Issued to the Medical Professionals Only

# AERRANE (Isoflurane USP)

## PRESENTATION

AERRANE (isoflurane USP) is a colourless volatile liquid for inhalation, containing 99.9% w/w isoflurane USP.

## INDICATIONS

AERRANE (isoflurane) is a volatile halogenated anaesthetic for general inhalation anaesthesia.

## DOSAGE AND ADMINISTRATION

AERRANE (isoflurane) should be administered only by persons trained in the administration of general anaesthesia. Facilities for maintenance of a patent airway, artificial ventilation, oxygen enrichment, and circulatory resuscitation must be immediately available.

AERRANE (isoflurane) is administered by inhalation. AERRANE (isoflurane) should be delivered from a vaporiser specifically designed for use with isoflurane .

Dosage for induction and maintenance must be individualised and titrated to the desired effect according to the patient's age and clinical status.

The need for premedication and type of premedicants must be determined on an individual basis.

With the exception of neonates, the minimum alveolar concentration (MAC) of AERRANE (isoflurane) decreases with increasing patient age.

AERRANE (isoflurane) MAC values according to age as shown below:

| Age | Average MAC Value in 100% Oxygen | Average MAC Value in 30% Oxygen and 70% $N_2O$ |
|---|---|---|
| 0 – 1 month | 1.60% | - |
| 1 – 6 months | 1.87% | - |
| 6 – 12 months | 1.80% | - |
| 1 – 5 years | 1.60% | - |
| 19 – 30 years | 1.28% | 0.56% |
| 32 – 55 years | 1.15% | 0.50% |
| 55 – 83 years | 1.05% | 0.37% |

### Induction of Anaesthesia

If AERRANE (Isoflurane) is used for induction of anaesthesia, a starting concentration of 0.5% is recommended. Concentrations of 1.3 – 3.0% usually bring about surgical anaesthesia within 7 to 10 minutes.

It is recommended that use be made of a hypnotic dose of a short acting barbiturate or another product such as propofol, etomidate, or midazolam in order to avoid coughing or laryngospasm, which can arise if induction is carried out with AERRANE (isoflurane) alone or in combination with oxygen or with an oxygen-nitrous oxide mixture.When using AERRANE (isoflurane) for induction, it should be considered that the risk of coughing, breath holding, laryngospasm, and bronchospasm during induction increases with the concentration of AERRANE (isoflurane).

### Maintenance of Anaesthesia

Anaesthesia can be maintained during surgery using a concentration of 1.0 – 2.5%, with the simultaneous administration of $N_2O$ and $O_2$. A higher concentration of 1.5 – 3.5% of AERRANE (isoflurane) is necessary if AERRANE (isoflurane) is administered with pure oxygen.

### Recovery

The concentration of AERRANE (isoflurane) must be reduced to 0.5% at the end of the operation, or to 0% during closure of the wound to allow prompt recovery. If all administration of anaesthetic agents has been stopped, the air passages of the patient should be ventilated several times with 100% oxygen until complete awakening occurs. If the vector gas is a mixture of 50% $O_2$ and 50% $N_2O$, the volume of the minimum alveolar concentration of AERRANE (isoflurane) is approximately 0.65%.

## CONTRAINDICATIONS

AERRANE (isoflurane) is contraindicated in patients:

- with known hypersensitivity to AERRANE (isoflurane) or to other halogenated inhalational anaesthetics
- with known or suspected susceptibility to malignant hyperthermia
- with a history of confirmed hepatitis due to halogenated inhalational anaesthetic or a history of unexplained moderate to severe hepatic dysfunction(e.g., jaundice associated with fever and/or eosinophilia) after anaesthesia with AERRANE (isoflurane) or other halogenated inhalational anaesthetics.
- Obstetric operation
- Nonselective MAOI (See Interactions)
- in whom general anaesthesia is contraindicated.

## SPECIAL WARNINGS AND PRECAUTIONS FOR USE

### Warnings

AERRANE (isoflurane) must only be used by a licensed anaesthetist. Since the depth of anaesthesia can change easily and rapidly with AERRANE (isoflurane). Only vaporisers that have been specially calibrated for this product may be used. The extent of blood-pressure reduction and respiratory depression can be an indication of the extent of anaesthesia.

Spontaneous respiration must be carefully monitored and must be assisted if necessary.

In susceptible individuals, AERRANE (isoflurane) anaesthesia may trigger a skeletal muscle hypermetabolic state leading to high oxygen demand and the clinical syndrome known as malignant hyperthermia.

