ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ISOFLURIN 1000 mg/g Inhalation Vapour, Liquid [BE, BG, CY, CZ, EL, ES, FR, HR, HU, IE, LT, LU, LV, NL, PL, PT, SI, SK, UK (NI)]

FUXIEN vet 1000 mg/g Inhalation Vapour, Liquid [DK, FI, NO, SE]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:
Active substance:
Isoflurane ..... 1000 mg

This veterinary medicinal product does not contain any excipient.

Clear, colourless, mobile, heavy liquid.

3. CLINICAL INFORMATION

3.1 Target species

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

3.2 Indications for use for each target species

Induction and maintenance of general anaesthesia.

3.3 Contraindications

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

3.4 Special warnings

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.

3.5 Special precautions for use

Special precautions for safe use in the target species:

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.

The use of the veterinary medicinal product in patients with cardiac disease should be considered only after a risk/ benefit assessment by the veterinarian.

It is important to monitor breathing and pulse for the frequency and its features. Respiratory arrest should be treated by assisted ventilation. It is important to maintain airways free and

properly oxygenate tissues during the maintenance of anaesthesia. In the case of cardiac arrest, perform a complete cardiopulmonary resuscitation.

The metabolism of isoflurane in birds and small mammals, can be affected by decreases in body temperature, that may occur secondary to a 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.

Like other inhalation anaesthetics of this type, isoflurane depresses the respiratory and cardiovascular systems.

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 anesthetics can harm the unborn child. The veterinary medicinal product should not be administered by pregnant women. Pregnant and breast-feeding women should not have any contact with the veterinary medicinal product and should avoid operating rooms 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 the veterinary medicinal product 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 the 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.

Special precautions for the protection of the environment:
To protect the environment, it is considered good practice to use charcoal filters with scavenging equipment.

3.6 Adverse events

Horse, dog, cat, ornamental bird, reptile, rat, mouse, hamster, chinchilla, gerbil, guinea pig, ferret:

Rare (1 to 10 animals / 10,000 animals treated):	Arrhythmia, bradycardia[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Cardiac arrest Respiratory arrest Malignant hyperthermia[2]
Undetermined frequency (cannot be estimated from the available data):	Hypotension[3] Respiratory depression[3]

[1] Transient
[2] Susceptible animals
[3] Dose-related

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder, or its local representative, or the national competent authority via the national reporting system. See also the package leaflet for respective contact details.

3.7 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.

3.8 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 section 3.9.

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

Isoflurane may be degraded to carbon monoxide by dried carbon dioxide absorbents.

3.9 Administration routes and dosage

Inhalation use. 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} values 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.

HORSES
The MAC for isoflurane in the horse is approximately 13.1 mg/g.

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, guiaphenesin, 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 guiaphenesin. Concentrations of 30 to 50 mg/g isoflurane may then be used to achieve the desired depth of anaesthesia in 5 to 10 minutes.
Isoflurane at a concentration of 30 to 50 mg/g in a high flow oxygen may be used for induction in foals.

Maintenance
Anaesthesia may be maintained using 15 to 25 mg/g isoflurane.

Recovery
Recovery is usually smooth and rapid.

DOGS
The MAC for isoflurane in the dog is approximately 12.8 mg/g.

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, medetomidine plus 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 propanolol 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 50 mg/g isoflurane, with or without premedication.

Maintenance
Anaesthesia may be maintained using 15 to 25 mg/g isoflurane.

Recovery
Recovery is usually smooth and rapid.

CATS
The MAC for isoflurane in the cat is approximately 16.3 mg/g.

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 40 mg/g isoflurane, with or without premedication.

Maintenance
Anaesthesia may be maintained using 15 to 30 mg/g isoflurane.

Recovery
Recovery is usually smooth and rapid.

