

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**CARTON BOX**

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Isothesia 1000 mg/g inhalation vapour, liquid for horses, dogs, cats, ornamental birds, reptiles, rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets

**2. STATEMENT OF ACTIVE SUBSTANCES**

100% isoflurane

**3. PHARMACEUTICAL FORM**

Inhalation vapour, liquid

Clear, colourless volatile liquid for the generation of gaseous anaesthetic, with a mildly pungent odour.

**4. PACKAGE SIZE**

250 ml

100 ml

**5. TARGET SPECIES**

For use in horses, dogs, cats, ornamental birds, reptiles, rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets.

**6. INDICATION(S)**

**Induction and maintenance of general anaesthesia.**

**7. METHOD AND ROUTE(S) OF ADMINISTRATION**

Read the package leaflet before use.  
Keep the bottle in the outer carton.

**8. WITHDRAWAL PERIOD (S)**

Withdrawal period: Horses: meat and offal: two days  
The product should not be used for the treatment of mares producing milk for human consumption.

**9. SPECIAL WARNING(S)**

Anaesthetics must be handled correctly. See package leaflet for operator warnings.

**10. EXPIRY DATE**

EXP {month/year}

**11. SPECIAL STORAGE CONDITIONS**

Do not store above 25°C.  
Store in the original bottle.  
Keep the bottle tightly closed.  
Protect from direct sunlight and heat.

**12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS.**

Dispose of waste material in accordance with local requirements.

**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**

Zoetis UK Limited  
5th Floor, 6 St. Andrew Street  
London  
EC4A 3AE

**16. MARKETING AUTHORISATION NUMBER**

Vm 42058/4197

**17. MANUFACTURER’S BATCH NUMBER**

Lot {number}

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE**

**BOTTLE LABEL**

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Isothesia 1000 mg/g inhalation vapour, liquid for horses, dogs, cats, ornamental birds, reptiles, rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets.

**2. STATEMENT OF ACTIVE SUBSTANCES**

100% isoflurane

**3. PHARMACEUTICAL FORM**

Inhalation vapour, liquid

Clear, colourless volatile liquid for the generation of gaseous anaesthetic, with a mildly pungent odour.

**4. PACKAGE SIZE**

250 ml

100 ml

**5. TARGET SPECIES**

For use in horses, dogs, cats, ornamental birds, reptiles, rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets.

**6. INDICATIONS**

Induction and maintenance of general anaesthesia

**7. METHOD AND ROUTE(S) OF ADMINISTRATION**

Read the package leaflet before use.

**8. WITHDRAWAL PERIOD(S)**

Withdrawal period: Horses: meat and offal: two days

The product should not be used for the treatment of mares producing milk for human consumption.

**9. SPECIAL WARNING(S), IF NECESSARY**

Anaesthetics must be handled correctly. See package leaflet for operator warnings.

**10. EXPIRY DATE**

EXP {month/year}

**11. SPECIAL STORAGE CONDITIONS**

Do not store above 25 °C.  
Store in the original bottle.  
Keep the bottle tightly closed.  
Protect from direct sunlight and heat.

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

**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 sight and reach of children.

**15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Zoetis UK Limited  
5th Floor, 6 St. Andrew Street  
London  
EC4A 3AE

**16. MARKETING AUTHORISATION NUMBER**

Vm 42058/4197

**17. MANUFACTURER’S BATCH NUMBER**

Lot {number}

## **B. PACKAGE LEAFLET**

## PACKAGE LEAFLET

**Isothesia 1000 mg/g inhalation vapour, liquid for horses, dogs, cats, ornamental birds, reptiles, rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets**

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

Marketing authorisation holder:

Zoetis UK Limited  
5th Floor, 6 St. Andrew Street  
London  
EC4A 3AE

Manufacturer responsible for batch release:

Aesica Queenborough Limited  
Queenborough  
Kent  
ME11 5EL  
UK

### **2. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Isothesia 1000 mg/g inhalation vapour, liquid for horses, dogs, cats, ornamental birds, reptiles, rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets.  
Isoflurane

### **3. STATEMENT OF THE ACTIVE SUBSTANCES AND OTHER INGREDIENT(S)**

A clear, colourless volatile liquid for the generation of gaseous anaesthetic, with a mildly pungent odour, containing 100% isoflurane.

### **4. INDICATIONS**

Induction and maintenance of general anaesthesia.

### **5. CONTRAINDICATIONS**

Do not use in case of known susceptibility to malignant hyperthermia.  
Do not use in case of hypersensitivity to isoflurane.