The syndrome includes non-specific features such as muscle rigidity, tachycardia, tachypnoea, cyanosis, arrhythmias, and unstable blood pressure. It should also be noted that many of these nonspecific signs may appear with light anaesthesia, acute hypoxia, etc.

An increase in overall metabolism may be reflected in an elevated temperature, (which may rise rapidly early or late in the case, but usually is not the first sign of augmented metabolism) and an increased usage of the $CO_2$ absorption system (hot canister).

$PaO_2$ and pH may decrease, and hyperkalaemia and a base deficit may appear.

Treatment includes discontinuance of triggering agents (e.g., AERRANE (isoflurane)), administration of intravenous dantrolene sodium, and application of supportive therapy. Such therapy includes vigorous efforts to decerase the patient's body temperature, respiratory and circulatory support as indicated, and management of electrolyte-fluid-acid-base derangements. (Consult prescribing information for dantrolene sodium intravenous for additional information on patient management.) Renal failure may appear later, and urine flow should be sustained if possible. Fatal outcome of malignant hyperthermia has been reported with AERRANE (isoflurane).

Use of inhaled anaesthetic agents has been associated with rare increases in serum potassium levels that have resulted in cardiac arrhythmias and death in paediatric 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 hyperkalaemia and resistant arrhythmias is recommended, as is subsequent evaluation for latent neuromuscular disease.

Cases of mild, moderate, and severe postoperative hepatic dysfunction or hepatitis with or without jaundice, including fatal hepatic necrosis and hepatic failure, have been reported with AERRANE (isoflurane). Such reactions can represent hypersensitivity hepatitis, a known risk of exposure to halogenated anaesthetic, including AERRANE (isoflurane).

Clinical judgment should be exercised when AERRANE (isoflurane) is used in patients with underlying hepatic conditions or under treatment with drugs known to cause hepatic dysfunction. See **CONTRAINDICATIONS.**

As with all halogenated anaesthetics, repeated anaesthesia within a short period of time should be approached with caution.

Allergic-type hypersensitivity reactions, including anaphylaxis, have been reported with AERRANE (isoflurane). Manifestations of such reactions have included hypotension, rash, difficulty breathing and cardiovascular collapse.

Some published studies in children have observed cognitive deficits after repeated or prolonged exposures to anaesthetic/sedative agents early in life. These studies have substantial limitations, and it is not clear if the observed effects are due to the anaesthetic/sedation drug administration or other factors such as the surgery or underlying illness.

QT Prolongation

Reports of QT prolongation, very rarely associated with torsade de pointes, have been received. Caution should be exercised when administering isoflurane to susceptible patients (e.g., patients with congenital Long QT syndrome or patients taking drugs that can prolong the QT interval).

### Precautions

All patients anaesthetised with AERRANE (isoflurane) should be continuously monitored (e.g., monitoring of the electrocardiogram, blood pressure, oxygen saturation, and end tidal $CO_2$).

AERRANE (isoflurane) is a profound respiratory depressant. Excessive respiratory depression may be related to depth of anaesthesia and respond to decreasing the inspired concentration of AERRANE (isoflurane). The depressant effect is accentuated by concurrent used of narcotics and other respiratory depressants. Respiration should be closely monitored, and assisted or controlled ventilation employed when necessary.

Relatively little metabolism of AERRANE (isoflurane) occurs in the human body. In the post operation period only 0.17% of the AERRANE (isoflurane) taken up can be recovered as urinary metabolites. Peak serum inorganic fluoride values usually average less than 5 µmol/liter and occur about four hours after anaesthesia, returning to normal levels within 24 hours. No signs of renal injury have been reported after AERRANE (isoflurane) administration.

There is insufficient experience of use in repeated anaesthesia to make a definite recommendation in this regard. As with all halogenated anaesthetics repeat anaesthesia within a short period of time should be approached with caution.

Patients with Myasthenia Gravis are extremely sensitive to drugs that produce respiratory depression. These effects are potentiated with some general anaesthetics. AERRANE (isoflurane) should be used with caution in these patients.

AERRANE (isoflurane) causes a dose-dependent reduction in systemic vascular resistance and blood pressure.

Particular care must be taken when selecting the dosage for patients who are hypovolaemic, hypotensive, or otherwise haemodynamically compromised, e.g., due to concomitant medications. Excessive decreases in blood pressure may be related to depth of anaesthesia and respond to reducing the inspired concentration of AERRANE (isoflurane).