ORNAMENTAL BIRDS
Few MAC/ED_{50} values have been recorded. Examples are 13.4 mg/g for the Sandhill crane, 14.5 mg/g for the racing pigeon, reduced to 8.9 mg/g by the administration of midazolam, and 14.4 mg/g for cockatoos, reduced to 10.8 mg/g 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 30 to 50 mg/g 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, 20 to 30 mg/g is suitable and safe.
Only 6 to 10 mg/g may be needed for some stork and heron species.
Up to 40 to 50 mg/g may be needed for some vultures and eagles.
35 to 40 mg/g 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 (eg. various species of lizard, tortoise, iguanas, chameleon and snakes).
The ED_{50} was determined in the desert iguana to be 31.4 mg/g at 35ºC and 28.3 mg/g 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 20 to 40 mg/g isoflurane.

Maintenance
10 to 30 mg/g is a useful concentration

Recovery
Recovery is usually smooth and rapid

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

Isoflurane has been recommended for anaesthesia of a wide variety of small mammals.
The MAC for mice has been cited as 13.4 mg/g, and for the rat as 13.8 mg/g, 14.6 mg/g and 24 mg/g.

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

Induction
Isoflurane concentration 20 to 30 mg/g.

Maintenance
Isoflurane concentration 2.5 to 20 mg/g.

Recovery
Recovery is usually smooth and rapid.

Guide to induction and maintenance of anaesthesia by species

Species	**MAC (%)**	**Induction (%)**	**Maintenance (%)**	**Recovery**
Horses	1.31	3.0 – 5.0 (foals)	1.5 – 2.5	Smooth and rapid
Dogs	1.28	Up to 5.0	1.5 – 2.5	Smooth and rapid
Cats	1.63	Up to 4.0	1.5 – 3.0	Smooth and rapid
Ornamental birds	See posology	3.0 – 5.0	See posology	Smooth and rapid
Reptiles	See posology	2.0 – 4.0	1.0 – 3.0	Smooth and rapid
Rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets	1.34 (mouse) 1.38/1.46/2.40 (rat)	2.0 – 3.0	0.25 – 2.0	Smooth and rapid

3.10 Symptoms of overdose (and where applicable, emergency procedures and 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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance.

3.12 Withdrawal periods

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

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QN01AB06

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

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.

5. PHARMACEUTICAL PARTICULARS

5.1 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.

5.2 Shelf life

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

5.3 Special precautions for storage

Do not store above 25ºC.
Store in the original container.
Protect from light.
Keep the bottle tightly closed.

5.4 Nature and composition of immediate packaging

Amber coloured glass bottle (Type III) containing 100ml or 250ml isoflurane. Bottles are closed with a black polypropylene screw cap.
Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Vetpharma Animal Health, S.L.

7. MARKETING AUTHORISATION NUMBER

{Marketing Authorization Number}

8. DATE OF FIRST AUTHORISATION

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

{DD month YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.
Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

{BOX}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ISOFLURIN 1000 mg/g Inhalation Vapour, Liquid [BE, BG, CY, CZ, EL, ES, FR, HR, HU, IE, LT, LU, LV, NL, PL, PT, SI, SK, UK (NI)]
FUXIEN vet 1000 mg/g Inhalation Vapour, Liquid [DK, FI, NO, SE]

2. STATEMENT OF ACTIVE SUBSTANCES

Isoflurane 1000 mg/g

3. PACKAGE SIZE

100 ml
250 ml

4. TARGET SPECIES

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

5. INDICATIONS

To be included only for medicinal products not subject to medical prescription.

6. ROUTES OF ADMINISTRATION

Inhalation use

7. WITHDRAWAL PERIODS

Withdrawal period:

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

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25ºC.
Store in the original container.
Protect from light.
Keep the bottle tightly closed.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

[UK(NI)]: Anaesthetics must be handled correctly. See package leaflet for user warnings.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

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

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Vetpharma Animal Health, S.L.

