SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Aivlosin 42.5 mg/g premix for medicated feeding stuff for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Tylvalosin (as tylvalosin tartrate) 42.5 mg/g

For the full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Premix for medicated feeding stuff.
A beige granular powder.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs

4.2 Indications for use, specifying the target species

Treatment and metaphylaxis of swine enzootic pneumonia caused by susceptible strains of *Mycoplasma hyopneumoniae* in pigs. At the recommended dose, lung lesions and weight loss are reduced but infection with *Mycoplasma hyopneumoniae* is not eliminated.

Treatment of porcine proliferative enteropathy (ileitis) caused by *Lawsonia intracellularis* in herds where there is a diagnosis based on clinical history, post-mortem findings and clinical pathology results.

Treatment and metaphylaxis of swine dysentery, caused by *Brachyspira hyodysenteriae* in herds where the disease has been diagnosed.

4.3 Contraindications

None.

4.4 Special warnings for each target species

Acute cases and severely diseased pigs with reduced food or water intake should be treated with a suitable injectable product.

Generally, strains of *B. hyodysenteriae* have higher minimal inhibitory concentration (MIC) values in cases of resistance against other macrolides, such as tylosin. The clinical relevance of this reduced susceptibility is not fully explored. Cross-resistance between tylvalosin and other macrolides cannot be excluded.

4.5 Special precautions for use

Special precautions for use in animals

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.

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 premix, 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.

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation in pigs. Use only in accordance with benefit-risk assessment by the responsible veterinarian.
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 Amounts to be administered and administration route

In-feed use.
For incorporation into dry feed only.

For treatment and metaphylaxis of swine enzootic pneumonia
The dose is 2.125 mg tylvalosin per kg bodyweight per day in-feed for 7 consecutive days.

Secondary infection by organisms such as *Pasteurella multocida* and *Actinobacillus pleuropneumoniae* may complicate enzootic pneumonia and require specific medication.

For treatment of porcine proliferative enteropathy (ileitis)
The dose is 4.25 mg tylvalosin per kg bodyweight per day in-feed for 10 consecutive days.

For treatment and metaphylaxis of swine dysentery
The dose is 4.25 mg tylvalosin per kg bodyweight per day in-feed for 10 consecutive days.

Indication	Dose of active substance	Duration of treatment	In feed inclusion rate
Treatment and metaphylaxis of swine enzootic pneumonia	2.125 mg/kg bodyweight/day	7 days	1 kg/tonne*
Treatment of PPE (ileitis)	4.25 mg/kg bodyweight/day	10 days	2 kg/tonne*
Treatment and metaphylaxis of swine dysentery	4.25 mg/kg bodyweight/day	10 days	2 kg/tonne*

Important: these inclusion rates assume a pig eats the equivalent of 5% bodyweight per day.

In older pigs, or in pigs with reduced appetite, or on restricted feed intake, inclusion levels may need to be increased to achieve target dose. Where feed intake is reduced, use the following formula:

$$\text{Kg premix/tonne feed} = \frac{\text{Dose rate (mg/kg bodyweight) x bodyweight (kg)}}{\text{Daily feed intake (kg) x Premix strength (mg/g)}}$$

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.

A horizontal ribbon mixer should be used to incorporate the product into the feeding stuff. It is recommended that Aivlosin is first mixed into 10 kg of the feeding stuff, followed by the rest of the feeding stuff and mixed well. Medicated feed may then be pelleted. Pelleting conditions involve a single pre-conditioning step with steam for 5 minutes and pelleting at not more than 70 °C under normal conditions.

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

No signs of intolerance have been observed in growing pigs at up to 10 times the recommended dose.

4.11 Withdrawal period(s)

Meat and offal: 2 days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antibacterials for systemic use, macrolides.

ATCvet code: QJ01FA92.

5.1 Pharmacodynamic properties

Tylvalosin tartrate is a macrolide antibiotic that has antibacterial activity against Gram-positive, some Gram-negative organisms and mycoplasma. It acts by inhibiting protein synthesis in the bacterial cell.

Macrolide antibiotics are metabolites or semi-synthetic derivatives of metabolites of soil organisms obtained by fermentation. They have differently sized lactone rings and are basic due to the dimethylamino group. Tylvalosin has a sixteen-membered ring.

Macrolides interfere with protein synthesis by reversibly binding to the 50S ribosome subunit. They bind to the donor site and prevent the translocation necessary for keeping the peptide chain growing. Their effect is essentially confined to rapidly dividing organisms. Macrolides are generally considered bacteriostatic and mycoplasmastatic.

It is considered that there are multiple mechanisms responsible for resistance development to macrolide compounds, namely alteration of the ribosomal target site, utilisation of active efflux mechanisms and production of inactivating enzymes.

Resistance to tylvalosin by *Mycoplasma hyopneumoniae* and *Lawsonia intracellularis* has not been reported or found in the field to date. No breakpoint for *Brachyspira hyodysenteriae* has been established.

Generally, strains of *B. hyodysenteriae* have higher MIC values in cases of resistance against other macrolides, such as tylosin. The clinical relevance of this reduced susceptibility is not fully explored. Cross-resistance between tylvalosin and other macrolide antibiotics cannot be excluded.

5.2 Pharmacokinetic particulars

Tylvalosin tartrate is rapidly absorbed after oral administration of Aivlosin.

After administration of the recommended dose, lung concentrations of 0.060–0.066 µg/ml were found at 2 and 12 hours post-treatment. The parent compound is widely distributed in the tissues with the highest concentrations found in the lungs, bile, intestinal mucosa, spleen, kidney and liver.

There is evidence that the concentration of macrolides is higher at the site of infection than in plasma, in particular in neutrophils, alveolar macrophages and alveolar epithelial cells.

In vitro metabolism studies have confirmed that the parent compound is rapidly metabolised to 3-O-acetyltylosin. In a trial with ^{14}C-labeled Aivlosin administered at 2.125 mg/kg to pigs for 7 days, over 70% of the dose was excreted in the faeces, with urinary excretion accounting for 3 to 4% of the dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrated magnesium silicate (sepiolite)
Wheat flour
Hydroxypropyl cellulose
Non-fat soyabean powder

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: 3 years.
Shelf life after first opening of the immediate packaging: 4 weeks.
Shelf life after incorporation into feed: 1 month in meal or pellets.

6.4 Special precautions for storage

Store below 30 °C.
Keep the container tightly closed.
Store in the original container.

6.5 Nature and composition of immediate packaging

One aluminium foil/polyester laminated bag containing 2 kg, 5 kg or 20 kg.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products 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 13277/5000

9. DATE OF FIRST AUTHORISATION

09 September 2004

10. DATE OF REVISION OF THE TEXT

September 2023

PROHIBITION OF SALE, SUPPLY AND/OR USE

Consideration should be given to official guidance on the incorporation of medicated premixes in final feed.

Approved 11 September 2023