

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE>

Bottle of 1 L
Can of 5 L

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

VETMULIN 125 mg/ml Solution for use in drinking water for pigs and chickens
Tiamulin hydrogen fumarate

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

Active substance

Tiamulin hydrogen fumarate (equivalent to tiamulin 101.2 mg)	125 mg
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Excipients:

Methyl parahydroxybenzoate (E218)	0.90mg
Propyl parahydroxybenzoate	0.10 mg

3. PHARMACEUTICAL FORM

Solution for use in drinking water

4. PACKAGE SIZE

1 Litre
5 Litre

5. TARGET SPECIES

Pigs and chickens (laying hens).

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

In drinking water use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Pigs

Meat and offal: 2 days (8.8 mg tiamulin hydrogen fumarate/ kg body weight equivalent to 7 ml of product/100 kg body weight)

Meat and offal: 4 days (20 mg tiamulin hydrogen fumarate/ kg body weight, equivalent to 16 ml product)/100 kg body weight)

Chickens (laying hens):

Meat and offal: 2 days

Eggs: Zero days

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP: {mm/yy}

Shelf-life after first opening the immediate packaging: 3 months

Once opened, use by:

Shelf-life after dilution in drinking water: 24 hours

11. SPECIAL STORAGE CONDITIONS

Store in the original container in order to protect from light.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

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

13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Huvepharma NV
Uitbreidingstraat 80
Antwerpen
B-2600
Belgium

16. MARKETING AUTHORISATION NUMBER(S)

Vm 30282/4040

17. MANUFACTURER'S BATCH NUMBER

Lot:

B. PACKAGE LEAFLET

PACKAGE LEAFLET:

VETMULIN 125 mg/ml Solution for use in drinking water for pigs and chickens

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation

Huvepharma NV
Uitbreidingstraat 80
2600 Antwerpen
Belgium

Manufacturer responsible for batch release

Biovet JSC
39 Petar Rakov Str.
4550 Peshtera
Bulgaria

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

VETMULIN 125 mg/ml Solution for use in drinking water for pigs and chickens

Tiamulin hydrogen fumarate

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Solution for use in drinking water.
Clear, colourless to slightly yellow liquid.

Each ml contains:

Active substance

Tiamulin hydrogen fumarate	125 mg
(equivalent to Tiamulin	101.2 mg)

Excipients:

Methyl parahydroxybenzoate (E218)	0.90 mg
Propyl parahydroxybenzoate	0.10 mg

4. INDICATION(S)

The presence of the disease in the herd must be established before the product is used.

In pigs

For the treatment of Swine Dysentery caused by tiamulin susceptible *Brachyspira hyodysenteriae*.

For the treatment of Porcine Colonic Spirochaetosis (spirochaetal diarrhoea or colitis) caused by tiamulin susceptible *Brachyspira pilosicoli*.

For the treatment of Porcine Proliferative Enteropathy (ileitis) caused by tiamulin susceptible *Lawsonia intracellularis*.

For the treatment and methaphylaxis of Enzootic pneumonia caused by tiamulin-susceptible *Mycoplasma hyopneumoniae*, including infections complicated by tiamulin-susceptible *Pasteurella multocida*.

In chickens (laying hens)

For the treatment and methaphylaxis of Chronic Respiratory Disease caused by tiamulin-susceptible *Mycoplasma gallisepticum* and Airsacculitis and Infectious Synovitis caused by tiamulin-susceptible *Mycoplasma synoviae*.

5. CONTRAINDICATIONS

Do not use in animals that could receive products containing monensin, narasin or salinomycin during or for at least seven days before or after treatment with tiamulin. Severe growth depression or death may result.

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

See section 12 for information regarding interaction between tiamulin and ionophores

6. ADVERSE REACTIONS

Pigs: In very rare cases, erythema or mild oedema of the skin (skin reactions) may occur in treated pigs.

Chickens (laying hens): none known.

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)

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 inform your veterinary surgeon

7. TARGET SPECIES

Pigs and chickens (laying hens).

