SPC, LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Lamulin 364.2 mg/g granules for oral solutionfor pigs
(in Cyprus, Greece, Hungary, Italy, Portugal, Spain)
Stalimox 364.2 mg/g granules for oral solution for pigs
(in Austria, Czech Republic, France, Germany, Slovakia)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One g granules for oral solution contains:

Active substance:	Tiamulin (as hydrogen fumarate)	364.2 mg
	Equivalent to	
	Tiamulin hydrogen fumarate	450.0 mg

Excipient QSP. 1 g

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Granules for oral solution.
White or yellowish-white granules.

4. CLINICAL PARTICULARS

4.1 Target species

Swine

4.2 Indications for use, specifying the target species

For treatment of swine dysentery caused by *Brachyspira hyodysenteriae* sensitive to tiamulin hydrogen fumarate.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substance or to any of the excipients. Do not administer the product with monensin, salinomycin and narasin and other monovalent ionophore-antibiotics 7 days before, during and 7 days after treatment of animals.
Do not use in the case of resistance to tiamulin.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

The uptake of medication by animals can be altered as a consequence of illness. In case of insufficient uptake of water, animals should be treated parenterally.
Use of the product should be based on susceptibility testing and take into account official and local antimicrobial policies.

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

After dissolution of the product in drinking water the pH of the medicated solution is slightly to moderately acidic depending on the concentration (in-use or proportioner concentrate, see section 4.9) used. Therefore, direct contact of the product with the skin, eyes and mucous membranes should be avoided.
People with known hypersensitivity to tiamulin should avoid contact with the veterinary medicinal product.
Wear protective gloves when reconstituting or administering the solution. Wash exposed skin after preparation. In case of accidental projection into the eyes, rinse abundantly with water.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

On rare occasions erythema or mild oedema of the skin may occur in pigs following the use of tiamulin hydrogen fumarate.

4.7 Use during pregnancy, lactation

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic, foetotoxic, maternotoxic effects.
The safety of the product has not been established in pregnant or lactating sows. Use only in accordance with risk/benefit assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

Tiamulin is known to produce clinically important – often lethal – interactions with antibiotics belonging to the ionophores. Therefore, pigs should not receive products containing monensin, narasin, salinomycin or semduramycin during or at least 7 days before and after treatment with the product.

4.9 Amounts to be administered and administration route

To be administered orally, in drinking water.
Dosage:

7.3 mg tiamulin (equivalent to 9.0 mg tiamulin hydrogen fumarate) per kg of body weight daily (equivalent to 20.0 mg product per kg of body weight), administered in the drinking water for 5 consecutive days.

Administration:

To ensure an intake of 7.3 mg tiamulin (equivalent to 9 mg tiamulin hydrogen fumarate) per kg daily, the product may be administered in two different ways, as follows. The daily dose rate, calculated on a live weight basis, may be administered in approximately one half of the daily water requirement. Unmedicated water should be provided each day after the medicated water has been consumed.

The product may also be administered continuously in the drinking water. The concentration to be used depends on the actual body weight and the water consumption of the animals and should be calculated, as follows:

$$\frac{\text{.....mg Lamulin/Stalimox 364.2 mg/g granules per kg body weight and day} \times \text{Average pig body weight (kg)}}{\text{Average daily water intake (l/animal)}} = \text{....mg Lamulin/Stalimox 364.2 mg/g granules per litre of drinking water}$$

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing. The required doses should be measured by suitably calibrated weighing equipment

Medicated water should be refreshed every 24 hours.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

During the target animal tolerance study, no adverse effect was observed even at the threefold therapeutic dose administered for two times the recommended duration.

If suspected toxic reactions do occur due to extreme overdose, the medication should be discontinued and appropriate symptomatic treatment should be initiated if necessary.

4.11 Withdrawal period(s)

Meat and offal: 2 days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: other antibacterials, ATCvet code: QJ01XX92

5.1 Pharmacodynamic properties

Tiamulin is a semisynthetic derivative of the naturally occuring diterpene antibiotic pleuromutilin. It acts by inhibiting protein synthesis at the ribosomal level, predominantly by binding to the 50S ribosomal subunit of bacteria. Tiamulin is a moderate-spectrum, bacteriostatic antibiotic. Its antibacterial activity is largely confined to gram-positive microorganisms, mycoplasma, certain gram-negative anaerobes such as *Brachyspira* and *Fusobacterium spp*, and the obligate intracellular bacterium, *Lawsonia intracellularis*. MIC_{90} value of tiamulin against *Brachyspira hyodysenteriae* isolated in Germany in 2002 was found to be 2.0 μg/ml.

