

PACKAGE LEAFLET

Package leaflet: Information for the patient

ISOFLURANE 100% Inhalation Vapour, Liquid

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, or nurse. This includes any possible side effects not listed in this leaflet. See section 4

What is in this leaflet

1. What Isoflurane is and what it is used for
2. What you need to know before you use Isoflurane
3. How to use Isoflurane
4. Possible side effects
5. How to store Isoflurane
6. Contents of the pack and other information

1. What Isoflurane is and what it is used for

Isoflurane is a general anaesthetic used which temporarily reduces the activity of the body's central nervous system. This causes a complete loss of sensation in the body, including loss of consciousness allowing surgery to be carried out without pain or distress.

Isoflurane is a clear colourless liquid that when put into a special anaesthetic machine (vaporiser) becomes a gas which is mixed with oxygen and you will be breathing in the mixture. It causes you to fall into a deep, painless sleep (induction of anaesthesia). It also maintains a deep, painless sleep during which you can undergo surgery (maintenance of anaesthesia).

2. What you need to know before you use Isoflurane

Do not use Isoflurane

- if you are hypersensitive/ allergic to Isoflurane or any of the other ingredients of this medicine (listed in section 6).
- You or anyone in your family, are susceptible to rapid rise in body temperature during anaesthesia (a condition known as malignant hyperthermia).

Warnings and precautions

Talk to your doctor or nurse before using Isoflurane:

- You have previously been given an inhaled anaesthetic, particularly if this was more than once over a short period (specifically in the last 3 months). Some anaesthetics can cause jaundice.
- You have reacted badly after previous administration of Isoflurane or other similar anaesthetics,

- e.g. you developed jaundice, fever, liver or blood problems.
- You have a disease of your liver
- You have coronary or other heart disease
- You have ever had QT prolongation (prolongation of a specific time interval in an ECG) or torsade de pointes (a specific type of heart rhythm), which may also be associated with QT prolongation. Isoflurane has sometimes been known to cause these.
- You have a mitochondrial disease.
- You have raised intracranial pressure. Isoflurane may raise pressure inside your skull. This could be a problem if you have a head injury, brain tumour or another condition that already raises pressure inside your head.
- You have low blood pressure, low blood volume or are debilitated. You may need a lower dose of Isoflurane.
- You have a condition that affects muscles (a neuromuscular disease e.g. Duchenne muscular dystrophy or myasthenia gravis).
- You suffer from bronchoconstriction (tightening of the lungs and airways leading to coughing, wheezing or shortness of breath).
- You are suffering from any other illness other than those connected with your operation, such as severe headaches, nausea, vomiting or a condition that affects muscles (a neuromuscular disease
- e.g. Duchenne muscular dystrophy or myasthenia gravis)
- You are pregnant or breastfeeding.

Other medicines and Isoflurane

As with all drugs, it is important that you tell your ward doctor, surgeon or anaesthetist which medications you are taking. This is particularly important if you are taking the following drugs:

- Amphetamines (stimulants)
- Beta blockers (used to treat high blood pressure and certain heart conditions)
- Non-selective MAO-inhibitors (a type of anti-depressants). These should be stopped 15 days before surgery
- Isoniazid (an antibiotic used to treat tuberculosis).
- Decongestant (ephedrine)
- Calcium antagonists
- Opioids and other sedatives
- Sympathomimetic agents such as isoprenaline

Please tell your doctor or nurse if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breast feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine Isoflurane may cause increased blood loss after operations involving the womb. If you have been breast feeding before being given Isoflurane, you should stop until the medicine is cleared from your body. Your doctor will let you know when it is safe for you to continue breast feeding.

Driving and using machines

You should not drive or use machines until your doctor advises that you are safe to do so.

Your mental alertness may be affected for 2-4 days, do not drive or operate machinery if you are affected after you have had a general anaesthetic.

3. How to use Isoflurane

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Isoflurane will be given by a trained anaesthetist during a surgery in hospital. The anaesthetist will decide on how much Isoflurane you need depending on your age, weight and the type of operation you are having and when it is to be given. Isoflurane has a strong smell, which is quite normal and will send you to sleep quickly.

