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

1 ml contains:

Active substance:
Tramadol hydrochloride 50 mg
(equivalent to 43.9 mg tramadol)

Excipient(s):
Benzyl alcohol (E1519) 10 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection
Clear and colourless solution

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

For the reduction of mild postoperative pain.

4.3 Contraindications

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.
Do not use in animals with epilepsy.

4.4 Special warnings for each target species

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-desmethyltramadol. In some dogs (non-responders) this may result in

the product failing to provide analgesia. Dogs should therefore be monitored regularly to ensure sufficient efficacy.

4.5 Special precautions for use

Special precautions for use in animals

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 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 product. See also section 4.8.

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 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 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.

4.6 Adverse reactions (frequency and seriousness)

Nausea and vomiting have occasionally been observed in dogs after administration of tramadol. In rare cases (more than 1 but less than 10 animals in 10,000 animals treated) hypersensitivity can occur. In cases of hypersensitivity reactions the treatment should be discontinued.

4.7 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.

4.8 Interaction with other medicinal products and other forms of interaction

Concomitant administration of the product with central nervous system depressants may potentiate the CNS and respiratory depressant effects.
When the product is administered together with 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 4.3.

4.9 Amounts to be administered and administration route

For intramuscular or intravenous injection: 2−4 mg tramadol hydrochloride per kg bodyweight, corresponding to 0.04−0.08 ml 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 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.

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

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.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Analgesics, other opioids
ATCvet code: QN02AX02.

5.1 Pharmacodynamic properties

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 μ-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.

5.2 Pharmacokinetic particulars

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Sodium acetate trihydrate
Hydrochloric acid, diluted (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Major incompatibilities

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

6.3 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

6.4 Special precautions for storage

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

6.5 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.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Le Vet Beheer B.V.
Wilgenweg 7
3421 TV Oudewater
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Vm 41821/4055

9. DATE OF FIRST AUTHORISATION

26 March 2018

10. DATE OF REVISION OF THE TEXT

June 2022

Approved 23 June 2022