**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Synthadon 5 mg/ml solution for injection for cats and dogs

Synthadon vet. 5 mg/ml solution for injection for cats and dogs (NO, SE, FI, DK, IS, EE)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

**Active substance:**
Methadone hydrochloride 5 mg
equivalent to methadone 4.47 mg

**Excipients:**

| **Qualitative composition of excipients and other constituents** | **Quantitative composition if that information is essential for proper administration of the veterinary medicinal product** |
|---|---|
| Methyl parahydroxybenzoate (E218) | 1.0 mg |
| Propyl parahydroxybenzoate (E216) | 0.2 mg |
| Sodium chloride | |
| Sodium hydroxide (for pH adjustment) | |
| Hydrochloric acid (for pH adjustment) | |
| Water for injections | |

A clear colourless to pale yellow solution.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Dogs and cats.

### 3.2 Indications for use for each target species

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

### 3.3 Contraindications

Do not use in 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.

### 3.4 Special warnings

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 veterinary medicinal 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.

### 3.5 Special precautions for use

Special precautions for safe use in the target species:
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 veterinary medicinal 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 veterinary medicinal 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.

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 personal protective equipment consisting of impermeable gloves should be worn when handling the veterinary medicinal 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 veterinary medicinal product.
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.
To the physician:
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 initiated. Administration of the opioid antagonist naloxone to reverse the symptoms is recommended.

Special precautions for the protection of the environment:
Not applicable.

### 3.6 Adverse events

Cats:

| | |
|---|---|
| Very common<br>(>1 animal / 10 animals treated): | Lip licking[1,2], diarrhoea[1,2], involuntary defecation[1,2]<br>Respiratory depression[2]<br>Vocalisation[1,2]<br>Urination[1,2]<br>Mydriasis[1,2]<br>Hyperthermia[1,2]<br>Hypersensitivity to pain[2] |

[1]Mild
[2]Transient

Dogs:

| | |
|---|---|
| Very common<br>(>1 animal / 10 animals treated): | Respiratory depression[2], panting[1,2], irregular breathing[1,2]<br>Bradycardia[2]<br>Lip licking[1,2], hypersalivation[1,2]<br>Vocalisation[1,2]<br>Hypothermia[1,2]<br>Staring[1,2], Tremor[1,2] |
| Very rare<br>(<1 animal / 10,000 animals treated, including isolated reports): | Urination[2,3]<br>Involuntary defecation[2,3] |

[1]Mild
[2]Transient
[3]Within first hour post dose

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

### 3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:

Methadone diffuses across the placenta.
Studies in laboratory animals have shown adverse effects on reproduction.
The safety of the veterinary medicinal product has not been established during pregnancy or lactation.
The use is not recommended during pregnancy and lactation.

### 3.8 Interaction with other medicinal products and other forms of interaction

For concurrent use with neuroleptics refer to section 3.9.
Methadone can potentiate the effects of analgesics, central nervous system inhibiters and substances that cause respiratory depression. Concomitant or subsequent use of the veterinary medicinal product with buprenorphine may lead to lack of efficacy.

### 3.9 Administration routes and dosage

Dogs:
Subcutaneous, intramuscular or intravenous use.

Cats:
Intramuscular use.

To ensure accuracy of dosing, bodyweight should be accurately measured and an appropriately calibrated syringe should be used to administer the veterinary medicinal product.

**Analgesia**
Dogs: 0.5 to 1 mg methadone hydrochloride per kg bodyweight, subcutaneously, intramuscularly or intravenously (corresponding to 0.1 to 0.2 ml/kg)
Cats: 0.3 to 0.6 mg methadone hydrochloride per kg bodyweight, intramuscularly (corresponding to 0.06 to 0.12 ml/kg)

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 0.5-1 mg/kg, IV, SC or IM

Combinations e.g.:
- Methadone HCl 0.5 mg/kg, IV + e.g. midazolam or diazepam

Induction with propofol, maintenance on isoflurane in oxygen.

- Methadone HCl 0.5 mg/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 -1.0 mg/kg, IV or IM + α2-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 0.6 mg/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. α2-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.

### 3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

A 1.5 fold overdose resulted in the effects described in section 3.6.

Cats: In case of overdoses (>2 mg/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 4 mg/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 0.1 mg/kg intravenously is recommended.

### 3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

### 3.12 Withdrawal periods

Not applicable.

## 4. PHARMACOLOGICAL INFORMATION

### 4.1 ATCvet code: QN02AC90

### 4.2 Pharmacodynamics

Methadone is 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 reuptake; 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 tranquilizers 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.