Isoflurane liquid is changed to vapour (gas) in a vapouriser. You will breathe it in as a vapour.

It may be used to put you to sleep before your operation or, if you are put to sleep with an injection, it may be used to maintain anaesthesia during the operation. Once the anaesthetist stops you from inhaling Isoflurane you will wake up within a few minutes.

If you have any further questions on the use of this product, ask your anaesthetist, doctor or nurse. Inducing sleep at the start of anaesthesia

Isoflurane is not recommended in infants and children for inducing sleep at the start of anaesthesia.

Medication before anaesthesia

Anaesthetist may decide to give your child medication to counter act the possible reduction in breathing and heart rate effects which may occur with the use of Isoflurane.

4. Possible side effects

Like all medicines, Isoflurane can cause side effects, although not everybody gets them. If you or your child suffer from any unusual or unexpected symptoms after an operation tell your doctor or anaesthetist IMMEDIATELY. The side effects will be managed by your surgeon or anaesthetist, as necessary, during or after the operation.

- After waking from Isoflurane anaesthesia, you may feel shivery, sick or you may vomit.
- You may experience an allergic or hypersensitivity reaction, skin rash or swelling of the face.
- Isoflurane may trigger malignant hyperthermia in some people. This condition may run in families. Affected patients develop a very high temperature after receiving certain anaesthetic drugs. Intensive care is usually needed and the condition may be fatal.
- Your blood pressure may fall after being given Isoflurane, especially if you are already taking medicines to lower blood pressure.
- Use of inhaled anaesthetic agents such as Isoflurane has been very rarely associated with increase in potassium levels in the blood (hyperkalaemia), resulting in abnormality of heart rhythm and death in children during the postoperative period. This event has been described in patients with latent as well as overt muscular disease, particularly Duchenne muscular dystrophy.
- You may experience breathing problems or rarely difficulty breathing (bronchospasm).
- You may experience increased heart rate and irregular heart beats (arrhythmias).
- The number of white blood cells in the blood may increase, levels of blood glucose may increase, blood levels of certain enzymes and other blood cells may be altered
- Agitation, delirium, altered mood, mental impairment, and convulsions have been reported.
- Effects on the liver have occurred after Isoflurane anaesthesia. There have been rare reports of mild, moderate and severe liver problems such as jaundice (causing yellowing of the skin and

- white of the eyes) and inflammation of the liver (hepatitis) causing pain in the abdomen.
- Isoflurane may cause increased blood loss after operations involving the womb.
 - As with other anaesthetics, small changes in moods and symptoms may persist for up to 6 days after administration.
 - Increase in blood fluoride levels (due to your body breaking down Isoflurane) with carbon monoxide levels.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Isoflurane

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton 'EXP'. The expiry date refers to the last day of that month.

Storage conditions: Do not store above 30⁰C.

6. Contents of the pack and other information

What Isoflurane contains:

The active substance is isoflurane. There are no other ingredients.

What Isoflurane looks like and contents of the pack:

Isoflurane is a colourless liquid available in 100 ml and 250 ml amber coloured glass bottles.

Marketing Authorisation Holder

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The following information is intended for healthcare professionals only:

PROFESSIONAL USER
LEAFLET ISOFLURANE
100% Inhalation Vapour, Liquid

Composition and Description

Isoflurane is a colourless non-flammable general inhalation anaesthetic which contains no additive or stabiliser. It is 1-chloro-2,2,2-trichloroethyl difluoromethyl ether.

Indications

Isoflurane is general inhalation anaesthetic for use in induction and maintenance.

Contraindications

Isoflurane is contraindicated in patients with known sensitivity to Isoflurane or to other halogenated anaesthetics.

It is also contraindicated in patients with known or suspected genetic susceptibility to malignant hyperthermia.

Precautions:

Vaporisers specially calibrated for isoflurane should be used so that the concentration of anaesthetic delivered can be accurately controlled. Hypotension and respiratory depression increase as anaesthesia is deepened.

Reports of QT prolongation, associated with torsade de pointes (in exceptional cases, fatal), have been received.

Caution should be exercised when administering isoflurane to patients at risk of QT prolongation.

