1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Aivlosin 625 mg/g granules for use in drinking water for chickens and turkeys

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Tylvalosin (as tylvalosin tartrate) 625 mg/g

Excipients:

Qualitative composition of excipients and other constituents
Lactose monohydrate

White granules.

3. CLINICAL INFORMATION

3.1 Target species

Chickens and turkeys.

3.2 Indications for use for each target species

Chickens
Treatment and metaphylaxis of respiratory infections caused by *Mycoplasma gallisepticum* in chickens. The presence of the disease in the flock must be established before the product is used.

As an aid in reducing the development of clinical signs and mortality from respiratory disease in flocks, where infection in ovum with *Mycoplasma gallisepticum* is likely because the disease is known to exist in the parent generation.

Turkeys
Treatment of respiratory disease associated with *Ornithobacterium rhinotracheale* in turkeys.

3.3 Contraindications

Do not use in cases of hypersensitivity to macrolide antibiotics or to any of the excipients.
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3.4 Special warnings

In field studies investigating the effect of treatment and metaphylaxis on mycoplasmosis, all birds (approximately 3 weeks old) received the product when clinical signs were evident in 2–5% of the flock. At 14 days after initiation of treatment, 16.7–25.0% morbidity and 0.3–3.9% mortality were observed in the treated group in comparison to 50.0–53.3% morbidity and 0.3–4.5% mortality in an untreated group.

In further field studies, chicks from parent stock with evidence of *Mycoplasma gallisepticum* infection were administered the veterinary medicinal product for the first three days of life followed by a second course at 16–19 days of age (a period of management stress). By 34 days after the initiation of treatment, 17.5–20.0% morbidity and 1.5–2.3% mortality were observed in the treated groups in comparison to 50.0–53.3% morbidity and 2.5–4.8% mortality in the untreated groups.

The strategy for *Mycoplasma gallisepticum* infection should include efforts to eliminate the pathogen from the parent generation.

Infection with *Mycoplasma gallisepticum* is reduced but not eliminated at the recommended dose. Medication should only be used for short-term amelioration of clinical signs in breeder flocks whilst awaiting confirmation of diagnosis of *Mycoplasma gallisepticum* infection.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Use of the product should be in accordance with official, national and regional antimicrobial policies.

An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

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

Use of the product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.
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 nondisposable 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.

3.6 Adverse events

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 the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lay

The safety of the veterinary medicinal product has not been established during lay in turkeys.

The product can be used in chickens laying eggs for human consumption and breeding birds producing eggs for hatching broiler stock or replacement layers.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

For use in drinking water.

Chickens
For treatment of respiratory disease associated with *Mycoplasma gallisepticum*:
The dose is 25 mg tylvalosin per kg bodyweight per day in drinking water for 3 consecutive days.

When used as an aid in reducing the development of clinical signs and mortality (where infection in ovum with *Mycoplasma gallisepticum* is likely):
The dose is 25 mg tylvalosin per kg bodyweight per day in drinking water for 3 consecutive days at 1 day old. This is followed by a second treatment with 25 mg tylvalosin per kg bodyweight per day in drinking water for 3 consecutive days at the period of risk, i.e. at times of management stress such as administration of vaccines (typically when birds are 2–3 weeks old).

Determine the combined bodyweight (in kg) of all the chickens to be treated. Select the correct number of sachets according to the amount of product required.

One sachet of 40 g is sufficient to treat a total of 1,000 kg of chicken (e.g. 20,000 birds with an average bodyweight of 50 g).

One sachet of 400 g is sufficient to treat a total of 10,000 kg of chicken (e.g. 20,000 birds with an average bodyweight of 500 g).

In order to achieve a correct dose, the preparation of a concentrated (stock) solution might be required (e.g. to treat a total of 500 kg total bird weight, only 50% of the prepared stock solution prepared from the 40 g sachet should be used).

