1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

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

Pheasants

4.2 Indications for use, specifying the target species

Treatment of respiratory disease associated with *Mycoplasma gallisepticum* in pheasants.

4.3 Contraindications

None.

4.4 Special warnings for each target species

Treat as soon as possible after clinical signs suggestive of mycoplasmosis are observed.
Treat all the birds in the affected flock.

4.5 Special precautions for use

Special precautions for use in animals

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

Use of the product should be based 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 the target bacteria.
Use of the veterinary medicinal product deviating from the instructions 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 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.

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 lay.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

For use in drinking water.

The dose is 25 mg tylvalosin per kg bodyweight per day in drinking water for 3 consecutive days.

Determine the combined bodyweight (in kg) of all the birds to be treated. For example, one sachet of 40 g is sufficient to treat a total of 1,000 birds with an average bodyweight of 1 kg; one sachet of 400 g is sufficient to treat a total of 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 veterinary medicinal product should be added to a volume of water that the birds will consume in one day. The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dose, the concentration of Aivlosin has to be adjusted accordingly.
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 veterinary medicinal 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 of 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.

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

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

4.11 Withdrawal period(s)

Meat and offal: 2 days.
Do not release pheasants for at least two days after the end of medication.

Not for use in birds producing or intended to produce eggs for human consumption.

Do not use within 14 days of the start of the laying period.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antibacterials for systemic use, macrolides.
ATCvet code: QJ01FA92.

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. Tylvalosin has activity against the following mycoplasma species found in poultry: *Mycoplasma gallisepticum*.

The minimum inhibitory concentration of tylvalosin for *M. gallisepticum* ranges from 0.007 to 0.25 µg/ml. 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.

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.

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.

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. 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.

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.
400 g sachet – 2 years.
Shelf life after first opening the immediate packaging: 5 weeks.
Shelf life of the medicated drinking water: 24 hours.

6.4. Special precautions for storage

40 g sachet: do not store above 25 ºC.
400 g sachet: do not store above 25 °C.

6.5 Nature and composition of immediate packaging

Aluminium foil laminated sachets containing 40 g or 400 g 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

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

7. MARKETING AUTHORISATION HOLDER

GB
Eco Animal Health Ltd
78 Coombe Road
New Malden
Surrey
KT3 4QS

NI
ECO Animal Health Europe Limited
6th Floor, South Bank House
Barrow Street
Dublin 4
D04 TR29
IRELAND

8. MARKETING AUTHORISATION NUMBERS

GB
VM 13277/5003

NI
EU/2/04/044/012 – 40 g
EU/2/04/044/014 – 400 g

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9 September 2004.
Date of last renewal: 9 September 2014.

10. DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (http://www.ema.europa.eu).

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.