

**ANNEX I**  
**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tralieve 50 mg/ml solution for injection for dogs

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

### Active substance:

Tramadol 43.9 mg  
(equivalent to 50 mg tramadol hydrochloride)

### Excipients:

Qualitative composition of excipients and other constituents	Quantitative composition if that information is essential for proper administration of the veterinary medicinal product
Benzyl alcohol (E1519)	10 mg
Sodium acetate trihydrate	
Hydrochloric acid, diluted (for pH adjustment)	
Sodium hydroxide (for pH adjustment)	
Water for injections	

Clear and colourless solution.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Dogs.

### 3.2 Indications for use for each target species

For the reduction of mild postoperative pain.

### 3.3 Contraindications

Do not use in animals with epilepsy.

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

Do not administer in conjunction with tricyclic antidepressants, monoamine oxidase inhibitors and serotonin reuptake inhibitors.

### 3.4 Special warnings

The analgesic effects of tramadol hydrochloride may be variable. This is thought to be due to individual differences in the metabolism of the drug to the primary active metabolite O-desmethytramadol. In some dogs (non-responders) this may result in the veterinary medicinal product failing to provide analgesia. Dogs should therefore be monitored regularly to ensure sufficient efficacy.

### 3.5 Special precautions for use

Special precautions for safe use in the target species:

Use with caution in dogs with renal or hepatic impairment. In dogs with hepatic impairment the metabolism of tramadol to the active metabolites may be decreased which may reduce the efficacy of the veterinary medicinal product. One of the active metabolites of tramadol is renally excreted and therefore in dogs with renal impairment the dosing regimen used may need to be adjusted. Renal and hepatic function should be monitored when using this veterinary medicinal product. See also section 3.8.

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

People with known hypersensitivity to tramadol or any of the excipients should avoid contact with the veterinary medicinal product.

The veterinary medicinal product may cause skin and eye-irritation. Avoid contact with the skin and eyes. Wash hands after use. In case of accidental eye exposure, rinse with clean water.

There is inadequate evidence available on the safety of tramadol in human pregnancy. Pregnant women and women of childbearing age should therefore take great care when handling this veterinary medicinal product and, in the event of exposure, seek medical advice immediately.

Tramadol may cause nausea and dizziness following accidental self-injection. If you develop symptoms following accidental exposure, seek medical advice and show the package leaflet or the label to the physician. However, DO NOT DRIVE as sedation may occur.

Special precautions for the protection of the environment:

Not applicable.

### 3.6 Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Hypersensitivity reaction*
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Vomiting, nausea

\*Treatment should be discontinued.

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:

Laboratory studies in mice and/or rats and rabbits have not produced any evidence of teratogenic, foetotoxic, maternotoxic effects.

Use only according to the benefit-risk assessment by the responsible veterinarian.

Lactation:

Laboratory studies in mice and/or rats and rabbits have not produced any evidence of adverse effects in the peri- and postnatal development of offspring.

Use only according to the benefit-risk assessment by the responsible veterinarian.

### Fertility:

In laboratory studies in mice and/or rats and rabbits, the use of tramadol at therapeutic doses did not adversely affect reproductive performance and fertility in males and females.

Use only according to the benefit-risk assessment by the responsible veterinarian.

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

Concomitant administration of the veterinary medicinal product with central nervous system depressants may potentiate the CNS and respiratory depressant effects.

When the veterinary medicinal product is administered together with veterinary medicinal products with a sedative effect, the duration of sedation may be increased.

Tramadol can induce convulsions and increase the effect of drugs that lower the seizure threshold.

Drugs that inhibit (e.g. cimetidine and erythromycin) or induce (e.g. carbamazepine) CYP450 mediated metabolism may have an effect on the analgesic effect of tramadol. The clinical relevance of these interactions has not been studied in dogs.

See also section 3.3.

## **3.9 Administration routes and dosage**

Intramuscular or intravenous use.

2–4 mg tramadol hydrochloride per kg bodyweight, corresponding to 0.04–0.08 ml veterinary medicinal product per kg bodyweight. Repeat doses can be administered every 6 to 8 hours (3–4 times daily). The recommended maximum daily dose is 16 mg/kg.

