ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Sachet (1 kg – 100 g)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Hydrotrim 500 mg/g + 100 mg/g powder for use in drinking water/milk

2. STATEMENT OF ACTIVE SUBSTANCE

Each gram contains:

Active substances:

500 mg Sulfadiazine equivalent to 543.9 mg Sulfadiazine sodium
100 mg Trimethoprim

3. PACKAGE SIZE

100 g
1 kg

4. TARGET SPECIES

Cattle (pre-ruminant calves), sheep (pre-ruminant lambs), pigs and chickens.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

In drinking water/milk replacer use.

7. WITHDRAWAL PERIODS

Withdrawal periods:

Cattle (pre-ruminant calves)
Meat and offal: 12 days.

Sheep (pre-ruminant lambs)
Meat and offal: 12 days.

Pigs
Meat and offal: 12 days.

Chickens
Meat and offal: 12 days.
Not for use in birds producing or intended to produce eggs for human consumption.

8. EXPIRY DATE

Exp. {mm/yyyy}
Once opened use within 3 months.
Once dissoluted in drinking water use within 24 hours.
Once dissoluted in milk replacer use within 1 hour.

9. SPECIAL STORAGE PRECAUTIONS

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

Huvepharma NV

14. MARKETING AUTHORISATION NUMBER

Vm 30282/3003

15. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Hydrotrim 500 mg/g + 100 mg/g powder for use in drinking water/milk for cattle, sheep, pigs and chickens

2. Composition

Each gram contains:

Active substances:

500 mg Sulfadiazine equivalent to 543.9 mg Sulfadiazine sodium
100 mg Trimethoprim

Excipients:

Qualitative composition of excipients and other constituents
Polysorbate 80
Maltodextrin

Off-white to light beige powder.

3. Target species

Cattle (pre-ruminant calves), sheep (pre-ruminant lambs), pigs and chickens.

4. Indications for use

Cattle (pre-ruminant calves) and sheep (pre-ruminant lambs)
Treatment and metaphylaxis of respiratory infections caused by *Mannheimia haemolytica* or *Pasteurella multocida* and infections caused by *Escherichia coli*.

The presence of the disease in the group must be established before the veterinary medicinal product is used.

Pigs
Treatment and metaphylaxis of respiratory infections caused by *Actinobacillus pleuropneumoniae* or *Pasteurella multocida* and infections caused by *Streptococcus suis* or *Escherichia coli*.

The presence of the disease in the group must be established before the veterinary medicinal product is used.

Chickens
Treatment and metaphylaxis of colibacillosis caused by *Escherichia coli*.

The presence of the disease in the flock must be established before the veterinary medicinal product is used.

5. Contraindications

Do not use in ruminating animals.
Do not use in animals suffering from severe liver or kidney disease, oliguria or anuria.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

Special warnings:

Severely diseased animals can have a decreased appetite and water consumption. If necessary, the concentration of the veterinary medicinal product in the drinking water should be adjusted to make sure that the recommended dosage is being consumed.

Pigs, cattle (pre-ruminant calves) and sheep (pre-ruminant lambs): the uptake of medication by animals may be altered as a consequence of illness. In case of insufficient water uptake, animals should be treated parenterally instead, using a suitable injectable veterinary medicinal product prescribed by the veterinarian.

Special precautions for safe use in the target species:

Due to the likely variability (time, geographical) in susceptibility of bacteria for potentiated sulfonamides, occurrence of resistance of bacteria may differ from country to country and even from farm to farm, and therefore bacteriological sampling and susceptibility testing are recommended. It is particularly of importance for *E. coli* infections where high percentages of resistance are observed (see section 4.2).

Use of the veterinary medicinal product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.

Use of the veterinary medicinal product deviating from the instructions given in the Summary of product characteristics (SPC) may increase the prevalence of bacteria resistant to sulfadiazine and trimethoprim and may also decrease the effectiveness of combinations of trimethoprim with other sulfonamides due to the potential for cross-resistance.

Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.

To avoid deterioration of the kidneys due to crystalluria during treatment, it should be ensured that the animal receives sufficient amount of drinking water.

This antimicrobial combination should only be used where diagnostic testing has indicated the need for simultaneous administration of each of the active substances.

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

This veterinary medicinal product contains sulfadiazine, trimethoprim and polysorbate 80, which can cause allergic reactions in some people. Hypersensitivity to sulfonamides may lead to cross reactions with other antibiotics. Allergic reactions to these substances may occasionally be serious.

People with known hypersensitivity (allergy) to sulfonamides, trimethoprim or polysorbate should avoid contact with the veterinary medicinal product.

Avoid skin and eye contact during preparation and administration. Wear personal protective equipment consisting of impervious (latex or nitrile) gloves (in compliance with Directive 89/686/EEC and EN374 norm), protective masks, eye protection and suitable protective clothing. In case of accidental contact with the eyes or skin, wash the affected area with plenty of water, and if skin rash occurs, seek medical advice immediately and show the package leaflet or the label to the physician.