In patients with coronary artery disease, maintenance of normal haemodynamics is important to avoid myocardial ischaemia.

AERRANE (isoflurane) can cause dose dependant coronary vasodilation and has been shown to divert blood from collateral-dependent myocardium to normally perfused areas in an animal model ("coronary steal"). The extent to which coronary steal occurs in patients with steal-prone coronary anatomy is unclear. AERRANE (isoflurane) should be used with caution in such patients.

In patients with or at risk for elevations of intracranial pressure (ICP), AERRANE (isoflurane) should be administered cautiously and in conjunction with ICP-reducing measures.

AERRANE (isoflurane) should not be administered to patients who can develop bronchoconstriction since bronchospasm can occur. In the case of neurosurgical operations, respiration should be adequately checked. As with other halogenated anaesthetics, AERRANE (isoflurane) increases the flow of blood through the brain and is accompanied by a transient increase in ICP. In most cases, this pressure increase can be prevented by hyperventilation.

AERRANE (isoflurane), like some other inhalational anaesthetics, can react with desiccated carbon dioxide ($CO_2$) absorbents to produce carbon monoxide, which may result in elevated levels of carboxyhaemoglobin in some patients. Barium hydroxide lime and soda lime become desiccated when fresh gases are passed through 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 administration of AERRANE (isoflurane).

The colour indicator of most $CO_2$ absorbents does not necessarily change as a result of desiccation. Therefore, the lack of significant colour change should not be taken as an assurance of adequate hydration. $CO_2$ absorbents should be replaced routinely regardless of the state of the color indicator, following current guidelines for use of anaesthesiology equipment.

AERRANE (isoflurane) may cause a decrease in intellectual function as well as changes in mood for several days after general anaesthesia.

With the exception of neonates, AERRANE (isoflurane) MAC decreases with increasing age.

In light of the fact that AERRANE (isoflurane) acts in an irritating manner on the mucous membranes, the product is difficult to use if inhalation anaesthesia is applied via mask. During the induction of anaesthesia in children, saliva flow and tracheobronchial secretion can increase and can be the cause of laryngospasm.

The following reactions have been reported following occupational exposure to AERRANE (isoflurane): dyspnoea, bronchospasm, stridor, cough, dizziness, paresthesia, hepatic reactions, flushing, rash, contact dermatitis, erythema, periorbital oedema, eye irritation, conjunctival hyperaemia, and headache. See Post-marketing Adverse Reactions.

In the case of patients who have undergone abortus provocatus, an increased loss of blood has been found. A transient increase in bromsulphthalein retention, blood glucose, and serum creatinine with a decrease in the serum urea level, serum cholesterol level, and alkaline phosphatase level, has been observed.

## INTERACTION WITH OTHER MEDICINAL PRODUCT AND OTHER FORMS OF INTERACTION

The simultaneous administration of AERRANE (isoflurane) and the following products requires strict supervision of the clinical and biologic condition of the patient.

### Contraindicated Combination

- Concomitant use of non-selective MAO inhibitors: May increase the risk of haemodynamic instability during surgery or medical procedures. Treatment should be stopped 15 days prior to surgery.

### Combinations Advised Against

- Beta-sympathomimetics (isoprenaline) and alpha- and beta-sympathomimetics (epinephrine or adrenaline; norepinephrine or noradrenaline): Risk of serious ventricular arrhythmia as a result of an increase in heart rate. AERRANE (isoflurane) is similar to sevoflurane in the sensitization of the myocardium to the arrhythmogenic effect of exogenously administered adrenaline. Doses of adrenaline greater than 5 mcg/kg, when administered submucosally, produce multiple ventricular arrhythmias.

