ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE AND THE IMMEDIATE PACKAGE

Outer carton
Glass vial of 100 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Propodine 10 mg/ml emulsion for injection/infusion for dogs and cats
propofol

2. STATEMENT OF ACTIVE SUBSTANCES

1 ml contains:
Propofol 10.0 mg

3. PHARMACEUTICAL FORM

Emulsion for injection/infusion.

4. PACKAGE SIZE

20 ml
50 ml
100 ml

5. TARGET SPECIES

Dogs and cats

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Intravenous use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP
Once broached use immediately.

11. SPECIAL STORAGE CONDITIONS

Do not freeze.
Store in the outer carton in order to protect from light.

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

Dechra Regulatory B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

Vm 50406/4007

17. MANUFACTURER'S BATCH NUMBER

Lot

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Glass vial of 20 ml
Glass vial of 50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Propodine 10 mg/ml emulsion for injection/infusion
Propofol

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

10 mg/ml

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

20 ml
50 ml

4. ROUTE(S) OF ADMINISTRATION

IV

5. WITHDRAWAL PERIOD(S)

6. BATCH NUMBER

Lot {number}

7. EXPIRY DATE

EXP
Once broached use immediately.

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Propodine 10 mg/ml emulsion for injection/infusion for dogs and cats

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

Marketing authorisation holder:
Dechra Regulatory B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

Manufacturer responsible for batch release:
Corden Pharma S.p.A
Viale dell'Industria 3
20867 Caponago
Italy

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Propodine 10 mg/ml emulsion for injection/infusion for dogs and cats
Propofol

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

1 ml contains
Active substance:
Propofol 10.0 mg

White or almost white homogeneous emulsion.

4. INDICATION(S)

- General anaesthesia for diagnostic or surgical procedures of short duration, lasting up to five minutes.
- Induction and maintenance of general anaesthesia.
- Induction of general anaesthesia where maintenance is provided by inhalation anaesthetic agents.

5. CONTRAINDICATIONS

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. ADVERSE REACTIONS

Induction is generally smooth, however evidence of excitation (e.g. paddling of limbs, nystagmus, focal muscle twitching/myoclonus, opisthotonus) is commonly observed in dogs and cats. Transient apnoea and mild hypotension may very commonly occur during induction of anaesthesia. An increase of arterial blood pressure followed by a decrease can be observed. See section 12 (Special precautions for use in animals). A reduction in the percentage of haemoglobin which is saturated with oxygen (SpO_2) may be observed in the absence of apnoea.

Cases of excessive salivation and vomiting have been reported uncommonly during the recovery phase in dogs. Excitation during the recovery phase has been observed rarely in dogs. Limb rigidity and persistent hiccough has been observed very rarely in dogs.
There has been an isolated report in a dog of green discolouration of urine following a prolonged propofol infusion.

In cats, sneezing, occasional retching and a paw/face licking characteristic during recovery have been observed in a small proportion of cases (uncommon). Repeated longer-duration (>20 minutes) anaesthesia with propofol in cats may cause oxidative injury and Heinz body formation, and non-specific signs such as anorexia, diarrhoea and mild facial oedema. Recovery may also be prolonged. Limiting repeated anaesthesia to intervals of more than 48 hours will reduce the likelihood.

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 in 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

Dogs and cats

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

For intravenous administration.

Induction of anaesthesia:
The induction dose of the veterinary medicinal product presented in the table below is based on published data from controlled laboratory and field studies as well as clinical experience and represents the average induction dose for dogs and cats. These doses are for guidance only. **The actual dose should be titrated against the response of the individual patient and may be significantly lower or higher than the average dose.**
The dosing syringe should be prepared based on the dose volume of product shown below, calculated according to bodyweight. The product should be administered to effect until the depth of anaesthesia is sufficient for endotracheal intubation. When inducing anaesthesia with propofol it should be injected sufficiently slowly to allow equilibration between the plasma and the effect site, and sufficiently quickly to avoid redistribution from the brain resulting in an inadequate plane of anaesthesia (i.e. administration over a period of approximately 10-40 seconds). Where propofol is used concurrently with an opioid, it should be administered more slowly, e.g. over 40-60 seconds. See section 12 (Interaction).
Use of pre-anaesthetic drugs (premedication) may markedly reduce propofol requirements dependent of on the type and dose of pre-anaesthetic drugs used. When propofol is used in combination with e.g. ketamine, fentanyl or benzodiazepines for induction of anaesthesia (so called co-induction), the total dose of propofol can be further reduced.

