

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Denagard 80% w/w Premix for Medicated Feed for Pigs, Chickens and Turkeys

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Tiamulin hydrogen fumarate - 800 mg/g

Excipients

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Premix for medicated feeding stuff

4. CLINICAL PARTICULARS

4.1 Target species

Pigs

Chickens (broiler, replacement pullet, layer/breeder)

Turkeys (poult (grower) and breeder)

4.2 Indications for use, specifying the target species

Pigs

For the treatment and metaphylaxis, when the disease is present in the group, of swine dysentery caused by *Brachyspira hyodysenteriae* susceptible to tiamulin. The presence of the disease in the group must be established before the product is used.

For the treatment of colitis caused by *Brachyspira pilosicoli*.

For the treatment of ileitis caused by *Lawsonia intracellularis*.

For the treatment of enzootic pneumonia caused by *Mycoplasma hyopneumoniae*.

Chickens

For the treatment and prevention of chronic respiratory disease (CRD) and air sacculitis caused by *Mycoplasma gallisepticum* and *Mycoplasma synoviae*.

Turkeys

For the treatment and prevention of infectious sinusitis and air sacculitis caused by *Mycoplasma gallisepticum*, *Mycoplasma meleagridis* and *Mycoplasma synoviae*.

4.3 Contraindications

Animals should not receive products containing ionophores (monensin, narasin or salinomycin) during or for at least seven days before or after treatment with tiamulin. Severe growth depression or death may result.

Refer to section 4.8 for information regarding interaction between tiamulin and ionophores

4.4 Special warning for each target species

In case of reduced feed intake, the inclusion levels in feed may need to be increased to achieve target dosage. Acute cases and severely diseased animals with reduced feed intake should be treated with a product of suitable formulation such as an injectable or water solution.

4.5 Special precautions for use

i. Special precautions for use in animals

It is sound clinical practice to base treatment 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.

Refer to section 4.8 for information regarding interaction between tiamulin and ionophores.

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

When mixing the veterinary medicinal product and handling the medicated feed, direct contact with eyes, skin and mucous membranes should be avoided. Personal protective equipment should be worn when mixing the veterinary medicinal product or handling the medicated feed: overalls, impervious gloves and either a disposable half-mask respirator conforming to European Standard EN 149 or a non-disposable respirator conforming to European Standard EN 140, with a filter to European Standard EN 143. Wash contaminated skin.

In case of accidental ingestion, seek medical advice immediately and show the package insert or label to the physician.

People with known hypersensitivity to tiarnulin should administer the product with caution.

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.

4.7 Use during pregnancy, lactation or lay

Can be used in pigs during pregnancy and lactation.
Can be used in laying and breeding chickens and turkeys.

4.8 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, administration of contaminated feed should be stopped immediately. The feed should be removed and replaced with fresh feed not containing the anticoccidials monensin, salinomycin or narasin.

4.9 Amounts to be administered and administration route

Calculations to achieve the correct dose rate and achieve the correct inclusion rate should be based on: - Inclusion rate (ppm) = dose rate (mg/kg bwt) x bodyweight (kg) / daily feed intake (kg).

To ensure a correct dosage, bodyweight should be determined as accurately as possible to avoid underdosing.

The intake of medicated feed depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of tiamulin hydrogen fumarate has to be adjusted accordingly.

Pigs

Treatment and metaphylaxis of Swine Dysentery caused by *B. hyodysenteriae*, treatment of Porcine Colonic Spirochaetosis (colitis) caused by *B. pilosicoli*

Dosage: 5 - 10 mg tiamulin hydrogen fumarate/kg bodyweight daily administered for 7 to 10 consecutive days. The dosage will normally be achieved by an inclusion level of 100 – 200 ppm tiamulin hydrogen fumarate in the finished feed provided that feed intake is unaffected.