### Combinations Requiring Precautions in Using

- Concomitant use of Beta-blockers: May exaggerate the cardiovascular effects of inhalational anaesthetics, including hypotension and negative inotropic effects. The action of beta-blockers can be suppressed during the operation with the use of beta-sympathicomimetic agents. In general, any medication with a beta-blocker need not be stopped and an abrupt reduction of the dosage should be avoided.
- Isoniazid: Risk of potentiating the hepatotoxic effect, with increased formation of toxic metabolites of isoniazid. Treatment with isoniazid should be suspended one week before the operation and should not be resumed until 15 days afterward.
- Epinephrine: Epinephrine utilized for its local haemostatic action, by subcutaneous or gingival injections: Risk of serious ventricular arrhythmia as a consequence of increased heart rate, although the myocardial sensitivity with respect to epinephrine is lower with the use of AERRANE (isoflurane) than in the case of other halogenated anaesthetics. Thus, the dosage should be limited to, for example, 0.1 mg epinephrine within 10 minutes or 0.3 mg within one hour in adults.
- Indirect sympathomimetics (amphetamines and their derivatives; psychostimulants, appetite suppressants, ephedrine and its derivatives): Risk of intraoperative hypersensitivity episode. In the case of a planned operation, it is preferable to interrupt the treatment a few days before the operation.
- In the majority of cases where a drug treatment is indispensable, there is no reason to suspend it before general anaesthesia. It suffices to inform the anaesthetist about it.
- Muscle relaxing agents: Risk of intensification of the action of depolarising relaxants and, in particular, nondepolarising relaxants. Thus it is recommended that approximately one third to one half of the usual dose of these substances be administered. The disappearance of the myoneural effect takes longer with AERRANE (isoflurane) than with other conventional anaesthetics. Neostigmine has an effect on the non depolarizing relaxants, but has no effect on the relaxing action of AERRANE (isoflurane) itself.
- Morphine analgesics: These products potentiate the depressive action of AERRANE (isoflurane) on respiration.
- Calcium antagonists: AERRANE (isoflurane) may lead to marked hypotension in patients treated with calcium antagonists, particularly dihydropyridine derivatives.
- Opioids: Decrease the Minimum Alveolar Concentration (MAC) of AERRANE (isoflurane). Opioids such as fentanyl and its analogues, when combined with AERRANE (isoflurane), may lead to synergistic fall in blood pressure and respiratory rate.
- $N_2O$: Decreases the MAC of AERRANE (isoflurane). See **DOSAGE AND ADMINISTRATION.**

## PREGNANCY AND LACTATION

There are no adequate data and well-controlled studies in pregnant women. AERRANE (Isoflurane) should be used during pregnancy only if the potential benefit justifies the potential risk of the foetus (see PRECLINICAL SAFETY DATA).

The administration of AERRANE (isoflurane) to pregnant mice has been shown to have a possible foetotoxic effect at anaesthetic concentrations (0.6%) for 4 hours/day for 10 days during organogenesis. In contrast, the administration of 1.05% isoflurane to pregnant rats for 6 hours/day for 3 days during organogenesis, the administration of 1.63-1.73% AERRANE (isoflurane) to pregnant rats for 1 hour/day for 5 days during organogenesis, and the administration of 2.28-2.34% AERRANE (isoflurane) to pregnant rabbits for 1 hour/day for 4 days during organogenesis produced no foetotoxic effects.

Insufficient information is available to recommend use in pregnancy or obstetrics other than for Caesarean section.

Because there is insufficient information regarding the excretion of AERRANE (isoflurane) in human milk, the potential risks and benefits for each specific patient should be carefully considered before AERRANE (isoflurane) is administered to nursing women. Breast feeding should not be given for up to 12 hours after the termination of anaesthesia.

AERRANE (isoflurane) exerts a relaxant effect on uterine smooth muscle. This can lead to increased blood lossin situations where uterine muscle contractions aids haemostasis, such as in obstetric surgery and in patients undergoing abortions.

## EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Patients should be advised that performance of activites requiring mental alertness, such as driving a vehicle or operating machinery, may be impaired for some time after general anaesthesia.Therefore,patients should not undertake hazardous tasks, such as driving, for at least 24 hours following administration of a general anaesthetic. The patient should only be sent home with an escort, and should not consume any alcohol.

# ADVERSE REACTIONS

## Adverse Reactions from Clinical Trials

The following adverse reactions were identified from controlled clinical studies of adult and paediatric subjects exposed to isoflurane. The studies were conducted using a variety of premedications, other anaesthetics, and surgical procedures of varying lengths.

