Formulation
• Water-soluble granules; suitable for both drinking water and stock solutions.

Indication
• Control of swine respiratory disease (SRD) associated with Bordetella bronchiseptica, Haemophilus parasuis, Pasteurella multocida, and Streptococcus suis in groups of swine in buildings experiencing an outbreak of SRD.

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

Packaging
• Cartons containing either 10 x 160-g or 5 x 400-g sachets.

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.

Precautions
• 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.

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

Withdrawal Period
• 0-days (no withdrawal needed).

Key Features
• Dual efficacy against both respiratory (SRD) and enteric (PPE) pathogens.

• Quick-acting, potent macrolide antibiotic that is not used in human health.

• Supports judicious, responsible antibiotic use.

• Wide safety margin; compatible when treating pigs with ionophores.

• No withdrawal period (0 days).

• Enters into white blood cells within two hours (in vitro).

• Easy, reliable dosing in drinking water for rapid control of new outbreaks.

• Palatable, non-clogging formulation.

Storage
• Store at or below 25°C (77°F).

• 2-year shelf-life for unopened sachets.
Important Safety Information: For use only in the drinking water of pigs. Not for use in lactating or pregnant females, or males and females intended for breeding. May cause skin irritation. People with known hypersensitivity to tylosin 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 Tylosin as Tylosin 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® (tylosin 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 tylosin as tylosin tartrate.

ANTIBIOTIC CLASSIFICATION:
Tylosin, the active component 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:
- Prepare drinking water medicated with 50 parts per million tylosin as shown in the following table.

<table>
<thead>
<tr>
<th>Aivlosin® Water Soluble Granules</th>
<th>40 grams</th>
<th>160 grams</th>
<th>400 grams</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tylosin content of sacher/gram</td>
<td>24</td>
<td>100</td>
<td>250</td>
</tr>
<tr>
<td>Recommended volume of stock solution (US gallons)</td>
<td>1</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Volume of drinking water (US gallons)</td>
<td>132</td>
<td>528</td>
<td>1320</td>
</tr>
<tr>
<td>Final tylosin inclusion rate in drinking water</td>
<td>50 parts per million (ppm)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 tylosin medicated water using equipment made of galvanized metal. Galvanized metal adversely affects the stability of tylosin 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 1-gram sachet per 40 US gallons or one 160-g sachet per 40 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 a pump to deliver the stock solution 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) 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 the 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. Tylosin tartrate has been shown to cause hypersensitivity reactions in laboratory animals.

People with known hypersensitivity to tylosin 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 and seek medical advice. If wearing contact lenses, immediately remove the eyes first, then remove contact lenses and continue to rinse the eyes thoroughly and seek medical advice. In case of bacterial protein synthesis and smoking during handling. Wash contaminated skin.

The Safety Data Sheet contains more detailed occupational safety and health information.

To report adverse effects in users, to obtain more information or obtain a 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 tylosin 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 tylosin in medicated drinking water and tylosin or another macrolide in medicated feed or by any other route of administration should be avoided. Tylosin 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 tylosin.
- 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 the same or another drug with tylosin as directed (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 the ASPCA Animal Product Safety Service at 1-800-345-4735 or the FDA at 1-888-FDA-VETS.

CLINICAL PHARMACOLOGY:
Tylosin 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 RNA of the 50S ribosomal subunit, thereby inhibiting protein synthesis.

The spectrum of activity of most available macrolides used in veterinary medicine is primarily against gram-positive bacteria, including some activity against Gram-negative fastidious bacteria. These compounds have no activity against the naturally resistant Enterobacteriaceae. 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 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 tylosin 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-valid gross PPE lesion scores. A conclusion of the effectiveness of 50 ppm tylosin for the control of PPE was determined based on statistically significant (p = 0.0103) improvement in the clinically-valid gross PPE lesion scores in the 50 ppm tylosin-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, and Streptococcus suis 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 tylosin-treated group (50 ppm tylosin 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 tylosin-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).

ANIMAL SAFETY: Swine:
- Margin of safety: Aivlosin® Water Soluble Granules given orally in drinking water at 50, 150, and 250 ppm tylosin (0, 1X, 3X and 5X the labeled dose), respectively, to 6 healthy pigs per treatment group over 15 days (3X the labeled dose) resulted 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. 14040 Industrial Road, Omaha, NE 68144 www.pharmgate.com

For 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 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. USPAPM46

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1800 Sir Tyler Drive
Wilmington, NC  28405
910.679.8364  Pharmgate.com