NDC: 11695-2800-1
Each mL contains 10 mg propofol
NADA 141-070, Approved by FDA

For Animals Only

HENRY SCHEIN® ANIMAL HEALTH

PropoThesia™

(propofol injectable emulsion)

Anesthetic Injection

Each mL contains 10 mg propofol
NADA 141-070
Emulsion for intravenous use in dogs and cats.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: PropoThesia™ (propofol) injection is a sterile, nonpyrogenic emulsion containing 10 mg/mL of propofol suitable for intravenous administration. Propofol is chemically described as 2,6-diisopropylphenol and has a molecular weight of 178.28. Propofol is very slightly soluble in water and is therefore formulated as a white, oil-in-water emulsion. Each mL contains propofol (10 mg), soybean oil (100 mg), glycerol (22.5 mg), egg yolk phospholipid (12 mg) and sodium metabisulfite (0.25 mg), with sodium hydroxide to adjust the pH. The propofol emulsion is isotonic and has a pH of 4.5-6.6.

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INDICATIONS: PropoThesia™ (propofol) is an anesthetic injection for use in dogs and cats as follows:

1. As a single injection to provide general anesthesia for short procedures.
2. For induction and maintenance of general anesthesia using incremental doses to effect.
3. For induction of general anesthesia where maintenance is provided by inhalant anesthetics.

Induction of general anesthesia will usually be observed within 30 to 60 seconds after the end of administration (administration should take 60 to 90 seconds). The doses for induction and maintenance vary depending upon species and preanesthetics. The duration of anesthesia varies depending upon species, dose, and preanesthetics.

In dogs, the duration of anesthesia following the recommended induction dose (5.5 to 7.0 mg/kg without premedication) is generally 5 to 7 minutes. The duration of anesthesia after maintenance doses varies from 2 to 6 minutes following 1.1 mg/kg to 6 to 10 minutes following 3.3 mg/kg. Full standing recovery is generally observed within 10 to 20 minutes after the end of anesthesia, regardless of the duration of anesthesia. Recovery may be delayed in sighthounds or if preanesthetics are administered.

In cats, the duration of anesthesia following the recommended induction dose (8.0 to 13.2 mg/kg without premedication) is generally 5 to 12 minutes. The duration of anesthesia after maintenance doses varies from 5 to 7 minutes following 1.1 mg/kg to 12 to 18 minutes following 4.4 mg/kg. Full standing recovery is generally observed within 30 to 45 minutes after the end of anesthesia, regardless of the duration of anesthesia. Recovery may be delayed if preanesthetics are administered.

DOSAGE AND ADMINISTRATION: Shake the vial thoroughly before opening. PropoThesia™ injection contains no antimicrobial preservatives. Strict aseptic techniques must always be maintained during handling since the vehicle is capable of supporting rapid growth of microorganisms.

Failure to follow aseptic handling procedures may result in microbial contamination causing fever, infection/sepsis, and/or other life-threatening illness. Do not use if contamination is suspected.

PropoThesia™ injection should be prepared for use just prior to initiation of each individual anesthetic procedure. The vial rubber stopper should be disinfected using 70% isopropyl alcohol. The entire contents of the vial should be drawn into sterile syringes immediately after vials are opened. Administration should commence promptly and be completed within 6 hours after the vials are opened. Any unused product should be discarded within 6 hours. Administer by intravenous injection only.

The emulsion should not be mixed with other therapeutic agents or injected into containers of infusion fluids prior to administration.

INDUCTION OF GENERAL ANESTHESIA:

For induction, PropoThesia™ injection should be titrated against the response of the patient over approximately 60 to 90 seconds or until clinical signs show the onset of anesthesia.

If PropoThesia™ injection is injected too slowly (greater than 90 seconds), an inadequate plane of anesthesia can occur. If this occurs, an additional low dose (1.1 mg/kg) of propofol may be administered to facilitate intubation or the transition to inhalant maintenance anesthesia.

The average induction dose ranges and dosage rates for healthy dogs given propofol alone, or when propofol is preceded by a premedicant, are indicated in the following table (the Table is for guidance only; in practice, the dose should be based upon patient response):

Induction Dosage Guidelines for Dogs

Preanesthetic	Propofol Induction Dose		Propofol Rate of Administration		
	mg/kg	mg/lb	Seconds	mg/kg/min	mL/kg/min
None	5.5-7.0	2.5-3.2	60-90	3.7-7.0	0.37-0.70
Acepromazine	4.0-4.4	1.8-2.0	60-90	2.7-4.4	0.27-0.44
Xylazine	2.2-3.3	1.0-1.5	60-90	1.5-3.3	0.15-0.33
Oxymorphone	2.2-3.3	1.0-1.5	60-90	1.5-3.3	0.15-0.33
Medetomidine	2.2-2.8	1.0-1.3	60-90	1.5-2.8	0.15-0.28

The required dose of tranquilizers, sedatives, or analgesics administered as preanesthetic medications (listed below) may be lower than the label directions for their use as a single medication[1].