In vitro resistance against tiamulin is known to develop slowly and stepwise. In the past 5-6 years, however, increasing number of *Brachyspira* isolates were reported to show decreased susceptibility to tiamulin. No cross-resistance between tiamulin and related classes of antimicrobials and no co-resistence to other classes of antimicrobials is known.

5.2 Pharmacokinetic particulars

After oral administration to pigs, tiamulin is rapidly absorbed from the gastrointestinal tract, well distributed in the body organs, intensively metabolized in the liver and rapidly eliminated from the blood with a terminal elimination half-life of 2.1 hours. Oral bioavailability in pigs is about 85-90%, maximum plasma concentration after a single oral dose of 10 mg/kg was reported to be 0.7 μg/ml. Approximately 65% of the metabolites is excreted via bile and 35% in the urine. Only 0.3 to 0.5% of the parent compound is excreted unchanged in the urine. Tiamulin concentration in the lung after water medication at a dosage of 60 mg/litre was measured to be 1.11 μg/g. The concentrations of tiamulin in the colon contents and mucosa after repeated oral administrations of the product at a daily dose of 9 mg/kg b.w. in drinking water were 5.31±1.26 and 2.41±0.89 μg/g, respectively. The tiamulin concentrations both in the lung and in the colon substantially exceed the MIC_{90} of the drug against the pathogens.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch
Lactose monohydrate

6.2 Incompatibilities

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

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: 3 months
Shelf-life after dilution or reconstitution according to directions: 24 hours

6.4. Special precautions for storage

Do not store above 25°C.
Store in the original container tightly closed in order to protect from moisture.

6.5 Nature and composition of immediate packaging

100 g polypropylene container with inner bag of LDPE.
1 kg polypropylene container with inner bag of LDPE.
5 kg polypropylene container with inner bag of LDPE.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

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

7. MARKETING AUTHORISATION HOLDER

Lavet Pharmaceuticals Ltd.
1161 Budapest
Ottó u. 14.
Hungary

For Germany:
VIRBAC S.A.
1ère avenue 2065 m L.I.D.
F-06516 Carros

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

In Italy:
Ricetta medico veterinaria in triplice copia non ripetibile.

LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

100 g polypropylene container with inner bag of LDPE.
1 kg polypropylene container with inner bag of LDPE.
5 kg polypropylene container with inner bag of LDPE.

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Lamulin 364.2 mg/g granules for oral solution for pigs
(in Cyprus, Greece, Hungary, Italy, Portugal, Spain)
Stalimox 364.2 mg/g granules for oral solution for pigs
(in Austria, Czech Republic, France, Germany, Slovakia)
Tiamulin (as hydrogen fumarate)

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Active substance:	Tiamulin (as hydrogen fumarate)	364.2 mg/g
	Equivalent to	
	Tiamulin hydrogen fumarate	450.0 mg/g

3. PHARMACEUTICAL FORM

Granules for oral solution

4. PACKAGE SIZE

100 g
1 kg
5 kg

5. TARGET SPECIES

Swine

6. INDICATION(S)

For treatment of swine dysentery caused by *Brachyspira hyodysenteriae* sensitive to tiamulin hydrogen fumarate.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

For in drinking water use.
Average dose: 7.3 mg tiamulin (equivalent to 9 mg tiamulin hydrogen fumarate) per kg of body weight daily.

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal period:
Meat and offal: 2 days.

9. SPECIAL WARNING(S), IF NECESSARY

Accidental contact with the mucosa is dangerous – see package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
After first opening of container: 3 months
After reconstitution in drinking water: 24 hours.

11. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.
Store in the original container tightly closed in order to protect from moisture.

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 products 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 REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Lavet Pharmaceutical Ltd.
1161 Budapest
Ottó u. 14.
Hungary

For Germany:
VIRBAC S.A.
1ère avenue 2065 m L.I.D.
F-06516 Carros

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch: {number}

PRODUCT INFORMATION

PACKAGE LEAFLET
Lamulin 364.2 mg/g granules for oral solutionfor pigs
(in Cyprus, Greece, Hungary, Italy, Portugal, Spain)
Stalimox 364.2 mg/g granules for oral solutionfor pigs
(in Austria, Czech Republic, France, Germany, Slovakia)

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

MAH: Lavet Pharmaceuticals Ltd., 1161 Budapest, Ottó u. 14., HUNGARY
For Germany:
VIRBAC S.A. – 1ère avenue – 2065 m L.I.D. – F-06516 CARROS

