ANNEX I

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

Excipients:

Qualitative composition of excipients and other constituents
Hydrated magnesium silicate (sepiolite)
Wheat flour
Hydroxypropyl cellulose
Non-fat soyabean powder

A beige granular powder.

3. CLINICAL INFORMATION

3.1 Target species

Pigs

3.2 Indications for use for each target species

The presence of the disease in the group must be established before the product is used.

- Treatment and metaphylaxis of swine enzootic pneumonia caused by *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 groups 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 groups where the disease has been diagnosed.

3.3 Contraindications

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

3.4 Special warnings

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 has been shown between tylvalosin and other macrolides. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to tylvalosin because its effectiveness may be reduced.

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 followed 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 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.

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 lactation

. Use only according to the benefit-risk assessment by the responsible veterinarian.
No signs of adverse effects were observed in sows or their offspring when tylvalosin 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.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

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:

$$\text{kg veterinary medicinal product/tonne feed} = \frac{\text{Dose rate (mg/kg bodyweight)} \times \text{Bodyweight (kg)}}{\text{Daily feed intake (kg)} \times \text{veterinary medicinal product strength (mg/g)}}$$

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 the veterinary medicinal product 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.

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

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

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

This veterinary medicinal product is intended to be used for the preparation of medicated feed.

Do not use for prophylaxis.

3.12 Withdrawal periods

Meat and offal: 2 days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01FA92

4.2 Pharmacodynamics

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.

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 proinflammatory CXCL-8, IL1α and LTB4 production, while inducing the release of pro-resolving Lipoxin A4 and Resolvin D1 in vitro.

4.3 Pharmacokinetics

Tylvalosin tartrate is rapidly absorbed after oral administration of the veterinary medicinal product.

After administration of the recommended dose, lung concentrations of 0.060–0.066 mcg/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 veterinary medicinal product 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.

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

5.3 Special precautions for storage

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

5.4 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.

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 or household waste.

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/2/04/044/001 – 20 kg
EU/2/04/044/002 – 5 kg
EU/2/04/044/020 – 2 kg

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).

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

Excipients:

Qualitative composition of excipients and other constituents
Lactose monohydrate

White granules.

3. CLINICAL INFORMATION

3.1 Target species

Pigs

3.2 Indications for use for each target species

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

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

The presence of the disease in the group must be established before the product is used..

3.3 Contraindications

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

3.4 Special warnings

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.
Cross-resistance has been shown between tylvalosin and other macrolides. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to tylvalosin because its effectiveness may be reduced.

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..

Good management and hygiene practices should be followed 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.

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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.

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 lactation

Use only according to the benefit-risk assessment by the responsible veterinarian.

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.

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.

To ensure a correct dosage, bodyweight should be determined as accurately as possible. The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage, the concentration of tylvalosin may need to be adjusted accordingly

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.
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Calculate the total amount of veterinary medicinal product required with the following formula:

Total weight of veterinary medicinal 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 *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:

The use of suitably calibrated measuring equipment is recommended.
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.

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

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

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, 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 proinflammatory CXCL-8, IL1α and LTB4 production, while inducing the release of pro-resolving Lipoxin A4 and Resolvin D1 in vitro.

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. 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.

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.
160 g sachet – 2 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, 160 g or 400 g of granules.

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/2/04/044/009 – 40 g
EU/2/04/044/010 – 160 g
EU/2/04/044/017 – 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).

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

Excipients:

Qualitative composition of excipients and other constituents
Lactose monohydrate

White granules.

3. CLINICAL INFORMATION

3.1 Target species

Pheasants

3.2 Indications for use for each target species

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

3.3 Contraindications

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

3.4 Special warnings

Treat as soon as possible after clinical signs suggestive of mycoplasmosis are observed. Treat all the birds in the affected flock.
Cross-resistance has been shown between tylvalosin and other macrolides. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to tylvalosin because its effectiveness may be reduced.

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

Laying birds

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

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.

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 the veterinary medicinal product 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.

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.

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

The minimum inhibitory concentration of tylvalosin for *Mycoplasma gallisepticum* ranges from 0.007 to 0.25 mcg/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.

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. 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 of granules.

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/2/04/044/012 – 40 g
EU/2/04/044/014 – 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).

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Aivlosin 42.5 mg/g oral powder for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Excipients:

Qualitative composition of excipients and other constituents
Hydrated magnesium silicate (sepiolite)
Wheat flour
Hydroxypropyl cellulose
Non-fat soyabean powder

A beige granular powder.

