobin in some patients. Case reports suggest that barium hydroxide lime and soda lime become desiccated when fresh gases are passedthrough the CO_2 absorber canister at high flow rates over many hours or days. When a clinician suspects that CO_2 absorbent may be desiccated, it should be replaced before the administration of Isoflurane, USP.

As with other halogenated anesthetic agents, Isoflurane, USP may cause sensitivity hepatitis in patients who have been sensitized by previous exposure to halogenated anesthetics (see **CONTRAINDICATIONS**).

Information for Patients
Isoflurane, as well as other general anesthetics, may cause a slight decrease in intellectual function for 2 or 3 days following anesthesia. As with other anesthetics, small changes in moods and symptoms may persist for up to 6 days after administration.

Laboratory Tests
Transient increases in BSP retention, blood glucose and serum creatinine with decrease in BUN, serum cholesterol and alkaline phosphatase have been observed.

Drug Interactions
Isoflurane potentiates the muscle relaxant effect of all muscle relaxants, most notably nondepolarizing muscle relaxants, and MAC (minimum alveolar concentration) is reduced by concomitant administration of N_2O.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Swiss ICR mice were given isoflurane to determine whether such exposure might induce neoplasia. Isoflurane was given at ½, 1/8 and 1/32 MAC for four in-utero exposures and for 24 exposures to the pups during the first nine weeks of life. The mice were killed at 15 months of age. The incidence of tumors in these mice was the same as in untreated control mice, which were given the same background gases, but not the anesthetic.

Pregnancy
Pregnancy Category C
Because of the possible risk of fetotoxicity isoflurane should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
It is not known if isoflurane is excreted in human milk, caution should be exercised when administered to nursing women.

ADVERSE REACTIONS
Adverse reactions encountered in the administration of Isoflurane, USP are in general dose dependent extensions of pharmaco-physiologic effects and include respiratory depression, hypotension and arrhythmias.
Shivering, nausea, vomiting and ileus have been observed in the postoperative period.
As with all other general anesthetics, transient elevations in white blood count have been observed even in the absence of surgical stress. See WARNINGS for information regarding malignant hyperthermia and elevated carboxyhemoglobin levels.
There have been rare reports of mild, moderate and severe (some fatal) postoperative hepatic dysfunction and hepatitis.
Isoflurane, USP has also been associated with perioperative hyperkalemia (see WARNINGS).
There have been rare reports of hepatic failure and hepatic necrosis associated with the use of potent volatile anesthetic agents, including Isoflurane, USP.
Due to the spontaneous nature of these reports, the actual incidence and relationship of Isoflurane, USP to these events cannot be established with certainty.

OVERDOSAGE
In the event of overdosage, or what may appear to be overdosage, the following action should be taken: Stop drug administration, establish a clear airway, and initiate assisted or controlled ventilation with pure oxygen.

DOSAGE AND ADMINISTRATION
Premedication
Premedication should be selected according to the need of the individual patient, taking into account that secretions are weakly stimulated by Isoflurane, USP, and the heart rate tends to be increased. The use of anticholinergic drugs is a matter of choice.

Inspired Concentration
The concentration of isoflurane being delivered from a vaporizer during anesthesia should be known. ***(For further information please see the full prescribing information).***

Induction
Induction with isoflurane in oxygen or in combination with oxygen-nitrous oxide mixtures may produce coughing, breath-holding, or laryngospasm. These difficulties may be avoided by the use of a hypnotic dose of an ultra-short-acting barbiturate. Inspired concentrations of 1.5 to 3.0% isoflurane usually produce surgical anesthesia in 7 to 10 minutes.

Maintenance
Surgical levels of anesthesia may be sustained with a 1.0 to 2.5% concentration when nitrous oxide is used concomitantly. An additional 0.5 to 1.0% may be required when isoflurane is given using oxygen alone. If added relaxation is required, supplemental doses of muscle relaxants may be used. The level of blood pressure during maintenance is an inverse function of isoflurane concentration in the absence of other complicating problems. Excessive decreases may be due to depth of anesthesia and in such instances may be corrected by lightening anesthesia.

HOW SUPPLIED
Isoflurane, USP is packaged in 250 mL ambercolored bottles.
250 mL NDC 66794-017-25

Safety and Handling
Occupational Caution
There is no specific work exposure limit established for Isoflurane, USP. However, the National Institute for Occupational Safety and Health Administration (NIOSH) recommends that no worker should be exposed at ceiling concentrations greater than 2 ppm of any halogenated anesthetic agent over a sampling period not to exceed one hour.

Storage
Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].

Manufactured by:
Piramal Enterprises Limited
N.H. 9, Digwal Village, KohirMandal, KohirCross Road, Medak Dist. 502 321 Andhra Pradesh, India.

Revised: January 2018.