Amount of THF (mg/g) per premix formulation	Amount of premix formulation per one tonne of feed
800.0	0.125 – 0.25 kg

Treatment of Porcine Proliferative Enteropathy (ileitis) caused by *L. Intracellularis*

Dosage: 7.5 mg tiamulin hydrogen fumarate/kg bodyweight daily administered for 10 to 14 consecutive days. The dosage will normally be achieved by an inclusion level of 150 ppm tiamulin hydrogen fumarate in the finished feed providing that feed intake is unaffected.

Amount of THF (mg/g) per premix formulation	Amount of premix formulation per one tonne of feed
800.0	0.188 kg

Treatment of Enzootic Pneumonia caused by *M. hyopneumoniae*

Dosage: 5.0 – 10.0 mg tiamulin hydrogen fumarate/kg bodyweight daily administered for 7 to 10 consecutive days. The dosage will normally be achieved by an inclusion level of 100 -200 ppm tiamulin hydrogen fumarate in the finished feed provided that feed intake is unaffected.

Secondary infection by organisms such as *Pasteurella multocida* and *Actinobacillus pleuropneumoniae* may complicate enzootic pneumonia and require specific medication.

Amount of THF (mg/g) per premix formulation	Amount of premix formulation per one tonne of feed
800.0	0.125 – 0.25 kg

Chicken (broiler, replacement pullet, laying and breeding hens)

Treatment and prevention of Chronic Respiratory Disease (CRD) caused by *M. gallisepticum* and air sacculitis and infectious synovitis caused by and *M. synoviae*.

Dosage – Treatment and prevention: 25 mg tiamulin hydrogen fumarate/kg bodyweight daily administered for the period of 3 to 5 consecutive days. This is normally achieved by an inclusion level of 250 - 500 ppm tiamulin hydrogen fumarate in finished feed provided that feed intake is unaffected. Inclusion levels in the higher range will in most cases be needed to avoid underdosing. In fast growing birds, e.g. broiler chickens during the first 2-4 weeks of life, inclusion levels in the lower range may be sufficient.

Amount of THF (mg/g) per premix formulation	Amount of premix formulation per one tonne of feed
800.0	0.313 - 0.625 kg

Turkey (young poults, breeding turkeys)

Treatment and prevention of infectious sinusitis and air sacculitis caused by *M. gallisepticum*, *M. synoviae* and *M. meleagridis*.

Dosage – Treatment and prevention: 40 mg tiamulin hydrogen fumarate/kg bodyweight daily administered for the period of 3 to 5 consecutive days. This is normally achieved by an inclusion level of 250 – 500 ppm tiamulin hydrogen fumarate in finished feed provided that feed intake is unaffected. Inclusion levels in the higher range will in most cases be needed to avoid underdosing. In fast growing birds, e.g. poults during the first 2-4 weeks of life, inclusion levels in the lower range may be sufficient.

Amount of THF (mg/g) per premix formulation	Amount of premix formulation per one tonne of feed
800.0	0.313 – 0.625 kg

Preventive treatment with tiamulin should only be initiated after confirmed infection with *M. gallisepticum*, *M. synoviae* or *M. meleagridis* and then as an aid in the prevention strategy to reduce the clinical signs and mortality from respiratory disease in flocks where infection in ovum is likely because the disease is known to exist in the parent generation. The prevention strategy should include efforts to eliminate the infection from the parent generation.

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

Pigs: Single oral doses of 100 mg/kg bodyweight in pigs caused hyperpnoea and abdominal discomfort. At 150 mg/kg no CNS effects were noted except for sedation. At 55 mg/kg given for 14 days a transient salivation and slight gastric irritation occurred. A minimum lethal dose has not been established in the pig.

Chickens and turkeys: The LD₅ for chickens is 1290 mg/kg and turkeys 840 mg/kg bodyweight.

The clinical signs of acute toxicity in chickens are – vocalization, clonic cramps and lateral recumbency. In turkeys signs of acute toxicity include clonic cramps, lateral or dorsal recumbency, salivation and ptosis.