3. CLINICAL INFORMATION

3.1 Target species

Pigs

3.2 Indications for use for each target species

The presence of the disease in the group must be established before the product is used.

- Treatment and metaphylaxis of swine enzootic pneumonia caused by *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 groups 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 groups where the disease has been diagnosed.

3.3 Contraindications

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

3.4 Special warnings

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 has been shown between tylvalosin and other macrolides. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to tylvalosin because its effectiveness may be reduced.

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.

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 oral powder, 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.

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 also the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation

Use only in accordance with benefit-risk assessment by the responsible veterinarian.

No signs of adverse effects were observed in sows or their offspring when tylvalosin 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.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

For use in individual pigs on farms where only a small number of pigs are to receive the treatment. Larger groups should be treated with medicated feeding stuff containing the premix.

For treatment and metaphylaxis of swine enzootic pneumonia
The dose is 2.125 mg tylvalosin per kg bodyweight per day 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 for 10 consecutive days.

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

This is achieved by thoroughly mixing the veterinary medicinal product into approximately 200–500 g of feed and then thoroughly mixing this pre-mixture into the remainder of the daily ration. Scoops of 2 sizes are provided for measuring the correct amount of veterinary medicinal product for mixing with the daily ration, according to the schedule below. The feed containing the oral powder should be provided as the sole ration for the periods recommended above.

The pig to be treated should be weighed and the amount of feed that the pig is likely to consume should be estimated, based on a daily feed intake equivalent to 5% of bodyweight. Consideration must be given to pigs whose daily feed intake is reduced or restricted. The correct quantity of the veterinary medicinal product should be added to the estimated quantity of daily ration for each pig, in a bucket or similar receptacle, and thoroughly mixed.
The veterinary medicinal product should only be added to dry non-pelleted feed.

Swine enzootic pneumonia 2.125 mg/kg bodyweight		
Bodyweight range (kg)	**Scoop size**	**Number of scoops**
7.5–12	1 ml	1
13–25	1 ml	2
26–38	1 ml	3
39–67	5 ml	1
68–134	5 ml	2
135–200	5 ml	3
201–268	5 ml	4

PPE (ileitis) and swine dysentery 4.25 mg/kg bodyweight		
Bodyweight range (kg)	**Scoop size**	**Number of scoops**
7.5–12	1 ml	2
13–19	1 ml	3
20–33	5 ml	1
34–67	5 ml	2
68–100	5 ml	3
101–134	5 ml	4
135–200	5 ml	6
201–268	5 ml	8

NB: A level scoop of the product should be measured

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

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

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.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QJ01FA92

4.2 Pharmacodynamics

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 bacteria cells.

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 mechanism 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.

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 proinflammatory CXCL-8, IL1α and LTB4 production, while inducing the release of pro-resolving Lipoxin A4 and Resolvin D1 in vitro.

4.3 Pharmacokinetics

Tylvalosin tartrate is rapidly absorbed after oral administration of the veterinary medicinal product.

After administration of the recommended dose lung concentrations of 0.060–0.066 mcg/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 veterinary medicinal product 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.

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: 3 years.
Shelf life after first opening of the immediate packaging: 4 weeks.
Feed to which the oral powder has been added should be replaced if not consumed within 24 hours.

5.3 Special precautions for storage

Store below 30 ºC.
Store in the original container.
Keep the container tightly closed.

5.4 Nature and composition of immediate packaging

One aluminium foil/polyester laminated bag containing 500 g. Scoops of 1 ml and 5 ml are attached.

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/2/04/044/013

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).

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.
.

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).

ANNEX II

OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

BAG

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE SUBSTANCES

Tylvalosin (as tylvalosin tartrate) 42.5 mg/g

3. PACKAGE SIZE

20 kg
5 kg
2 kg

4. TARGET SPECIES

Pigs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

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

7. WITHDRAWAL PERIODS

Withdrawal period: Meat and offal: 2 days.

8. EXPIRY DATE

Exp. {mm/yyyy}
Shelf life after incorporation into meal or pelleted feed: 1 month.
Once opened use within 4 weeks

9. SPECIAL STORAGE PRECAUTIONS

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

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

ECO Animal Health Europe Limited

14. MARKETING AUTHORISATION NUMBERS

EU/2/04/044/001 (20 kg)
EU/2/04/044/002 (5 kg)
EU/2/04/044/020 (2 kg)

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

SACHET

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE SUBSTANCES

Tylvalosin (as tylvalosin tartrate) 625 mg/g

3. PACKAGE SIZE

40 g
160 g
400 g

4. TARGET SPECIES

Pigs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

In drinking water use

7. WITHDRAWAL PERIODS

Withdrawal period: Meat and offal: 2 days.