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

Turkeys
For treatment of respiratory disease associated with *Ornithobacterium rhinotracheale*:
The dose is 25 mg tylvalosin per kg bodyweight per day in drinking water for 5 consecutive days.

Determine the combined bodyweight (in kg) of all the turkeys to be treated. Select the correct number of sachets according to the amount of product required.

One sachet of 40 g is sufficient to treat a total of 1,000 kg of turkeys (e.g. 10,000 birds with an average bodyweight of 100 g).

One sachet of 400 g is sufficient to treat a total of 10,000 kg of turkeys (e.g. 10,000 birds with an average bodyweight of 1 kg).

In order to achieve a correct dose, the preparation of a concentrated (stock) solution might be required (e.g. to treat a total of 500 kg total bird weight, only 50% of the prepared stock solution prepared from the 40 g sachet should be used).

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

Mixing instructions:

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 per 1,500 ml or 400 g of product per 15 litres water and it is necessary to mix the solution for 10 minutes. After this time, any remaining cloudiness will not affect efficacy of the 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.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

No signs of intolerance have been observed in poultry species at up to 150 mg tylvalosin per kg bodyweight per day for 5 days.

No adverse effects on egg production, egg fertility, hatchability and chick viability were observed in broiler breeder stock administered 75 mg tylvalosin per kg bodyweight per day for 28 consecutive days.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable

3.12 Withdrawal periods

Meat and offal: 2 days.
Eggs (chicken): zero days.

Turkeys: Not for use in birds producing or intended to produce eggs for human consumption. Do not use within 21 days before the start of the laying period.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QJ01FA92

4.2 Pharmacodynamics

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.
Macrolides (including tylvalosin) have been shown to have effects on the innate immune system, which may augment the direct effects of the antibiotic on the pathogen and aid the clinical situation.

Chicken
Tylvalosin has activity against the following mycoplasma species found in chicken: *Mycoplasma gallisepticum*.
The minimal inhibitory concentration (MIC) of tylvalosin for *Mycoplasma gallisepticum* ranges from 0.007 to 0.25 mcg/ml.

Turkeys
Tylvalosin has activity against *Ornithobacterium rhinotracheale*, a Gram-negative organism found in turkeys and chickens.
The MIC of tylvalosin for *Ornithobacterium rhinotracheale* ranges from 0.016 to 32 μg/ml.

Efficacy of tylvalosin against *O. rhinotracheale* in turkeys was demonstrated in a challenge model using co-infection with avian metapneumovirus and a single strain of *O. rhinotracheale* under strictly controlled conditions. These studies demonstrated a modest but statistically significant reduction in the incidence of lower respiratory lesions (lung and air sac) and clinical signs in turkeys treated with tylvalosin compared with negative controls. Efficacy studies under field conditions have not been conducted.

Bacteria can develop resistance to antimicrobial substances. There are multiple mechanisms responsible for resistance development to macrolide compounds.
Cross-resistance within the macrolide group of antibiotics cannot be excluded. Reduced susceptibility for tylvalosin was generally noted in tylosin resistant strains.

4.3 Pharmacokinetics

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.

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.

The terminal half-lives for the elimination of tylvalosin and its active metabolite 3-AT range from 1 to 1.45 hours in the chicken. Six hours after treatment, the concentration of tylvalosin in the gastrointestinal tract mucosa has a mean concentration of 133 ng/g and in the gastrointestinal contents of 1,040 ng/g. The active metabolite 3-AT has a mean concentration of 57.9 ng/g and 441 ng/g, respectively.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale:
40 g sachet – 3 years.
400 g sachet – 2 years.
Shelf life after first opening the immediate packaging: 5 weeks.
Shelf life of the medicated drinking water: 24 hours.

5.3 Special precautions for storage

Do not store above 25 °C.

5.4 Nature and composition of immediate packaging

Aluminium foil laminated sachet containing 40 g or 400 g.

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

ECO Animal Health Europe Limited

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/04/044/018 – 40 g
EU/2/04/044/019 – 400 g

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 09/09/2004

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

{MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).