SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Isofane 100% *w/w* Inhalation vapour, liquid.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance: Isoflurane 100% w/w
For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Inhalation vapour, liquid
A clear colourless liquid with a characteristic odour.

4. CLINICAL PARTICULARS

Summary presentation of the active substance: Isoflurane is a volatile liquid halogenated hydrocarbon. Although the exact mode of action is poorly understood it is thought that, in common with other general anaesthetics, isoflurane acts by competing with endogenous ligands for binding to specific neuroreceptors.

4.1 Target species

Horses, dogs, cats, small mammals, ornamental birds and reptiles.

4.2 Indications for use, specifying the target species

To induce and maintain anaesthesia in all types of veterinary surgery.

4.3 Contraindications

Do not use in animals sensitive to isoflurane or other halogenated or inhalation anaesthetic agents. Do not use in animals with a known susceptibility to malignant hyperthermia.

4.4 Special warnings for each target species

Horses: Recovery from isoflurane anaesthesia is generally smooth and rapid. However, one report suggests that horses recovering from isoflurane anaesthesia may appear un-coordinated. It is important to provide adequate post-anaesthetic analgesia since isoflurane anaesthetised horses may become aware of their surroundings more rapidly than horses recovering from halothane anaesthesia.

Other species: none

4.5 Special precautions for use

i. Special precautions for use in animals None known
ii. Special precautions for the person administering the veterinary medicinal product to animals

Do not breathe the vapour. The Occupational Exposure Standard (OES) for isoflurane has been set at 50 ppm on an 8-hour weighted average.
Operating rooms and recovery areas should be provided with adequate ventilation or scavenging systems to prevent the accumulation of anaesthetic vapour.
All scavenging/extraction systems must be adequately maintained. To protect the environment it is considered good practice to use charcoal filters with scavenging/ventilation equipment.
Avoid using masking procedures for prolonged induction and maintenance of general anaesthesia. Use cuffed endotracheal intubation when possible for the administration of Isofane during maintenance of general anaesthesia.
Care should be taken when dispensing isoflurane, with any spillage removed immediately using an inert and absorbent material e.g. sawdust.
Pregnant and breast-feeding 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 catecholamines may cause cardiac dysrhythmias.

4.6 Adverse reactions (frequency and seriousness)

Heart rate usually remains stable with isoflurane, however both respiration and blood pressure are depressed in a dose-related manner. Pulse and respiration should be assessed for both rate and character in all patients. Consideration should be given to supplemental ventilation, especially in animals which have sustained injuries which may lead to increased CO_2 levels or a depressed heart rate. In animals with head injuries consider supplemental ventilation to maintain normal circulating CO_2 levels such that cerebral blood flow does not increase. Blood pressure should be assessed throughout anaesthesia. Hypotension, if related to depth of anaesthesia, can be corrected by a reduction in delivered isoflurane concentration.

In horses, as with all anaesthetic agents, it may sometimes be necessary to administer an ionotropic agent in hypotension. Isoflurane appears to sensitise the myocardium to the dysrhythmogenic effects of circulating catecholamines to a lesser extent than halothane.

4.7 Use during pregnancy, lactation or lay

Isoflurane has been successfully used in pregnant animals, including the horse, dog and cat, for Caesarean section. Reproduction studies in mice, rats and rabbits show no evidence of effect on foetal malformation specifically attributable to isoflurane at clinically relevant doses.
However, specific studies in the target species to show the effect on pregnant, lactating or breeding animals have not been undertaken.

4.8 Interaction with other medicinal products and other forms of interaction

Muscle relaxation with isoflurane is normally adequate for the majority of surgical procedures. If a more profound muscle relaxation is required, e.g. for thoracic surgery, additional muscle relaxants may be employed. All commonly available non-depolarising muscle relaxants are potentiated by isoflurane and the effects will be maintained for longer than is usual with these agents. In dogs, care should be taken if administering a midazolamketamine combination to an animal already anaesthetised with isoflurane.

4.9 Posology and method of administration

The product should only be used in an accurately calibrated isoflurane specific vaporiser.

Pre-medication: The pre-medication should be chosen according to the type and condition of the animal and the surgical procedure planned.
Isoflurane has been shown to be compatible with the most commonly used veterinary premedicant agents. The use of sedative or analgesic drugs is likely to reduce the concentration of isoflurane required to induce or maintain anaesthesia.