8. EXPIRY DATE

Exp. {mm/yyyy}
Medicated drinking water should be replaced every 24 hours.
Once opened use within 5 weeks

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 ºC.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

ECO Animal Health Europe Limited

14. MARKETING AUTHORISATION NUMBERS

EU/2/04/044/009 (40g)
EU/2/04/044/010 (160g)
EU/2/04/044/017 (400g)

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

SACHET

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE SUBSTANCES

Tylvalosin (as tylvalosin tartrate) 625 mg/g

3. PACKAGE SIZE

40 g
400 g

4. TARGET SPECIES

Pheasants

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

In drinking water use

7. WITHDRAWAL PERIODS

Withdrawal period: 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 before the start of the laying period.

8. EXPIRY DATE

Exp. {mm/yyyy}
Medicated drinking water should be replaced every 24 hours.
Once opened use within 5 weeks

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 ºC.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

ECO Animal Health Europe Limited

14. MARKETING AUTHORISATION NUMBERS

EU/2/04/044/012 (40g)
EU/2/04/044/014 (400g)

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

BAG

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Aivlosin 42.5 mg/g oral powder for pigs

2. STATEMENT OF ACTIVE SUBSTANCES

Tylvalosin (as tylvalosin tartrate) 42.5 mg/g

3. PACKAGE SIZE

500 g

4. TARGET SPECIES

Pigs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.
Only to be added to dry food.

7. WITHDRAWAL PERIODS

Withdrawal period: Meat and offal: 2 days.

8. EXPIRY DATE

Exp. {mm/yyyy}
Feed to which the oral powder has been added should be replaced if not consumed within 24 hours.
Once opened use within 4 weeks

9. SPECIAL STORAGE PRECAUTIONS

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

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

ECO Animal Health Europe Limited

14. MARKETING AUTHORISATION NUMBERS

EU/2/04/044/013

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

SACHET

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE SUBSTANCES

Tylvalosin (as tylvalosin tartrate) 625 mg/g

3. PACKAGE SIZE

40 g
400 g

4. TARGET SPECIES

Chickens and Turkeys

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

In drinking water use

7. WITHDRAWAL PERIODS

Withdrawal periods:
Meat and offal: 2 days.
Eggs (chickens): 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.

8. EXPIRY DATE

Exp. {mm/yyyy}
Medicated drinking water should be replaced every 24 hours.
Once opened use within 5 weeks

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 ºC.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

ECO Animal Health Europe Limited

14. MARKETING AUTHORISATION NUMBERS

EU/2/04/044/018 (40g)
EU/2/04/044/019 (400g)

15. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

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

2. Composition

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

A beige granular powder.

3. Target species

Pigs

4. Indications for use

The presence of the disease in the group must be established before the product is used.
Treatment and metaphylaxis of swine enzootic pneumonia caused by *Mycoplasma hyopneumoniae*. 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 groups where there is a diagnosis based on clinical history, post-mortem findings and clinical pathology results.
Treatment and metaphylaxis of swine dysentery in groups, caused by *Brachyspira hyodysenteriae,* where the disease has been diagnosed.

5. Contraindications

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

6. Special warnings

Special warnings:

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 has been shown between tylvalosin and other macrolides. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to tylvalosin because its effectiveness may be reduced.

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 followed 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 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.

Pregnancy and lactation:

Use only in accordance with benefit-risk assessment by the responsible veterinarian.

No signs of adverse effects were observed in sows or their offspring when tylvalosin 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.

Overdose:

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

Special restrictions for use and special conditions for use:
This veterinary medicinal product is intended to be used for the preparation of medicated feed.
Do not use for prophylaxis.

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

7. Adverse events

None known.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the

medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system:
HPRA Pharmacovigilance
Website: www.hpra.ie
or
Website: https://www.gov.uk/report-veterinary-medicine-problem/animal-reacts-medicine
e-mail: adverse.events@vmd.gov.uk

8. Dosage for each species, routes and method of administration

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:

$$\text{kg veterinary medicinal product/tonne feed} = \frac{\text{Dose rate (mg/kg bodyweight)} \times \text{Bodyweight (kg)}}{\text{Daily feed intake (kg)} \times \text{veterinary medicinal product strength (mg/g)}}$$

Acute cases and severely diseased pigs with reduced food and water intake should be treated with a suitable injectable product.
In addition to medical treatment, good management and hygiene practices should be established on the farm in order to reduce the risk of infection and to control the build-up of resistance.
The medicated feed should be fed as the sole ration.

