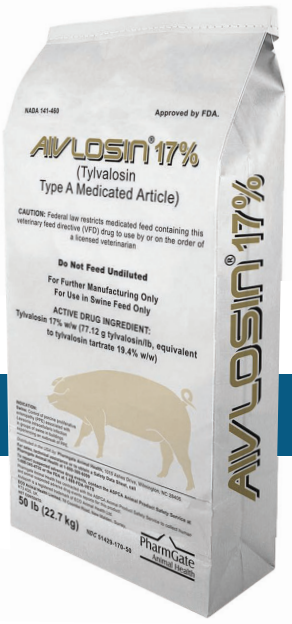
AIVLOSIN® 17%

(Tylvalosin Type A Medicated Article)



The powerful new tool for cost-effective ileitis control

- Great economics
- Quick acting
- Outstanding results
- Convenient in-feed dosing
- No withdrawal

Fast-Facts

Indication

For control of porcine proliferative enteropathy (PPE) associated with *Lawsonia intracellularis* infection in groups of swine in buildings experiencing an outbreak of PPE.

Active ingredient

Tylvalosin, a new unique macrolide antibiotic for oral use in feed.

Formulation

Free-flowing granules containing 17% tylvalosin (as tylvalosin tartrate).

Dosage and Administration

Feed Type C medicated feed containing 38.6 grams tylvalosin/ton (42.5 ppm) as the sole ration for 14 consecutive days.

Withdrawal

0 days (no withdrawal needed).

Availability

Veterinary feed directive drug (VFD).

Pharmgate
ANIMAL HEALTH

The labeling contains complete use information, including cautions and warnings. Always read, understand and follow the labeling and use directions. See the back page for use directions and additional information.

AIVLOSIN® 17%

(Tylvalosin Type A Medicated Article)

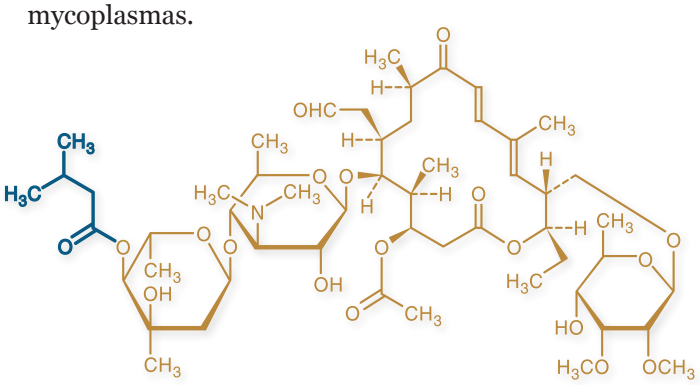
The powerful new tool for cost-effective ileitis control

New, Unique Feed Medication for Ileitis Control

- Aivlosin® 17% is an entirely new product for swine.
- Tylvalosin, the active ingredient of Aivlosin 17%, is a novel antibiotic that provides rapid and cost-effective control of ileitis caused by the intracellular pathogen *Lawsonia intracellularis*.

Powerful Second-Generation Macrolide

- Tylvalosin (Aivlosin 17%) is a macrolide antibiotic that interferes with bacterial protein synthesis by binding to ribosomes. It is active mainly against Gram-positive bacteria, some fastidious Gram-negative bacteria, and mycoplasmas.



Lipophilic isovaleryl group (blue) on the tylvalosin molecule allows rapid penetration of cellular lipid membranes. Subsequent binding to bacterial ribosomes interferes with protein synthesis.

Quick Results, Greater and Rapid Accumulation

Research: Uptake by gut epithelial cells (in vitro)

- Tylvalosin entered epithelial cells much **more rapidly and at much higher concentration than tilmicosin or tylosin** (Figure 1).[1]

Research: Uptake by swine neutrophils (in vitro)

- Tylvalosin rapidly entered swine white blood cells and **achieved high concentrations 8.9-times the extracellular concentration, much greater than that achieved by tilmicosin or tylosin.**[1]

Research: Pharmacokinetics in swine (in vivo)

- Tylvalosin is rapidly absorbed and concentrates in target tissues. Concentrations of tylvalosin and 3-AT (a microbiologically active metabolite) in small intestines and lungs exceeded those in blood (Table 1).[2]

Intracellular concentration (µg/g)

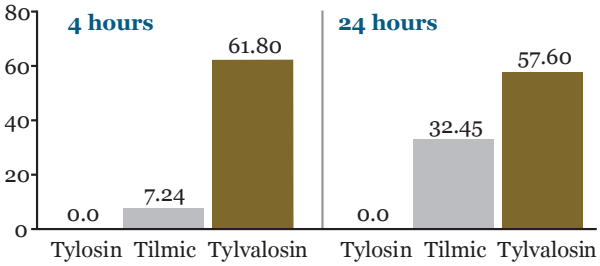


Figure 1: *Intracellular concentrations of tylvalosin, tilmicosin, and tylosin in HRT-18 cells after 4 and 24 hours incubation (mean of duplicate samples).*