| System Organ Class (SOC) | Adverse Reaction | Frequency Category |
|---|---|---|
| **BLOOD AND LYMPATHIC SYSTEM DISORDERS** | White blood cell count increased | Very Common[1] |
| **METABOLISM AND NUTRITION DISORDERS** | Blood glucose increased | Not Known |
| **PSYCHIATRIC DISORDERS** | Delirium | Common |
| | Mood changes | Uncommon |
| | Nightmare | Uncommon |
| | Confusional state | Not Known |
| | Nervousness | Not Known |
| **NERVOUS SYSTEM DISORDERS** | Agitation (Excitement) (induction) | Very common[2] |
| | Movement (maintenance) | Common |
| | Convulsive pattern on electroencephalogram | Uncommon |
| | Seizure | Rare |
| | Ataxia | Not Known |
| | Dizziness | Not Known |
| | Drowsiness | Not Known |
| | Intellectual function decreased | Not Known |
| **CARDIAC DISORDERS** | Ventricular arrhythmia (intraoperative) | Common[3] |
| | Nodal arrhythmia (intraoperative) | Common[3] |
| | Atrial arrhythmia (intraoperative) | Common[3] |
| | Arrhythmia (postoperative) | Common[3] |
| **VASCULAR DISORDERS** | Hypotension | Intraoperative: Not Known |
| | | Postoperative: Not Known |
| | Hypertension | Intraoperative: Not Known |
| | | Postoperative: Rare |
| **RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS** | Breath holding | Overall: Very Common[2,3] |
| | | Induction: Very Common[2] |
| | | Maintenance: Common[2] |
| | Cough | Overall: Very Common[2,3] |
| | | Induction: Very Common[2] |
| | | Maintenance: Common[2] |
| | Laryngospasm | Overall: Common[2,3] |
| | | Induction: Common[2] |
| | | Maintenance: Uncommon[2] |
| | Secretions | Overall: Uncommon[2,3] |
| | | Induction: Uncommon[2] |
| | | Maintenance: -[4] |
| **GASTROINTESTINAL DISORDERS** | Nausea | Recovery: Very Common |
| | Vomiting | Induction: Uncommon[2] |
| | | Recovery: Common |
| | Retching | Induction: Uncommon[2] |
| | | Maintenance: Uncommon[2] |
| **HEPATOBILIARY DISORDERS** | Blood bilirubin increased | Not Known |
| | Bromosulpthalein clearance decreased | Not Known |
| | Alanine aminotransferase increased | Not Known |
| | Aspartate aminotransferase increased | Not Known |
| | Blood alkaline phosphatase increased | Not Known |
| | Blood lactate dehydogenase increased | Not Known |
| **SKIN AND SUBCUTANEOUS TISSUE DISORDERS** | Diaphoresis | Overall: Uncommon[2,3] |
| | | Induction: Uncommon[2] |
| | | Maintenance: -[4] |
| **MUSCULOSKELETAL CONNECTIVE TISSUE AND BONE DISORDERS** | Myalgia | Not Known |
| **GENERAL DISORDERS AND ADMINISTRATIVE SITE CONDITIONS** | Chills/shivering | Very Common |
| | Asthenia | Not Known |
| | Fatigue | Not Known |

ADR frequency is based upon the following scale: Very Common (≥1/10); Common (≥1/100 - <1/10), Uncommon (≥1/1,000 - <1/100), Rare (≥1/10,000 - <1/1,000), Very Rare (<1/10,000)

[1] Increases in white blood cell count were reported to rise for all patients in the first 1 to 2 days and 3 to 5 days postoperatively.

[2] Frequency/denominator reflects patients not receiving intravenous induction agents or muscle relaxants for intubation (i.e., patients receiving inhalation induction)

[3] Overall frequency category determined based on the data for the individual anesthesia phases.

[4] Seen in (0/359) patients during maintenance. Frequency/denominator reflects patients not receiving intravenous induction agents or muscle relaxants for intubation (i.e., patients receiving inhalation induction).

## Post-marketing Adverse Reactions

The following adverse reactions have been reported in the post-marketing

experience, listed by MedDRA System Organ Class (SOC), then by Preferred Term in

order of severity.

**BLOOD AND LYMPHATIC SYSTEM DISORDERS:** Carboxyhaemoglobin increased

**IMMUNE SYSTEM DISORDERS:** Anaphylactic reaction

**METABOLISM AND NUTRITION DISORDERS:** Hyperkalaemia

**PSYCHIATRIC DISORDERS:** Withdrawal syndrome (following multi-day exposure; symptoms include seizure, hallucination, ataxia, agitation, confusion)

**NERVOUS SYSTEM DISORDERS:** Brain oedema, Intracranial pressure increased, Migraine, Myoclonus, Nystagmus, Pupils unequal, Headache

