

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetmulin 450 mg/g granules for use in drinking water for pigs, chickens and turkeys
Tiamulin hydrogen fumarate

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each gram contains Tiamulin hydrogen fumarate 450.0 mg (equivalent to tiamulin 364.2 mg)

3. PHARMACEUTICAL FORM

Granules for use in drinking water.

4. PACKAGE SIZE

1 kg

5. TARGET SPECIES

Pigs, chickens, turkeys.

6. INDICATION(S)

Read the package leaflet before use.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral administration through the drinking water.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Pigs

Meat and offal: 2 days (8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of product)/kg body weight)

Meat and offal: 4 days (20 mg tiamulin hydrogen fumarate (equivalent to 44.4 mg of product)/kg body weight)

Chickens

Meat and offal: 2 days

Eggs: Zero days

Turkeys

Meat and offal: 6 days

9. SPECIAL WARNING(S), IF NECESSARY

Animals should not receive products containing monensin, salinomycin or narasin during or for at least seven days before or after treatment with the product.

10. EXPIRY DATE

<EXP {month/year}>

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

Shelf life after dilution or reconstitution according to directions: 24 hours.

Once opened, use by

11. SPECIAL STORAGE CONDITIONS

Store in the original container. Do not refrigerate or freeze.

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
2600 Antwerpen
Belgium

16. MARKETING AUTHORISATION NUMBER(S)

Vm 30282/4002

17. MANUFACTURER'S BATCH NUMBER

<Batch> <Lot> <BN> {number}

PACKAGE LEAFLET

Vetmulin 450 mg/g granules for use in drinking water for pigs, chickens and turkeys
Tiamulin hydrogen fumarate

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

Marketing authorisation holder

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 450 mg/g granules for use in drinking water for pigs, chickens and turkeys.
Tiamulin hydrogen fumarate

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

Each gram contains Tiamulin hydrogen fumarate 450.0 mg (equivalent to tiamulin
364.2 mg)

White to pale yellow granules

4. INDICATION(S)

Pigs

Treatment of Swine Dysentery caused by *Brachyspira hyodysenteriae* susceptible to tiamulin.

Treatment of Porcine Colonic Spirochaetosis (colitis) caused by *Brachyspira pilosicoli* susceptible to tiamulin.

Treatment of Porcine Proliferative Enteropathy (ileitis) caused by *Lawsonia intracellularis* susceptible to tiamulin.

Treatment and metaphylaxis of Enzootic Pneumonia caused by *Mycoplasma hyopneumoniae*, including infections complicated by *Pasteurella multocida* susceptible to tiamulin.

Treatment of Pleuropneumonia caused by *Actinobacillus pleuropneumoniae* susceptible to tiamulin.

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

Chickens

Treatment and metaphylaxis of Chronic Respiratory Disease caused by *Mycoplasma gallisepticum* and Airsacculitis and Infectious Synovitis caused by *Mycoplasma synoviae* susceptible to tiamulin.

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

Treatment and metaphylaxis of Infectious Sinusitis and Airsacculitis caused by *Mycoplasma gallisepticum*, *Mycoplasma synoviae* and *Mycoplasma meleagridis* susceptible to tiamulin.

The presence of the disease in the herd or flock must be established before use.

5. CONTRAINDICATIONS

Do not use in animals with known hypersensitivity to the active ingredient or to any of the excipients.

Do not use in pigs and birds 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. See section 4.8 for information regarding interaction between tiamulin and ionophores.

6. ADVERSE REACTIONS

On very rare occasions erythema or mild oedema of the skin may occur in pigs following the use of Tiamulin

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 serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Pigs, chickens and turkeys.

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

For oral administration through the drinking water.

When medicating large volumes of water, prepare a concentrated solution first and then dilute to the required final concentration.

Fresh solutions of tiamulin-medicated drinking water should be made up each day.

To ensure the correct dosage, body weight should be determined as accurately as possible to avoid underdosing. The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of tiamulin has to be adjusted accordingly.

In order to avoid interactions between the ionophores and tiamulin, the veterinarian and farmer should check that the feed label does not state that it contains salinomycin, monensin and narasin.

The dosage of the product to be incorporated should be established according to the following formula:

$$\frac{\text{Dose (mg product per kg body weight per day)}}{\text{Mean body weight (kg) of animals to be treated}} \times \text{Mean daily water consumption (litre) per animal per day} = \text{...mg product per litre of drinking water}$$

Mean daily water consumption (litre) per animal per day'

Chickens:

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 (equivalent to 55.6 mg of product)/kg body weight daily administered for the period of 3 to 5 consecutive days.

Turkeys:

For the treatment and metaphylaxis of Infectious Sinusitis and Airsacculitis caused by *Mycoplasma gallisepticum*, *Mycoplasma synoviae* and *Mycoplasma meleagridis*:

The dosage is 40 mg tiamulin hydrogen fumarate (equivalent to 88.9 mg of product)/kg body weight daily administered for the period of 3 to 5 consecutive days.

Pigs:

For the treatment of Swine Dysentery caused by *Brachyspira hyodysenteriae*:

The dosage is 8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of product)/kg body weight daily administered 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.

For the treatment of Porcine Colonic Spirochaetosis (colitis) caused by *Brachyspira pilosicoli*:

The dosage is 8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of product)/kg body weight daily administered 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.

For the treatment of Porcine Proliferative Enteropathy (ileitis) caused by *Lawsonia intracellularis*:

The dosage is 8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of product)/kg body weight daily administered in the drinking water of pigs for 5 consecutive days.