9. Advice on correct administration

A horizontal ribbon mixer should be used to incorporate the veterinary medicinal product into feeding stuff. It is recommended that the veterinary medicinal product is first mixed with 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.

10. Withdrawal periods

Meat and offal: 2 days.

11. Special storage precautions

Keep out of the sight and reach of children.
Store below 30 °C.
Store in the original container.
Keep the bag tightly closed.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after "Exp".
Shelf life after first opening the immediate packaging: 4 weeks.
Shelf life after incorporation into feed: meal and pellets: 1 month.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription

14. Marketing authorisation numbers and pack sizes

EU/2/04/044/001 – 20 kg
EU/2/04/044/002 – 5 kg
EU/2/04/044/020 – 2 kg

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

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

16. Contact details

Marketing authorisation holder:

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

Manufacturer responsible for batch release:
Acme Drugs s.r.l.
Via Portella della Ginestra 9/a
42025 CAVRIAGO (RE)
ITALY
Or
Provet A.E.
Nikiforou Foka & Agíon Anargyron
Thesi Vrago
Aspropyrgos
193 00
Greece

Local representative and contact details to report suspected adverse reactions:
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

België/Belgique/Belgien Ecuphar NV/SA Legeweg 157-I, BE-8020 Oostkamp Tel: +32 50 31 42 69 Email: animal.health@ecuphar.be	**Lietuva** Magnum Veterinarija, UAB Martinavos g. 8, Martinavos k., LT-54463 Kauno r., Lietuva Tel.: +370 688 96944 Email: info@magnumvet.lt
Република България ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND телефон: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Luxembourg/Luxemburg** ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com
Česká republika Sevaron s.r.o. Palackého třída 163a 612 00 Brno Tel: +42 (0) 54 1426 370 Email: info@sevaron.cz	**Magyarország** Dunavet-B ZRt, 7020 Dunaföldvár, Ady E. u. 5. Tel: +36 75 542 940 Email: dunavet-bp@dunavet.hu

Danmark Salfarm Danmark A/S, Nordager 19, 6000 Kolding Tel: +45 75 52 94 13 E-mail: sal@salfarm.dk www.salfarm.com	**Malta** ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com
Deutschland Ecuphar GmbH Brandteichstrasse 20, 17489 Greifswald, Deutschland, E-mail: info@ecuphar.de Tel: +49 (0)38348 3584 0	**Nederland** Ecuphar BV Verlengde Poolseweg 16 NL-4818 CL Breda Tel : +31 (0)88 033 38 00 Email: info@ecuphar.nl
Eesti AS Magnum Veterinaaria Vae 16, Laagri, Harju mk Tel: +372 6 501 920	**Norge** Salfarm Scandinavia AB Florettgatan 29C, 2. Vån 25 467 Helsingborg Sweden Phone: 0046 767 834 910 Email: Scan@salfarm.com
Ελλάδα DG Nucleus ΕΠΕ Ν.Χαρίτου 11 43100 Καρδιτσα Τηλ:+302441073034 Email: info@vkk.gr	**Österreich** Ecuphar GmbH Brandteichstrasse 20, 17489 Greifswald, Deutschland, E-mail: info@ecuphar.de Tel: +49 (0)38348 3584 0
España Ecuphar Veterinaria S.L.U. C/Cerdanya, 10-12 Planta 6º, 08173 Sant Cugat del Vallés, Barcelona (España). Tel: +34 (0)935 955 000	**Polska** Calier Polska Sp. z o.o. ul. Magazynowa 5, 66-446 Deszczno Tel: +48 95 7214521 E-mail: calierpolska@calier.com.pl HURTOWNIA LEKÓW WETERYNARYJNYCH "AGA-VET" ul. Turkowska 58c 62-720 Brudzew Tel: **+48 (63) 279 70 04** Email: hurtownia@agavet.com.pl