Acepromazine	0.03-0.1	mg/kg	IM, SC, IV
Xylazine	0.25-0.5	mg/kg	IV
Xylazine	0.5-1.0	mg/kg	IM, SC
Oxymorphone	0.1-0.2	mg/kg	IM, SC, IV
Medetomidine	5.0-10.0	µg/kg	IM

The use of the drugs listed above as preanesthetics for dogs markedly reduces propofol requirements. As with other sedative hypnotic agents, the amount of phenothiazine, opioid, and/or alpha$_2$-agonist premedication will influence the response of the patient to an induction dose of PropoThesia™ injection. The induction dose will also be influenced by the interval between the administration of premedication and induction, and by the rate of administration of propofol.

The average induction dose ranges and dosage rates for healthy cats given propofol alone, or when propofol is preceded by a premedicant, are indicated in the following table (the Table is for guidance only; in practice, the dose should be based upon patient response):

Induction Dosage Guidelines for Cats

Preanesthetic	Propofol Induction Dose		Propofol Rate of Administration		
	mg/kg	mg/lb	Seconds	mg/kg/min	mL/kg/min
None	8.0-13.2	3.6-6.0	60-90	5.3-13.2	0.53-1.32
Acepromazine	8.0-13.2	3.6-6.0	60-90	5.3-13.2	0.53-1.32
Butorphanol	8.0-13.2	3.6-6.0	60-90	5.3-13.2	0.53-1.32
Oxymorphone	8.0-13.2	3.6-6.0	60-90	5.3-13.2	0.53-1.32
Xylazine	7.0-12.0	3.2-5.5	60-90	4.7-12.0	0.47-1.20

The required dosage of tranquilizers, sedatives, or analgesics administered as preanesthetic medications (listed below) may be lower than the label directions for their use as a single medication[1,8,9].

Acepromazine	0.03-0.1	mg/kg	IM, SC, IV
Butorphanol	0.1-0.4	mg/kg	IM, SC
Oxymorphone	0.1-0.4	mg/kg	IM, SC, IV
Xylazine	0.25-0.5	mg/kg	IV
Xylazine	0.5-1.0	mg/kg	IM, SC

The use of the drugs listed above as preanesthetics for cats may reduce propofol requirements. As with other sedative hypnotic agents, the amount of phenothiazine, opioid and/or alpha$_2$-agonist premedication will influence the response of the patient to an induction dose of PropoThesia™ injection. The induction dose will also be influenced by the interval between the administration of premedication and induction, and by the rate of administration of propofol.

MAINTENANCE OF GENERAL ANESTHESIA

A. Intermittent Propofol Injections: Anesthesia can be maintained by administering propofol in intermittent IV injections. Clinical response will be determined by the amount, the rate of administration, and the frequency of maintenance injections. The following Tables are provided for guidance:

Maintenance Dosage Guidelines for Dogs

Preanesthetic	Propofol Maintenance Dose		Propofol Rate of Administration		
	mg/kg	mg/lb	Seconds	mg/kg/min	mL/kg/min
None	1.1-3.3	0.5-1.5	30-60	1.1-3.3	0.11-0.33
Acepromazine	1.1	0.5	30-60	1.1-2.2	0.11-0.22
Xylazine	1.1	0.5	30-60	1.1-2.2	0.11-0.22
Oxymorphone	1.1	0.5	30-60	1.1-2.2	0.11-0.22
Medetomidine	1.1	0.5	30-60	1.1-2.2	0.11-0.22

Repeated maintenance doses of propofol do not result in increased recovery times, indicating that the anesthetic effects of propofol are not cumulative in dogs.

Maintenance Dosage Guidelines for Cats

Preanesthetic	Propofol Maintenance Dose		Propofol Rate of Administration		
	mg/kg	mg/lb	Seconds	mg/kg/min	mL/kg/min
None	1.1-4.4	0.5-2.0	30-60	1.1-4.4	0.11-0.44
Acepromazine	1.1-4.4	0.5-2.0	30-60	1.1-4.4	0.11-0.44
Butorphanol	1.1-4.4	0.5-2.0	30-60	1.1-4.4	0.11-0.44
Oxymorphone	1.1-4.4	0.5-2.0	30-60	1.1-4.4	0.11-0.44
Xylazine	1.1-2.2	0.5-1.0	30-60	1.1-2.2	0.11-0.22
Acepromazine/Butorphanol	1.1-3.3	0.5-1.5	30-60	1.1-3.3	0.11-0.33
Acepromazine/Oxymorphone	1.1-3.3	0.5-1.5	30-60	1.1-3.3	0.11-0.33

Repeated maintenance doses of propofol may result in slightly increased recovery times, indicating that the anesthetic effects of propofol may be cumulative in cats.