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

In drinking water use

Pigs

- i) For the treatment of Swine Dysentery caused by *Brachyspira hyodysenteriae*. The dosage is 8.8 mg tiamulin hydrogen fumarate/kg body weight (equivalent to 7 ml of product/100 kg body weight) administered daily in the drinking water of pigs for 3 to 5 consecutive days depending on the severity of the infection and/or the duration of the disease.
- ii) For the treatment of Porcine Colonic Spirochaetosis (colitis) caused by *Brachyspira pilosicoli*. The dosage is 8.8 mg tiamulin hydrogen fumarate /kg body weight (equivalent to 7 ml of product/100 kg body weight) administered daily in the drinking water of pigs for 3 to 5 consecutive days depending on the severity of the infection and/or the duration of the disease.
- iii) For the treatment of Porcine Proliferative Enteropathy (ileitis) caused by *Lawsonia intracellularis*. The dosage is 8.8 mg tiamulin hydrogen fumarate /kg body weight (equivalent to 7 ml of product/100 kg body weight) administered daily in the drinking water of pigs for 5 consecutive days.
- iv) For the treatment and metaphylaxis of Enzootic Pneumonia caused by *Mycoplasma hyopneumoniae*, including infections complicated by *Pasteurella multocida* susceptible to tiamulin. The dosage is 20 mg tiamulin hydrogen fumarate/kg body weight (equivalent to 16 ml of product/100 kg body weight) administered daily for 5 consecutive days.

Chickens (laying hens)

For the treatment and metaphylaxis of Chronic Respiratory Disease caused by *Mycoplasma gallisepticum* and Airsacculitis and Infectious Synovitis caused by *Mycoplasma synoviae*. the dosage is 25 mg tiamulin hydrogen fumarate/kg body weight (equivalent to 20 ml of product/100 kg body weight) administered daily for the period of 3 to 5 consecutive days.

9. ADVICE ON CORRECT ADMINISTRATION

Administration:

To ensure a correct dosage, body weight should be determined as accurately as possible to avoid underdosing. The intake of medicated water depends on the actual body weight, the water consumption, the clinical condition of the animals, the environment and the age of the animal. In order to obtain the correct dosage, the concentration of tiamulin should be adjusted accordingly. Follow the instructions below to calculate the required daily amount of product:

$$\frac{\text{..... ml product per kg} \times \text{body weight per day} \times \text{average body weight (kg)}}{\text{water intake (litre/animal/day)}} = \text{ml of the product per litre of drinking water per day}$$

Use a sufficiently accurate device to obtain the required volume of product. Use clean containers for preparation of the medicated drinking water. Stir the medicated drinking water prepared with the product for at least 1 minute after preparation in order to assure homogeneity. When medicating large volumes of water, prepare a concentrated solution first and then dilute to the required final concentration. The maximum solubility of the product is 200 mL/ L

Medicated drinking water should be refreshed or replaced every 24 hours.

In order to avoid interactions between the ionophores and tiamulin, the veterinarian and farmer should check with the feed mill that the feed does not contain salinomycin, monensin and narasin.

For chickens, in order to avoid interactions between the incompatible ionophores monensin, narasin and salinomycin and tiamulin, the feed mill supplying the birds feed should be notified that tiamulin will be used and that these anticoccidials should not be included in the feed or contaminate the feed. The feed should be tested for the ionophores prior to use if there is any suspicion that contamination of the feed might have occurred.

If an interaction does occur, stop tiamulin medication immediately and replace with fresh drinking water. Remove contaminated feed as soon as possible and replace with feed not containing salinomycin, monensin or narasin.

10. WITHDRAWAL PERIOD(S)

Pigs:

Meat and offal: 2 days (8.8 mg tiamulin hydrogen fumarate/ kg body weight equivalent to 7 ml of product/100 kg body weight)

Meat and offal: 4 days (20 mg tiamulin hydrogen fumarate/ kg body weight, equivalent to 16 ml product/100 kg body weight)

Chickens (laying hens):

Meat and offal: 2 days

Eggs: Zero days

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Store in the original container in order to protect from light.

