comfortan®

With Comfortan®, improved analgesia and anaesthesia management is now within your reach

- First EU veterinary authorised methadone HCl 10 mg/ml
- Strong opioid analgesia
- Ability to redose until the desired effect is reached
- Dose dependant sedation
- Minimal cardiovascular and respiratory effects
- Quick onset: IV < 10 min, IM < 15 min
- Optimal duration of action: approx. 4 hours
- Solution for injection in dogs
- 10 ml multidose vial
- 3 year shelf life
- 28 days shelf life after opening

For more further information about Comfortan®, please contact Eurovet on 01223 257933

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1. NAME OF THE VETERINARY MEDICAL PRODUCT
Comfortan® 10 mg/ml solution for injection for dogs.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each ml contains:
- Active substance: Methadone HCl 0.5 mg/kg equivalent to methadone hydrochloride 10 mg
- Excipients:
  - Methylparaben (E218) 1.0 mg
  - Propylparaben (E216) 0.2 mg
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Solution for injection.
A clear colourless to pale yellow solution.

4. CLINICAL PARTICULARS
4.1 Target species
Dogs.

4.2 Indications for use, specifying the target species

4.3 Contra-indications
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.

4.4 Special warnings for each target species
Due to the variable individual response to methadone, animals should be regularly monitored to ensure sufficient analgesia or the desired effect duration. Use of the product must be preceded by a thorough clinical examination. Greyhounds may require higher doses than other breeds to achieve effective plasma levels.

4.5 Special precautions for use
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 may cause respiratory depression. To ensure safe use of the product, treated animals should be monitored regularly, including examination of heart rate and respiratory rate.

4.6 Adverse reactions (frequency and seriousness)
Respiratory depression may be seen. Mild reactions have been observed: panting, lip licking, and occasional pruritus.

4.7 Premedication and/or neuroleptanalgesia
Induction with thiopentone or propofol to effect, maintenance on isoflurane in oxygen.

4.8 Interaction with other medicinal products and other forms of interaction

4.9 Amounts to be administered and administration route

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

4.11 Withdrawal period
Not applicable.

5. PHARMACOLOGICAL PARTICULARS
Pharmacotherapeutic group: Diphenylpropylamine derivatives. ATCvet code: N02AC 02

5.1 Pharmacodynamic properties
Methadone is a structurally unrelated to other opium-derived analgesics and exists as a racemic mixture. Each enantiomer has a separate mode of action; the d-isomer noncompetitively antagonizes the NMDA receptor and inhibits norepinephrine uptake; the l-isomer is a µ-opioid receptor agonist. There are two subtypes µ1 and µ2. The analgesic effects of methadone are believed to be mediated by both the µ1 and µ2 subtypes, whereas the µ2 subtype appears to mediate respiratory depression and inhibition of gastrointestinal motility. The µ1 subtype produces supraspinal analgesia and the µ2 receptors produce spinal analgesia.
Methadone has the ability to produce profound analgesia. It can also be used for premedication and it can assist in the production of sedation in combination with tranquillizers or sedatives. The duration of effects may vary from 1.5 to 6.5 hours. Opioids produce a dose-dependent respiratory depression. Very high doses may result in convulsions.

5.2 Pharmacokinetic Particulars
Each dogs methadone is absorbed very rapidly (Tmax 0.1-0.5 min) following intramuscular injection of 0.3 to 0.5 mg/kg. Tmax tends to be later at the higher dose levels indicating that an increase in dose tends to delay the absorption phase. The rate and extent of systemic exposure of dogs to methadone appears to be characterised by dose-independent (linear) kinetics following intramuscular administration. The bioavailability is high and ranges between 65.4 ± 100 %, with a mean estimate of 49 %. Following subcutaneous administration of 0.4 mg/kg methadone is absorbed slower (Tmax 15 – 140 min) and bioavailability is 67.2 ± 22 %. In dogs volume of distribution at steady state (Vss) was 44.4 ± 5.1 L/kg in males and females respectively. The terminal half-life in the range 0.9 to 2.2 hours following intramuscular administration, and is independent of dose and sex. The terminal half-life fails to significantly change following intravenous administration. The terminal half-life ranges from 6.4 to 10 hours following subcutaneous administration. Total plasma clearance (CL) of methadone following intravenous administration is high 39.2 to 3.6 L/H/kg or ca 70 % to 85 % of the cardiac plasma output in dogs (4.18 L/min).

Methadone is extensively protein bound (60 to 90 %). The opioids are lipophilic and weak bases. These properties make them favourable for extravascular administration. Consequently, opioids have a large volume of distribution, which greatly exceeds total body water. A small amount (3 to 4 % in the dogs) of the administered dose is excreted unchanged in the urine; the remainder is metabolised in the liver and subsequently excreted.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Methadone hydrochloride (E 218) Propyl paraben (E 216) Sodium chloride Hydrochloric acid (for pH adjustment)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
Not applicable.

6.4 Special precautions for storage

6.5 Nature and composition of immediate packaging
-Vials of uncoated glass type I (Ph. Eup.) filled with 5, 10, 20, 25, 30 and 50 ml
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7. MARKETING AUTHORIZATION HOLDER
Eurovet Animal Health B.V.
Handelsweg 25
5553 AL Bälden
The Netherlands

8. MARKETING AUTHORIZATION NUMBER
VM 16849/4022

9. DATE OF FIRST AUTHORISATION
March 2011

10. DATE OF REVISION OF THE TEXT
March 2011

PROHIBITION OF SALE, SUPPLY AND/OR USE
This product falls within the regime of controlled drugs Schedule II.