### 4.3 Pharmacokinetics

In dogs methadone is absorbed very rapidly (Tmax 5-15 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 prolong 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 and 100%, with a mean estimate of 90 %. Following subcutaneous administration of 0.4 mg/kg methadone is absorbed slower (Tmax 15 – 140 min) and bioavailability is 79 ± 22%. In dogs volume of distribution at steady state (Vss) was 4.84 and 6.11 L/kg in males and females respectively. The terminal half-life is in the range 0.9 to 2.2 hours following intramuscular administration, and is independent of dose and sex. The terminal half-life may be slightly longer following intravenous administration. The terminal half-life ranges from 6.4 to 15 hours following subcutaneous administration. Total plasma clearance (CL) of methadone following intravenous administration is high 2.92 to 3.56 L/h/kg or ca 70% to 85% of the cardiac plasma output in dogs (4.18 L/h/kg).

In cats methadone is also rapidly absorbed following intramuscular injection (peak values occur at 20 min), however when the veterinary medicinal product is administered inadvertently subcutaneously (or in another poorly vascularised area) absorption will be slower. The terminal half-life is in the range of 6 to 15 hours. Clearance is medium to low with a mean (sd) value of 9.06 (3.3) ml/kg/min.

Methadone is extensively protein bound (60 to 90%). The opioids are lipophilic and weak bases. These physiochemical properties favour intracellular accumulation. Consequently, opioids have a large volume of distribution, which greatly exceeds total body water. A small amount (3 to 4% in the dog) of the administered dose is excreted unchanged in the urine; the remainder is metabolized in the liver and subsequently excreted.

## 5. PHARMACEUTICAL PARTICULARS

### 5.1 Major incompatibilities

Do not mix with any other veterinary medicinal product except the infusion solutions indicated in section 3.9.

The veterinary medicinal product is incompatible with injection fluids containing meloxicam or any other nonaqueous solution.

### 5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life after first opening the immediate packaging: 28 days
Shelf-life after dilution according to directions: 4 hours, protected from light

### 5.3 Special precautions for storage

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

### 5.4 Nature and composition of immediate packaging

Nature of container:
Clear colourless type I glass vial
Teflon coated bromobutyl rubber 20 mm stopper
Aluminium 20 mm cap

Pack size:
Cardboard box containing 1 vial of 5, 10, 20, 25, 30 or 50 mL

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater <or household waste>.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

## 6. NAME OF THE MARKETING AUTHORISATION HOLDER

Le Vet Beheer B.V.

## 7. MARKETING AUTHORISATION NUMBER(S)

## 8. DATE OF FIRST AUTHORISATION

## 9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

## 10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

**ANNEX III**

**LABELLING AND PACKAGE LEAFLET**

# A. LABELLING

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**Outer carton**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Synthadon 5 mg/ml solution for injection

## 2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

| | |
|---|---|
| Methadone hydrochloride | 5 mg |
| equivalent to methadone | 4.47 mg |

## 3. PACKAGE SIZE

5 ml
10 ml
20 ml
25 ml
30 ml
50 ml

## 4. TARGET SPECIES

Dogs and cats

## 5. INDICATIONS

## 6. ROUTES OF ADMINISTRATION

Dogs: subcutaneous, intramuscular or intravenous use.
Cats: intramuscular use.

## 7. WITHDRAWAL PERIODS

## 8. EXPIRY DATE

Exp. {mm/yyyy}
Once broached use within 28 days. Use by …

## 9. SPECIAL STORAGE PRECAUTIONS

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

## 10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

## 11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

## 12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

## 13. NAME OF THE MARKETING AUTHORISATION HOLDER

Le Vet Beheer B.V.

## 14. MARKETING AUTHORISATION NUMBERS

## 15. BATCH NUMBER

Lot {number}

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**5, 10, 20, 25, 30 or 50 ml vials**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Synthadon

## 2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Methadone hydrochloride 5 mg/ml

## 3. BATCH NUMBER

Lot {number}

## 4. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 28 days. Use by…

# B. PACKAGE LEAFLET

# PACKAGE LEAFLET

## 1. Name of the veterinary medicinal product

Synthadon 5 mg/ml solution for injection for cats and dogs

## 2. Composition

Each ml contains:

| | | |
|---|---|---|
| **Active substance**: | Methadone hydrochloride | 5 mg |
| | equivalent to methadone | 4.47 mg |
| **Excipients**: | Methyl parahydroxybenzoate (E218) | 1.0 mg |
| | Propyl parahydroxybenzoate (E216) | 0.2 mg |

A clear colourless to pale yellow solution.

## 3. Target species

Dogs and cats.

## 4. Indications for use

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

## 5. Contraindications

Do not use in 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.