Caution should be exercised in administering general anaesthesia, including isoflurane, to patients with mitochondrial disorders.

Isoflurane, like other inhalational agents, has relaxant effects on the uterus with the potential risk for uterine bleeding.

Clinical judgement should be observed when using isoflurane during obstetric anaesthesia.

Consideration should be taken to use the lowest possible concentration of isoflurane in obstetrical operations (see 'Use in pregnancy').

Isolated cases of increased carboxyhaemoglobin have been reported with the use of halogenated inhalation agents with a -CF₂H moiety (i.e., desflurane, enflurane and isoflurane). No clinically

significant concentrations of carbon monoxide are produced in the presence of normally hydrated

absorbents. Care should be taken to follow manufacturer's instructions for CO₂ absorbents.

Isoflurane has been reported to interact with dry carbon dioxide absorbents during closed circuit anaesthesia, to form carbon monoxide. In order to minimize the risk of formation of carbon monoxide in rebreathing circuits and the possibility of elevated carboxyhaemoglobin levels, carbon dioxide adsorbents should not be allowed to dry out.

Rare cases of extreme heat, smoke and/or spontaneous fire in the anaesthesia machine have been reported during the administration of general anaesthesia with drugs in this class when used in conjunction with desiccated CO₂ absorbents, specifically those containing potassium hydroxide (e.g. Baralyme). When a clinician suspects that the CO₂ absorbent may be desiccated, it should be replaced before administration of isoflurane. The colour indicator of most CO₂ 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. CO₂ absorbents should be replaced routinely regardless of the state of the colour indicator.

Because levels of anaesthesia can be altered easily and quickly with Isoflurane, only vaporisers which produce a predictable concentration with a good degree of accuracy or techniques during which inspired or expired concentrations can be monitored, should be used.

The degree of hypotension and respiratory depression may provide some indication of anaesthetic depth.

As with any potent general anaesthetic, isoflurane should only be administered in an adequately equipped anaesthetising environment by those who are familiar with the pharmacology of the drug and qualified by training and experience to manage the anaesthetised patient.

Reports demonstrate that Isoflurane can produce hepatic injury ranging from mild transient increases of liver enzymes to fatal hepatic necrosis in very rare instances.

It has been reported that previous exposure to halogenated hydrocarbon anaesthetics, especially if the interval is less than 3 months, may increase the potential for hepatic injury. Cirrhosis, viral hepatitis or other pre-existing liver disease can be a reason to select an anaesthetic other than a halogenated anaesthetic.

Regardless of the anaesthetics employed, maintenance of normal haemodynamics is important to the avoidance of myocardial ischaemia in patients with coronary artery disease.

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

Isoflurane must be used with caution in patients with increased intracranial pressure. In such cases hyperventilation may be necessary.

Use of isoflurane in hypovolaemic, hypotensive and debilitated patients has not been extensively investigated. A lower concentration of isoflurane is recommended for use in these patients. All commonly used muscle relaxants are markedly potentiated by isoflurane, the effect being most profound with non-depolarising agents.

Isoflurane may cause a slight decrease in intellectual function for 2-4 days following anaesthesia. Small changes in moods and symptoms may persist for up to 6 days after administration. This must be taken into account when patients resume normal daily activities, including driving or operating heavy machinery (see 'Effects on Ability to Drive and Use Machines').

A potentiation of neuromuscular fatigue can be seen in patients with neuromuscular diseases, such as myasthenia gravis. Isoflurane should be used with caution in these patients. Isoflurane should be administered with caution to patients who can develop bronchoconstriction since bronchospasm can occur (see 'Undesirable Effects').

Isoflurane may cause respiratory depression which may be augmented by narcotic premedication or other agents causing respiratory depression. Respiration should be supervised and if necessary, assisted (see 'Undesirable Effects').

During the induction of anaesthesia, saliva flow and tracheobronchial secretion can increase and can be the cause of laryngospasm, particularly in children.

Paediatric population

Children under two years of age

Caution should be exercised when Isoflurane is used in small children due to limited experience with this patient group.

During the induction of anaesthesia, saliva flow and tracheobronchial secretion can increase and can be the cause of laryngospasm, particularly in children.

