Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Tramvetol 50 mg/ml solution for injection for dogs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Tramadol (as hydrochloride) 43.9 mg
Equivalent to 50 mg of tramadol hydrochloride

Excipients:
For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection.
Clear and colourless solution, free from visible particles.

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

4.6 Adverse reactions (frequency and seriousness)

Nausea and vomiting have occasionally been observed in dogs after administration of this product. In rare cases hypersensitivity can occur. In cases of hypersensitivity reactions the treatment should be discontinued.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Pregnancy:
In laboratory studies conducted on mice and / or rats and rabbits respectively, the use of tramadol did not reveal the existence of teratogenic, foetotoxic, maternotoxic effects. Use only according to the benefit-risk assessment by the responsible veterinarian.

Lactation:
In laboratory studies conducted on mice and / or rats and rabbits, respectively, the use of tramadol did not show any adverse effects in the peri and post-natal period of offspring. Use only according to the benefit-risk assessment by the responsible veterinarian.

Fertility:
In laboratory studies conducted on mice and / or rats and rabbits respectively, the use of tramadol at therapeutic doses did not induce the appearance of unfavourable reactions on reproductive parameters and fertility in the male and female. Use only according to the benefit-risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interactions

Concomitant administration of this product with central nervous system depressants may potentiate the effects on C.N.S. and respiratory depressant effects.

When the product is administered together with medicinal products with a sedative effect, the duration of sedation may be increased.
This product can induce seizures and increase the effect of drugs that lower the convulsive 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.
The combination with mixed agonist/antagonists (e.g. buprenorphine, butorphanol) and tramadol is not advisable, because the analgesic effect of a pure agonist may be theoretically reduced in such circumstances.

4.9 Amounts to be administered and administration route

For intramuscular or intravenous use: 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 includes, in particular, miosis, vomiting, cardiocirculatory collapse, disturbances of consciousness up to coma, convulsions and respiratory depression up to the 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 or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Analgesics, other opioids, tramadol.
ATC vet 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

Sodium acetate trihydrate
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: 2 years.
Shelf life after first opening the immediate packaging: use immediately.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Type I colourless glass ampoule with engraved cut line, containing 1 ml of solution for injection.
Pack size: box containing 10 ampoules

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

Virbac S.A.
1ère avenue
2065 M LID
06516 Carros
France

8 MARKETING AUTHORISATION NUMBER(S)

VPA10988/112/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30th August 2019

10 DATE OF REVISION OF THE TEXT