Intravenous administration must be carried out very slowly.

As the individual response to tramadol is variable, 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 tailored using the above dose and re-treatment interval ranges. In the event of the veterinary medicinal product failing to provide adequate analgesia by 30 minutes following administration or for the duration of any planned re-treatment interval, a suitable alternative analgesic should be used.

To ensure a correct dosage, body weight should be determined as accurately as possible.

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

In cases of intoxication with tramadol symptoms similar to those observed with other centrally acting analgesics (opioids) are likely to occur. This includes in particular miosis, vomiting, cardiovascular collapse, consciousness disorders up to coma, convulsions and respiratory depression up to respiratory arrest.

General emergency measures: Maintain a patent airway; support cardiac and respiratory function depending on the symptoms. The antidote for respiratory depression is naloxone. However, the decision to use naloxone in the event of an overdose should be made following an assessment of the benefit-risk ratio for the individual as it may only partially reverse some of the other effects of tramadol and may increase the risk of seizures, although data on the latter are conflicting. In case of seizures, administer diazepam.

## **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**

For administration by a veterinarian or under their direct supervision.

## **3.12 Withdrawal periods**

Not applicable.

## **4. PHARMACOLOGICAL INFORMATION**

**4.1 ATCvet code:**  
QN02AX02

### **4.2 Pharmacodynamics**

Tramadol is a centrally acting analgesic agent with a complex mode of action exerted by its 2 enantiomers and primary metabolite, involving opioid, norepinephrine, and serotonin receptors. The (+) enantiomer of tramadol inhibits serotonin uptake. The (-) enantiomer inhibits norepinephrine reuptake. The metabolite O-desmethyltramadol has greater affinity for the  $\mu$ -opioid receptors. Unlike morphine, tramadol does not have depressing effects on respiration for an extensive analgesic dose range. Likewise, it does not affect gastrointestinal motility. The effects on the cardiovascular system tend to be mild. The analgesic potency of tramadol is about 1/10 to 1/6 of that of morphine. In humans genotypic differences result in up to 10% of individuals being non-responders to tramadol hydrochloride. In these individuals the analgesic effect of tramadol is decreased or absent. A similar phenomenon is known to exist in dogs, however the percentage of dogs affected is not known.

### **4.3 Pharmacokinetics**

After intramuscular administration, the absorption is almost total, with a bioavailability of 92%. Protein binding is moderate (15%). Tramadol is metabolized in the liver by cytochrome P450 mediated demethylation followed by conjugation with glucuronic acid. Elimination occurs mainly via the kidneys, with an elimination half-life of about 0.5-2 hours.

## **5. PHARMACEUTICAL PARTICULARS**

### **5.1 Major incompatibilities**

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

### **5.2 Shelf life**

Shelf life of the veterinary medicinal product as packaged for sale: 30 months.  
Shelf life after first opening the immediate packaging: 8 weeks.

### **5.3 Special precautions for storage**

This veterinary medicinal product does not require any special storage conditions.

### **5.4 Nature and composition of immediate packaging**

Clear type I glass vials closed with a coated bromobutyl rubber stopper and aluminium cap in a carton box.

#### Pack sizes:

Box with 1 vial of 10 ml  
Box with 1 vial of 20 ml  
Box with 1 vial of 50 ml

Multi-pack with 6 boxes each containing 1 vial of 10 ml  
Multi-pack with 6 boxes each containing 1 vial of 20 ml  
Multi-pack with 6 boxes each containing 1 vial of 50 ml  
Multi-pack with 10 boxes each containing 1 vial of 10 ml  
Multi-pack with 10 boxes each containing 1 vial of 20 ml

Multi-pack with 10 boxes each containing 1 vial of 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)**

VPA10475/034/001

### **8. DATE OF FIRST AUTHORISATION**

16/03/2018

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

11/09/2024

### **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) (<https://medicines.health.europa.eu/veterinary>).

**ANNEX III**

**LABELLING AND PACKAGE LEAFLET**

## **5. LABELLING**



**PARTICULARS TO APPEAR ON THE OUTER PACKAGE****{Cardboard box}****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Tralieve 50 mg/ml solution for injection

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each ml contains:

Tramadol 43.9 mg

(equivalent to 50 mg tramadol hydrochloride)

**3. PACKAGE SIZE**

1 x 10 ml

1 x 20 ml

1 x 50 ml

6 x 10 ml

6 x 20 ml

6 x 50 ml

10 x 10 ml

10 x 20 ml

10 x 50 ml

**4. TARGET SPECIES**

Dogs.