France Laboratoire LCV Z.I. Plessis Beucher 35220 Châteaubourg Tél : +33 (0)2 99 00 92 92	**Portugal** Belphar LDA Sintra Business Park No 7, Edifício 1- Escritório 2K Zona Industrial de Abrunheira 2710-089 Sintra Tel: +35 (0)13088 08321
Hrvatska ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**România** SC MARAVET SA Baia Mare Maravet, Street No 1 Tel: +40 262 211 964 Email: office@maravet.com
Ireland ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Slovenija** ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com
Ísland ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Slovenská republika** Sevaron s.r.o. Palackého třída 163a 612 00 Brno Česká Republika Tel: +42 (0) 54 1426 370 Email: info@sevaron.cz
Italia Ecuphar Italia S.R.L. Viale Francesco Restelli, 3/7, piano 1 20124 Milano Tel: +39 (0)02829 50604	**Suomi/Finland** Vetcare Oy PL 99 24101 Salo Tel: +358 (0)20 144 3360 Email: vetcare@vetcare.fi
Κύπρος Panchris Feeds (Veterinary) Ltd Industrial Area Aradippou, 7100, Larnaca, POB 40261, 6302, Larnaca, Τηλ: + 357 24813333	**Sverige** Salfarm Scandinavia AB Florettgatan 29C, 2. Vån 25 467 Helsingborg Phone: 0046 767 834 910 Email: Scan@salfarm.com

Latvija Magnum Veterinārija SIA Ulbrokas iela 23, Rīga, LV-1021, Tel: +371 671 60091	**United Kingdom (Northern Ireland)** ECO Animal Health Limited The Grange, 100 The High Street London N14 6BN Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

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

2. Composition

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

White granules.

3. Target species

Pigs

4. Indications for use

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

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

The presence of the disease in the group must be established before the product is used.

5. Contraindications

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

6. Special warnings

Special warnings:

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.
Cross-resistance has been shown between tylvalosin and other macrolides. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to tylvalosin because its effectiveness may be reduced.

Special precautions for safe use in the target species:

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

Good management and hygiene practices should be followed 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.

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.
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.

Pregnancy and lactation:

Use only according to the benefit-risk assessment by the responsible veterinarian.

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.

Overdose:

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

Major incompatibilities:

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

7. Adverse events

None known.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system:
HPRA Pharmacovigilance
Website: www.hpra.ie

or
Website: https://www.gov.uk/report-veterinary-medicine-problem/animal-reacts-medicine
e-mail: adverse.events@vmd.gov.uk

8. Dosage for each species, routes and method of administration

For use in drinking water.

To ensure a correct dosage, bodyweight should be determined as accurately as possible. The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage, the concentration of tylvalosin may need to be adjusted accordingly.

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 veterinary medicinal product required with the formula:
Total weight of veterinary medicinal 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 and size 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 *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.

9. Advice on correct administration

The use of suitably calibrated measuring equipment is recommended.

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 400g 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.

10. Withdrawal periods

Meat and offal: 2 days.

11. Special storage precautions

Keep out of the sight and reach of children.
Do not store above 25 ºC

Do not use this veterinary medicinal product after the expiry date which is stated on the label after "EXP".
Shelf life after first opening the immediate packaging: 5 weeks.
Shelf life of the medicated drinking water: 24 hours.

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription

14. Marketing authorisation numbers and pack sizes

EU/2/04/044/009 – 40 g
EU/2/04/044/010 – 160 g
EU/2/04/044/017 – 400 g

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

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

16. Contact details

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

Manufacturer responsible for batch release:
Acme Drugs s.r.l.
Via Portella della Ginestra 9/a
42025 CAVRIAGO (RE)
ITALY
or
Provet A.E.
Nikiforou Foka & Agíon Anargyron Thesi Vrago
Aspropyrgos
193 00
Greece

Local representatives and contact details to report suspected adverse reactions:
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

België/Belgique/Belgien Vaccifar BVBA Sint Damiaanstraat 18 B-2160 Wommelgem BELGIUM Tel : +32 3 355 29 50 Email : info@vaccifar.com	**Lietuva** Magnum Veterinarija, UAB Martinavos g. 8, Martinavos k., LT-54463 Kauno r., Lietuva Tel.: +370 688 96944 Email: info@magnumvet.lt

