

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

IsoCare 100% w/v Inhalation vapour, liquid

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Qualitative composition

Quantitative composition

Active substances

Isoflurane

%w/v

100

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Inhalation vapour, liquid

Clear, colourless liquid

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

Cats

Horses

4.2 Indications for use, specifying the target species

Isoflurane is a volatile inhalation anaesthetic for induction and maintenance of general anaesthesia in puppies and adult dogs, and cats and kittens.

In horses isoflurane can be used for induction of anaesthesia of unweaned horses and for maintenance of anaesthesia of horses of all ages.

4.3 Contraindications

Isoflurane should not be administered to animals with a known history of sensitivity to halogenated anaesthetics including signs of malignant hyperthermia.

4.4 Special warnings for each target species

Respiratory complications, especially in cats, are often linked to inadequate consideration of reducing the MAC (see 4.8. for definition) of Isoflurane required. Use of greater than 1.3 to 1.6 MAC should be avoided in cats.

When using isoflurane to anaesthetise an animal with a head injury, consideration should be given as to whether artificial ventilation is appropriate to maintain normal CO₂ levels, so that cerebral blood flow does not increase.

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

Isoflurane produces respiratory depression in horses. It is recommended that horses anaesthetised for longer than 2 hours should be mechanically ventilated to prevent atelectasis, hypoxaemia and respiratory alkalosis.

4.5 Special precautions for use

i. Special precautions for use in animals

None

ii. Special precautions for the person administering the veterinary medicinal product to animals

Do not breathe the vapour. Users should consult their National Authority for advice on occupational exposure standards for Isoflurane.

Operating rooms and recovery areas should be provided with adequate ventilation or scavenging to prevent the accumulation of anaesthetic vapour. Make sure that the ventilation system in the operating room assures a number of air changes that is at least equal to 12 times the percentage of isoflurane in the anaesthetic multiplied by the applied flow rate (in litres per minute) and divided by the volume of the operating room (in m³). All scavenging/extraction systems must be adequately maintained.

Avoid using masking procedures for prolonged induction and maintenance of general anaesthesia. Use cuffed endotracheal intubation when possible for the administration of ISOCARE during maintenance of general anaesthesia.

Care should be taken when dispensing isoflurane, with any spillage removed immediately using an inert and absorbent material eg. sawdust.

Pregnant and breastfeeding women should avoid exposure to the product and should avoid operating rooms and animal recovery areas.

Wash any splashes from skin and eyes immediately and avoid contact with the mouth.

In the event of severe accidental exposure: remove the operator from the source of the exposure and seek urgent medical assistance and show this label.

Halogenated anaesthetic agents may induce liver damage. In the case of isoflurane this is an idiosyncratic response very rarely seen after repeated exposure.

Advice to doctors: maintain a patent airway and give symptomatic and supportive treatment. Note that adrenaline and catchecoleamines may cause cardiac dysrhythmias.

iii. Other precautions

To protect the environment it is considered good practice to use charcoal filters with scavenging/ventilation equipment.

4.6 Adverse reactions (frequency and seriousness)

Hypotension, respiratory depression with hypercapnia and cardiac arrhythmias have been reported. These can often be controlled by decreasing the level of anaesthesia.

In sensitive dogs and cats, isoflurane anaesthesia can induce a hypermetabolic state in the skeletal muscles, which leads to a high oxygen consumption and a clinical syndrome known as malignant hyperthermia.

4.7 Use during pregnancy, lactation or lay

Isoflurane has been safely used for anaesthesia during Caesarean section in the dog and cat.

Reproduction studies have been performed in mice and rats and have provided no evidence of embryotoxicity, teratogenicity, nor any other negative effect on reproduction performance attributable to isoflurane at clinically relevant concentrations. However, full comprehensive data concerning the use of isoflurane in pregnant or lactating dogs, cats or horses have not been obtained.

4.8 Interaction with other medicinal products and other forms of interaction

Interactions: Interactions with other drugs should always be kept in mind before any anaesthesia.

The simultaneous administration of isoflurane and the following products requires strict supervision of the patient's clinical and biological condition.

Muscle relaxing agents: Intensification of the action of depolarising relaxants and especially, non-depolarising relaxants such as atracurium, pancuronium or vecuronium. Thus it is recommended that $\pm 1/3$ to $1/2$ of the usual dose of these substances is administered. The disappearance of the myoneural effect takes longer with isoflurane than with other conventional anaesthetics. Neostigmine reverses the effect of the non-depolarising muscle relaxants, but does not reverse the direct neuromuscular depression activity of Isoflurane.

Sedatives and analgesics. The concurrent use of sedative or analgesic drugs may reduce the level of isoflurane required to induce and maintain anaesthesia. For example, opiates, alpha-2-agonists, phenothiazines and benzodiazepines have been reported to reduce the MAC values. Particular caution should be exercised if administering dissociative combinations to a dog already anaesthetised with isoflurane. Respiratory complications are often linked to inadequate consideration of reducing the MAC of isoflurane required.

