AIVLOSIN- tylvalosin tartrate granule, for solution
Pharmgate Animal Health LLC

Approved by FDA under NADA # 141-336

AIVLOSIN®

(62.5% w/w Tylvalosin as Tylvalosin Tartrate)

Water Soluble Granules

For use only in the drinking water of swine intended for slaughter.

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.

ANTIBIOTIC CLASSIFICATION:

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

INDICATIONS:

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

Control of swine respiratory disease (SRD) associated with *Bordetella bronchiseptica, Haemophilus parasuis, Pasteurella multocida, Streptococcus suis,* and *Mycoplasma hyopneumoniae* in groups of swine intended for slaughter in buildings experiencing an outbreak of SRD.

DOSAGE AND ADMINISTRATION:

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

Aivlosin® Water Soluble Granules sachet size	**160 grams**	**400 grams**
Tylvalosin content of sachet (grams)	100	250
Recommended volume of stock solution (US gallons)	4	10

Volume of drinking water (US gallons)	528	1320
Final tylvalosin inclusion rate in drinking 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:

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:

NOT FOR USE IN HUMANS.
KEEP OUT OF REACH OF CHILDREN.

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 Safety Data Sheet contains more detailed occupational safety information.

To report adverse effects in users, to obtain more information or obtain a Safety Data Sheet, call Pharmgate Animal Health LLC. at 1-833-531-0114.

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.

To assure both food safety and responsible use in swine, concurrent use of tylvalosin in medicated drinking water and tylvalosin or another macrolide in medicated feed or by any other route of administration should be avoided. Tylvalosin belongs to the macrolide antimicrobial drug class. Macrolides are ranked as a critically important drug in human medicine; therefore, minimizing the risk of development of antimicrobial resistance to this class of drug is very important. The following conditions of use and restrictions listed below are critical for
the FDA's strategy of risk management associated with tylvalosin:

Always treat the fewest number of animals necessary to control a respiratory disease or PPE outbreak.

Do not immediately follow this macrolide treatment with another macrolide treatment via any route.

Prescriptions should not be renewed or refilled for animals already treated with one course of therapy with tylvalosin asdirected (See Dosage and Administration above).

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 Pharmgate Animal Health LLC. at 1-833-531-0114. For additional information about adverse drug

experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or at www.fda.gov/reportanimalae.

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:

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.

Control of Swine Respiratory Disease (SRD):

The effectiveness of Aivlosin® Water Soluble Granules for the control of swine respiratory disease (SRD) associated with *Bordetella bronchiseptica, Haemophilus parasuis, Pasteurella multocida, Streptococcus suis* and *Mycoplasma hyopneumoniae* was investigated in a natural field infection study conducted in the United States (three study sites) and Canada (one study site). Day 0 was defined when at least 15% of the candidate pigs were deemed clinically affected with SRD (moderate or severe respiratory score, moderate or severe
depression score, and rectal temperature greater than or equal to 104.0 °F). On Day 0 a total of 980 pigs were enrolled and randomly assigned to a tylvalosin-treated group (50 ppm tylvalosin in drinking water for 5 consecutive days) or a non-medicated control group. Treatment success was evaluated on Day 7 and was defined as a pig with normal or mild respiratory score, normal or mild depression score, and rectal temperature less than 104.0 °F. The proportion of pigs meeting the definition of treatment success was numerically higher in the tylvalosin-treated group (48.5%) compared to the proportion of pigs meeting the definition of treatment success in the non-medicated control group (41.6%), and the observed difference was statistically significant ($p=0.0353$).

Additional data to demonstrate the effectiveness of Aivlosin® Water Soluble Granules for the control of SRD associated with *Mycoplasma hyopneumoniae* was obtained in an experimentally-induced infection model study. Two hundred and forty (240) commercial crossbred pigs were challenged endotracheally with a representative isolate of *M. hyopneumoniae*. One hundred and ninety-two (192) study pigs were randomly assigned to either a tylvalosin-treated group (50 ppm tylvalosin in drinking water for 5 consecutive days) or a nonmedicated control group. Treatment was started when at least four of eight randomly pre-selected sentinel pigs exhibited a minimum of 3% weighted gross lung lesions consistent with *M. hyopneumoniae* infection. After a 5-day treatment period and a 5-day post-treatment period, study pigs were euthanized and necropsy performed to determine lung lesion scores. The analysis included 95 tylvalosin-treated pigs and 93 nonmedicated control pigs. There was a statistically significant ($P<0.0001$) improvement in pen mean *M. hyopneumoniae* lung lesion scores in the 50 ppm tylvalosin treated pigs (5.1%) compared to negative control (10.9%).