Република България ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND телефон: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Luxembourg/Luxemburg** Vaccifar BVBA Sint Damiaanstraat 18 B-2160 Wommelgem BELGIUM Tel : +32 3 355 29 50 Email : info@vaccifar.com
Česká republika Sevaron s.r.o. Palackého třída 163a 612 00 Brno Tel: +42 (0) 54 1426 370 Email: info@sevaron.cz	**Magyarország** Dunavet-B ZRt, 7020 Dunaföldvár, Ady E. u. 5. Tel: +36 75 542 940 Email: dunavet-bp@dunavet.hu
Danmark Salfarm Danmark A/S, Nordager 19, 6000 Kolding Tel: +45 75 52 94 13 E-mail: sal@salfarm.dk	**Malta** ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com
Deutschland Ecuphar GmbH Brandteichstrasse 20, 17489 Greifswald, Deutschland, E-mail: info@ecuphar.de Tel: +49 (0)38348 3584 0	**Nederland** Vaccifar BVBA Sint Damiaanstraat 18 B-2160 Wommelgem BELGIUM Tel : +32 3 355 29 50 Email : info@vaccifar.com
Eesti AS Magnum Veterinaaria Vae 16, Laagri, Harju mk Tel: +372 6 501 920	**Norge** Salfarm Scandinavia AB Florettgatan 29C, 2. Vån 25 467 Helsingborg Sweden Phone: 0046 767 834 910 Email: Scan@salfarm.com
Ελλάδα DG Nucleus ΕΠΕ Ν.Χαρίτου 11 43100 Καρδιτσα Τηλ:+302441073034 Email: info@vkk.gr	**Österreich** Ecuphar GmbH Brandteichstrasse 20, 17489 Greifswald, Deutschland, E-mail: info@ecuphar.de Tel: +49 (0)38348 3584 0

España Ecuphar Veterinaria S.L.U. C/Cerdanya, 10-12 Planta 6º, 08173 Sant Cugat del Vallés, Barcelona (España). Tel: +34 (0)935 955 000	**Polska** Calier Polska Sp. z o.o. ul. Magazynowa 5, 66-446 Deszczno Tel: +48 95 7214521 fax: +48 95 7214532 E-mail: calierpolska@calier.com.pl HURTOWNIA LEKÓW WETERYNARYJNYCH "AGA-VET" ul. Turkowska 58c 62-720 Brudzew Tel: **+48 (63) 279 70 04** Email: hurtownia@agavet.com.pl" Group-On-Vet Sp. Z o.o. Ludwinów 31B, 42-320 Niegowa Polska.
France Laboratoire LCV Z.I. Plessis Beucher 35220 Châteaubourg Tél : +33 (0)2 99 00 92 92	**Portugal** Belphar LDA Sintra Business Park No 7, Edifício 1- Escritório 2K Zona Industrial de Abrunheira 2710-089 Sintra Tel: +35 (0)13088 08321
Hrvatska Mount Trade d.o.o., Inductrijska 13, 43280 Garesnica, Croatia Tel: +385 (0) 43 485 914 Email: skladiste@mount-trade.hr	**România** SC MARAVET SA Baia Mare Maravet, Street No 1 Tel: +40 262 211 964 Email: office@maravet.com
Ireland ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Slovenija** ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com

Ísland ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Slovenská republika** Sevaron s.r.o. Palackého třída 163a 612 00 Brno Česká Republika Tel: +42 (0) 54 1426 370 Email: info@sevaron.cz
Italia Ecuphar Italia S.R.L. Viale Francesco Restelli, 3/7, piano 1 20124 Milano Tel: +39 (0)02829 50604	**Suomi/Finland** Vetcare Oy PL 99 24101 Salo Tel: +358 (0)20 144 3360 Email: vetcare@vetcare.fi
Κύπρος Panchris Feeds (Veterinary) Ltd Industrial Area Aradippou, 7100, Larnaca, POB 40261, 6302, Larnaca, Τηλ: + 357 24813333	**Sverige** Salfarm Scandinavia AB Florettgatan 29C, 2. Vån 25 467 Helsingborg Phone: 0046 767 834 910 Email: Scan@salfarm.com
Latvija Magnum Veterinārija SIA Ulbrokas iela 23, Rīga, LV-1021, Tel: +371 671 60091	**United Kingdom (Northern Ireland)** ECO Animal Health Limited The Grange, 100 The High Street London N14 6BN Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

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

2. Composition

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

White granules.

3. Target species

Pheasants

4. Indications for use

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

5. Contraindications

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

6. Special warnings

Special warnings:

Treat as soon as possible after clinical signs suggestive of mycoplasmosis are observed.
Treat all the birds in the affected flock.
Cross-resistance has been shown between tylvalosin and other macrolides. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to tylvalosin because its effectiveness may be reduced.

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 in order 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 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.

Laying birds:

Use only in accordance with benefit-risk assessment by the responsible veterinarian.