Tissue	Drug conc.	Ratio tissue:blood
Blood	5.3 µg/mL	
Small intestine	14.43 µg/g	3.2×
Lung	7.7 µg/g	1.7×

Table 1: *Drug concentrations (tylvalosin+3-AT) 2 hours after oral tylvalosin at 50 mg/kg BW.*

Tylvalosin Offers Advantages Compared to Earlier/Older Macrolides

- **Reaches gut epithelial cells (site of infection) much faster and at much higher levels.**
- **Reaches high tissue concentrations, especially in lungs and small intestine.**
- **Rapidly penetrates white blood cells at concentrations much higher than other macrolides.**

Great Performance for Ileitis

The clinical effectiveness of Aivlosin® 17% for control of ileitis (PPE) was evaluated in two masked, randomized complete block design, challenge studies conducted in the US and Canada.[3,4] Both sites followed a common protocol:

- 144 PPE-free commercial cross-bred male and female pigs (4-5 wk of age, 18-31 lb) were randomly allocated at each site to 2 treatment groups of 72 pigs each.
- Pigs were orally challenged with an intestinal mucosal homogenate containing *L. intracellularis* prepared from a field case of acute hemorrhagic PPE.
- When at least 15% of pigs showed signs of diarrhea (day 6-7), Aivlosin treatment was initiated in one group (via medicated feed as sole ration for 14 consecutive days) while the other group (control) remained non-medicated.
- Clinical scores were recorded daily; intestines scored for PPE lesions at necropsy.

Results - Site A:

- Aivlosin significantly reduced (P = 0.03) PPE intestinal lesion scores (Figure 2), & mortality fell 73% (P = 0.03).
- Average daily gain (ADG) significantly improved by 87.5% (P = 0.0004) in the Aivlosin group (Figure 2).

Results - Site B:

- Aivlosin significantly reduced (P = 0.02) PPE intestinal lesion scores (Figure 3).
- Fecal scores (Figure 3) and abdominal appearance scores were significantly improved (P = 0.0001 and P = 0.004 respectively).

Conclusions:

Aivlosin was highly effective in providing control of ileitis challenge infections.

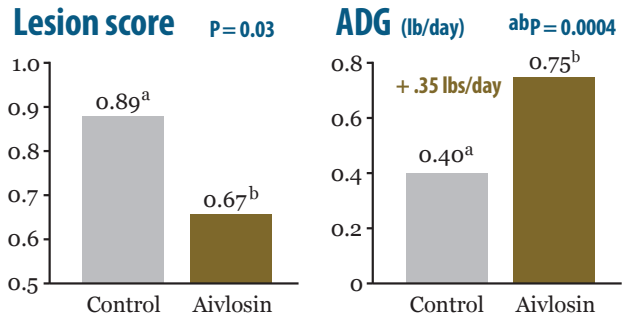


Figure 2: *Site A – average PPE lesion scores and ADG. (lesions scored on a range of 0 to 3, 0=normal, 3=severe).*

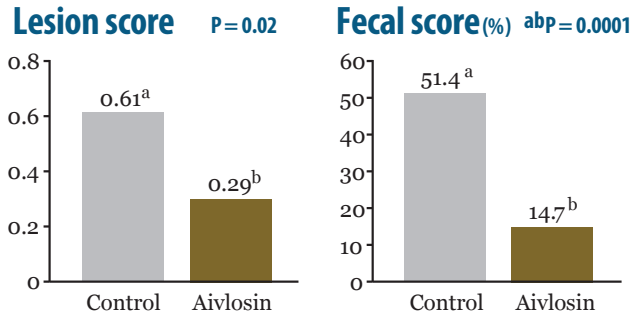


Figure 3: *Site B - average PPE lesion scores and fecal scores. (lesions scored on a range of 0 to 3, 0=normal, 3=severe; fecal score represents proportion of pen pig alive days with abnormal fecal scores).*

Physical Characteristics

- **Excellent homogeneity in feed**
- **Convenient in mills**
- **Excellent flowability**
- **Little or no dust**
- **Low risk of contamination**

AIVLOSIN® 17%

The powerful *NEW* tool for ileitis

- **Excellent disease control, reducing mortality and supporting optimal performance.**
- **Powerful action for Ileitis.**
- **Ideal for strategic, targeted control programs.**
- **Zero-day withdrawal time.**
- **Convenient free-flowing granular formulation.**
- **Wide safety margin.**
- **Long shelf life.**
- **Flexible medication options via feed, or via drinking water using Aivlosin® Water Soluble Granules.**

Important Safety Information: Available under Veterinary Feed Directive only. AIVLOSIN is indicated only for the control of PPE caused by *Lawsonia intracellularis* in groups of swine in a house experiencing an outbreak of this disease. For use only in the feed of pigs. Not for use in lactating or pregnant females, or males and females intending for breeding. May cause skin irritation. People with known hypersensitivity to Tylvalosin Tartrate should avoid contact with this product. When handling Aivlosin® 17% Tylvalosin Type A Medicated Article, avoid direct contact with eyes and skin. Wear a dust mask, coveralls, and impervious gloves when mixing and handling this product. Eye protection is recommended. When used in accordance with label directions, no withdrawal period is required before slaughter for human consumption.