ANIMAL SAFETY:

Margin of safety:

Aivlosin® Water Soluble Granules given orally in drinking water at 0, 50, 150 and 250 ppm tylvalosin (0, 1×, 3× and 5× the labeled dose, respectively) to 8 healthy pigs per treatment group over 15 days (3× 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 160- and 400-gram sachets supplied in boxes holding 10 and 5 sachets respectively.

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

Distributed in the USA by:
Pharmgate Animal Health LLC.
14040 Industrial Road,
Omaha, NE 68144
www.pharmgateah.com

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

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

PRINCIPAL DISPLAY PANEL - 160 g Packet and Carton

NDC 51429-625-16

***AIV*LOSIN®**
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Aivlosin® Water Soluble Granules sachet size	**160 grams**
Tylvalosin content of sachet (grams)	**100**
Recommended volume of stock solution (US gallons)	**4**
Volume of drinking water (US gallons)	**528**
Final tylvalosin inclusion rate in drinking 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: See Product Information provided in the package insert for details.

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Net contents: 160 grams

Aivlosin® Water Soluble Granules

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PharmGate
Animal Health

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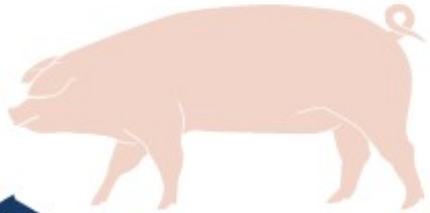


Net contents: 160 grams

Aivlosin® Water Soluble Granules

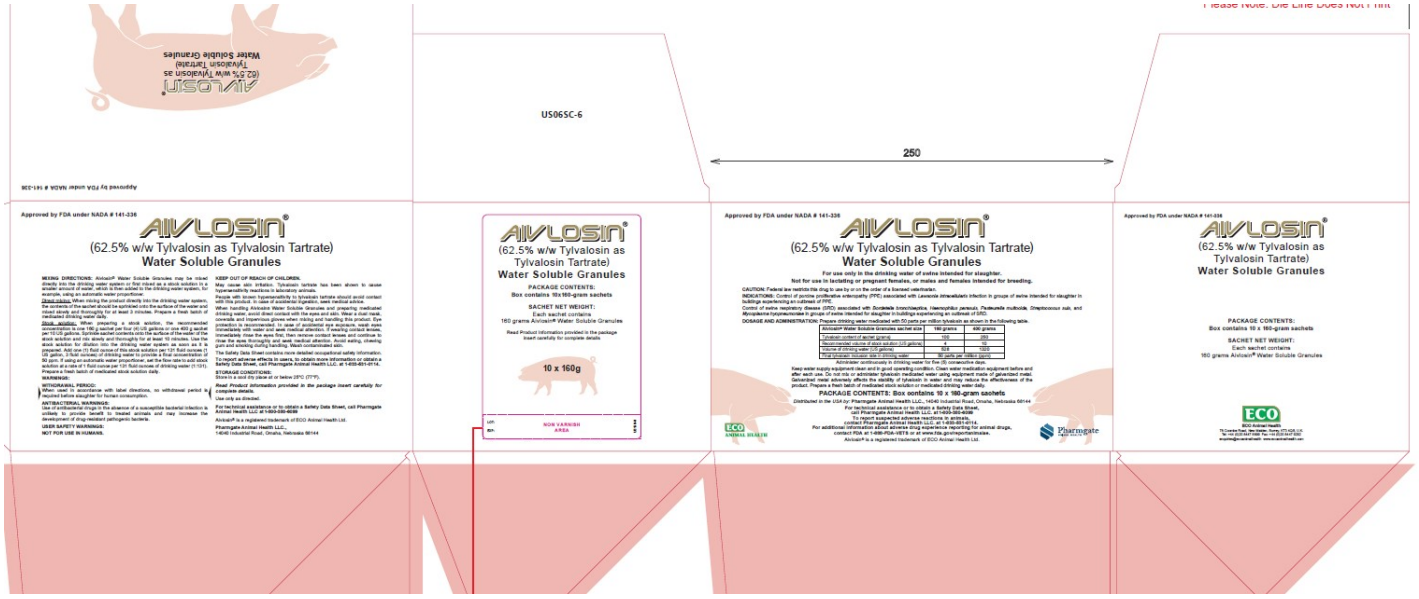
Approved by FDA under NADA # 141-336

Pharmgate ANIMAL HEALTH

Rev 01/21
US160SM-4

CLEAR AREA FOR LOT & EXP DETAILS 120 X 15mm

PACKAGE CONTENTS: Box contains 10 x 160-gram sachets



PRINCIPAL DISPLAY PANEL - 400 g Packet and Carton

NDC 51429-625-40

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Aivlosin® Water Soluble Granules sachet size	**400 grams**
Tylvalosin content of sachet (grams)	**250**

Recommended volume of stock solution (US gallons)	**10**
Volume of drinking water (US gallons)	**1320**
Final tylvalosin inclusion rate in drinking 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: See Product Information provided in the package insert for details.