14. MARKETING AUTHORISATION NUMBER

EU/0/00/000/000

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

{IMMEDIATE PACKAGE: Flask 100 and 250 ml}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ISOFLURIN 1000 mg/g Inhalation Vapour, Liquid [BE, BG, CY, CZ, EL, ES, FR, HR, HU, IE, LT, LU, LV, NL, PL, PT, SI, SK, UK]
FUXIEN vet 1000 mg/g Inhalation Vapour, Liquid [DK, FI, NO, SE]

2. STATEMENT OF ACTIVE SUBSTANCES

Isoflurane 1000 mg/g

3. TARGET SPECIES

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

4. ROUTES OF ADMINISTRATION

Inhalation use. Read the package leaflet before use.

5. WITHDRAWAL PERIODS

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

6. EXPIRY DATE

Exp. {month/year}

7. SPECIAL STORAGE PRECAUTIONS

Do not store above 25ºC.
Store in the original container.
Protect from light.
Keep the bottle tightly closed.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Vetpharma Animal Health, S.L.

9. BATCH NUMBER

Lot {number}

B. LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

ISOFLURIN 1000 mg/g Inhalation Vapour, Liquid [BE, BG, CY, CZ, EL, ES, FR, HR, HU, IE, LT, LU, LV, NL, PL, PT, SI, SK, UK]

FUXIEN vet 1000 mg/g Inhalation Vapour, Liquid [DK, FI, NO, SE]

2. Composition

Each g contains:
Active substance:
Isoflurane 1000 mg

Clear, colourless, mobile, heavy liquid.

3. Target species

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

4. Indications for use

Induction and maintenance of general anaesthesia.

5. Contraindications

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

6. Special warnings

Special warnings:
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 safe use in the target species:

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.
The use of the veterinary medicinal product in patients with cardiac disease should be considered only after a risk/benefit assessment by the veterinarian.
It is important to monitor breathing and pulse for the frequency and its features. Respiratory arrest should be treated by assisted ventilation.
It is important to maintain airways free and properly oxygenate tissues during the maintenance of anaesthesia. In the case of cardiac arrest, perform a complete cardiopulmonary resuscitation.

The metabolism of isoflurane in birds and small mammals, can be affected by decreases in body temperature, that may occur secondary to a 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.

Like other inhalation anaesthetics of this type, isoflurane depresses the respiratory and cardiovascular systems.
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 veterinary medicinal product and should avoid operating rooms 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 the veterinary medicinal product 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 the 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.

Special precautions for the protection of the environment:
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 section 8.
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.

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.

7. Adverse events

Horse, dog, cat, ornamental bird, reptile, rat, mouse, hamster, chinchilla, gerbil, guinea pig, ferret:

Rare (1 to 10 animals / 10,000 animals treated):	Arrhythmia, bradycardia[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Cardiac arrest Respiratory arrest Malignant hyperthermia[2]
Undetermined frequency (cannot be estimated from the available data):	Hypotension[3] Respiratory depression[3]

[1] Transient
[2] Susceptible animals
[3] Dose-related

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder, the local representative of the marketing authorisation holder, using the contact details at the end of this leaflet, or via your national reporting system {national system details}.

8. Dosage for each species, routes and method of administration

Inhalation use. Isoflurane may be administered in oxygen or oxygen/nitrous oxide mixtures. The MAC (minimal alveolar concentration in oxygen) or effective dose ED_{50} values 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.

HORSES

The MAC for isoflurane in the horse is approximately 13.1 mg/g.

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, guiaphenesin, 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 guiaphenesin. Concentrations of 30 to 50 mg/g isoflurane may then be used to achieve the desired depth of anaesthesia in 5 to 10 minutes.

Isoflurane at a concentration of 30 to 50 mg/g in a high flow oxygen may be used for induction in foals.

Maintenance

Anaesthesia may be maintained using 15 to 25 mg/g isoflurane.

Recovery

Recovery is usually smooth and rapid.

DOGS

The MAC for isoflurane in the dog is approximately 12.8 mg/g.

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, medetomidine plus 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 propanolol 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 50 mg/g isoflurane, with or without premedication.

