

TYVALOSIN[®]

Water Soluble Granules

Novel therapeutic antibiotic, setting the new standard for cost-effective treatment of ileitis.

INDICATIONS

- For the treatment of porcine proliferative enteropathy (PPE) associated with *Lawsonia intracellularis* in pigs.

PRODUCT DESCRIPTION

- Water-soluble antibiotic for oral use by administration in the drinking water.
- Contains 62.5% w/w tylvalosin (as tylvalosin tartrate), a macrolide antibiotic.
- Veterinary use only; for use in drinking water of swine.

WITHDRAWAL PERIOD

- 24 hours.

PACKAGING

- Cartons containing either 20 × 40-g, 10 × 160-g, or 5 × 400-g sachets.

STORAGE

- Store at or below 25°C.

FORMULATION

- Water-soluble granules; concentrated for drinking water and stock solutions.

DOSAGE & ADMINISTRATION

- May be mixed directly into the drinking water system or first mixed as a stock solution (e.g., for automatic water proportioners).
- Prepare drinking water medicated with 50 ppm tylvalosin daily. Administer continuously for 5 consecutive days.
- Based on a theoretical daily water consumption rate of 10% of body weight, 50 ppm tylvalosin in drinking water provides the target dose rate of 5 mg tylvalosin/kg body weight per day.
- Prepare fresh medicated drinking water daily.

EXPIRATION PERIOD

- 3-year shelf-life for unopened sachets.

KEY FEATURES

- Quick-acting, potent macrolide antibiotic that is not used in human health.
- Accumulates rapidly in target tissues with intracellular concentrations many times extracellular levels.
- Enhances macrophage activity.
- Easy, reliable dosing in drinking water for immediate treatment of new outbreaks.
- Flexible usage; compatible with clinical or subclinical disease management programs.
- Palatable, non-clogging formulation.
- Brief 24-hour withdrawal period.
- Wide safety margin.

Veterinary use only

AIVLOSIN®

Water Soluble Granules

EN:**62.5% w/w tylvalosin (as tylvalosin tartrate)**

DESCRIPTION: Aivlosin® Water Soluble Granules is a water soluble granular powder containing 62.5% w/w tylvalosin (as tylvalosin tartrate) for oral use by administration in the drinking water.

THERAPEUTIC CLASSIFICATION: Tylvalosin, the active ingredient in Aivlosin® Water Soluble Granules, is a macrolide antibiotic.

INDICATIONS: For the treatment of Porcine Proliferative Enteropathy (PPE) associated with *Lawsonia intracellularis* in pigs.

TARGET SPECIES: Pigs.

DOSAGE AND ADMINISTRATION:**For use in drinking water of swine only.**

Administer continuously in drinking water. Medicated water should be the only source of drinking water during the treatment period. If improvement is not observed within 5 days, the diagnosis should be reconfirmed. Keep water supply equipment clean and in good operating condition. Clean water medication equipment before and after each use. Only a sufficient amount of medicated drinking water should be prepared to cover daily requirements.

Do not mix or administer medicated water using equipment made of galvanized metal. Galvanized metal adversely affects the stability of tylvalosin in water and may reduce the effectiveness of the product. Prepare a fresh batch of medicated stock solution or medicated drinking water daily.

Aivlosin® Water Soluble Granules may be mixed directly into the drinking water system or first mixed as a stock solution in a smaller amount of water, which is then added to the drinking water system, for example, using an automatic water proportioner.

When mixing the product directly into the drinking water system, the contents of the sachet should be sprinkled onto the surface of the water and mixed slowly and thoroughly until a clear solution is produced (usually within 3 minutes).

When preparing a stock solution for an automatic water proportioner, the recommended maximum concentration is one-40 g sachet per 4 L (~1 US gallon), one-160 g sachet per 16 L (~4 US gallons) or one-400 g sachet per 40 L (~10 US gallons). Sprinkle contents onto the surface of the water and mix slowly and thoroughly for 10 minutes. After this time, any remaining cloudiness will not affect tylvalosin concentration. Use the stock solution for dilution into the drinking water system as soon as it is prepared. Add 32 mL of this stock solution per 4 L drinking water to provide a final concentration of 50 ppm.