Induction: The dose for induction of anaesthesia will vary according to species, but is generally between 2% and 5% concentration in an oxygen, or oxygen/nitrous oxide mixture. The table below presents a guide to the concentrations required for induction of anaesthesia by species based on use of Isofane with oxygen. When used in conjunction with oxygen/nitrous oxide a lower concentration of isoflurane may be required. Speed of induction and the concentration of isoflurane required may vary according to several different influences, including the health and medication status of the patient.
Observation of effect and clinical judgement will be required to determine the most appropriate induction dose in each case.
Maintenance: A guide to maintenance dose by species based on use of the product with oxygen is presented in the table below. When used in conjunction with oxygen/nitrous oxide a lower concentration of isoflurane may be required. The specific dose required may vary according to several different influences, including the health and medication status of the patient.
Clinical judgement will be required to determine the most appropriate dose in each case.

Recovery: Recovery from anaesthesia is generally rapid, uneventful and smooth.

Guide to induction and maintenance of anaesthesia by species
(Isofane concentration in oxygen)

Species	Induction (%)	Maintenance (%)	MAC* (%)
Horse	3.0 – 5.0 (Foals)	1.5 – 2.5	1.31
Dog	Up to 5.0	1.5 – 2.5	1.3
Cat	Up to 4.0	1.5 – 3.0	1.61
Ornamental birds	Up to 5.0	2.0 – 3.0	1.5
Reptiles	2.0 - 4.0	1.0 – 3.0	N/a
Small Mammals	2.0 – 3.0	0.25 – 2.0	Rabbit 2.05 Mouse 1.34 Rat 1.38 – 2.4

* Minimum Alveolar Concentration at which 50% of anaesthetised patients show no response to a stimulus.

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

Isoflurane causes dose related respiratory and cardiovascular depression. It is important that both respiration and cardiovascular function is monitored for both rate and character. Respiratory arrest should be treated by assisted ventilation, preferably with oxygen supplementation. Maintain a patent airway and adequate tissue oxygenation throughout the period of anaesthesia.

4.11 Withdrawal periods

Not to be used in animals intended for human consumption. Treated horses may never be slaughtered for human consumption. The horse must have been declared as not intended for human consumption under national horse passport legislation.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

In common with other anaesthetics, increasing concentrations of isoflurane produce respiratory depression characterised by decreased respiratory rate and/or tidal volume and by concurrent increases in arterial CO_2 tension and respiratory acidosis in all species. Cardiovascular effects are more varied, including falls in arterial pressure, total peripheral resistance and baroreflex sensitivity. Heart rate tends to remain stable or increase and cardiac output remains stable in cats and dogs but falls in horses. Prolonged anaesthesia causes initial respiratory depression but parameters remain stable thereafter.
In the horse, heart rate, left ventricular work and arterial pressure may increase. Otherwise, these and other cardiovascular parameters tend to remain stable. Isoflurane also protects against atrial fibrillation and sensitises the myocardium to catecholamine-induced arrhythmias to a lesser degree than other anaesthetics.

The effects on the CNS include loss of consciousness, analgesia and muscle relaxation. Cerebral autoregulation in response to changes in $PaCO_2$ or blood pressure at high isoflurane concentrations is depressed, as are cerebral vascular resistance and metabolism. The cerebral blood flow tends to increase.
There are no signs of CNS irritability or increased cerebrospinal fluid production in dogs; in cats there are signs of mild CNS irritability (possibly due to hypocapnia) and a small increase in intracranial pressure. Isoflurane has no clinically significant effects on the liver and kidneys or on blood chemistry or cell counts.

5.2 Pharmacokinetic properties

Isoflurane is administered by inhalation. Absorption takes place across the alveolar exchange membranes at a rate determined by the rate and depth of respiration, by the cardiac output and by the solubility of isoflurane in the blood. Isoflurane has a low blood/gas partition coefficient (i.e. it is poorly soluble) and equilibration between alveolar gas and the circulation is therefore rapid, in the order of 30 minutes. Distribution of isoflurane is dependent on cardiac output and the partition coefficients of the various tissues. Again these tend to be low so distribution is rapid.
Isoflurane is very stable and metabolism is minimal. 95% or more is excreted unchanged, the remainder is believed to be metabolised by the liver to fluoride ions, trifluoroacetic acid and HCI. Peak serum fluoride ion concentrations stay well below the levels considered to be harmful for the kidneys.
Excretion occurs mostly via the lungs and is dependent on the same parameters determining absorption and distribution. In dogs, 92-96% of absorbed isoflurane is excreted unchanged via the lungs with a half-life of 150±42 minutes. The metabolites of isoflurane are excreted in the urine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None

6.2 Incompatibilities

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 carboxyhaemaglobin 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

Do not store above 25°C.
Keep the container tightly closed. Protect from light.

6.5 Nature and composition of immediate packaging

Type III amber glass bottles containing 100 ml or 250 ml of isoflurane, fitted with a black polypropylene or a black phenolic/urea screw cap with a translucent low-density polyethylene cone insert.

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 veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

Vm 37071/4001

9. DATE OF FIRST AUTHORISATION

28 June 1999

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