Overdose:

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

Major incompatibilities:

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

7. Adverse events

None known.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system:
HPRA Pharmacovigilance
Website: www.hpra.ie
or
Website: https://www.gov.uk/report-veterinary-medicine-problem/animal-reacts-medicine
e-mail: adverse.events@vmd.gov.uk

8. Dosage for each species, routes and method of administration

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 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 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 veterinary medicinal product has to be adjusted accordingly. No other source of drinking water should be available during the medication period.

9. Advice on correct administration

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 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.

10. Withdrawal periods

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 before the start of the laying period

11. Special storage precautions

Keep out of the sight and reach of children.
Do not store above 25 ºC

Do not use this veterinary medicinal product after the expiry date which is stated on the label after "EXP".
Shelf life after first opening the immediate packaging: 5 weeks.
Shelf life of the medicated drinking water: 24 hours.

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription

14. Marketing authorisation numbers and pack sizes

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

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

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

16. Contact details

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

Manufacturer responsible for batch release:
Acme Drugs s.r.l.
Via Portella della Ginestra 9/a
42025 CAVRIAGO (RE)
ITALY
Or
Provet A.E.
Nikiforou Foka & Agíon Anargyron Thesi Vrago
Aspropyrgos
193 00
Greece

Local representatives and contact details to report suspected adverse reactions:
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

België/Belgique/Belgien Ecuphar NV/SA Legeweg 157-I, BE-8020 Oostkamp Tel: +32 50 31 42 69 Email: animal.health@ecuphar.be	**Lietuva** Magnum Veterinarija, UAB Martinavos g. 8, Martinavos k., LT-54463 Kauno r., Lietuva Tel.: +370 688 96944 Email: info@magnumvet.lt

Република България ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND телефон: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Luxembourg/Luxemburg** ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com
Česká republika Sevaron s.r.o. Palackého třída 163a 612 00 Brno Tel: +42 (0) 54 1426 370 Email: info@sevaron.cz	**Magyarország** Dunavet-B ZRt, 7020 Dunaföldvár, Ady E. u. 5. Tel: +36 75 542 940 Email: dunavet-bp@dunavet.hu
Danmark Salfarm Danmark A/S, Nordager 19, 6000 Kolding Tel: +45 75 52 94 13 E-mail: sal@salfarm.dk	**Malta** ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com
Deutschland Ecuphar GmbH Brandteichstrasse 20, 17489 Greifswald, Deutschland, E-mail: info@ecuphar.de Tel: +49 (0)38348 3584 0	**Nederland** Ecuphar BV Verlengde Poolseweg 16 NL-4818 CL Breda Tel : +31 (0)88 033 38 00 Email: info@ecuphar.nl
Eesti AS Magnum Veterinaaria Vae 16, Laagri, Harju mk Tel: +372 6 501 920	**Norge** Salfarm Scandinavia AB Florettgatan 29C, 2. Vån 25 467 Helsingborg Sweden Phone: 0046 767 834 910 Email: Scan@salfarm.com
Ελλάδα DG Nucleus ΕΠΕ Ν.Χαρίτου 11 43100 Καρδιτσα Τηλ:+302441073034 Email: info@vkk.gr	**Österreich** Ecuphar GmbH Brandteichstrasse 20, 17489 Greifswald, Deutschland, E-mail: info@ecuphar.de Tel: +49 (0)38348 3584 0

España Ecuphar Veterinaria S.L.U. C/Cerdanya, 10-12 Planta 6º, 08173 Sant Cugat del Vallés, Barcelona (España). Tel: +34 (0)935 955 000	**Polska** Calier Polska Sp. z o.o. ul. Magazynowa 5, 66-446 Deszczno Tel: +48 95 7214521 E-mail: calierpolska@calier.com.pl HURTOWNIA LEKÓW WETERYNARYJNYCH "AGA-VET" ul. Turkowska 58c 62-720 Brudzew Tel: **+48 (63) 279 70 04** Email: hurtownia@agavet.com.pl
France Laboratoire LCV Z.I. Plessis Beucher 35220 Châteaubourg Tél : +33 (0)2 99 00 92 92	**Portugal** Belphar LDA Sintra Business Park No 7, Edifício 1- Escritório 2K Zona Industrial de Abrunheira 2710-089 Sintra Tel: +35 (0)13088 08321
Hrvatska ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**România** SC MARAVET SA Baia Mare Maravet, Street No 1 Tel: +40 262 211 964 Email: office@maravet.com
Ireland ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Slovenija** ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com
Ísland ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Slovenská republika** Sevaron s.r.o. Palackého třída 163a 612 00 Brno Česká Republika Tel: +42 (0) 54 1426 370 Email: info@sevaron.cz

