Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Active substance:
Propofol 10.0 mg

Excipient(s):
For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Emulsion for injection/infusion.
White or almost white homogeneous emulsion.

4 CLINICAL PARTICULARS

4.1 Target Species

Dogs and cats

4.2 Indications for use, specifying the target species

- 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.

4.3 Contraindications

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

4.4 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.

4.5 Special precautions for use

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 4.8.
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.

4.6 Adverse reactions (frequency and seriousness)

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 4.5. 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).

4.7 Use during pregnancy, lactation or lay

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, exposure (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.

4.8 Interaction with other medicinal products and other forms of interactions

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 4.9.
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 4.5.
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 anaesthesia.

4.9 Amounts to be administered and administration route

For intravenous administration.
Shake the vial gently but thoroughly before opening. See section 4.4.

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 4.8.
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 4.8 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.

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

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.

4.11 Withdrawal period(s)

Not applicable

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anaesthetics, general
ATC Vet Code: QN01AX10

5.1 Pharmacodynamic properties

Propofol is a general anaesthetic characterised by rapid onset and short duration of anaesthesia. Recovery from anaesthesia is usually rapid.
Propofol primarily acts by enhancing the inhibitory synaptic neurotransmission mediated by GABA (gamma-aminobutyric acid) through binding to the GABA type A ($GABA_A$) receptor. However, the glutaminergic and noradrenergic neurotransmitter systems are also thought to have a role in mediating the effects of propofol.

5.2 Pharmacokinetic particulars

After intravenous injection, blood concentrations of propofol are characterised by a rapid distribution phase, elimination of drug from the body and a slower redistribution phase from a deep compartment. This first phase, with a distribution half-life of approximately 10 min, is clinically relevant, since recovery from anaesthesia occurs subsequent to the redistribution of propofol from the brain. The terminal phase is considered to represent the slow release of the drug from poorly vascularised tissues, which is of little relevance to its practical use. In dogs, no accumulation of blood levels has been observed after repeated daily dosing. Generally, clearance is higher in dogs than in cats, although breed differences exist in dogs, probably due to differences in metabolism. In dogs, clearance is higher than hepatic blood flow, suggesting the presence of extrahepatic metabolism. However, clearance is reduced during prolonged infusion (4h), most likely caused by a reduction in hepatic blood flow. The volume of distribution is high in both dogs and cats.
Propofol is highly bound to plasma protein (96-98%).
Clearance of the drug occurs through hepatic metabolism followed by renal elimination of the conjugated metabolites. A small amount is excreted in the faeces.
Drug accumulation has not been evaluated in cats. However, based on available pharmacokinetic data, it is likely that drug accumulation occurs in this species upon repeated daily dosing.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Egg phospholipids for injection
Glycerol
Soya-bean oil refined
Sodium hydroxide (for pH adjustment)
Water for injections
Nitrogen

6.2 Major incompatibilities

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

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years
Shelf life after first opening the immediate packaging: use immediately

6.4 Special precautions for storage

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.

6.5 Nature and composition of immediate packaging

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.

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

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

7 MARKETING AUTHORISATION HOLDER

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

8 MARKETING AUTHORISATION NUMBER(S)

VPA22622/034/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28 June 2019

10 DATE OF REVISION OF THE TEXT

April 2020