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 as packaged for sales: 3 years.
Shelf life after first opening the immediate packaging: 3 months
Shelf life after dilution in drinking water: 24 hours

12. SPECIAL WARNING(S)

Special warnings for each target species

Water intake may be depressed during the administration of tiamulin in birds. Water intake should be monitored at frequent intervals, especially in hot weather.

Pigs with reduced water intake and/or in a debilitated (weak) condition should be treated parenterally (intravenously or intramuscularly).

Special precautions for the use in animals

Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of target bacteria.

Use of the product deviating from the instructions of the package leaflet may increase the prevalence of bacteria resistant to tiamulin.

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

People with known hypersensitivity to tiamulin or parabens should administer the veterinary medicinal product with caution.

Both the product and the diluted product in drinking water may cause hypersensitivity reactions due to contact. Avoid contact of both the product and medicated water with the skin. Do not smoke, eat or drink when handling the product. Wear protective clothes and gloves when mixing and handling the product, and wash hands after use. In case of accidental contact with skin, rinse with plenty of clean water. Contaminated clothing should be removed.

Ingestion of the product or medicated water should be avoided. In the event of accidental ingestion, rinse mouth with plenty of clean water and seek medical advice immediately.

Pregnancy and lactation

Can be used in pigs during pregnancy and lactation.

Lay

Can be used in laying chickens

Interaction with other medicinal products and other forms of interaction:

Severe growth depression, ataxia, paralysis (lameness) or death may result from the interaction of tiamulin with ionophores such as monensin, salinomycin and narasin.

Animals should not receive products containing monensin, salinomycin or narasin during or at least 7 days before or after treatment with tiamulin. If signs of an interaction do occur, stop both the administration of tiamulin-medicated drinking water and the administration of ionophore-contaminated feed immediately. The feed should be removed and replaced with fresh feed not containing the anticoccidials monensin, salinomycin or narasin.

Simultaneous use of tiamulin and lasalocid or semduramicin do not appear to cause any

interaction. Simultaneous use of maduramicin and tiamulin may lead to a mild to moderate growth depression in chickens. The situation is transient and recovery normally occurs within 3- 5 days following withdrawal of tiamulin treatment.

Overdose (symptoms, emergency procedures, antidotes)

In pigs, single oral doses of 100 mg tiamulin hydrogen fumarate/kg body weight caused hyperpnoea and abdominal discomfort. At a dose of 150 mg tiamulin hydrogen fumarate/kg body weight, the only effect on the central nervous system was sedation. A dose of 55 mg tiamulin hydrogen fumarate/kg body weight during 14 days caused a transient salivation and a mild irritation of the stomach. Tiamulin hydrogen fumarate has an adequate therapeutic index in the pig (meaning that the dose that has a therapeutic effect is much lower than the dose causing toxicity), and therefore a minimum lethal dose for pigs has not been established.

The LD₅₀ (the dose at which 50% of a tested chicken population died after a specified test duration) in chickens, is 1090 mg/kg body weight. Tiamulin hydrogen fumarate has a relatively high therapeutic index in birds. The likelihood of an overdose is low as water intake and hence tiamulin hydrogen fumarate intake is reduced if abnormally high doses are given. The clinical signs of acute toxicity in chickens are: vocalisation, clonic cramps and lying in a lateral position.

If signs of poisoning occur, rapidly remove the medicated water and replace it with fresh unmedicated water. Appropriate symptomatic treatment should be initiated.

Incompatibilities

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

Other information

Tiamulin only degrades slowly in soils and may accumulate over years.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

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

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

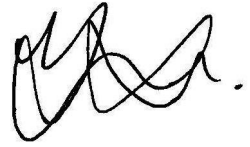
To be completed nationally

15. OTHER INFORMATION

The product is presented in 1 litre high density polyethylene (HDPE) bottles closed with polypropylene (PP) screw cap and low density polyethylene (LDPE) seal disc and 5 litre high density polyethylene (HDPE) jars, closed with HDPE ribbed cap with a tamper-evident ring.

Not all pack sizes may be marketed.

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

A handwritten signature in black ink, consisting of several loops and a final horizontal stroke.

Approved: 06 June 2023