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Net contents: 400 grams

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Animal Health

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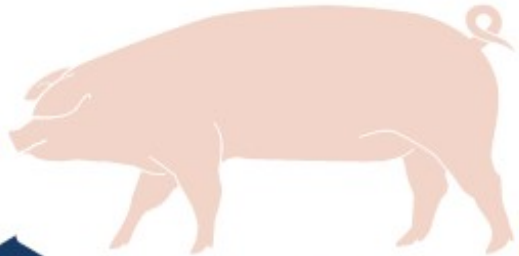


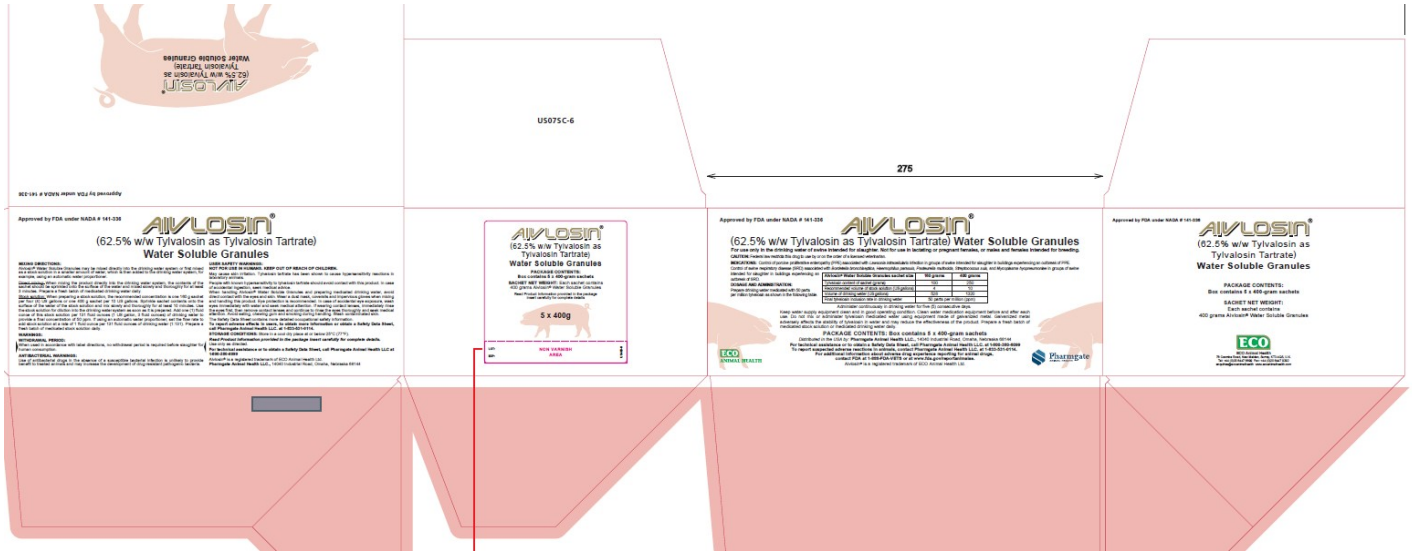
Net contents: 400 grams
Aivlosin® Water Soluble Granules
Approved by FDA under NADA # 141-336

Pharmgate ANIMAL HEALTH

Rev 01/21
US400SM-4

CLEAR AREA FOR LOT & EXP DETAILS 144 X 18mm

PACKAGE CONTENTS: Box contains 5 x 400-gram sachets



AIVLOSIN

tylvalosin tartrate granule, for solution

Product Information			
Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:51429-625
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Tylvalosin tartrate (UNII: AL5667FY0W) (Tylvalosin - UNII:9T02S42WQO)	Tylvalosin	62.5 g in 100 g

Inactive Ingredients	
Ingredient Name	**Strength**
Lactose monohydrate (UNII: EWQ57Q8I5X)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:51429-625-16	160 g in 1 PACKET		
2	NDC:51429-625-40	400 g in 1 PACKET		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141336	09/05/2012	

Labeler - Pharmgate Animal Health LLC (833270817)

Registrant - ECO Animal Health (831287599)

Revised: 11/2021

Pharmgate Animal Health LLC