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 (equivalent to 44.4 mg of product)/kg body weight daily administered for 5 consecutive days.

For the treatment of Pleuropneumonia caused by *Actinobacillus pleuropneumoniae* susceptible to tiamulin:

The dosage is 20 mg tiamulin hydrogen fumarate (equivalent to 44.4 mg of product)/kg body weight daily administered for 5 consecutive days.

9. ADVICE ON CORRECT ADMINISTRATION

Use suitably calibrated weighing equipment to weigh the necessary amount of product

The maximum solubility of the product is 10 gram/liter.

In order to avoid interactions between the ionophores and tiamulin, the veterinarian and farmer should check that the feed label does not state that it contains salinomycin, monensin and narasin.

For chickens and turkeys, 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 occur.

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 the tiamulin-incompatible ionophores.

10. WITHDRAWAL PERIOD

Pigs

Meat and offal: 2 days (8.8 mg tiamulin hydrogen fumarate (equivalent to 19.6 mg of product)/kg body weight)

Meat and offal: 4 days (20 mg tiamulin hydrogen fumarate (equivalent to 44.4 mg of product)/kg body weight)

Chickens
Meat and offal: 2 days
Eggs: Zero days

Turkeys
Meat and offal: 6 days

11. SPECIAL STORAGE PRECAUTIONS

Shelf life after first opening the immediate packaging: 3 months
Shelf life after dilution or reconstitution according to directions: 24 hours
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.

Store in the original container.
Do not refrigerate or freeze.

Keep out of the sight and reach of children.

12. SPECIAL WARNING(S)

Special warnings (for each target species)

Animals with reduced water intake and/or in a debilitated condition should be treated parenterally.

Water intake may be depressed during the administration of tiamulin in birds. It appears to be concentration-dependent with 500 mg tiamulin hydrogen fumarate (equivalent to 1.11 g of product) in 4 litres of water reducing intake by approximately 10% and 500 mg tiamulin hydrogen fumarate (equivalent to 1.11 g of product) in 2 litres of water by 15% in chickens. It does not appear to have any adverse effect on overall performance of the birds or efficacy of the veterinary medicinal product but water intake should be monitored at frequent intervals, especially in hot weather. In turkeys, it is more marked, with approximately 20% reduction and therefore it is recommended not to exceed a concentration of 500 mg tiamulin hydrogen fumarate in 2 litres of the drinking water. **Special precautions for 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. Inappropriate use of the veterinary medicinal product may increase the prevalence of bacteria resistant to tiamulin.

User Warnings

Direct contact with the skin, eyes and mucous membranes should be avoided by wearing overalls, impermeable rubber gloves and safety glasses when preparing or handling the product.

In case of accidental eye contact, rinse the eyes thoroughly with clean running water immediately. Seek medical advice if irritation persists.

When handling the product, inhalation of the dust must be avoided by wearing a disposable half-mask respirator conforming to European Standard EN 149 or a non-disposable respirator to European Standard EN 140 with a filter to EN 143.

Contaminated clothing should be removed and any splashes on to the skin should be washed off immediately.

Wash hands after use.

Accidental ingestion should be avoided. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or label to the physician.

People with known hypersensitivity to tiamulin should avoid contact with the product.

Use during pregnancy, lactation or lay

Pigs

The product can be used during pregnancy and lactation.

Chickens and turkeys

Can be used in laying chickens and in breeding chickens and turkeys.

Interaction with other medicinal products and other forms of interaction

Tiamulin has been shown to interact with ionophores such as monensin, salinomycin and narasin and may result in signs indistinguishable from an ionophore toxicosis. Animals should not receive products containing monensin, salinomycin or narasin during or at least 7 days before or after treatment with tiamulin. Severe growth depression, ataxia, paralysis or death may result.

If signs of an interaction do occur, stop both the administration of tiamulin-medicated drinking water and also 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.

Concomitant use of tiamulin and the divalent ionophore anticoccidials lasalocid and semduramicin do not appear to cause any interaction, however the concomitant use of maduramicin 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), if necessary**

Chickens and turkeys:

Regarding poultry, there is a relatively high therapeutic index with tiamulin hydrogen fumarate and the likelihood of an overdose is considered remote especially as water intake and hence tiamulin hydrogen fumarate intake is reduced if abnormally high concentrations are given. The LD5 is 1090 mg/kg body weight for chickens and 840 mg/kg body weight for turkeys. The clinical signs of toxicity in chickens are vocalisation, clonic cramps and lying in a lateral position. Signs in turkeys are: clonic cramps, lateral or dorsal lying position, salivation and ptosis.

Pigs:

Single oral doses of 100 mg tiamulin hydrogen fumarate/kg body weight in pigs caused hyperpnoea and abdominal discomfort. At 150 mg tiamulin hydrogen fumarate/kg body weight no central nervous system effects were noted except for tranquillisation. At 55 mg tiamulin hydrogen fumarate/kg body weight daily given for 14 days, a transient salivation and slight gastric irritation occurred. Tiamulin hydrogen fumarate is considered to have an adequate therapeutic index in the pig and a minimum lethal dose has not been established. If signs of intoxication do occur promptly remove the medicated water and replace with fresh water.

Incompatibilities

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

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 product should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Block bottomed zipped 1 kg bag of polyethylene terephthalate/aluminium/low density Polyethylene.

When the container is opened for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the label.

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

Revised: August 2018
AN: 00077/2018

A handwritten signature in black ink, appearing to be 'Alan', with a horizontal line underneath.

Approved: 23 August 2018