Isoflurane has a weaker sensitising action on the myocardium to the effects of circulating dysrhythmogenic catecholamines than halothane.

Isoflurane has been reported to interact with dry carbon dioxide absorbents to form carbon monoxide. In order to minimise the risk of this in rebreathing circuits, and the possibility of elevated carboxyhaemoglobin levels, absorbents should not be allowed to dry out.

4.9 Amount(s) to be administered and administration route

THE DELIVERED CONCENTRATION OF ISOFLURANE MUST BE REGULATED ACCURATELY, VAPORISERS SPECIALLY CALIBRATED FOR THE AGENT SHOULD BE USED.

Isoflurane may be vaporised from a flow-over vaporiser specifically calibrated for isoflurane.

Vaporisers delivering a saturated vapour which is then diluted (flow-through vaporisers) may also be used. Isoflurane may be administered in oxygen or oxygen/nitrous oxide mixtures.

Instructions for use for the keyed bottle collar (for use with key-fill vaporiser)

- To attach a keyed bottle adapter, remove the cap and the seal from the anaesthetic bottle.
 - Check that the anaesthetic bottle neck is not chipped or damaged.
 - Note that the colour of the keyed bottle collar will match the colour of the adapter.
 - Match the keyed bottle adapter to the keyed bottle collar and screw together until tight.
 - Now connect the bottle to the vapouriser filler receptacle.
- The potency of inhalation anaesthetics is expressed by its required Minimum Alveolar Concentration (MAC) which prevents gross purposeful movements in response to a pain stimulus in 50% of the animals. For adult dogs, this MAC % for isoflurane in oxygen is 1.28, for cats 1.63 and for horses 1.3.1.

Pre-anaesthetic management

Healthy dogs, cats and horses should not receive food 8 to 12 hours before anaesthesia.

Water should be allowed by free choice. Animals should be examined clinically before anaesthesia. Other factors such as age, pre-existing disease, medication and surgical sites should also be considered before using isoflurane.

Pre-medication

Dogs and cats: Depending upon the patient status, a short-acting barbiturate or an anticholinergic, a tranquilliser or a muscle relaxant may be used to avert excitement during induction (see interactions).

Horses: Acepromazine or xylazine can be used as preanaesthetic agents, while in certain patients an anticholinergic may also be indicated.

Induction of anaesthesia

Dogs and cats: Following a recommended dose of barbiturate or other appropriate induction agent, mask induction using inspired concentrations of 2.0-2.5% isoflurane alone with oxygen is usually employed. Pure mask induction with isoflurane alone with oxygen may require concentrations of up to 5.0% in dogs or 4.0% in cats. These concentrations can be expected to produce surgical anaesthesia within 5 to 10 minutes. Pharyngeal and laryngeal reflexes are rapidly diminished, as a result of which tracheal intubation is made easy. Intubation should be effected quickly in cats before anaesthesia lightens and the glottis closes.

Horse: Anaesthesia may be induced using intravenous administration of glyceryl guaiacolate followed by either a short acting barbiturate or ketamine hydrochloride. In unweaned foals, anaesthesia can be induced by face mask delivery of isoflurane at the maximum vaporiser concentration (5%) with an oxygen flow of 8 L/min.

Maintenance of anaesthesia

The concentration of isoflurane necessary to maintain anaesthesia is less than the required concentration for induction.

Dogs: Surgical anaesthesia may be maintained during surgery using a concentration of 1.5-1.8% isoflurane alone with oxygen.

Cats: Surgical anaesthesia may be maintained during surgery using a concentration of 1.5 to 3.0% maximum isoflurane along with oxygen.

Horses: After induction and intubation, isoflurane may be delivered in either 100% oxygen or oxygen/nitrous oxide mixture (1:1). At the start isoflurane concentrations in the inspired air should usually be set at the maximum level allowed by the vaporiser (4-5%). Oxygen flow rates of 13-22 ml/min/kg are used to fill the anaesthetic machine rapidly with isoflurane. The vaporiser setting should then, based on the horse's reactions, be gradually decreased to 3.5% and further down to reach the optimum concentration, to 2%, or between 1.5 and 2.5%.

Table: Induction and maintenance of anaesthesia

<i>Species</i>	<i>MAC (%)</i>	<i>Induction (%)</i>	<i>Maintenance (%)</i>
Cats	1.63	Up to 4.0	1.5-3.0
Dogs	1.28	Up to 5.0	1.5-1.8
Horses	1.31	-	1.5-2.5
Unweaned foals	1.31	3.0-5.0	1.5-2.5

Body temperature, blood pressure and respiration should be monitored at all times during anaesthesia. These effects are dose dependent, and the anaesthetic flow should be adjusted to compensate for changes.

Recovery

Consideration should be given to the analgesic requirements of the patient before recovery from anaesthesia takes place.

