

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Aivlosin 625 mg/g granules for use in drinking water for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance :

Tylvalosin (as tylvalosin tartrate) 625 mg/g

For the full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Granules for use in drinking water.

White granules.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs

4.2 Indications for use, specifying the target species

Treatment and metaphylaxis of porcine proliferative enteropathy (ileitis) caused by *Lawsonia intracellularis*.

Treatment and metaphylaxis of swine enzootic pneumonia caused by susceptible strains of *Mycoplasma hyopneumoniae*.

The presence of the disease in the group must be established before metaphylaxis.

4.3 Contraindications

None

4.4 Special warnings for each target species

In severely diseased pigs, if water intake is reduced, pigs should be treated with a suitable injectable veterinary medicinal product prescribed by a veterinarian. At the recommended dose, lung lesions and clinical signs are reduced but infection with *Mycoplasma hyopneumoniae* is not eliminated.

4.5 Special precautions for use

Special precautions for use in animals

Official, national and regional antimicrobial policies should be taken into account when the product is used.

Good management and hygiene practices should be followed to reduce the risk of re-infection.

It is sound clinical practice to base treatment on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of target bacteria.

Use of the veterinary medicinal product deviating from the instructions in the SPC may increase the risk of development and selection of resistant bacteria and decrease the effectiveness of treatment with other macrolides due to the potential for cross-resistance.

An antibacterial with a lower risk of antimicrobial resistance selection, if available for the same indication, should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Tylvalosin has been shown to cause hypersensitivity (allergic) reactions in laboratory animals; therefore, people with known hypersensitivity to tylvalosin should avoid contact with this product.

When mixing the veterinary medicinal product and handling the medicated water, direct contact with eyes, skin and mucous membranes should be avoided. Personal protective equipment consisting of impervious gloves and a half-mask respirator conforming to European Standard EN 149 or a non-disposable respirator conforming to European Standard EN 140 with a filter conforming to European Standard EN 143 should be worn when mixing the product. Wash contaminated skin.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:

Not applicable.

Other precautions:

Not applicable.

4.6 Adverse reactions (frequency and seriousness)

Pigs.

None known.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See also section 16 of the package leaflet for contact details.

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has been established during pregnancy and lactation in pigs.

No signs of adverse effects were observed in sows or their offspring when the veterinary medicinal product was administered orally and continuously for 195 days to sows, from before insemination to weaning, at an inclusion rate of 150 mg tylvalosin per kg water, corresponding to an average of 4.6 mg tylvalosin per kg body weight per day.

Laboratory studies in animals have not produced any evidence of a teratogenic effect. Maternal toxicity in rodents has been observed at doses of 400 mg tylvalosin per kg bodyweight and above. In mice, a slight reduction in the foetal bodyweight was seen at doses causing maternal toxicity.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amount(s) to be administered and administration route

For use in drinking water.

To ensure a correct dosage, bodyweight should be determined as accurately as possible. Water consumption should be monitored, and the concentration of the product adjusted if needed to avoid underdosing.

The product should be added to a volume of water that the pigs will consume in one day. No other source of drinking water should be available during treatment.

Porcine proliferative enteropathy (ileitis) caused by *Lawsonia intracellularis*

The dose is 5 mg tylvalosin per kg bodyweight per day in drinking water for 5 consecutive days.

Calculate the total amount of product required with the following formula:

Total weight of product in grams = total bodyweight of the heaviest pig to be treated in kg x number of pigs x 5/ 625.

Select the correct number of sachets according to the amount of product required.

The 40 g sachet is sufficient to treat a total of 5,000 kg of pigs (e.g. 250 pigs with the heaviest pig weighing 20 kg) for one day.

The 160 g sachet is sufficient to treat a total of 20,000 kg of pigs (e.g. 400 pigs with the heaviest pig weighing 50 kg) for one day.

The 400 g sachet is sufficient to treat a total of 50,000 kg of pigs (e.g. 1000 pigs with the heaviest pig weighing 50 kg) for one day.

Swine enzootic pneumonia caused by susceptible strains of *Mycoplasma hyopneumoniae*

The dose is 10 mg tylvalosin per kg bodyweight per day in drinking water for 5 consecutive days.

Calculate the total amount of product required with the following formula:

Total weight of product in grams = total bodyweight of the heaviest pig to be treated in kg x number of pigs to be treated x 10 / 625.

Select the correct number of sachets according to the amount of product required.

The 40 g sachet is sufficient to treat a total of 2,500 kg of pigs (e.g. 125 pigs with the heaviest pig weighing 20 kg) for one day.

The 160 g sachet is sufficient to treat a total of 10,000 kg of pigs (e.g. 200 pigs with the heaviest pig weighing 50 kg) for one day.

The 400 g sachet is sufficient to treat a total of 25,000 kg of pigs (e.g. 500 pigs with the heaviest pig weighing 50 kg) for one day.

