ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tramsan 20 mg chewable tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Tramadol hydrochloride 20 mg

3. PACKAGE SIZE

10 tablets
20 tablets
30 tablets
40 tablets
50 tablets
60 tablets
70 tablets
80 tablets
90 tablets
100 tablets
120 tablets
250 tablets

4. TARGET SPECIES

Dogs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 30°C.

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

Accidental ingestion of this veterinary medicinal product can be harmful. 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

Alfasan Nederland B.V.

14. MARKETING AUTHORISATION NUMBERS

Vm 36408/3036

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Aluminium blisters

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tramsan 20 mg

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Tramadol hydrochloride 20 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Tramsan 20 mg chewable tablets for dogs
Tramsan 80 mg chewable tablets for dogs

2. Composition

Each 20 mg tablet contains:
Active substance:
Tramadol hydrochloride 20 mg
equivalent to 17.6 mg tramadol

Each 80 mg tablet contains:
Active substance:
Tramadol hydrochloride 80 mg
equivalent to 70.3 mg tramadol

White to off-white round and convex chewable tablet with a cross-shaped break line on one side, size 7 mm or size 13 mm.
Tablets can be divided into 2 or 4 equal parts.

3. Target species

Dogs

4. Indications for use

For the reduction of acute and chronic mild soft tissue and musculoskeletal pain.

5. Contraindications

Do not administer in conjunction with tricyclic antidepressants, monoamine oxidase inhibitors and serotonin reuptake inhibitors.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in animals with epilepsy.

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-desmethyltramadol. In some dogs (non-responders) this may result in the product failing to provide analgesia. For chronic pain, multimodal analgesia should be considered. Dogs should be monitored regularly by a veterinarian to ensure adequate pain relief. In case of recurrence of pain or insufficient analgesia the analgesic protocol may need to be reconsidered.

Special precautions for safe use in the target species:
The tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of 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. Cessation of long-term analgesic therapy should be done gradually whenever possible.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Tramadol and vanillin may cause hypersensitivity (allergic) reactions. People with known hypersensitivity to these substances should avoid contact with the product. Wash hands after use. Seek medical advice in case of hypersensitivity reactions.

This veterinary medicinal product may cause eye irritation, e.g., if dust is formed when broken into smaller parts. Avoid contact with the eyes, including hand-to-eye contact. If the veterinary medicinal product comes into contact with the eyes, rinse immediately with plenty of water.

Tramadol may cause sedation, nausea, and dizziness after accidental ingestion. To avoid accidental ingestion, particularly by a child, unused part tablets should be returned to the open blister space, inserted back into the carton, and kept in a safe place out of the sight and reach of children. In case of accidental ingestion, particularly by children, seek medical advice and show the package leaflet or the label to the physician. In case of accidental ingestion by adults: DO NOT DRIVE as sedation may occur.

Pregnancy and lactation:
Laboratory studies in mice and/or rats and rabbits have not produced any evidence of teratogenic, foetotoxic, maternotoxic effects and 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 product with central nervous system depressants, may potentiate the CNS and respiratory depressant effects. Tramadol can 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.
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. See also the section on contraindications.

Overdose:
In cases of intoxication with tramadol, symptoms similar to those observed with other centrally acting analgesics (opioids) are likely to occur. These 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. Inducing vomiting in order to empty the stomach is suitable unless the affected animal is showing reduced consciousness, in which case gastric lavage may be considered.
The antidote for respiratory depression is naloxone. However, naloxone may not be useful in all cases of tramadol overdose as it may only partially reverse some of the other effects of tramadol. In case of seizures, administer diazepam.

7. Adverse events

Dogs:

Frequency	Adverse event
Common (1 to 10 animals / 100 animals treated):	Sedation[1,2]; drowsiness – neurological disorder[2]
Uncommon (1 to 10 animals / 1000 animals treated)	Nausea; vomiting
Rare (1 to 10 animals / 10,000 animals treated):	Hypersensitivity[3]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Convulsion[4]

[1] Mild.
[2] Especially when higher doses are given.
[3] In cases of hypersensitivity reactions the treatment should be discontinued.
[4] In dogs with a low seizure threshold.

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

Oral use.
The recommended dose is 2-4 mg tramadol hydrochloride per kg body weight every 8 hours or as needed based on the intensity of pain.
The minimum dosing interval is 6 hours. The recommended maximum total daily dose is 16 mg/kg. 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. The dog should be examined regularly by a veterinarian to assess if additional analgesia is subsequently required. Additional analgesia can be administered by increasing the tramadol dose until the maximum daily

dose is reached, and/or by following a multimodal analgesic approach with the addition of other suitable analgesics.

Please note that this dosing table is intended as a guide for dispensing the product at the high end of the dose range: 4 mg/kg bodyweight. It states the number of tablets required to administer 4 mg tramadol hydrochloride per kg bodyweight.

The recommended dose is 2-4 mg tramadol HCl per kg. In these tables an example of 4 mg tramadol HCl per kg is stated.

Body weight	Veterinary medicinal product 20 mg
1.25 kg	
2.5 kg	
3.75 kg	
5 kg	
6.25 kg	
7.5 kg	
10 kg	
15 kg	

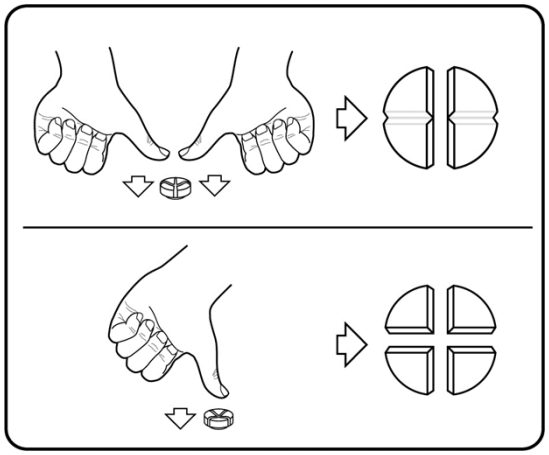
Body weight	Veterinary medicinal product 80 mg
20 kg	
30 kg	
40 kg	
50 kg	
60 kg	

= ¼ Tablet = ½ Tablet = ¾ Tablet = 1 Tablet

The most appropriate tablet strengths should be used in order to minimise divided tablets to be kept until the next dosing. The remaining tablet fraction(s) should be used in the next administration(s).
To ensure a correct dosage, body weight should be determined as accurately as possible.

9. Advice on correct administration

Tablets can be divided into 2 or 4 equal parts to ensure accurate dosing. Place the tablet on a flat surface, with its scored side facing up and the convex (rounded) side facing the surface.



Two equal parts: press down with your thumbs on both sides of the tablet.
Four equal parts: press down with your thumb in the middle of the tablet.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Do not store above 30°C.
Do not use this veterinary medicinal product after the expiry date which is stated on the package after Exp. The expiry date refers to the last day of that month.

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

Vm 36408/3036
Vm 36408/3037

PVC/PE/PVDC-aluminium blisters, containing 10 tablets each.
Cardboard box of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 120 or 250 tablets.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{DD month YYYY}

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 manufacturer responsible for batch release:
Alfasan Nederland B.V.
Kuipersweg 9
3449 JA Woerden
The Netherlands

Manufacturer responsible for batch release:
Lelypharma B.V.
Zuiveringsweg 42
8243 PZ Lelystad
The Netherlands

Local representatives and contact details to report suspected adverse reactions:
Anupco Ltd T/A Kela Animal Health
Office 39, Lodge House Lodge Park, Lodge Lane,
Langham, Colchester, Essex, CO4, 5NE
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17. Other information

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