**5. INDICATIONS****6. ROUTES OF ADMINISTRATION**

Intravenous or intramuscular use.

**7. WITHDRAWAL PERIODS****8. EXPIRY DATE**

Exp. {mm/yyyy}

Shelf life after first opening the immediate packaging: 8 weeks.

Once broached use by ...

<b>9. SPECIAL STORAGE PRECAUTIONS</b>
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<b>10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”</b>
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Read the package leaflet before use.

<b>11. THE WORDS “FOR ANIMAL TREATMENT ONLY”</b>
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For animal treatment only.

<b>12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”</b>
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Keep out of the sight and reach of children.

<b>13. NAME OF THE MARKETING AUTHORISATION HOLDER</b>
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Le Vet. Beheer B.V.

<b>14. MARKETING AUTHORISATION NUMBERS</b>
--------------------------------------------

VPA10475/034/001

<b>15. BATCH NUMBER</b>
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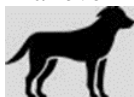
Lot {number}

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

**Glass vials of 10, 20 or 50 ml**

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Tralieve



**2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES**

Tramadol hydrochloride 50 mg/ml

**3. BATCH NUMBER**

Lot {number}

**4. EXPIRY DATE**

Exp. {mm/yyyy}

Shelf life after first opening the immediate packaging: 8 weeks.

Once broached use by ...

## **B. PACKAGE LEAFLET**

## PACKAGE LEAFLET

### 1. Name of the veterinary medicinal product

Tralieve 50 mg/ml solution for injection for dogs

### 2. Composition

Each ml contains:

**Active substance:**

Tramadol 43.9 mg  
(equivalent to 50 mg tramadol hydrochloride)

**Excipients:**

Benzyl alcohol (E1519) 10 mg

Clear and colourless solution.

### 3. Target species

Dogs.

### 4. Indications for use

For the reduction of mild postoperative pain.

### 5. Contraindications

Do not use in animals with epilepsy.

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

Do not administer in conjunction with tricyclic antidepressants, monoamine oxidase inhibitors and serotonin reuptake inhibitors.

### 6. Special warnings

Special warnings:

The analgesic effects of tramadol hydrochloride may be variable. This is thought to be due to individual differences in the metabolism of the drug to the primary active metabolite O-desmethytramadol. In some dogs (non-responders) this may result in the veterinary medicinal product failing to provide analgesia. Dogs should therefore be monitored regularly to ensure sufficient efficacy.

Special precautions for safe use in the target species:

Use with caution in dogs with renal or hepatic impairment. In dogs with hepatic impairment the metabolism of tramadol to the active metabolites may be decreased which may reduce the efficacy of the veterinary medicinal product. One of the active metabolites of tramadol is renally excreted and therefore in dogs with renal impairment the dosing regimen used may need to be adjusted. Renal and hepatic function should be monitored when using this veterinary medicinal product. See also section on Interactions.

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

People with known hypersensitivity to tramadol or any of the excipients should avoid contact with the veterinary medicinal product.

The veterinary medicinal product may cause skin and eye-irritation. Avoid contact with the skin and eyes. Wash hands after use. In case of accidental eye exposure, rinse with clean water.

There is inadequate evidence available on the safety of tramadol in human pregnancy. Pregnant women and women of childbearing age should therefore take great care when handling this veterinary medicinal product and, in the event of exposure, seek medical advice immediately.

Tramadol may cause nausea and dizziness following accidental self-injection. If you develop symptoms following accidental exposure, seek medical advice and show the package leaflet or the label to the physician. However, DO NOT DRIVE as sedation may occur.

