SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ISOFLUTEK 1000 mg/g inhalation vapour, liquid [BE, CZ, DE, EE, ES, HU, LU, NL, PT, RO, CY, DK, EL, IT, LT, LV, SK]
ISOFLUTEK VET [SE]
ISOTEK 1000 mg/g inhalation vapour, liquid [PL]
ISORANE 1000 mg/g inhalation vapour, liquid [FR]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

Active substance:
Isoflurane 1000 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Inhalation vapour, liquid.
A clear, colourless, mobile, heavy liquid.

4. CLINICAL PARTICULARS

4.1 Target species

Horses, dogs, cats, ornamental birds, reptiles, rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets.

4.2 Indications for use, specifying the target species

Induction and maintenance of general anaesthesia.

4.3 Contraindications

Do not use in cases of known susceptibility to malignant hyperthermia.
Do not use in cases of hypersensitivity to isoflurane or to other halogenated agents/ halogenated inhalation anaesthetics.

4.4 Special warnings for each target species

The ease and rapidity of alteration of the depth of anaesthesia with isoflurane and its low metabolism may be considered advantageous for its use in special groups of patients such as the old or young, and those with impaired hepatic, renal or cardiac function.

4.5 Special precautions for use

Special precautions for use in animals

Isoflurane has little or no analgesic properties. Adequate analgesia should always be given before surgery. The analgesic requirements of the patient should be considered before the general anaesthesia is ended.
Isoflurane causes depression of the cardiovascular and respiratory systems.

It is important to monitor pulse quality and rate in all patients. The use of the product in patients with cardiac disease should only be considered after a benefit risk assessment by the responsible veterinary surgeon. In the case of cardiac arrest, complete cardiopulmonary resuscitation should be performed. It is important to monitor respiratory rate and quality.
It is also important to maintain an open airway and to properly oxygenate tissues during the maintenance of anaesthesia. Respiratory arrest should be treated by assisted ventilation.
The metabolism of birds, and to an extent small mammals, is affected more profoundly by decreases in body temperature, due to high surface area to body weight ratio. Therefore, body temperature should be monitored and kept stable during treatment.
Drug metabolism in reptiles is slow and highly dependent upon environmental temperature. Reptiles may be difficult to induce with inhalation agents due to breath holding.
When using isoflurane to anaesthetise an animal with a head injury, consideration should be given as to whether artificial ventilation is appropriate to help avoid increased cerebral blood flow by maintaining normal CO_2 levels.

Special precautions to be taken by 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 systems to prevent the accumulation of anaesthetic vapour. All scavenging/extraction systems must be adequately maintained.
Exposure to anaesthetics can harm the unborn child. Pregnant and breast-feeding women should not have any contact with the product and should avoid operating room and animal recovery areas. Avoid using masking procedures for prolonged induction and maintenance of general anaesthesia.
Use cuffed endotracheal intubation when possible for the administration of isoflurane 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. Wash any splashes from skin and eyes, and avoid contact with the mouth. If severe accidental exposure occurs remove the operator from the source of exposure, seek urgent medical assistance and show this label.
Halogenated anaesthetic agents may induce liver damage. In case of isoflurane this is an idiosyncratic response very rarely seen after repeated exposure.
Advice to Doctors: Ensure a patent airway and give symptomatic and supportive treatment. Note that adrenaline and catecholamines may cause cardiac dysrhythmias.

Other precautions

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

4.6 Adverse reactions (frequency and seriousness)

Isoflurane produces hypotension and respiratory depression in a dose-related manner. Cardiac arrhythmias and transient bradycardia have been reported rarely.
Malignant hyperthermia has been reported very rarely in susceptible animals.
Cardiac and/or respiratory arrest has been very rarely reported.
The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals ***treated*** displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Pregnancy:
Use only according to the benefit/risk assessment by the responsible veterinarian. Isoflurane has been safely used for anaesthesia during caesarean section in the dog and cat.

Lactation:
Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

The action of muscle relaxants in man, especially those of the nondepolarising (competitive) type such as atracurium, pancuronium or vecuronium, is enhanced by isoflurane. Similar potentiation might be expected to occur in the target species, although there is little direct evidence to this effect. Concurrent inhalation of nitrous oxide enhances the effect of isoflurane in man and similar potentiation might be expected in animals.
The concurrent use of sedative or analgesic drugs is likely to reduce the level of isoflurane required to produce and maintain anaesthesia.
Some examples are given in 4.9.
Isoflurane has a weaker sensitising action on the myocardium, to the effects of circulating dysrhythmogenic catecholamines, than halothane.
Isoflurane may be degraded to carbon monoxide by dried carbon dioxide absorbents.