This veterinary medicinal product may be harmful if ingested. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Wash hands after use.

Special precautions for the protection of the environment:

Not applicable.

Pregnancy, lactation or lay:

Do not use during pregnancy, lactation or lay.
Laboratory studies in rats and rabbits have shown evidence of teratogenic and foetotoxic effects.

Interaction with other medicinal products and other forms of interaction:

Do not administer concomitantly with coccidiostats or veterinary medicinal products containing sulfonamides.

Do not associate with PABA (para-aminobenzoic acid).

Sulfamides potentiate anticoagulants action.

Overdose:

Sulfonamides overdose causes renal toxicity. In this case, the administration of the veterinary medicinal product has to be stopped.

Special restrictions for use and special conditions for use:

Not applicable.

Major incompatibilities:

Do not add to drinking water treated with sodium hypochlorite at 5 ppm.

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

7. Adverse events

Chickens:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Decreased drinking
Undetermined frequency (cannot be estimated from the available data):
Hypersensitivity reactions

Cattle (pre-ruminant calves), sheep (pre-ruminant lambs) and pigs:

Undetermined frequency (cannot be estimated from the available data):
Hypersensitivity reactions

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 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

For use in drinking water/milk replacer.

Cattle (pre-ruminant calves) and sheep (pre-ruminant lambs):

12.5 mg of sulfadiazine and 2.5 mg of trimethoprim per kg body weight (corresponding to 25 mg of the veterinary medicinal product per kg body weight), every 12 hours for 4 to 7 consecutive days, to be dissolved in the milk replacer.

Pigs:
25 mg of sulfadiazine and 5 mg of trimethoprim per kg body weight per day (corresponding to 50 mg of the veterinary medicinal product per kg body weight per day), for 4 to 7 consecutive days, to be dissolved in drinking water.

Chickens:

25 mg of sulfadiazine and 5 mg of trimethoprim per kg body weight per day (corresponding to 50 mg of the veterinary medicinal product per kg body weight per day), for 4 to 7 consecutive days, to be dissolved in drinking water.

Guidance for preparing veterinary medicinal product solutions:
To ensure a correct dosage, body weight should be determined as accurately as possible.

The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage, the concentration of sulfadiazine and trimethoprim should be adjusted accordingly.

The use of suitably calibrated measuring equipment is recommended.

Based on the recommended dose and the number and weight of animals to be treated, the exact daily concentration of the veterinary medicinal product should be calculated according to the following formula:

$$\frac{\text{mg veterinary medicinal product/kg body weight/day} \times \text{average body weight (kg) of animals to be treated}}{\text{average daily water intake (l/animal)}} = \text{mg veterinary medicinal product per litre of drinking water/milk replacer}$$

9. Advice on correct administration

Prepare the solution with fresh tap water (or milk replacer for cattle (pre-ruminant calves)) immediately before use. Milk replacer should be prepared prior to the addition of the veterinary medicinal product. The solution should be vigorously stirred for 5 minutes. Medicated milk replacer should be consumed immediately after preparation. Water uptake should be monitored at frequent intervals during medication. The medicated drinking water should be the sole source of drinking water for the treatment duration. Any medicated drinking water which is not consumed within 24 hours should be discarded. After the end of the medication period, the water supply system should be cleaned appropriately to avoid intake of sub-therapeutic amounts of the active substance.

The maximum solubility of the veterinary medicinal product is 1g/L. During dissolution, the solution should be stirred for at least 2 minutes. Solutions should be checked visually for complete dissolution.
For stock solutions and when using a proportioner, take care not to exceed the maximum solubility. Adjust flow rate settings of the dosing pump according to concentration of the stock solution and water intake of the animals to be treated.

10. Withdrawal periods

Cattle (pre-ruminant calves)
Meat and offal: 12 days.

Sheep (pre-ruminant lambs)
Meat and offal: 12 days.

Pigs
Meat and offal: 12 days.

Chickens
Meat and offal: 12 days.
Not for use in birds producing or intended to produce eggs for human consumption.

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 label after Exp. The expiry date refers to the last day of that month.

Shelf life after first opening the immediate package: 3 months.
Shelf life after dissolution in drinking water according to directions: 24 hours.
Shelf life after dissolution in milk replacer according to directions: 1 hour.

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 30282/3003

100 g pillow sachet and 1 kg resealable block-bottom zipped sachet made of polyethylene/aluminium/polyethylene terephthalate laminate.

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>:

Huvepharma NV
Uitbreidingstraat 80
2600 Antwerpen
Belgium
<Tel: +32 3 288 18 49>
<E-mail: pharmacovigilance@huvepharma.com>

Manufacturer responsible for batch release:

Biovet JSC
39 Petar Rakov Str
4550 Peshtera
Bulgaria

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

<17. Other information>

Trimethoprim is persistent in soils.

Approved 03 October 2023