Pregnancy:

Laboratory studies in mice and/or rats and rabbits have not produced any evidence of teratogenic, foetotoxic, maternotoxic effects.

Use only according to the benefit-risk assessment by the responsible veterinarian.

Lactation:

Laboratory studies in mice and/or rats and rabbits have not produced any evidence of adverse effects in the peri- and postnatal development of offspring.

Use only according to the benefit-risk assessment by the responsible veterinarian.

Fertility:

In laboratory studies in mice and/or rats and rabbits, the use of tramadol at therapeutic doses did not adversely affect reproductive performance and fertility in males and females.

Use only according to the benefit-risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:

Concomitant administration of the veterinary medicinal product with central nervous system depressants may potentiate the CNS and respiratory depressant effects.

When the veterinary medicinal product is administered together with veterinary medicinal products with a sedative effect, the duration of sedation may be increased.

Tramadol can induce convulsions and increase the effect of drugs that lower the seizure threshold.

Drugs that inhibit (e.g. cimetidine and erythromycin) or induce (e.g. carbamazepine) CYP450 mediated metabolism may have an effect on the analgesic effect of tramadol. The clinical relevance of these interactions has not been studied in dogs.

See also section Contraindications.

Overdose:

In cases of intoxication with tramadol symptoms similar to those observed with other centrally acting analgesics (opioids) are likely to occur. This include in particular miosis, vomiting, cardiovascular collapse, consciousness disorders up to coma, convulsions and respiratory depression up to respiratory arrest.

General emergency measures: Maintain a patent airway; support cardiac and respiratory function depending on the symptoms. The antidote for respiratory depression is naloxone. However, the decision to use naloxone in the event of an overdose should be made following an assessment of the benefit-risk ratio for the individual as it may only partially reverse some of the other effects of tramadol and may increase the risk of seizures, although data on the latter are conflicting. In case of seizures, administer diazepam.

Special restrictions for use and special conditions for use:

For administration by a veterinarian or under their direct supervision.

Major incompatibilities:

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

## **7. Adverse events**

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Hypersensitivity reaction*
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Vomiting, nausea

\*Treatment should be discontinued.

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: HPRA Pharmacovigilance Website: [www.hpra.ie](http://www.hpra.ie)

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

Intramuscular or intravenous use.

2–4 mg tramadol hydrochloride per kg bodyweight, corresponding to 0.04–0.08 ml veterinary medicinal product per kg bodyweight.

Repeat doses can be administered every 6 to 8 hours (3–4 times daily). The recommended maximum daily dose is 16 mg/kg.

Intravenous administration must be carried out very slowly.

As the individual response to tramadol is variable, 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 tailored using the above dose and re-treatment interval ranges. In the event of the veterinary medicinal product failing to provide adequate analgesia by 30 minutes following administration or for the duration of any planned re-treatment interval, a suitable alternative analgesic should be used.

To ensure a correct dosage, body weight should be determined as accurately as possible.

## **9. Advice on correct administration**

None.

## **10. Withdrawal periods**

Not applicable.

## **11. Special storage precautions**

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton after Exp. The expiry date refers to the last day of that month.  
Shelf life after first opening the immediate packaging: 8 weeks.

## **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**

VPA10475/034/001

### Pack sizes:

Cardboard box with 1 vial of 10 ml, 20 ml or 50 ml.

Multi-pack with 6 boxes each containing 1 vial of 10 ml, 20 ml or 50 ml.

Multi-pack with 10 boxes each containing 1 vial of 10 ml, 20 ml or 50 ml.

Not all pack sizes may be marketed.

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

11/09/2024

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

## **16. Contact details**

### 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

### Local representatives and contact details to report suspected adverse reactions:



Dechra Veterinary Products Limited  
Sansaw Business Park  
Hadnall  
Shrewsbury  
Shropshire  
SY4 4AS  
United Kingdom  
Tel: +44 (0) 1939 211200

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

**17. Other information**

<b>POM</b> (Prescription Only)
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