**CARDIAC DISORDERS:** Cardiac arrest, Ventricular fibrillation, Torsade de pointes, Myocardial infarction, Myocardial ischaemia, Atrioventricular block complete, Atrioventricular block second degree, Atrial fibrillation, Electrocardiogram QT prolonged, Atrioventricular block first degree, Ventricular tachycardia, Ventricular extrasystoles, Tachycardia, Bradycardia, Cardiac output decreased

**VASCULAR DISORDERS:** Flushing

**RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS:** Apnoea, Hypoxia, Bronchospasm, Airway obstruction, Respiratory depression, Hypercapnia, Stridor, Hiccough

**GASTROINTESTINAL DISORDERS:** Pancreatitis

**HEPATOBILIARY DISORDERS:** Hepatic failure, Hepatic necrosis, Hepatitis fulminant, Cholestatic hepatitis, Hepatitis, Hepatic steatosis, Jaundice, Gammaglutamyltransferase increased

**SKIN AND SUBCUTANEOUS TISSUE DISORDERS:** Rash

**MUSCULOSKELETAL, CONNECTIVE TISSUE AND BONE DISORDERS:** Rhabdomyolysis

**RENAL AND URINARY DISORDERS:** Acute renal failure**, Oliguria**

**GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS:** Malignant hyperthermia, Hypothermia

**INJURY, POISONING, AND PROCEDURAL COMPLICATIONS*:** Unwanted awareness during anaesthesia; Dyspnoea, Bronchospasm, Stridor, Cough, Dizziness, Paresthesia, Hepatic reactions, Flushing, Rash, Contact dermatitis, Erythema, Periorbital oedema, Eye irritation, Conjunctival hyperaemia, Headache

***All reactions categorized within this SOC, with the exception of, Unwanted awareness during anaesthesia, were from occupational exposure in non-patients.**

****Cases of acute renal failure and oliguria have been reported after AERRANE (isoflurane) anaesthesia. These events may be secondary to hypotension or other effects of AERRANE (isoflurane).**

# OVERDOSAGE

In the event of apparent overdosage, the following actions should be taken, as appropriate: discontinue administration ofAERRANE (isoflurane), maintain a patent airway, initiate assisted or controlled ventilation with oxygen and maintain adequate cardiovascular function.

# PRECLINICAL SAFETY DATA

Published animal studies of some anaesthetic/sedation drugs have reported adverse effects on brain development in early life and late pregnancy. These studies have demonstrated that anaesthetic and sedation drugs that block N-methyl-D-aspartate (NMDA) receptors and/or potentiate gamma-aminobutyric acid (GABA) activity during the period of rapid brain growth or synaptogenesis may result in neuronal and oligodendrocyte cell loss in the developing brain and alterations in synaptic morphology and neurogenesis when used for longer than 3 hours. The clinical significance of these non-clinical findings is yet to be determined. However, based on comparisons across species, the window of vulnerability to these changes is believed to correlate with exposures in the third trimester through the first several months of life, but may extend out to approximately 3 years of age in humans.

# PHARMACOLOGICAL PROPERTIES

AERRANE (isoflurane) is an inhalation-type anaesthetic, belonging to the group of halogenated anaesthetics. Induction and recovery from anaesthesia rapidly take place with AERRANE (isoflurane).

AERRANE (isoflurane) has the slightly irritating odour of ether, which can limit the speed of induction.

Pharyngeal and laryngeal reflexes are rapidly diminished as a result of which tracheal intubation is rendered easy.

Typically, blood pressure decreases with induction of anaesthesia but may return toward normal with surgical stimulation.

AERRANE (isoflurane) undergoes minimal biotransformation in man. In the post-anaesthesia period, 0.17% of the isoflurane absorbed can be recovered as urinary metabolites. The principal metabolite is trifluoroacetic acid. The average serum level of inorganic fluoride in patients administered AERRANE (isoflurane) anaesthesia is between 3 and 4 µmol/litre.

In patients anaesthetised with AERRANE (isoflurane), the mean peak serum concentration of inorganic fluorides is usually less than 5 µmol/litre and occurs about four hours after anaesthesia, returning to normal levels within 24 hours. This should not alter renal function in a normal subject.

# PHARMACEUTICAL PARTICULARS

FPO

Storage: Store below 30°C. Store bottle in an upright position. To avoid leakage apply bottle cap firmly but not too tightly. AERRANE (isoflurane) must be kept in the original container until immediately prior to use.

This product has a shelf life of 60 months from the date of manufacture.

AERRANE (isoflurane) is packaged in amber colour glass bottle containing 100 mL and 250 mL isoflurane.



Baxter

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