### **6. ADVERSE REACTIONS**

Isoflurane produces hypotension and respiratory depression in a dose-related manner. It is important that respiration and pulse should be monitored for both rate and character. Respiratory arrest should be treated by assisted ventilation with air or, preferably, with oxygen supplementation. It is important that a patent airway be



maintained and adequate tissue oxygenation achieved throughout the period of anaesthesia. Should cardiac arrest occur, full cardiopulmonary resuscitation methods should be applied. Cardiac arrhythmias and transient bradycardia have been reported rarely. However, isoflurane has a weaker sensitising action on the myocardium, to the effects of dysrhythmogenic circulating catecholamines, than halothane.

Malignant hyperthermia has been reported very rarely in susceptible animals.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports)

If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon.

## 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

### Premedication:

Isoflurane may be used with other drugs commonly used in veterinary anaesthetic regimes. Drugs used for premedication should be selected for the individual patient. See Contra-indications, warnings etc for potential drug interactions.

The MAC (minimal alveolar concentration) in oxygen given below for the target species should be used as a guide only. The actual concentrations required in practice will depend on many variables including the concomitant use of other drugs and the clinical status of the patient.

Induction, Maintenance and Recovery: See table below:

Species	MAC (%)	Induction (%)*	Maintenance (%)
Horses	1.31	3.0-5.0 (foals)	1.5-2.5
Dogs	1.28	up to 5.0	1.5-2.5
Cats	1.63	up to 4.0	1.5-3.0
Ornamental Birds	1.45 (pigeon)	3.0-5.0	0.6-5.0
Reptiles	Not published	2.0-4.0	1.0-3.0
Rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets	1.34 (mouse) 1.38-2.40 (rat) 1.55 (gerbils) 1.62 (hamster)	2.0-3.0	0.25-2.0

\* Induction usually occurs via a face mask. In all species, recovery is normally smooth and rapid.

Species specific interactions:

*Horses:*

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

*Dogs:*

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 propranolol on myocardial contractility are reduced during isoflurane anaesthesia, indicating a moderate degree of  $\beta$ -receptor activity.

*Cats:*

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 sensitivity of the heart to adrenalin (epinephrine).

*Ornamental Birds:*

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

*Reptiles and small mammals:*

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

## **9. ADVICE ON CORRECT ADMINISTRATION**

**Isothesia should be used only in an isoflurane specific vaporiser.**

Isoflurane should be administered using an accurately calibrated vaporiser in an appropriate anaesthetic circuit since levels of anaesthesia may be altered rapidly and easily. The lowest effective dose should be administered, and, as with all anaesthetics, the correct dose is the minimum that achieves the desired level of anaesthesia. Isoflurane may be administered in oxygen or oxygen/nitrous oxide mixtures.

## **10. WITHDRAWAL PERIOD(S)**

Horses: meat and offal: two days

The product should not be used for the treatment of mares producing milk for human consumption.

## **11. SPECIAL STORAGE PRECAUTIONS**

Keep out of the sight and reach of children.

Do not store above 25°C. Protect from direct sunlight and heat.

Store in the original bottle and keep the bottle tightly closed

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

## 12. SPECIAL WARNING(S)

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 CO<sub>2</sub> levels, so that cerebral blood flow does not increase.

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.

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

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

It's important to monitor breathing and pulse for the frequency and its features.

Respiratory arrest should be treated by assisted ventilation. It's important to maintain airways free and properly oxygenate tissues during the maintenance of anaesthesia.

In the case of cardiac arrest, perform a complete cardio pulmonary resuscitation.

Treated animals should be kept warm and at a constant temperature, both during the procedure and recovery. Monitoring of body temperature is recommended.

The action of muscle relaxants in man, especially those of the non-depolarising 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. For example, opiates, alpha-2-agonists, acepromazine, and benzodiazepines have been reported to reduce the MAC values. The concomitant administration of midazolam/ketamine during isoflurane anaesthesia may result in marked cardiovascular effects, particularly arterial hypotension.

Birds and small mammals are particularly susceptible to decreases in body temperature, due to their high surface area to body weight ratio. This, in turn, can affect the metabolism of isoflurane. 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.

Use in pregnant and lactating animals should be limited to cases in which the benefits outweigh the risks.

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

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.

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 general anaesthesia is ended.

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. 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.

#### Operator Warnings:

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 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 Isothesia 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:

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.

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

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

### **14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED**

### **15. OTHER INFORMATION**

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.

Isoflurane produces unconsciousness by its action on the central nervous system. It has little or no analgesic properties and consideration should be given to the analgesic requirements of the patient before the termination of general anaesthesia. The use of analgesia for painful procedures is consistent with good veterinary practice.

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

Package Quantities: 100 ml and 250 ml bottle  
Not all pack sizes may be marketed.