If signs of intoxication do occur promptly remove the medicated feed, replace with fresh unmedicated feed and apply supportive, symptomatic therapy.

4.11 Withdrawal period(s)

Pigs

Treatment (at 5-10 mg/kg bwt): 6 days

Chickens

Meat and offal: 1 day

Eggs: 0 days

Turkeys

Meat and offal: 4 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antibacterial for systemic use

ATCvet code: QJ01XQ01

5.1 Pharmacodynamic properties

Tiamulin is a bacteriostatic semi-synthetic antibiotic belonging to the pleuromutilin group of antibiotics and acts at the ribosomal level to inhibit bacterial protein synthesis.

Tiamulin has shown a in-vitro activity against a wide range of bacteria such as *Brachyspira hyodysenteriae*, *Brachyspira pilosicoli*, *Lawsonia intracellularis* and *Mycoplasma* spp.

Tiamulin is bacteriostatic at therapeutic concentrations and has been shown to act at the 70S ribosome level and the primary binding site is on the 50S subunit and possibly a secondary site where the 50S and 30S subunits join. It appears to inhibit microbial protein production by producing biochemical inactive initiation complexes, which prevent elongation of the polypeptide chain.

Mechanisms responsible for resistance development in *Brachyspira* spp to the pleuromutilin class of antibiotics are considered to be based on mutations at the ribosomal target site. Clinically relevant resistance to tiamulin requires combinations of mutations around the tiamulin binding site.

Resistance to tiamulin may be associated with decreased susceptibility to other pleuromutilins.

5.2 Pharmacokinetic particulars

Pig

Tiamulin is well absorbed in the pig (over 90%) following oral administration and widely distributed through the body. Following a single oral dose of 10 mg and 25 mg tiamulin/kg bodyweight, the C_{max} was 1.03 µg/ml and 1.82 µg/ml respectively by microbiological assay and the T_{max} was 2 hours for both.

Tiamulin has been shown to concentrate in the lung, a target tissue, and also in liver, where it is metabolised and excreted (70-85%) in the bile, the remainder is excreted via the kidney (15-30%). Tiamulin which has not been absorbed or metabolised, passes down the intestines to the colon and concentrates there.

Chicken

Tiamulin is well absorbed in chickens (70-95%) after oral administration.

Tiamulin distributes widely through the body and has been shown to concentrate in the liver and kidney (sites of excretion) and in the lung (30 times serum level). Excretion is mainly via the bile (55-65%) and kidney (15-30%) as mainly microbiologically inactive metabolites and is quite rapid, 99% of the dose within 48 hours.

Turkey

In turkeys, serum levels of tiamulin are similar to chickens. In breeders on 0.025% tiamulin the average serum level was 0.36 µg/ml (range 0.22-0.5 µg/ml).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gelatin

6.2 Incompatibilities

None known

6.3 Shelf-life

Shelf life of veterinary medicinal product as packaged for sale: 3 years.

Shelf life after incorporation into meal or pellet feed: 3 months.

6.4 Special precautions for storage

Do not store above 25°C. Store in a dry place. Protect from light.
The product will remain stable in the finished feed or vitamin/mineral premixes for 3 months.

6.5 Nature and composition of immediate packaging

Low density polyethylene bags containing 5 kg or 25 kg.

Not all pack sizes may be marketed.

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

Any unused product or waste material should be disposed of in accordance with national requirements.

7. MARKETING AUTHORISATION HOLDER

Elanco Europe Ltd
Lilly House
Priestley Road
Basingstoke
Hampshire
RG24 9NL

8. MARKETING AUTHORISATION NUMBER

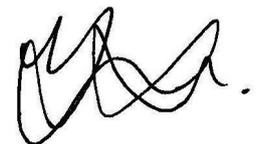
Vm 00879/4054

9. DATE OF FIRST AUTHORISATION

07 January 1993

10. DATE OF REVISION OF THE TEXT

March 2021



Approved: 03 March 2021