B. Maintenance by Inhalant Anesthetics: Clinical trials using propofol have shown that it may be necessary to use a higher initial concentration of the inhalant anesthetic than is usually required following induction using barbiturate anesthetics, due to rapid recovery from PropoThesia™ injection.

OVERDOSAGE

Rapid administration or accidental overdosage of PropoThesia™ injection may cause neurologic and cardiopulmonary depression. Respiratory arrest (apnea) may be observed. In cases of respiratory depression, stop drug administration, establish a patent airway, and initiate assisted or controlled ventilation with oxygen. Cardiovascular depression should be treated with plasma expanders, pressor agents, antiarrhythmic agents or other techniques as appropriate for the observed abnormality.

In feline safety studies using healthy cats and elevated doses of propofol, unexplained decreases in albumin, globulin, and total protein values were noted. Increases in bile acids and triglycerides were also noted and were probably due to the lipid content of the drug formulation. These transient changes were not clinically significant in healthy cats.

CONTRAINDICATIONS

PropoThesia™ injection is contraindicated in dogs and cats with a known hypersensitivity to propofol or its components, or when general anesthesia or sedation are contraindicated.

WARNINGS:

Induction of anesthesia with PropoThesia™ injection is frequently associated with apnea and respiratory depression. Hypotension and oxygen desaturation can occur also, especially following rapid bolus administration. Apnea is observed less frequently following maintenance doses of PropoThesia™ injection when given as the sole maintenance agent, or when a maintenance dose is administered during inhalant anesthesia.

When using PropoThesia™ injection, patients should be continuously monitored and facilities for the maintenance of a patent airway, artificial ventilation, and oxygen supplementation must be immediately available. The clinical use of propofol without available supplemental oxygen and artificial ventilation has not been adequately evaluated and is not recommended.

PRECAUTIONS:

1. PropoThesia™ injection contains no antimicrobial preservatives. Strict aseptic techniques must always be maintained during handling since the vehicle is capable of supporting rapid growth of microorganisms. Failure to follow aseptic handling procedures may result in microbial contamination causing fever, infection/sepsis, and/or other life-threatening illness. Do not use if contamination is suspected.
2. When using PropoThesia™ injection, patients should be continuously monitored, and facilities for the maintenance of a patent airway, artificial ventilation, and oxygen supplementation must be immediately available. The clinical use of propofol without available supplemental oxygen and artificial ventilation has not been adequately evaluated and is not recommended.
3. Anesthesia effects: Careful monitoring of the patient is necessary when using PropoThesia™ injection as a maintenance anesthetic due to the possibility of rapid arousal. Apnea may occur following maintenance doses of PropoThesia™ injection.

   Following induction, additional PropoThesia™ injection at the lower maintenance dose may be needed to complete the transition to inhalant maintenance anesthesia due to rapid recovery from propofol. Doses administered during the transition to inhalant anesthesia or during inhalant maintenance anesthesia may result in apnea.
4. Physiological effects: During induction of anesthesia, mild hypotension and increased heart rate may occur when PropoThesia™ injection is used alone.
5. Premedicants: Premedicants may increase the anesthetic or sedative effect of PropoThesia™ injection and result in more pronounced changes in systolic, diastolic and mean arterial blood pressures. The use of ketamine (an approved compound for restraint in cats) is not recommended as a preanesthetic prior to propofol due to an increased number of patients experiencing apnea.
6. Breeding animals: Adequate data concerning the safe use of PropoThesia™ injection in pregnant, lactating, and breeding dogs and cats have not been obtained. Propofol crosses the placenta, and as with other general anesthetic agents, the administration of propofol may be associated with neonatal depression.
7. Puppies and Kittens: The use of propofol has not been evaluated in puppies or kittens.
8. Compromised or debilitated dogs and cats: Doses may need adjustment for geriatric or debilitated patients. The administration of PropoThesia™ injection to patients with renal failure and/or hepatic failure has not been evaluated. As with other anesthetic agents, caution should be exercised in dogs or cats with cardiac, respiratory, renal or hepatic impairment, or in hypovolemic or debilitated dogs and cats.
9. Sighthounds: PropoThesia™ injection induction followed by inhalant anesthetic agents produced satisfactory anesthesia and recovery times in sighthounds. Propofol alone in 6 greyhounds and 7 non-grey hounds showed satisfactory, but longer recovery times in the greyhounds (averages of 47 and 18 minutes, respectively).[2] In a propofol pharmacokinetics study, greyhounds had higher propofol levels in plasma, a lower volume of distribution, slower total body clearance rates, and longer recovery times than did mixed-breed dogs. The elimination half-life was similar in both groups.[3]
10. Arrhythmogenicity: In one study in dogs, propofol increased myocardial sensitivity to the development of epinephrine-induced ventricular arrhythmias in a manner similar to other anesthetics.[4]
11. Consecutive day treatment: Heinz bodies increased dramatically in cats following repeat administration of propofol on consecutive days and were associated with decreases in RBC count and hematocrit. Large numbers of Heinz bodies can lead to hemolytic anemia.[5,6] In one study in cats, treatment with propofol once a day for 3 days led to a marked increase in Heinz bodies. Treatment for 5 or more consecutive days resulted in generalized malaise and/or facial edema; clinical signs of illness resolved within 24 to 48 hours after cessation of propofol.
12. Concurrent medication: No significant adverse interactions with commonly used drugs have been observed.
13. Perivascular administration: Perivascular administration does not produce local tissue reaction.