Prepare drinking water medicated with 50 parts per million tylvalosin as shown in the following table:

Aivlosin® Water Soluble Granules sachet size	40 g	160 g	400 g
Tylvalosin content of sachet (g)	25	100	250
Volume of drinking water (L)	500	2000	5000
Volume of drinking water (US gallons)	132	528	1320
Tylvalosin inclusion rate in water	50 parts per million (ppm)		

Administer continuously in drinking water for five (5) consecutive days. Based on a theoretical daily water consumption rate of 10% body weight, 50 ppm tylvalosin in drinking water will provide a dose rate of 5 mg tylvalosin/kg body weight per day.

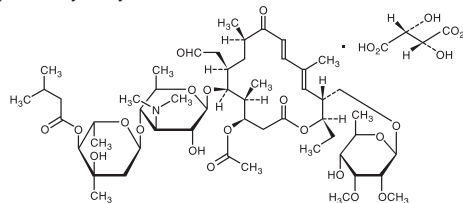
CAUTIONS: Not for use in breeding animals. The effects of tylvalosin on swine reproductive performance, pregnancy and lactation have not been determined.

WARNINGS: Treated swine must not be slaughtered for use in food for at least 24 hours after the latest treatment with this drug. Tylvalosin has been shown to cause hypersensitivity reactions in laboratory animals; therefore, people with known hypersensitivity to tylvalosin tartrate should avoid contact with this product. When mixing Aivlosin® Water Soluble Granules and handling the medicated water, direct contact with eyes, skin and mucous membranes should be avoided. Keep out of reach of children.

ADVERSE REACTIONS: No adverse reactions related to the drug were observed during clinical or target animal safety trials.

CLINICAL PHARMACOLOGY:**Chemical Nomenclature and Structure**

(4R,5S,6S,7R,9R,11E,13E,15R,16R)-15-[[[6-deoxy-2,3-di-O-methyl-β-D-allopyranosyl]oxy]methyl]-6-[[[3,6-dideoxy-4-O-[2,6-dideoxy-3-C-methyl-4-O-(3-methylbutanoyl)-α-L-ribo-hexopyranosyl]-3-(dimethylamino)-β-D-glucopyranosyl]oxy]-16-ethyl-5,9,13-trimethyl-2,10-dioxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-dien-4-yl acetate (2R,3R)-2,3-dihydroxybutanedioate.

**Mechanism of Action:**

Tylvalosin is a 16-membered macrolide ring structure. Macrolides inhibit bacterial protein synthesis. They penetrate the bacterial cell wall and cell membrane to reach the cytoplasm, where they bind to the 50S ribosomal sub-unit with a specific target in the 23S ribosomal RNA molecule. Consequently, they prevent peptide chain elongation by interfering with the formation of the peptide bonds. The macrolide class of antimicrobials is used therapeutically.

MICROBIOLOGY: The spectrum of activity of most available macrolides used in veterinary medicine is primarily against Gram-positive bacteria and mycoplasmas with some activity against Gram-negative fastidious bacteria but no activity against the naturally resistant *Enterobacteriaceae* including *Escherichia coli* and *Salmonella* spp. MIC data for *Lawsonia intracellularis* have been generated (Table 1). The MIC of each antibiotic was defined as the lowest concentration tested which consistently inhibited growth (<1% of the control growth).

Table 1. MIC Data for Tylvalosin against *Lawsonia intracellularis*

Strain Tested	Intracellular MIC (µg/mL)	Reference
51/89	32	McOrist (2002)
KM 01	32	
916/91 ^a	32	Gebhart (2000)
VP4 ^b	>64 (cytopathic activity)	

^aUK strain, ^bUS strain

Use of antibacterial drugs in the absence of a susceptible bacterial infection is unlikely to provide benefit to treated animals and may increase the development of drug-resistant pathogenic bacteria.

HANDLING PRACTICES: When handling animals, the possibility of spreading infections between facilities and contracting zoonoses should be considered. The use of Good Infection Control Practices is recommended, and should include the use of impermeable gloves and clean clothing at each facility visited. Washing hands after each facility visit is recommended.

STORAGE: Store at or below 25°C.

HOW SUPPLIED: Aivlosin® Water Soluble Granules is packaged in cartons containing either 20 x 40 g, 10 x 160 g or 5 x 400 g sachets.

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