LABELLING AND PACKAGE LEAFLET

LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Bottles of 250 ml

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]

Isoflurane

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each g contains:

Active substance:
Isoflurane 1000 mg

3. PHARMACEUTICAL FORM

Inhalation vapour, liquid.

4. PACKAGE SIZE

250 ml

5. TARGET SPECIES

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

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Inhalation use. Read the package leaflet before use.

8. WITHDRAWAL PERIOD

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

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once opened use within 3 months
Once opened use by…..

11. SPECIAL STORAGE CONDITIONS

Keep the bottle tightly closed

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

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

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

LABORATORIOS KARIZOO, S.A.
Polígono Industrial La Borda
Mas Pujades, 11-12
08140 – CALDES DE MONTBUI (Barcelona)
SPAIN

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton box for bottles of 250 ml

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]

Isoflurane

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each g contains:

Active substance:
Isoflurane 1000 mg

3. PHARMACEUTICAL FORM

Inhalation vapour, liquid.

4. PACKAGE SIZE

250 ml

5. TARGET SPECIES

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

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Inhalation use. Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal period:
Horses
Meat and offal: 2 days.

Not authorised for use in mares producing milk for human consumption.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once opened use within 3 months
Once opened use by…..

11. SPECIAL STORAGE CONDITIONS

Keep the bottle tightly closed.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

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

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

LABORATORIOS KARIZOO, S.A.
Polígono Industrial La Borda
Mas Pujades, 11-12
08140 – CALDES DE MONTBUI (Barcelona)
SPAIN

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch

PACKAGE LEAFLET

PACKAGE LEAFLET:
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]

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:
LABORATORIOS KARIZOO, S.A.
Polígono Industrial La Borda
Mas Pujades, 11-12
08140 – CALDES DE MONTBUI (Barcelona)
Spain

2. 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]

Isoflurane

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each g contains:

Active substance:
Isoflurane 1000 mg

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

4. INDICATION(S)

Induction and maintenance of general anaesthesia.

5. 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.

6. ADVERSE REACTIONS

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).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon
Alternatively you can report via your national reporting system {national system details}

7. TARGET SPECIES

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

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Inhalation route.
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 or

guaiphenesin. 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 8 section	3 - 5	See 8 section
Reptiles	See 8 section	2 - 4	1 - 3
Rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets	1.34 (mice) 1.38, 1.46 and 2.4 (rat)	2 - 3	0.25 - 2

9. ADVICE ON CORRECT ADMINISTRATION

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.

10. WITHDRAWAL PERIOD

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

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

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

Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Shelf life after first opening the container: 3 months.

12. SPECIAL WARNING(S)

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.

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.

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.

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 "DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION".
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.

Overdose (symptoms, emergency procedures, antidotes):
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.

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.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Pack size:
Box with 1 bottle of 250 ml

Marketing authorisation number:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.