AIVLOSIN®
Water Soluble Granules

Indications

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

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 prescription; for use in drinking water of swine.

Withdrawal Period

- 0 days (no withdrawal needed).

Packaging

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

Storage

- Store at or below 25°C (77°F).

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 a fresh batch of medicated stock solution or medicated drinking water daily.
- 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.

Expiration Period

- 2-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.[1,2]
- Enhances macrophage activity.[1]
- Easy, reliable dosing in drinking water for immediate control of new outbreaks.
- Flexible usage; compatible with clinical or subclinical disease management programs.
- Palatable, non-clogging formulation.
- No withdrawal period (0 days).
- Wide safety margin.

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

Important Safety Information: 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 drinking water 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® Water Soluble Granules and preparing medicated drinking water, 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 141-336 **Approved by FDA.**

AIVLOSIN®

(62.5% w/w Tylvalosin as Tylvalosin Tartrate)

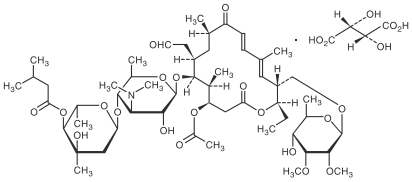
Water Soluble Granules

Use only as directed.
For use only in the drinking water of pigs.
Not for use in lactating or pregnant females, or males and females intended for breeding.

CAUTION:
Federal law restricts this drug to use by or on the order of a licensed veterinarian.

PRODUCT DESCRIPTION:
Aivlosin® (Tylvalosin Tartrate) Water Soluble Granules is a water soluble granular powder for oral use by administration in the drinking water. Each gram of Aivlosin® Water Soluble Granules contains 0.625 grams of tylvalosin as tylvalosin tartrate.

TYLVALOSIN TARTRATE CHEMICAL NOMENCLATURE AND STRUCTURE:
(4*R*,5*S*,6*S*,7*R*,9*R*,11*E*,13*E*,15*R*,16*R*)-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 (2*R*,3*R*)-2,3-dihydroxybutanedioate.



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

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

DOSAGE AND ADMINISTRATION:
Swine:
Control of Porcine Proliferative Enteropathy

Prepare drinking water medicated with 50 parts per million Tylvalosin as shown in the following table.

Aivlosin® Water Soluble Granules sachet size	40 grams	160 grams	400 grams
Tylvalosin content of sachet (grams)	25	100	250
Volume of drinking water (liters)	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.

Keep water supply equipment clean and in good operating condition. Clean water medication equipment before and after each use. Do not mix or administer Tylvalosin 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.

MIXING DIRECTIONS:
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.

Direct mixing: 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 for at least 3 minutes. Prepare a fresh batch of medicated drinking water daily.

Stock solution: When preparing a stock solution, the recommended concentration is one 40-gram sachet per US gallon, or one 160-g sachet per four (4) US gallons or one 400-gram sachet per 10 US gallons. Sprinkle sachet contents onto the surface of the water of the stock solution and mix slowly and thoroughly for at least 10 minutes. Use the stock solution for dilution into the drinking water system as soon as it is prepared. Add one (1) fluid ounce of this stock solution per 131 fluid ounces (1 US gallon, 3 fluid ounces) of drinking water to provide a final concentration of 50 ppm. If using an automatic water proportioner, set the flow rate to add stock solution at a rate of 1 fluid ounce per 131 fluid ounces of drinking water (1:131). Prepare a fresh batch of medicated stock solution daily.

WARNINGS:
NOT FOR HUMAN USE.
KEEP OUT OF REACH OF CHILDREN.

WITHDRAWAL PERIOD:
When used in accordance with label directions, 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 pathogenic bacteria.

USER SAFETY WARNINGS:
May cause skin irritation.

Tylvalosin Tartrate has been shown to cause hypersensitivity reactions in laboratory animals.

People with known hypersensitivity to Tylvalosin Tartrate should avoid contact with this product.

In case of accidental ingestion, seek medical advice.

When handling Aivlosin® Water Soluble Granules and preparing medicated drinking water, 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. If irritation persists, seek medical attention.

Avoid eating, chewing gum and smoking during handling.

Wash contaminated skin.

The Material Safety Data Sheet contains more detailed occupational safety information.

To report adverse effects in users, to obtain more information or obtain a Material Safety Data Sheet, call the ASPCA Animal Product Safety Service at 1-800-345-4735.

PRECAUTIONS:
Not for use in lactating or pregnant females, or males and females intended for breeding. The effects of Tylvalosin on swine reproductive performance, pregnancy and lactation have not been determined. The safety and efficacy of this formulation in species other than swine have not been determined.

ADVERSE REACTIONS IN ANIMALS:
No adverse reactions related to the drug were observed during clinical or target animal safety trials. To report suspected adverse reactions in animals, contact the ASPCA Animal Product Safety Service at 1-800-345-4735 or the FDA at 1-888-FDA-VETS.

CLINICAL PHARMACOLOGY:
Tylvalosin is a 16-membered semi-synthetic macrolide antibiotic. Macrolides are generally considered to be bacteriostatic agents that exert their antibiotic effect by reversibly binding to the 23S rRNA of the 50S ribosomal subunit, thereby inhibiting bacterial protein synthesis. 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. These compounds have no activity against the naturally resistant Enterobacteriaceae including *Escherichia coli* and *Salmonella* spp. Typically, macrolides achieve higher concentrations in tissues than in plasma.

EFFECTIVENESS: Swine:
Control of Porcine Proliferative Enteropathy (PPE): A multi-location challenge model study was conducted to confirm the effectiveness of AIVLOSIN® Water Soluble Granules for the control of PPE associated with *Lawsonia intracellularis*. Pigs were challenged by intragastric gavage with a mucosal homogenate containing a North American isolate of *Lawsonia intracellularis* isolated in 2005 that induces representative disease in challenged pigs. When at least 15% of the study pigs were showing signs of infection based on abnormal fecal scores, pigs were provided water containing tylvalosin at an inclusion rate of 50 ppm for five consecutive days, or were provided non-medicated water. Effectiveness was evaluated using clinical scores (pig demeanor score, abdominal appearance score, and fecal score) and clinically-validated gross PPE lesion scores. A conclusion of the effectiveness of 50 ppm tylvalosin for the control of PPE was determined based on a statistically significant ($p = 0.0103$) improvement in the clinically-validated gross PPE lesion scores in the 50 ppm tylvalosin-treated group compared to the non-medicated group.

ANIMAL SAFETY: Swine:
Margin of safety: Aivlosin® Water Soluble Granules given orally in drinking water at 0, 50, 150 and 250 ppm tylvalosin (0, 1X, 3X and 5X the labeled dose, respectively) to 8 healthy pigs per treatment group over 15 days (3X the labeled duration) did not result in drug-induced clinical signs, gross pathologic lesions, histopathologic lesions or clinically-relevant clinical pathology abnormalities.

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

HOW SUPPLIED: Aivlosin® Water Soluble Granules is packaged in 40-, 160- and 400-gram sachets supplied in boxes holding 20, 10 and 5 sachets respectively.

LOT NO.: Printed on label.
EXPIRY: Printed on label.

Distributed in the USA by:
Pharmgate Animal Health.
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For technical assistance or to obtain a Material 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 FDA at 1-888-FDA-VETS.

Aivlosin® is a registered trademark of ECO Animal Health Ltd.

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1. Stuart et al. *Pig J* 2007; 60:26-35.
2. Data on file. ECO Animal Health.