Dosing recommendations for induction of anaesthesia:

	Dose mg/kg bodyweight	**Dose volume ml/kg bodyweight**
DOGS		
Unpremedicated	6.5 mg/kg	0.65 ml/kg
Premedicated		
With non-α-2 agonist (acepromazine-based)	4.0 mg/kg	0.40 ml/kg
With α-2 agonist	2.0 mg/kg	0.20 ml/kg
CATS		
Unpremedicated	8.0 mg/kg	0.80 ml/kg
Premedicated		
With non-α-2 agonist (acepromazine-based)	6.0 mg/kg	0.60 ml/kg
With α-2 agonist	4.5 mg/kg	0.45 ml/kg

Propofol has been used as an induction agent in combination with other premedication regimens, see section 12 (Interaction) for further detail.

Maintenance of anaesthesia:
Following induction of anaesthesia with the veterinary medicinal product, the animal may be intubated and maintained on the veterinary medicinal product or an inhalation anaesthetic agent. Maintenance doses of the veterinary medicinal product may be given as repeat bolus injections or as continuous infusion. Continuous and prolonged exposure may lead to slower recovery, particularly in cats.

Repeat bolus injection:
Where anaesthesia is maintained by repeat bolus injections, the dose rate and duration of effect will vary between animals. An incremental dose of approximately 1-2 mg/kg (0.1-0.2 ml/kg b.w.) in dogs and 0.5-2 mg/kg (0.05-0.2 ml/kg b.w.) in cats may be given to effect when anaesthesia becomes too light. This dose may be repeated as required to maintain an appropriate depth of anaesthesia.
Continuous infusion:
For continuous infusion anaesthesia the suggested starting dose rate is 0.3-0.4 mg/kg/min (1.8-2.4 ml/kg/hour) in dogs and 0.2-0.3 mg/kg/min (1.2-1.8 ml/kg/hour) in cats. Use of pre-anaesthetic drugs (premedication) or concomitant infusion of e.g. ketamine or opioids may reduce propofol requirements dependent on the type and dose of drugs used. The actual infusion rate should be based on the response of the individual patient and the desired depth of anaesthesia and can be adjusted by 0.01-0.05 mg/kg/minute (0.06-0.3 ml/kg/hour) increments based on assessment of anaesthetic depth and cardiovascular response. When a rapid increase in anaesthetic depth is warranted, an additional bolus of propofol (0.5-1 mg/kg [0.05-0.1 ml/kg] in dogs and 0.2-0.5 mg/kg [0.02-0.05 ml/kg] in cats) can be administered.

9. ADVICE ON CORRECT ADMINISTRATION

Shake the vial gently but thoroughly before opening. See section 12 (Special warnings for each target species).

10. WITHDRAWAL PERIOD(S)

Not applicable

11. SPECIAL STORAGE PRECAUTIONS

Do not freeze.
Store in the outer carton in order to protect from light.
Withdrawn product should be used immediately. Product remaining in the vial should be discarded.
Keep out of the sight and reach of children.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of that month.

Shelf life after first opening the container: use immediately.

12. SPECIAL WARNING(S)

Special warnings for each target species:
This product is a stable emulsion. Prior to use, the product should be inspected visually for the absence of visible droplets or extraneous foreign particles and discarded if present. Do not use if evidence of phase separation remains after gentle shaking.
If the product is injected too slowly, an inadequate plane of anaesthesia can occur, due to failure to reach the appropriate threshold of pharmacological activity.

Special precautions for use in animals:
During induction of anaesthesia, mild hypotension and transient apnoea may occur. If the product is injected too rapidly, cardiopulmonary depression may occur (apnoea, bradycardia, hypotension).
When using the veterinary medicinal product, facilities for the maintenance of a patent airway, artificial ventilation and oxygen enrichment must be available.
Following induction of anaesthesia, the use of an endotracheal tube is recommended. It is advisable to administer supplemental oxygen during maintenance of anaesthesia.
Caution should be exercised in dogs and cats with cardiac, respiratory, renal or hepatic impairment, or in hypovolaemic or debilitated animals.
When propofol is used concomitantly with opioids, an anticholinergic agent (e.g. atropine) may be used in cases of bradycardia according to the benefit/risk assessment by the responsible veterinarian. See section on Interactions.
Care should be taken when administering the product to patients with hypoproteinaemia, hyperlipidaemia or very thin animals since these animals may be more susceptible to adverse effects.
Propofol does not have analgesic properties, therefore supplementary analgesic agents should be provided in cases where procedures are anticipated to be painful.
It has been reported that clearance of propofol is slower and incidence of apnoea is greater in dogs over 8 years of age than in younger animals. Extra care should be taken when administering the product to these animals, for example, a lower dose of propofol may be adequate for induction in such cases.
The safety of the product has not been established in dogs or cats younger than 4 months and should be used in these animals only according to the risk/benefit assessment by the responsible veterinarian.
Sighthounds have been reported to show a slower clearance of propofol and may have a slightly longer duration of recovery from anaesthesia compared to other breeds of dog.
Use aseptic techniques when administering the product as it does not contain an antimicrobial preservative.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Propofol is a potent drug: particular care should be taken to avoid accidental self-administration. A guarded needle should preferably be used until the moment of injection.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician, but DO NOT DRIVE as sedation may occur.
Avoid contact with the skin and eyes as this product can cause irritation. Wash off splashes from the skin and eyes immediately with plenty of water. Seek medical advice if irritation persists.
This product may cause hypersensitivity (allergy) reactions in those that are already sensitised to propofol or other drugs, soya or egg. People with known hypersensitivity to these substances should avoid contact with the veterinary medicinal product.

