synthadon® 10mg/ml

Solution for Injection for Cats and Dogs

Methadone hydrochloride

Statement of the active substances and other ingredients

Description:

A clear colourless to pale yellow solution.

Each ml contains:

Active substance:

Methadone hydrochloride (equivalent to methadone 8.9mg)	10mg

Excipients:

Methyl parahydroxybenzoate (E218)	1.0mg
Propyl parahydroxybenzoate	0.2mg

Indications

Analgesia in dogs and cats.

Premedication for general anaesthesia or neuroleptanalgesia in dogs and cats in combination with a neuroleptic drug.

Contraindications

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

Do not use in animals with advanced respiratory failure.

Do not use in animals with severe liver and renal dysfunction.

Adverse reactions

Cats: Respiratory depression may be seen. Mild excitatory reactions have been observed: lip licking, vocalisation, urination, defaecation, mydriasis, hyperthermia and diarrhoea. Hyperalgesia has been reported. All reactions were transient.

Dogs: Respiratory depression may be seen. Mild reactions have been observed: panting, lip licking, salivation, vocalisation, irregular breathing, hypothermia, fixed stare and body tremors. Occasional urination and defaecation can be seen within the first hour post-dose. All reactions were transient.

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

Target species

Dogs and cats.

Dosage for each species, route(s) and method of administration

Analgesia

Dogs: 0.5 to 1mg methadone hydrochloride per kg bodyweight, subcutaneously, intramuscularly or intravenously (corresponding to 0.05 to 0.1ml/kg).

Cats: 0.3 to 0.6mg methadone hydrochloride per kg bodyweight, intramuscularly (corresponding to 0.03 to 0.06ml/kg).

To ensure accuracy of dosing, an appropriately calibrated syringe should be used to administer the product.

As the individual response to methadone is varied, and depends partly on the dosage, the age of the patient, individual differences in pain sensitivity and general condition, the optimal dosing regimen should be individually based. In dogs onset of action is 1 hour following subcutaneous administration, approximately 15 minutes following intramuscular injection and within 10 minutes following intravenous injection. Duration of effect is approximately 4 hours following intramuscular or intravenous administration. In cats onset of action is 15 minutes following administration and the duration of effect is 4 hours in average. The animal should be examined regularly to assess if additional analgesia is subsequently required.

Premedication and/or neuroleptanalgesia

Dogs:

- Methadone HCl 0.5-1mg/kg, IV, SC or IM.

Combinations e.g.:

- Methadone HCl 0.5mg/kg, IV + e.g., midazolam or diazepam.
  Induction with propofol, maintenance on isoflurane in oxygen.
- Methadone HCl 0.5mg/kg + e.g., acepromazine.
  Induction with thiopentone or propofol to effect, maintenance on isoflurane in oxygen or induction with diazepam and ketamine.
- Methadone HCl 0.5-1.0mg/kg, IV or IM + α_2-agonist (e.g., xylazine or medetomidine).
  Induction with propofol, maintenance with isoflurane in combination with fentanyl or total intravenous anaesthesia (TIVA) protocol: maintenance with propofol in combination with fentanyl.

TIVA protocol: induction propofol, to effect. Maintenance with propofol and remifentanil.

Chemical-physical compatibility has only been demonstrated for dilutions 1:5 with the following solutions for infusion: sodium chloride 0.9%, Ringer solution and glucose 5%.

Cats:

- Methadone HCl 0.3 to 0.6mg/kg, IM:
  - Induction with benzodiazepine (e.g., midazolam) and dissociative (e.g., ketamine);
  - With a tranquilizer (e.g., acepromazine) and NSAID (meloxicam) or sedative (e.g., α_2-agonist);
  - Induction with propofol, maintenance with isoflurane in oxygen.

Doses depend on the desired degree of analgesia and sedation, desired duration of effect and the concurrent use of other analgesics and anaesthetics.

When used in combination with other products, lower dosages can be used.

For safe use with other pharmaceuticals, reference must be made to the relevant product literature.

The stopper should not be punctured more than 20 times.

Special storage precautions

Keep out of the sight and reach of children.

Store in the original package in order to protect from light.

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

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.

Shelf-life after first opening of the immediate packaging: 28 days.

Shelf-life after dilution according to directions: 4 hours, protected from light.

When the container is broached (opened) for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the label.