When used in excitable horses, consideration should be given to the administration of a sedative to cover the period of recovery from isoflurane anaesthesia.

The concentration of isoflurane must be reduced to 0% at the end of surgery to allow prompt recovery. This recovery of dogs and cats from isoflurane anaesthesia is typically uneventful.

When the administration of isoflurane has been stopped, the air passages of the patient should be ventilated several times with 100% oxygen until complete awakening.

Due to the low solubility of isoflurane in blood rapid changes in anaesthetic depth and a rapid recovery may be seen. Isoflurane administration should therefore not be discontinued until the surgical procedure and the preparations for recovery are completed.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

Symptoms

Overdose with isoflurane produces marked hypotension and respiratory depression and hypercapnia. Respiratory failure occurs at concentrations exceeding 2 MAC.

Emergency procedure

In the event of an overdose, or an adverse effect, stop drug administration, establish a clear airway and initiate assisted or controlled ventilation with pure oxygen. Administration of fluids may be beneficial.

4.11 Withdrawal period(s)

Not to be used in horses intended for human consumption

Treated horses may never be slaughtered for human consumption

The horse must have been declared for human consumption under the national horse passport legislation

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group:

Isoflurane is an inhalation anaesthetic, belonging to the group of halogenated ether anaesthetics:

ATC Vet Code:

QN01AB06

5.1 Pharmacodynamic properties

Isoflurane produces general anaesthesia after inhalation. The exact mode of action is not well understood but is similar to that of halothane. Isoflurane has a low blood to gas solubility coefficient and so induction, recovery and the response to changed levels of isoflurane, takes place rapidly with minimal lipid uptake. As the anaesthetic dose is increased, both tidal volume and respiratory rate decrease. The animal will demonstrate a progressive loss of consciousness, muscle tone and reflexes.

The respiratory depression is partially mitigated by surgical stimulation even at deeper levels of anaesthesia. No convulsive activity occurs with isoflurane even with hypocapnia, deep levels of anaesthesia or auditory stimulation.

Blood pressure drops in dogs and cats over the first 30 minutes of anaesthesia and then remains stable, whereas heart rate remains unchanged.

Also in horses isoflurane has a depressant effect on arterial blood pressure, mainly due to decreased peripheral resistance, whilst there is only a limited effect on cardiac output. Horses anaesthetised with isoflurane frequently show a slower respiratory rate mainly due to prolonged expiration time. These pharmacological changes spontaneously return to pre-treatment values during the recovery period.

Isoflurane is a good muscle relaxant for surgical procedures (see the information in Section 4.8).

5.2 Pharmacokinetic properties

Isoflurane is metabolised minimally in animals. On average, 94% or more of the Isoflurane dose is exhaled unaltered. The serum inorganic fluoride level after isoflurane anaesthesia in dogs increased rapidly but only minimally with peak levels of $\pm 3 \mu\text{mol/L}$ at the end of a 3-hour anaesthesia. Critical levels for kidney damage are thought to be $50 \mu\text{mol/L}$ and these levels are unlikely to occur. Isoflurane metabolism is thought to involve breakdown by cytochrome P-450 to yield fluoride ions. No increase of urinary excretion of fluoride above normal levels was detected after a 3 hour anaesthesia.

In horses, levels of isoflurane in expired air are reduced by 50% as early as 3 minutes after withdrawal of isoflurane, and by 90% after 25 minutes. Other specific pharmacokinetic parameters (e.g. plasma half life, body clearance, volume of distribution) for isoflurane in horses are not available.

5.3 Environmental properties

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None

6.2 Incompatibilities

Isoflurane can be used in combination with the commonly used vector gases. Isoflurane has been reported to interact with dry carbon dioxide absorbents to form carbon monoxide. In order to minimise the risk of formation of carbon monoxide in rebreathing circuits, and the possibility of elevated carboxyhaemoglobin levels, absorbents should not be allowed to dry out.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 5 years

6.4 Special precautions for storage

Protect from direct sunlight

Handle and store the bottles so as to avoid breakage. Isoflurane is non-flammable and non-explosive and it is non-reactive to metal used in anaesthetic equipment.

Store in a tightly closed original container.

6.5 Nature and composition of immediate packaging

100ml or 250ml glass amber type IV bottle with black phenolic resin or polypropylene screw cap (screw fit) with a conical low density polyethylene washer.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products, if appropriate

Any unused product or waste material derived from such veterinary medicinal products should be disposed of in accordance with national requirements.

7. MARKETING AUTHORISATION HOLDER

Baxter Healthcare Ltd.
Caxton Way
Thetford
Norfolk
IP24 3SE

8. MARKETING AUTHORISATION NUMBER(S)

Vm 00116/4000

9. DATE OF FIRST AUTHORISATION

Date: 21st July 1997

10. DATE OF REVISION OF THE TEXT

Date: December 2008