Malignant Hyperthermia

In susceptible individuals, 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 nonspecific features such as muscle rigidity, tachycardia, tachypnoea, cyanosis, arrhythmias, and unstable blood pressures. (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 CO₂ absorption system (hot canister). PaO₂ and pH may decrease, and hyperkalaemia and a base deficit may appear. Treatment includes discontinuance of triggering agents (e.g. isoflurane), intravenous administration of 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 on patient management.)

Renal failure may appear later.

There have been postmarketing reports of malignant hyperthermia. Some of these reports have been fatal.

Perioperative hyperkalaemia

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 age group 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 creatine kinase levels and, in some cases, changes in urine consistent with myoglobinuria. Despite the similarity in presentation to malignant hyperthermia, these patients did NOT have classical signs or symptoms of malignant hyperthermia such as muscle rigidity or hypermetabolic state. Prompt and vigorous

treatment for hyperkalaemia and resistant arrhythmias is recommended as is subsequent evaluation for latent neuromuscular disease.

Drug Interactions:

Combinations advised against:

Beta- sympathomimetic agents like isoprenaline and alpha- and beta- sympathomimetic agents like adrenaline and noradrenaline should be used with caution during isoflurane narcosis, due to a potential risk of ventricular arrhythmia. Non-selective MAO-inhibitors: Risk of crisis during the operation. Treatment should be stopped 15 days prior to surgery.

Combinations requiring precautions in using:

Indirect-acting sympathomimetics (amphetamines and their derivatives, psychostimulants, appetite suppressants, ephedrine and its derivatives): Risk of peri-operative hypertension. In patients undergoing elective surgery, treatment should ideally be discontinued several days before surgery.

Adrenaline, by subcutaneous or gingival injections: risk of serious ventricular arrhythmia as a consequence of increased heart rate, although the myocardial sensitivity with respect to adrenaline is lower with the use of Isoflurane than in the case of Halothane.

Calcium antagonists, in particular dihydropyridine derivatives:

Isoflurane may lead to marked hypotension in patients treated with calcium antagonists. Caution should be exercised when calcium antagonists are used concomitantly with inhalation anaesthetics due to risk of additive negative inotropic effect.

Beta-blockers: Cardiovascular compensation reactions may be impaired by beta-blockers.

Inducers of CYP2E1

Medicinal products and compounds that increase the activity of cytochrome P450 isoenzyme CYP2E1, such as isoniazid and alcohol, may increase the metabolism of isoflurane and lead to significant increases in plasma fluoride concentrations.

Use of Isoflurane and Isoniazid can increase the risk of potentiation of the hepatotoxic effects.

Opioids, benzodiazepines and other sedative agents are associated with respiratory depression, and caution should be exercised when concomitantly administered with Isoflurane.

Concomitant use of succinylcholine with 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 post-operative period.

All commonly used muscle relaxants are markedly potentiated by Isoflurane. Neostigmine has an effect on the non-depolarising relaxants, but has no effect on the relaxing action of Isoflurane itself.

MAC (minimum alveolar concentration) is reduced by concomitant administration of N₂O in adults. Pregnancy

There are no or limited amount of data from the use of isoflurane in pregnant women. Studies in animals

have shown reproductive toxicity. Isoflurane should only be used during pregnancy if the benefit outweighs the potential risk.

Isoflurane, like other inhalational agents, has relaxant effects on the uterus with the potential risk for uterine bleeding. Clinical judgement should be observed when using isoflurane during obstetric anaesthesia. Consideration should be taken to use the lowest possible concentration of isoflurane in obstetrical operations.

Use in Caesarean Section

Isoflurane, in concentrations up to 0.75%, has been shown to be safe for the maintenance of anaesthesia for caesarean section.

Breastfeeding

It is not known whether isoflurane/metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when isoflurane is administered to a nursing woman.

Effects on Ability to Drive and Use Machines

Patients should be advised that performance of activities requiring mental alertness, such as operating a motor vehicle or hazardous machinery, may be impaired for 2-4 days after anaesthesia with isoflurane. As with other anaesthetics, small changes in moods and symptoms may persist for up to 6 days after administration.