4.9 Amounts to be administered and administration route

Inhalation route.
Isoflurane should be administered using an accurately calibrated vaporiser in an appropriate anaesthetic circuit, since levels of anaesthesia may be altered rapidly and easily.
Isoflurane may be administered in oxygen or oxygen/nitrous oxide mixtures.
The MAC (minimal alveolar concentration in oxygen) or effective dose ED_{50} and suggested concentrations given below for the target species should be used as a guide or starting point only. The actual concentrations required in practice will depend on many variables, including the concomitant use of other drugs during the anaesthetic procedure and the clinical status of the patient.
Isoflurane may be used in conjunction with other drugs commonly used in veterinary anaesthetic regimes for premedication, induction and analgesia. Some specific examples are given in the individual species information. The use of analgesia for painful procedures is consistent with good veterinary practice.
Recovery from isoflurane anaesthesia is usually smooth and rapid. The analgesic requirements of the patient should be considered before the termination of general anaesthesia.
Although anaesthetics have a low potential for damage to the atmosphere, it is good practice to use charcoal filters with scavenging equipment, rather than to discharge them into the air.

HORSE

The MAC for isoflurane in the horse is approximately 1.31%.

Premedication

Isoflurane may be used with other drugs commonly used in veterinary anaesthetic regimes. The following drugs have been found to be compatible with isoflurane: acepromazine, alfentanil, atracurium, butorphanol, detomidine, diazepam, dobutamine, dopamine, guaiphenesin, ketamine, morphine, pentazocine, pethidine, thiamylal, thiopentone and xylazine. Drugs used for premedication should be selected for the individual patient. However, the potential interactions below should be noted.

Interactions:

Detomidine and xylazine have been reported to reduce the MAC for isoflurane in horses.

Induction

As it is not normally practicable to induce anaesthesia in adult horses using isoflurane, induction should be by the use of a short acting barbiturate such as thiopentone sodium, ketamine orguaiphenesin. Concentrations of 3 to 5% isoflurane may then be used to achieve the desired depth of anaesthesia in 5 to 10 minutes.
Isoflurane at a concentration of 3 to 5% in high flow oxygen may be used for induction in foals.

Maintenance

Anaesthesia may be maintained using 1.5 % to 2.5 % isoflurane.

Recovery

Recovery is usually smooth and rapid.

DOG

The MAC for isoflurane in the dog is approximately 1.28 %.

Premedication

Isoflurane may be used with other drugs commonly used in veterinary anaesthetic regimes. The following drugs have been found to be compatible with isoflurane: acepromazine, atropine, butorphanol, buprenorphine, bupivacaine, diazepam, dobutamine, ephedrine, epinephrine, etomidate, glycopyrrolate, ketamine, medetomidine, midazolam, methoxamine, oxymorphone, propofol, thiamylal, thiopentone and xylazine. Drugs used for premedication should be selected for the individual patient. However, the potential interactions below should be noted.

Interactions

Morphine, oxymorphone, acepromazine, medetomidine, and midazolam have been reported to reduce the MAC for isoflurane in dogs.
The concomitant administration of midazolam/ketamine during isoflurane anaesthesia may result in marked cardiovascular effects, particularly arterial hypotension.
The depressant effects of propranolol on myocardial contractility are reduced during isoflurane anaesthesia, indicating a moderate degree of β-receptor activity.

Induction

Induction is possible by face mask using up to 5% isoflurane, with or without premedication.

Maintenance

Anaesthesia may be maintained using 1.5% to 2.5% isoflurane.

Recovery

Recovery is usually smooth and rapid.

CAT

The MAC for isoflurane in the cat is approximately 1.63%.

Premedication

Isoflurane may be used with other drugs commonly used in veterinary anaesthetic regimes. The following drugs have been found to be compatible with isoflurane: acepromazine, atracurium, atropine, diazepam, ketamine, and oxymorphone. Drugs used for premedication should be selected for the individual patient. However, the potential interactions below should be noted.

Interactions:
Intravenous administration of midazolam-butorphanol has been reported to alter several cardio-respiratory parameters in isoflurane-induced cats as has epidural fentanyl and medetomidine. Isoflurane has been shown to reduce the sensitivity of the heart to adrenaline (epinephrine).

Induction:

Induction is possible by face mask using up to 4% isoflurane, with or without premedication.

Maintenance:

Anaesthesia may be maintained using 1.5% to 3% isoflurane.

Recovery

Recovery is usually smooth and rapid.

ORNAMENTAL BIRDS

Few MAC/ED_{50} have been recorded. Examples are 1.34% for the Sandhill crane, 1.45% for the racing pigeon, reduced to 0.89% by the administration of midazolam, and 1.44% for cockatoos, reduced to 1.08% by the administration of butorphanol analgesic.
The use of isoflurane anaesthesia has been reported for many species, from small birds such as zebra finches, to large birds such as vultures, eagles and swans.

Drug interactions/compatibilities

Propofol has been demonstrated in the literature to be compatible with isoflurane anaesthesia in swans.