Mixing instructions:

In order to achieve a correct dose, accurate and properly calibrated equipment should be used for weighing out the required amount of product.

The veterinary medicinal product may be mixed directly into the drinking water system or first mixed as a stock solution into a smaller amount of water, which is then added into the drinking water system.

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 thoroughly until a clear solution is produced (usually within 3 minutes).

When preparing a stock solution, the maximum concentration should be 40 g of product per 1,500 ml, 160 g of product per 6,000 ml or 400 g of product per 15,000 ml water and it is necessary to mix the solution for 10 minutes. After this time, any remaining cloudiness will not affect the efficacy of the veterinary medicinal product.

Only a sufficient amount of medicated drinking water should be prepared to cover the daily requirements.

Medicated drinking water should be replaced every 24 hours.

After end of the medication period, the water supply system should be cleaned appropriately to avoid intake of subtherapeutic amounts of the active substance.

As an adjunct to medication, good management and hygiene practices should be introduced in order to reduce the risk of infection and to control the build-up of resistance.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

No signs of intolerance have been observed in pigs at up to 100 mg tylvalosin per kg bodyweight per day for 5 days.

4.11 Withdrawal period(s)

Meat and offal: 2 days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group:

ATCvet code:

QJ01FA92

Pharmacotherapeutic group: antibacterials for systemic use, macrolides.

5.1 Pharmacodynamic properties

Tylvalosin is a macrolide antibiotic. Macrolides are metabolites or derivatives of metabolites of soil organisms obtained by fermentation. They interfere with protein synthesis by reversibly binding to the 50S ribosome subunit. They are generally considered bacteriostatic.

Tylvalosin has activity against pathogenic organisms isolated from a range of animal species-mainly Gram-positive organisms and mycoplasma but also some Gram-negative organisms, including *Lawsonia intracellularis*. At concentrations above MIC, *in vitro* studies have shown a bactericidal effect of tylvalosin against *Mycoplasma hyopneumoniae* strains.

Bacteria can develop resistance to antimicrobial substances. There are multiple mechanisms responsible for resistance development to macrolide compounds. The mechanisms involve the alteration of the ribosomal target site (e.g. encoded by *erm* genes), the utilization of active efflux mechanism (e.g. due to *mef*, *msr* genes) and the production of inactivating enzymes (e.g. caused by *mph* genes). Bacterial resistance to macrolides may be chromosomal or plasmid-encoded and may be transferable if associated with transposons or plasmids. In Mycoplasmas, resistance may be transferable if associated with

mobile genetic elements. Cross-resistance within the macrolide group of antibiotics cannot be excluded.

Scientific evidence suggests that macrolides act synergistically with the host immune system. Macrolides appear to enhance phagocyte killing bacteria.

In addition to their antimicrobial properties, immunomodulating and anti-inflammatory effects have been described for some macrolides in experimental studies. Tylvalosin has been shown to induce apoptosis of porcine neutrophils and macrophages, promote efferocytosis and inhibit pro-inflammatory CXCL-8, IL1 α and LTB4 production, while inducing the release of pro-resolving Lipoxin A4 and Resolvin D1 in vitro”.

5.2 Pharmacokinetic particulars

Tylvalosin tartrate is rapidly absorbed after oral administration of the veterinary medicinal product. Tylvalosin is widely distributed in tissues, with the highest concentrations found in the respiratory tissues, bile, intestinal mucosa, spleen, kidney and liver. The t_{max} for tylvalosin is about 2.2 hours; the terminal half-life for the elimination is approximately 2.2 hours.

Tylvalosin has been shown to concentrate in phagocytic cells and gut epithelial cells. Concentrations (up to 12 times) were achieved in the cells (intracellular), compared to the extracellular concentration. In vivo studies have shown tylvalosin to be present in higher concentrations in the mucous lining of the respiratory and gut tissues compared to the plasma.

The major metabolite of tylvalosin is 3-acetyltylosin (3-AT), which is also microbiologically active.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate

6.2 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale:

40 g sachet – 3 years.

160 g sachet – 2 years.

400 g sachet – 2 years.

Shelf life after first opening of the immediate packaging: 5 weeks.

Shelf life of the medicated drinking water: 24 hours.

6.4 Special precautions for storage

Do not store above 25 °C.

6.5 Nature and composition of immediate packaging

Aluminium foil laminated sachet containing 40 g, 160 g or 400 g of granules.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater.

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

ECO Animal Health Ltd
The Grange
100 High Street
London
N14 6BN
United Kingdom

8. MARKETING AUTHORISATION NUMBER

Vm 13277/5004

9. DATE OF FIRST AUTHORISATION

09 September 2004

10. DATE OF REVISION OF THE TEXT

July 2024

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

11. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCT

Veterinary medicinal product subject to prescription.

Gavin Hall
Approved: 01 December 2024