Special warnings

Special precautions for use in animals

Methadone may occasionally cause respiratory depression and, as with other opioid drugs, care should be taken when treating animals with impaired respiratory function or animals that are receiving drugs that can cause respiratory depression. To ensure safe use of the product, treated animals should be monitored regularly, including examination of heart rate and respiratory rate.

As methadone is metabolised by the liver, its intensity and duration of action may be affected in animals with impaired liver function. In case of renal, cardiac or hepatic dysfunction or shock, there may be greater risk associated with the use of the product. The safety of methadone has not been demonstrated in dogs less than 8 weeks and cats less than 5 months of age. The effect of an opioid on head injury is dependent on the type and severity of the injury and the respiratory support supplied. Safety has not been fully evaluated in clinically compromised cats. Due to the risk of excitation, repeated administration in cats should be used with care. Use in the above mentioned cases should be in accordance with a benefit/risk assessment by the responsible veterinarian.

Due to the variable individual response to methadone, animals should be regularly monitored to ensure sufficient efficacy for the desired effect duration. Use of the product must be preceded by a thorough clinical examination. In cats pupil dilatation is seen long after the analgesic effect has disappeared. It is therefore not an adequate parameter to assess clinical efficacy of the administered dose.

Greyhounds may require higher doses than other breeds to achieve efficacious plasma levels.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Methadone can cause respiratory depression following spillage on the skin or accidental self-injection. Avoid skin, eyes and mouth contact and wear impermeable gloves when handling the product. In case of spilling on the skin or splashing in the eyes, wash immediately with large amounts of water. Remove contaminated clothes.

People with known hypersensitivity to methadone should avoid contact with the veterinary medicinal product.

Methadone has the potential to cause stillbirths. Pregnant women are advised not to handle the product.

In the case of accidental self-injection, seek medical advice immediately and show the package insert to the physician but DO NOT DRIVE as sedation may occur.

ADVICE TO DOCTORS: Methadone is an opioid whose toxicity may cause clinical effects including respiratory depression or apnoea, sedation, hypotension and coma. When respiratory depression occurs controlled ventilation should be installed. Administration of the opioid antagonist naloxone to reverse the symptoms is recommended.

Pregnancy, lactation

Methadone diffuses across the placenta.

Studies in laboratory animals have shown adverse effects on reproduction.

The safety of the product during pregnancy and lactation has not been assessed in target species.

The use of the product is not recommended during pregnancy.

Interaction with other medicinal products and other forms of interaction

For concurrent use with neuroleptics refer to the 'Dosage, routes and method of administration' section.

Methadone can potentiate the effects of analgesics, central nervous system inhibitors and substances that cause respiratory depression. Concomitant or subsequent use of the veterinary medicinal product with buprenorphine may lead to lack of efficacy.

Overdose (symptoms, emergency procedures, antidotes)

A 1.5-fold overdose resulted in the effects described in the 'Adverse reactions' section.

Cats: In case of overdoses (>2mg/kg) the following signs can be observed: increased salivation, excitation, hind leg paralysis and loss of righting reflex. Seizures, convulsion and hypoxia were also recorded in some cats. A dose of 4mg/kg could be fatal in cats. Respiratory depression has been described.

Dogs: Respiratory depression has been described.

Methadone can be antagonized by naloxone. Naloxone should be given to effect. A starting dose of 0.1mg/kg intravenously is recommended.

Incompatibilities

Do not mix with any other veterinary medicinal product except the infusion solutions indicated in the 'Dosage, routes and method of administration' section.

The product is incompatible with injection fluids containing meloxicam or any other non-aqueous solution.

Special precautions for the disposal of unused product or waste material, if any

Medicines should not be disposed of via wastewater or household waste. Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

Date on which the package leaflet was last approved: December 2015

Pack sizes

Cardboard box containing 1 vial of 5, 10, 20, 25, 30 or 50ml. Not all pack sizes may be marketed.

Marketing Authorisation Holder:
Le Vet Beheer B.V., Wilgenweg 7,
3421 TV Oudewater, The Netherlands

Manufacturer responsible for batch release:
Produlab Pharma B.V., Forellenweg 16
4941 SJ Raamsdonksveer, The Netherlands

Distributed by:
Animalcare Ltd, 10 Great North Way, York, YO26 6RB, UK

For animal treatment only.

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