Dosage and administration

Posology MAC values for Isoflurane vary with age. The table below indicates average MAC values for different age groups.

ADULTS*		
AGE	Average MAC value	
	In 100% Oxygen	70% N2O
26 ± 4 years	1.28%	0.56%
44 ± 7 years	1.15%	0.50%
64 ± 5 years	1.05%	0.37%
PAEDIATRIC POPULATION		
Age	Average MAC Value in 100% Oxygen	
Preterm neonates < 32 weeks gestational age	1.28%	
Preterm neonates 32-37 weeks gestational age	1.41%	
0-1 month	1.60%	
1-6 months	1.87%	
6-12 months	1.80%	
1-5 years	1.60%	

Premedication:

Premedication drugs should be selected according to the needs of the patient. The respiratory depressant effect of Isoflurane should be taken into account. The use of anticholinergic drugs is a matter of choice, but may be advisable for inhalation induction in paediatrics.

Induction:

As Isoflurane has a mild pungency, inhalation should usually be preceded by the use of a short acting barbiturate, or other intravenous induction agent, to prevent coughing. Alternatively, Isoflurane with oxygen or with an oxygen/ nitrous oxide mixture may be administered.

It is recommended that induction with Isoflurane be initiated at a concentration of 0.5%. Concentrations of 1.5-3.0% usually produce surgical anaesthesia in 7-10 minutes.

Induction of anaesthesia in children: Isoflurane is not recommended for use as an inhalation induction agent in infants and children because of the occurrence of cough, breath-holding, desaturation, increased secretions and laryngospasm.

Maintenance:

Adequate anaesthesia for surgery may be sustained with an inspired Isoflurane concentration of 1.0% to 2.5% in an oxygen/nitrous oxide mixture. Additional Isoflurane (0.5% to 1.0%) may be required when Isoflurane is given with oxygen alone.

For caesarean section, 0.5-0.75% isoflurane in a mixture of oxygen/nitrous oxide is suitable to maintain anaesthesia for this procedure.

Arterial pressure levels during maintenance tend to be inversely related to alveolar Isoflurane concentration in the absence of other complicating factors. Provided there are no other complicating factors this is probably due to peripheral vasodilation. Excessive falls in blood pressure may be due to the depth of anaesthesia and, in such circumstances, can be corrected by reducing the inspired Isoflurane concentration.

Elderly:

As with other agents, lesser concentrations of isoflurane are normally required to maintain surgical anaesthesia in elderly patients. See above for MAC values related to age.

Method of Administration:

Vaporisers specially calibrated for Isoflurane should be used so that the concentration of anaesthetic can be accurately controlled.

Isoflurane is not recommended as an induction agent in children.

Undesirable Effects:

a. Summary of the safety profile

Adverse reactions encountered in the administration of Isoflurane are in general dose dependent extensions of pharmacophysiological effects and include hypotension, respiratory depression and arrhythmias. Potential serious undesirable effects include malignant hyperthermia, hyperkalaemia, elevated serum creatine kinase, myoglobinuria, anaphylactic reactions and liver adverse reactions (see 'Precautions'). Shivering, nausea, vomiting, ileus, agitation and delirium have been observed in the post-operative period.

Cardiac arrest, bradycardia and tachycardia have been observed with general inhalation anaesthetic drugs including isoflurane.

Reports of QT prolongation, associated with torsade de pointes (in exceptional cases, fatal) have been received and ileus has been observed..

b. Tabulated summary of adverse reactions

The following table displays adverse reactions reported in clinical trials and from postmarketing

experience. Frequency cannot be estimated from the available data, therefore it is "not known".