NADA 141-460 **Approved by FDA.**

AIVLOSIN® 17%

(Tylvalosin Type A Medicated Article)

CAUTION: Federal law restricts medicated feed containing this veterinary feed directive (VFD) drug to use by or on the order of a licensed veterinarian

Do Not Feed Undiluted – For Further Manufacturing Only – For Use in Swine Feed Only

ACTIVE DRUG INGREDIENT: Tylvalosin 17% w/w (77.12 g tylvalosin/lb, equivalent to tylvalosin tartrate 19.4% w/w)

INDICATION: Swine: Control of porcine proliferative enteropathy (PPE) associated with *Lawsonia intracellularis* infection in groups of swine in buildings experiencing an outbreak of PPE.

DIRECTIONS FOR USE:

MIXING DIRECTIONS:

Swine:

Control of Porcine Proliferative Enteropathy

Preparation of Type B medicated feed containing 3,856 grams per ton (4,250 ppm) tylvalosin:

Prepare tylvalosin Type B medicated feed in mash form only.
To manufacture one ton of Type B medicated feed containing 3,856 g/ton (4,250 ppm) tylvalosin, mix 50 pounds of Aivlosin® 17% Type A Medicated Article with 1950 pounds of non-medicated feed.

Preparation of Type C medicated feed containing 38.6 grams per ton (42.5 ppm) tylvalosin:

To manufacture one ton of Type C medicated feed containing 38.6 g/ton (42.5 ppm) tylvalosin, mix 0.5 pound of Aivlosin® 17% Type A Medicated Article with 1999.5 pounds of non-medicated feed.

To aid in the even distribution of drug in the finished feed, add the full amount of Aivlosin® 17% Type A Medicated Article into a small portion of the feed and mix. Blend this mixture into the remainder of the feed and mix thoroughly. Pelleted Type C medicated feed must bear an expiration date of 30 days after the date of manufacture. Crumbled Type C medicated feeds must bear an expiration date of 7 days after the date of manufacture.

FEEDING DIRECTIONS: Feed Type C medicated feed containing 38.6 grams tylvalosin/ton as the sole ration for 14 consecutive days.

CAUTION: To assure both food safety and responsible use in swine, concurrent use of tylvalosin Type A medicated article in medicated feed and tylvalosin or another macrolide in medicated drinking water or by any other route of administration should be avoided. Not for use in swine intended for breeding. The effects of tylvalosin on swine reproductive performance, pregnancy, and lactation have not been determined. VFDs for tylvalosin shall not be refilled.

WARNINGS:

WITHDRAWAL PERIOD:

No withdrawal period is required before slaughter for human consumption.

ANTIBACTERIAL WARNINGS:

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 bacteria.

USER SAFETY WARNINGS:

Not for use in humans. Keep out of reach of children.
May cause skin irritation. Tylvalosin has been shown to cause hypersensitivity reactions in laboratory animals.
People with known hypersensitivity to tylvalosin should avoid contact with this product. In case of accidental ingestion or inhalation, seek medical attention. When handling Aivlosin® 17% Type A Medicated Article and preparing medicated feeds, avoid direct contact with the eyes and skin. Wear a dust mask, coveralls and impervious gloves when mixing and handling this product. Eye protection is recommended. In case of accidental eye exposure, wash eyes immediately with water and seek medical attention. If wearing contact lenses, immediately rinse the eyes first, then remove contact lenses and continue to rinse the eyes thoroughly and seek medical attention.

In case of accidental skin exposure, wash contaminated skin thoroughly.

The Safety Data Sheet contains more detailed occupational safety information.

STORAGE: Store in a cool dry place at or below 25°C (77°F).

NET CONTENTS: 50 lb (22.7 kg).50 lb (22.7 kg) **Use only as directed.**

Distributed in the USA by: **Pharmgate Animal Health**, 14040 Industrial Road, Omaha, NE 68144.

For sales, technical assistance or to obtain a Safety Data Sheet, call Pharmgate Animal Health at 1-800-380-6099

To report suspected adverse drug events, contact the ASPCA Animal Product Safety Service at 1-800-345-4735 or the FDA at 1-888-FDA-VETS. Pharmgate Animal Health has contracted with the ASPCA Animal Product Safety Service to collect human and animal suspected adverse drug events reports for this product.

1. Stuart A et al. Intra-cellular accumulation and trans-epithelial transport of Aivlosin, tylosin and tilmicosin. *Pig J* 2007; 60:26-35.
2. ECO Animal Health Report.
3. ECO Animal Health report EFF.US.070142.
4. ECO Animal Health report EFF.US.090170.

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