Manufacturer for the batch release:
Lavet Pharmaceuticals Ltd., 2143, Kistarcsa Batthyány u. 6., HUNGARY
or
VIRBAC S.A. – 1ère avenue – 2065 m L.I.D. – F-06516 CARROS

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Lamulin 364.2 mg/g granules for oral solutionfor pigs
(in Cyprus, Greece, Hungary, Italy, Portugal, Spain)
Stalimox 364.2 mg/g granules for oral solution for pigs
(in Austria, Czech Republic, France, Germany, Slovakia)
Tiamulin (as hydrogen fumarate)

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

Active substance:	Tiamulin (as hydrogen fumarate)	364.2 mg/g
	Equivalent to	
	Tiamulin hydrogen fumarate	450.0 mg/g

4. INDICATION(S)

For treatment of swine dysentery caused by *Brachyspira hyodysenteriae* sensitive to tiamulin hydrogen fumarate.

5. CONTRAINDICATIONS

Do not use in case of hypersensitivity to the active substance or to any of the excipients. Do not administer the product with monensin, salinomycin and narasin and other monovalent ionophore-antibiotics 7 days before, during and 7 days after treatment of animals.
Do not use in the case of resistance to tiamulin.

6. ADVERSE REACTIONS

On rare occasions erythema or mild oedema of the skin may occur in pigs following the use of tiamulin hydrogen fumarate.
If you notice any serious effect or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Swine

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

Dosage:
7.3 mg tiamulin (equivalent to 9.0 mg tiamulin hydrogen fumarate) per kg of body weight daily (equvivalent to 20.0 mg product per kg of body weight), administered in the drinking water for 5 consecutive days.

9. ADVICE ON CORRECT ADMINISTRATION

Administration:
To ensure an intake of 7.3 mg tiamulin (equivalent to 9 mg tiamulin hydrogen fumarate) per kg daily, the product may be administered in two different ways, as follows. The daily dose rate, calculated on a live weight basis, may be administered in approximately one half of the daily water requirement. Unmedicated water should be provided each day after the medicated water has been consumed.
The product may also be administered continuously in the drinking water. The concentration to be used depends on the actual body weight and the water consumption of the animals and should be calculated, as follows:

$$\frac{\text{.....mg Lamulin/Stalimox 364.2 mg/g granules per kg body weight and day} \times \text{Average pig body weight (kg)}}{\text{Average daily water intake (l/animal)}} = \text{....mg Lamulin/Stalimox 364.2 mg/g granules per litre of drinking water}$$

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing. The required doses should be measured by suitably calibrated weighing equipment
Medicated water should be refreshed every 24 hours.

10. WITHDRAWAL PERIOD

Meat and offal: 2 days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.

Do not store above 25°C.
Store in the original container tightly closed in order to protect from moisture.

Do not use after the expiry date stated on the label.
Shelf life of the product as packaged for sale: 2 years.
Shelf-life after first opening the container: 3 months.
Shelf-life after dilution or reconstitution according to directions: 24 hours.

12. SPECIAL WARNING(S)

During the target animal tolerance study, no adverse effect was observed even at the threefold therapeutic dose administered for two times the recommended duration.
If suspected toxic reactions do occur due to extreme overdose, the medication should be discontinued and appropriate symptomatic treatment should be initiated if necessary.
The uptake of medication by animals can be altered as a consequence of illness. In case of insufficient uptake of water, animals should be treated parenterally.
Use of the product should be based on susceptibility testing and take into account official and local antimicrobial policies.
After dissolution of the product in drinking water the pH of the medicated solution is slightly to moderately acidic depending on the concentration (in-use or proportioner concentrate, see section 4.9) used. Therefore, direct contact of the product with the skin, eyes and mucous membranes should be avoided.
People with known hypersensitivity to tiamulin should avoid contact with the veterinary medicinal product.
Wear protective gloves when reconstituting or administering the solution. Wash exposed skin after preparation. In case of accidental projection into the eyes, rinse abundantly with water.
The safety of the veterinary medicinal product has not been established in pregnant or lactating sows. Use only in accordance with risk/benefit assessment by the responsible veterinarian.
Tiamulin is known to produce clinically important – often lethal – interactions with antibiotics belonging to the ionophores. Therefore, pigs should not receive products containing monensin, narasin, salinomycin or semduramycin during or at least 7 days before and after treatment with the Lamulin/Stalimox product.
In absence of compatibility studies, the product must not mixed with other veterinary medicinal product.

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

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Pack sizes:
100 g polypropylene container with inner bag of LDPE.

1 kg polypropylene container with inner bag of LDPE.
5 kg polypropylene container with inner bag of LDPE.
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.