Interactions

Butorphanol has been reported to reduce the MAC for isoflurane in cockatoos. Midazolam has been reported to reduce the MAC for isoflurane in pigeons.

Induction

Induction with 3 to 5% isoflurane is normally rapid. Induction of anaesthesia with propofol, followed by isoflurane maintenance, has been reported for swans.

Maintenance

The maintenance dose depends on the species and individual.
Generally, 2 to 3% is suitable and safe.
Only 0.6 to 1% may be needed for some stork and heron species.
Up to 4 to 5% may be needed for some vultures and eagles.
3.5 to 4% may be needed for some ducks and geese.
Generally, birds respond very rapidly to changes in concentration of isoflurane.

Recovery

Recovery is usually smooth and rapid.

REPTILES

Isoflurane is considered by several authors to be the anaesthetic of choice for many species. The literature records its use on a wide variety of reptiles (e.g. various species of lizard, tortoise, iguanas, chameleon and snakes).
The ED_{50} was determined in the desert iguana to be 3.14% at 35ºC and 2.83% at 20ºC.

Drug interactions/compatibilities

No specific publications on reptiles have reviewed compatibilities or interactions of other drugs with isoflurane anaesthesia.

Induction

Induction is usually rapid at 2 to 4% isoflurane.

Maintenance

1 to 3% is a useful concentration.

Recovery

Recovery is usually smooth and rapid.

RATS, MICE, HAMSTERS, CHINCHILLAS, GERBILS, GUINEA PIGS AND FERRETS

Isoflurane has been recommended for anaesthesia of a wide variety of small mammals.

The MAC for mice has been cited as 1.34%, and for the rat as 1.38%, 1.46% and 2.4%.

Drug interactions/compatibilities

No specific publications on small mammals have reviewed compatibilities or interactions of other drugs with isoflurane anaesthesia.

Induction

Isoflurane concentration 2 to 3%.

Maintenance

Isoflurane concentration 0.25 to 2%.

Recovery

Recovery is usually smooth and rapid.

Species	MAC (%)	Induction (%)	Maintenance (%)
Horse	1.31	3 - 5	1.5 - 2.5
Dog	1.28	up to 5	1.5 - 2.5
Cat	1.63	up to 4	1.5 - 3
Ornamental birds	See 4.9 section	3 - 5	See 4.9 section
Reptiles	See 4.9 section	2 - 4	1 - 3
Rats, mice, hamsters, chinchillas,	1.34 (mice) 1.38, 1.46 and 2.4 (rat)	2 - 3	0.25 - 2

gerbils, guinea pigs and ferrets			

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

Isoflurane overdose may result in profound respiratory depression. Therefore, respiration must be monitored closely and supported when necessary with supplementary oxygen and / or assisted ventilation.
In cases of severe cardiopulmonary depression, administration of isoflurane should be discontinued, the breathing circuit should be flushed with oxygen, the existence of a patent airway ensured, and assisted or controlled ventilation with pure oxygen initiated.
Cardiovascular depression should be treated with plasma expanders, pressor agents, antiarrhythmic agents or other appropriate techniques.

4.11 Withdrawal period(s)

Horses
Meat and offal: 2 days.
Not authorised for use in mares producing milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anaesthetic, general – halogenated hydrocarbons
ATCvet code: QN01AB06

5.1 Pharmacodynamic properties

Isoflurane produces unconsciousness by its action on the central nervous system. It has little or no analgesic properties.
Like other inhalation anaesthetics of this type, isoflurane depresses the respiratory and cardiovascular systems. Isoflurane is absorbed on inhalation and is rapidly distributed via the bloodstream to other tissues, including the brain. Its blood/gas partition coefficient at 37ºC is 1.4. The absorption and distribution of isoflurane and the elimination of non-metabolised isoflurane by the lungs are all rapid, with the clinical consequences of rapid induction and recovery and easy and rapid control of the depth of anaesthesia.

5.2 Pharmacokinetic particulars

Metabolism of isoflurane is minimal (about 0.2%, mainly to inorganic fluoride) and almost all of the administered isoflurane is excreted unchanged by the lungs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None

6.2 Major Incompatibilities

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, carbon dioxide absorbents should not be allowed to dry out.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 30 months
Shelf life after first opening the immediate packaging: 3 months

6.4. Special precautions for storage

This veterinary medicinal product does not require any special temperature storage conditions.
Keep the bottle tightly closed.

6.5 Nature and composition of immediate packaging

Type III amber glass bottle containing 250 mL isoflurane, closed with a polypropylene/polyethylene roll-on pilfer-proof cap and a high-density polyethylene neck collar with wing, which is fitted over the cap and bottle neck.

Pack size:
Box with 1 bottle of 250 mL"

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

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

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: DD/MM/YYYY
Date of last renewal: DD/MM/YYYY

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

For animal treatment only.
To be supplied only on veterinary prescription.