HUMAN USER SAFETY

Not for human use. Keep out of reach of children.

PropoThesia™ injection should be managed to prevent the risk of diversion, through such measures as restriction of access and the use of drug accountability procedures appropriate to the clinical setting. Rare cases of self-administration of propofol have been reported, including dose-related fatalities.

Preventive care should be taken to avoid self-administration; for example, use of a guarded needle until the moment of injection is recommended. Symptoms of self-administration may include cardiovascular and/or respiratory depression. Anaphylaxis to propofol may occur during its first use, especially in patients with a history of drug allergy.[7] In the event of accidental self-administration, seek medical attention immediately.

Contact of this product with skin, eyes, and clothes should be avoided. If contact occurs, skin and eyes should be liberally flushed with water for 15 minutes. If irritation develops and continues, consult a physician.

Initial arousal following propofol anesthesia can be extremely rapid. Caution should be used at this time in manipulations involving the mouth, such as removing an endotracheal tube.

ADVERSE REACTIONS:

The primary side effect of PropoThesia™ injection is respiratory depression and apnea. Apnea was observed in 20% of the dog cases in the clinical trial. Apnea was observed in 1.4% of the cat cases in the clinical trial. All apnea cases responded satisfactorily to oxygen supplementation and/or controlled ventilation.

Apnea lasting less than 1 minute in healthy dogs or cats may cause no harm. Animals breathing atmospheric air that become apneic may show signs of cerebral damage after 2 minutes. Animals breathing 100% oxygen that become apneic may not show signs of cerebral damage for 5 to 8 minutes.

Ventricular arrhythmias may occur secondary to hypoxia induced by apnea.

The primary side effect of PropoThesia™ injection in cats is paddling during recovery. Paddling was observed in 11% of the cat cases in the clinical trial.

Other transient side effects in dogs or cats are observed infrequently or rarely:

- **Respiratory:** panting, reverse sneezing, cyanosis
- **Musculoskeletal:** paddling during recovery, tremors, tenseness, movements, fasciculations
- **Cardiovascular:** bradycardia, hypotension, cyanosis, tachycardia, premature ventricular contractions
- **Central Nervous System:** excitation, opisthotonus, seizure
- **Injection Site:** pain during injection
- **Gastrointestinal:** emesis/retching
- **Other:** rubbing at face or nose during recovery, vocalization during recovery, chewing or licking the injection site during recovery.

CLINICAL PHARMACOLOGY: After a single dose, propofol blood level profiles are characterized by a rapid distribution phase and a rapid elimination phase. The liver is the main site of metabolism with the major portion of metabolites being excreted in urine. No change in pharmacokinetics occurs after multiple daily dosing in dogs. Concomitant medication may affect the pharmacokinetics of either propofol or other medications.

In dogs, PropoThesia™ injection has been used in association with acepromazine, atropine, glycopyrrolate, halothane, isoflurane, medetomidine, oxymorphone, and xylazine. No pharmacological incompatibility has been encountered.

In cats, PropoThesia™ injection has been used in association with acepromazine, atropine, glycopyrrolate, butorphanol, oxymorphone, xylazine, and halothane. No pharmacological incompatibility has been encountered.

Heidi Rudolph

HSAH Marketing Approval: 4/21/17

Corrina Paz

HSAH Regulatory

To report suspected adverse drug events, call 1-855-724-3461.

To obtain a copy of the Safety Data Sheet (SDS) or for technical assistance go to www.henryscheinvet.com.

For additional information about adverse drug experience reporting for animal drugs, Contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinarySafetyHealth.

STORAGE:

Store between 4 – 25°C (40-77°F). Do not freeze.

Shake well before use. Discard opened vial with care. Within 6 hours after opening, any withdrawn unused product should be discarded safely.

HOW SUPPLIED:

PropoThesia™ injection is supplied in cartons of five-20 mL vials containing 10 mg propofol per mL.

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