Advice to the doctor:
Do not leave the patient unattended. Maintain airways and give symptomatic and supportive treatment.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy (in foetuses/neonates) and during lactation.

Propofol crosses the placenta. Studies using propofol in pregnant rats and rabbits have demonstrated no deleterious effects on gestation of the treated animals, or on the reproductive performance of their offspring. However, according to available scientific literature (non-human primates: moderate plane of anaesthesia for 5h; rats: 0.3-0.6 mg/kg/min for 1-2h) to propofol during the period of brain development may adversely affect the neurological development in foetuses and neonates.
Studies in humans showed that small quantities (<0.1% of maternal dose within 24h after dosing) of propofol are excreted in human breastmilk.
Use only according to the benefit/risk assessment by the responsible veterinarian.
Propofol has been safely used in dogs for the induction of anaesthesia prior to delivery of puppies by caesarean section. Owing to risk of neonatal death, the use of propofol for the maintenance of anaesthesia during caesarean section is not recommended.

Interaction with other medicinal products and other forms of interaction:
Propofol has been used in association with commonly used premedicants (e.g. atropine, acepromazine, benzodiazepines [e.g. diazepam, midazolam], α-2-agonists [e.g. medetomidine, dexmedetomidine], opioids [e.g. methadone, buprenorphine]), other induction agents (e.g. ketamine) and prior to maintenance with inhalational agents (e.g. halothane, nitrous oxide, isoflurane, sevoflurane).
The concurrent use of sedative or analgesic drugs is likely to reduce the dose of propofol required for induction and maintenance of anaesthesia. See section 8.
Concomitant use of propofol and opioids may cause significant respiratory depression and a profound decrease in heart rate. Cardiac arrest has been observed in dogs that received propofol followed by alfentanil. To reduce the risk of apnoea, propofol should be administered slowly, for example, over 40-60 seconds. See also section on Special precautions for use in animals..
Co-administration of propofol and opioid (e.g. fentanyl, alfentanil) infusions for maintenance of general anaesthesia may result in a prolonged recovery.
Administration of propofol with other drugs that are metabolised by cytochrome P450 (isoenzyme 2B11 in the dog) such as e.g. chloramphenicol, ketoconazole and loperamide, reduces propofol clearance and prolongs recovery from propofol anaesthesia.

Overdose (symptoms, emergency procedures, antidotes):
Accidental overdosage is likely to cause cardio-respiratory depression. Respiratory depression should be treated by assisted or controlled ventilation with oxygen. Cardiovascular function should be supported by administering pressor agents and intravenous fluids.
In dogs, doses greater than 9 mg/kg administered at a rate of 2 mg/s may cause cyanosis of the mucous membranes. Mydriasis may also be observed upon overdose. Cyanosis and mydriasis serve as an indication that supplemental oxygen is necessary. At doses above 16.5 mg/kg administered at a rate of 2 mg/s, apnoea lasting longer than 90 seconds has been reported. At doses of 20 mg/kg and above administered at a rate of 0.5 mg/s, death has been reported.
In dogs, repeated infusions of 0.6-0.7 mg/kg/min for approximately 1 hour per day for 14 consecutive days resulted in an increase in heart rate and mean arterial blood pressure, while decreases in red blood cell count, haemoglobin and haematocrit were noted. Although the animals were mechanically ventilated, there was evidence of respiratory acidosis, likely due to depression of respiratory centres resulting in insufficient alveolar ventilation and CO_2 accumulation.
Death from apnoea has been reported in a cat subsequent to injection of 19.5 mg/kg, administered as a single dose.

Incompatibilities:
Do not mix with other veterinary medicinal products, with the exception of dextrose 5% intravenous infusion or sodium chloride 0.9% intravenous infusion.

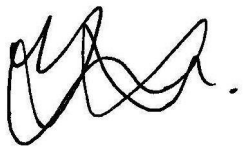
13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product 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

Colourless Type I glass vials of 20 ml, 50 ml and 100 ml closed with a coated bromobutyl rubber stopper and aluminium cap in a carton box.
Not all pack sizes may be marketed.



Approved: 07 September 2023