**TYLVALOSURE 625MG/G GRANULES**

**Description and Composition**
TYLVALOSURE 625MG/G GRANULES are off-white granules. Each gram contains 625mg of Tylvalosin (as tartrate) as its active ingredient.

**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.

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

Turkeys:
Tylvalosin has activity against *Ornithobacterium rhinotracheale*, a Gram-negative organism found in turkeys and chickens.

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.

**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.

**Indication**
Chickens:
Treatment and metaphylaxis of respiratory infections caused by *Mycoplasma gallisepticum* in chickens. The presence of the disease in the flock should be established before metaphylactic treatment. 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 tylvalosin sensitive strains of *Ornithobacterium rhinotracheale* in turkeys.

**Recommended Dose**
**Chickens:**
For treatment of respiratory disease associated with *Mycoplasma gallisepticum*:
The dose is 25mg tylvalosin per kg body weight 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 body weight 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 body weight 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 body weight (in kg) of all the chickens to be treated. Select the correct number of pack size according to the amount of product required.

A pouch of 100g is sufficient to treat a total of 2,500kg of chickens, (e.g. 50,000 birds with an average weight of 50g). A pouch of 500g is sufficient to treat a total of 12,500kg of chickens (e.g. 25,000 birds with an average body weight of 500g).

In order to achieve a correct dose, the preparation of a concentrated (stock) solution might be required (e.g. to treat a total of 1,250kg total bird weight, only 50% of the prepared stock solution prepared from the 100g pouch should be used.

The product should be added to a volume of water that the chickens 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 25mg tylvalosin per kg body weight per day in drinking water for 5 consecutive days.
Determine the combined body weight (in kg) of all the turkeys to be treated. Select the correct number of pack size according to the amount of product required.

One pouch of 100g is sufficient to treat a total of 2,500kg of turkeys (e.g. 25,000 birds with an average body weight of 100g). A pouch of 500g is sufficient to treat a total of 12,500kg of turkeys (e.g. 12,500 birds with an average body weight of 1kg).

In order to achieve a correct dose, the preparation of a concentrated (stock) solution might be required (e.g. to treat a total of 1,250kg total bird weight, only 50% of the prepared stock solution prepared from the 100g pouch 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 pouch 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 100g per 3.75 litres or 500g of product per 18.75 liters 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.

**Route of Administration**
For oral administration via drinking water.

**Contraindication**
None.

**Warning and Precautions**
**Special warnings for each target species**
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.

**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. 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 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 or a non-disposable respirator with a filter 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.

**Interaction with Other Medicaments**
None known.

**Pregnancy and Lactation**
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.

**Side Effects**
None known.

**Symptoms and Treatment of Overdose**
No signs of intolerance have been observed in poultry species at up to 150mg tylvalosin per kg body weight per day for 5 days.
No adverse effects on egg production, egg fertility, hatchability and chick viability were observed in broiler breeder stock administered 75mg tylvalosin per kg body weight per day for 28 consecutive days.

**Storage Condition**
Store below 30ºC.

**Shelf life**
3 years.
To be used within 24 hours after dilution.

**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 of the start of the laying period.

**Packing**
100g, 200g, 500g, 1kg, 10kg, 25kg.

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