Maintenance
Anaesthesia may be maintained using 15 to 25 mg/g isoflurane.

Recovery
Recovery is usually smooth and rapid.

CATS

The MAC for isoflurane in the cat is approximately 16.3 mg/g.

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 40 mg/g isoflurane, with or without premedication.

Maintenance
Anaesthesia may be maintained using 15 to 30 mg/g isoflurane.

Recovery
Recovery is usually smooth and rapid.

ORNAMENTAL BIRDS

Few MAC/ED_{50} values have been recorded. Examples are 13.4 mg/g for the Sandhill crane, 14.5 mg/g for the racing pigeon, reduced to 8.9 mg/g by the administration of midazolam, and 14.4 mg/g for cockatoos, reduced to 10.8 mg/g 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 30 to 50 mg/g 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, 20 to 30 mg/g is suitable and safe.

Only 6 to 10 mg/g may be needed for some stork and heron species.
Up to 40 to 50 mg/g may be needed for some vultures and eagles.
35 to 40 mg/g 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 (eg. various species of lizard, tortoise, iguanas, chameleon and snakes).
The ED_{50} was determined in the desert iguana to be 31.4 mg/g at 35ºC and 28.3 mg/g 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 20 to 40 mg/g isoflurane.

Maintenance
10 to 30 mg/g is a useful concentration

Recovery
Recovery is usually smooth and rapid

RATS, MICE, HAMSTERS, CHINCHILLAS, GERBILS, GUNIEA PIGS AND FERRETS
Isoflurane has been recommended for anaesthesia of a wide variety of small mammals.
The MAC for mice has been cited as 13.4 mg/g, and for the rat as 13.8 mg/g, 14.6 mg/g and 24 mg/g.

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

Induction
Isoflurane concentration 20 to 30 mg/g.

Maintenance
Isoflurane concentration 2.5 to 20 mg/g.

Recovery
Recovery is usually smooth and rapid.

Guide to induction and maintenance of anaesthesia by species

Species	MAC (%)	Induction (%)	Maintenance (%)	Recovery
Horses	1.31	3.0 – 5.0 (foals)	1.5 – 2.5	Smooth and rapid
Dogs	1.28	Up to 5.0	1.5 – 2.5	Smooth and rapid
Cats	1.63	Up to 4.0	1.5 – 3.0	Smooth and rapid
Ornamental birds	See posology	3.0 – 5.0	See posology	Smooth and rapid
Reptiles	See posology	2.0 – 4.0	1.0 – 3.0	Smooth and rapid
Rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets	1.34 (mouse) 1.38/1.46/2.40 (rat)	2.0 – 3.0	0.25 – 2.0	Smooth and rapid

9. Advice on correct administration

Inhalation use. Isoflurane should be administered using an accurately calibrated vaporiser in an appropriate anaesthetic circuit, since levels of anaesthesia may be altered rapidly and easily.

10. Withdrawal periods

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.

Do not store above 25ºC.
Store in the original container.
Protect from light.
Keep the bottle tightly closed.

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

12. Special precautions for disposal

[BE, BG, CY, CZ, EL, ES, FR, HR, HU, IE, LT, LU, LV, NL, PL, PT, SI, SK, DK, FI, NO, SE]: Medicines should not be disposed of via wastewater or household waste.

[PL]: Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

[UK(NI)]: Medicines should not be disposed of via wastewater.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.
Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

14. Marketing authorization numbers and pack sizes

Pack sizes: cardboard box containing 100 ml or 250 ml amber glass bottle.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{DD month YYYY}

16. Contact details

Marketing authorisation holder:
Vetpharma Animal Health, S.L.
Gran Via Carles III, 98, 7ª
08028 Barcelona
Spain

Manufacturer responsible for batch release:

LABORATORIOS KARIZOO, S.A.
Mas Pujades, 11 – 12, Polígono Industrial La Borda
Caldes de Montbui, 08014 Barcelona,
Spain

Local representatives and contact details to report suspected adverse reactions:

17. Other information