SUMMARY OF MOST FREQUENT ADVERSE DRUG REACTIONS		
SOC	FREQUENCY	ADVERSE REACTIONS
Blood and lymphatic system disorders	Not known	Carboxyhaemoglobinaemia ²
Immune system disorders	Not known	Anaphylactic reaction ¹
	Not known	Hypersensitivity ¹
Metabolism and nutrition disorders	Not known	Hyperkalaemia ²
	Not known	Blood glucose increased ¹
Psychiatric disorders	Not known	Agitation
	Not known	Delirium
	Not known	Mood altered ⁵
Nervous system disorders	Not known	Convulsion
	Not known	Mental impairment ⁴
Cardiac disorders	Not known	Arrhythmia
Vascular disorders	Not known	Hypertension ²
	Not known	Haemorrhage ³
Respiratory, thoracic and mediastinal disorders	Not known	Bronchospasm ²
	Not known	Dyspnoea ¹
	Not known	Wheezing ¹
	Not known	Respiratory depression ²
	Not known	Laryngospasm ²
Gastrointestinal disorders	Not known	Ileus
	Not known	Vomiting
	Not known	Nausea
Hepatobiliary disorders	Not known	Hepatic necrosis ²
	Not known	Hepatocellular injury ²
	Not known	Blood bilirubin increased ¹
Skin and subcutaneous tissue disorders	Not known	Swelling face ¹
	Not known	Dermatitis contact ¹
	Not known	Rash ¹

Renal and urinary disorders	Not known	Blood creatinine increased ¹
	Not known	Blood urea decreased ¹
General disorders and administration site conditions	Not known	Hyperthermia malignant ²
	Not known	Chest discomfort ¹
	Not known	Chills
Investigations	Not known	White blood cell count increased ¹
	Not known	Hepatic enzyme increased ²
	Not known	Fluoride increased ¹
	Not known	Electroencephalogram abnormal
	Not known	Blood cholesterol decreased ¹
	Not known	Blood alkaline phosphatase decreased ¹

¹See 'c. Description of selected adverse reactions' below

²See 'Precautions'

³In patients undergoing induced abortion.

⁴May cause a slight decrease in intellectual function for 2-4 days after anaesthesia. See 'Precautions'.

⁵Small changes in moods and symptoms may persist for up to 6 days. See 'Precautions'.

c. Description of selected adverse reactions

Transient increases in blood bilirubin, blood glucose and serum creatinine with decrease in BUN, serum cholesterol and alkaline phosphatase have been observed. As with other general anaesthetics, transient elevations in white blood count have been observed even in the absence of surgical stress.

Rare reports of hypersensitivity (including dermatitis contact, rash, dyspnoea, wheezing, chest discomfort, swelling face, or anaphylactic reaction) have been received, especially in association with long-term occupational exposure to inhaled anaesthetic agents, including isoflurane. These reactions have been confirmed by clinical testing (e.g., methacholine challenge). The etiology of anaphylactic reactions experienced during inhalational anaesthetic exposure is, however, unclear because of the exposure to multiple concomitant drugs, many of which are known to cause such reactions.

Minimally raised levels of serum inorganic fluoride occur during and after isoflurane anaesthesia, due to biodegradation of the agent. It is unlikely that the low levels of serum inorganic fluoride observed (mean 4.4 µmol/l in one study) could cause renal toxicity, as these are well below the proposed threshold levels for kidney toxicity.

d. Paediatric population

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 post-operative period.

During the induction of anaesthesia, saliva flow and tracheobronchial secretion can increase and can be the cause of laryngospasm.

e. Other special populations

Neuromuscular disease:

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 post-operative period. Patients with latent as well as overt neuromuscular disease, particularly Duchenne muscular dystrophy, appear to be most vulnerable. Early and aggressive intervention to treat the hyperkalaemia and resistant arrhythmias is recommended, as is subsequent evaluation for latent neuromuscular disease.

Elderly:

Lesser concentrations of isoflurane are normally required to maintain surgical anaesthesia in elderly patients.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Overdose

As with other halogenated anaesthetics, hypotension and respiratory depression have been observed. Close monitoring of blood pressure and respiration is recommended. Supportive measures may be necessary to correct hypotension and respiratory depression resulting from excessively deep levels of anaesthesia.

Pharmaceutical Precautions:

Do not store above 30°C. Keep the container tightly closed. Keep out of the sight and reach of children.

Shelf Life:

5 years.

Legal Category: P

Package Information:

Isoflurane is supplied in bottles of 100 ml or 250 ml.
PL 37071/0002

Text Revised: February 2019.

MA Holder:

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