## 6. Special warnings

Special warnings:
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 veterinary medicinal 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 for safe use in the target species:
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 veterinary medicinal 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 veterinary medicinal 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.

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 personal protective equipment consisting of impermeable gloves should be worn when handling the veterinary medicinal 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 veterinary medicinal product.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or label to the physician but DO NOT DRIVE as sedation may occur.
To the physician**:**
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 and lactation:
Methadone diffuses across the placenta.
Studies in laboratory animals have shown adverse effects on reproduction.
The safety of the veterinary medicinal product has not been established during pregnancy or lactation. The use is not recommended during pregnancy and lactation.

Interaction with other medicinal products and other forms of interaction:
For concurrent use with neuroleptics refer to section 8.
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:
A 1.5-fold overdose resulted in the effects described in section 7.

Cats: In case of overdoses (>2 mg/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 4 mg/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 0.1 mg/kg intravenously is recommended.

<Special restrictions for use and special conditions for use:>

Major incompatibilities:
Do not mix with any other veterinary medicinal product except the infusion solutions indicated in section 8.
The veterinary medicinal product is incompatible with injection fluids containing meloxicam or any other non-aqueous solution.

## 7. Adverse events

Cats:

| | |
|---|---|
| Very common<br>(>1 animal / 10 animals treated): | Lip licking[1,2], diarrhoea[1,2], involuntary defecation[1,2]<br>Respiratory depression[2]<br>Vocalisation[1,2]<br>Urination[1,2]<br>Mydriasis (dilated pupils)[1,2]<br>Hyperthermia (elevated body temperature)[1,2]<br>Hypersensitivity to pain[2] |

[1]Mild
[2]Transient

Dogs:

| | |
|---|---|
| Very common<br>(>1 animal / 10 animals treated): | Respiratory depression[2], panting[1,2], irregular breathing[1,2]<br>Bradycardia (slow heart rate)[2]<br>Lip licking[1,2], hypersalivation (increased salivation)[1,2]<br>Vocalisation[1,2]<br>Hypothermia (low body temperature)[1,2]<br>Staring[1,2], Tremor[1,2] |
| Very rare<br>(<1 animal / 10,000 animals treated, including isolated reports): | Urination[2,3]<br>Involuntary defecation[2,3] |

[1]Mild
[2]Transient
[3]Within first hour post dose

Reporting adverse events is important. It allows continuous safety monitoring of a product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder <or the local representative of the marketing authorisation holder> using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

## 8. Dosage for each species, routes and method of administration

Dogs:
Subcutaneous, intramuscular or intravenous use.

Cats:
Intramuscular use.

To ensure accuracy of dosing, bodyweight should be accurately measured and an appropriately calibrated syringe should be used to administer the veterinary medicinal product.

**Analgesia**
Dogs: 0.5 to 1 mg methadone hydrochloride per kg bodyweight, subcutaneously, intramuscularly or intravenously (corresponding to 0.1 to 0.2 ml/kg)
Cats: 0.3 to 0.6 mg methadone hydrochloride per kg bodyweight, intramuscularly (corresponding to 0.06 to 0.12 ml/kg)

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 0.5-1 mg/kg, IV, SC or IM

Combinations *e.g.*:
- Methadone HCl 0.5 mg/kg, IV + *e.g.*, midazolam or diazepam

Induction with propofol, maintenance on isoflurane in oxygen.

- Methadone HCl 0.5 mg/kg + *e.g.*, acepromazine

Induction with thiopentone or propofol to effect, maintenance on isoflurane in oxygen or induction with diazepam and ketamine

- Methadone HCl 0.5-1.0 mg/kg, IV or IM + $\alpha_2$-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 0.6 mg/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.*, $\alpha_2$-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.

## 9. Advice on correct administration

The stopper should not be punctured more than 20 times.

## 10. Withdrawal periods

Not applicable.

## 11. 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 carton and the label after Exp. The expiry date refers to the last day of that month.

Shelf-life after first opening 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 veterinary medicinal 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.

## 12. Special precautions for disposal

Medicines should not be disposed of via wastewater or <household waste>.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your <veterinary surgeon> <or> <pharmacist> how to dispose of medicines no longer required.

## 13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

## 14. Marketing authorisation numbers and pack sizes

Pack sizes: Cardboard box containing 1 vial of 5, 10, 20, 25, 30 or 50 mL.

Not all pack sizes may be marketed.

## 15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

## 16. Contact details

Marketing authorisation holder <and contact details to report suspected adverse reactions>:
Le Vet Beheer B.V.
Wilgenweg 7
3421 TV Oudewater
The Netherlands
<Tel. : +31 348 563434>

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

<Local representatives <and contact details to report suspected adverse reactions>:>

## <17. Other information>