Italia Ecuphar Italia S.R.L. Viale Francesco Restelli, 3/7, piano 1 20124 Milano Tel: +39 (0)02829 50604	**Suomi/Finland** Vetcare Oy PL 99 24101 Salo Tel: +358 (0)20 144 3360 Email: vetcare@vetcare.fi
Κύπρος Panchris Feeds (Veterinary) Ltd Industrial Area Aradippou, 7100, Larnaca, POB 40261, 6302, Larnaca, Τηλ: + 357 24813333	**Sverige** Salfarm Scandinavia AB Florettgatan 29C, 2. Vån 25 467 Helsingborg Phone: 0046 767 834 910 Email: Scan@salfarm.com
Latvija Magnum Veterinārija SIA Ulbrokas iela 23, Rīga, LV-1021, Tel: +371 671 60091	**United Kingdom (Northern Ireland)** ECO Animal Health Limited The Grange, 100 The High Street London N14 6BN Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Aivlosin 42.5 mg/g oral powder for pigs

2. Composition

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

A beige granular powder.

3. Target species

Pigs

4. Indications for use

The presence of the disease in the group must be established before the product is used.
Treatment and metaphylaxis of swine enzootic pneumonia caused by *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 groups 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 groups where the disease has been diagnosed.

5. Contraindications

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

6. Special warnings

Special warnings:

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 has been shown between tylvalosin and other macrolides. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to tylvalosin because its effectiveness may be reduced.
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.

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.

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

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 oral powder, 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.

Pregnancy and lactation:

Use only in accordance with benefit-risk assessment by the responsible veterinarian.
No signs of adverse effects were observed in sows or their offspring when tylvalosin 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.

Overdose:

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

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

7. Adverse events

None known.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system:

HPRA Pharmacovigilance
Website: www.hpra.ie
or
Website: https://www.gov.uk/report-veterinary-medicine-problem/animal-reacts-medicine
e-mail: adverse.events@vmd.gov.uk

8. Dosage for each species, routes and method of administration

For oral use.

The oral powder is for use in individual pigs on farms where only a small number of pigs are to receive the treatment. Larger groups should be treated with medicated feeding stuff containing the premix.

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 for 10 consecutive days.

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

9. Advice on correct administration

This is achieved by thoroughly mixing the veterinary medicinal product into approximately 200–500 g of feed and then thoroughly mixing this pre-mixture into the remainder of the daily ration.

Scoops of 2 sizes are provided for measuring the correct amount of the veterinary medicinal product for mixing with the daily ration, according to the schedule below. The feed containing the oral powder should be provided as the sole ration for the periods recommended above.

The pig to be treated should be weighed and the amount of feed that the pig is likely to consume should be estimated, based on a daily feed intake equivalent to 5% of bodyweight. Consideration must be given to pigs whose daily feed intake is reduced or restricted. The correct quantity of the veterinary medicinal product should then be added to the estimated quantity of daily ration for each pig, in a bucket or similar receptacle, and thoroughly mixed.

The veterinary medicinal product should only be added to dry non-pelleted feed.

Swine enzootic pneumonia 2.125 mg/kg bodyweight		
Bodyweight range (kg)	**Scoop size**	**Number of scoops**
7.5–12	1 ml	1
13–25	1 ml	2
26–38	1 ml	3
39–67	5 ml	1
68–134	5 ml	2
135–200	5 ml	3
201–268	5 ml	4

PPE (ileitis) and swine dysentery 4.25 mg/kg bodyweight		
Bodyweight range (kg)	**Scoop size**	**Number of scoops**
7.5–12	1 ml	2
13–19	1 ml	3
20–33	5 ml	1
34–67	5 ml	2
68–100	5 ml	3
101–134	5 ml	4
135–200	5 ml	6

			201–268	5 ml	8

NB: A level scoop of the product should be measured**.**

10. Withdrawal periods

Meat and offal: 2 days.

11. Special storage precautions

Keep out of the sight and reach of children.
Store below 30 °C.
Store in the original container.
Keep the container tightly closed.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after "EXP".
Shelf life after first opening the immediate packaging: 4 weeks.
Feed to which the oral powder has been added should be replaced if not consumed within 24 hours.

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription

14. Marketing authorisation numbers and pack sizes

EU/2/04/044/013

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

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

16. Contact details

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

Manufacturer responsible for batch release:
Acme Drugs s.r.l.
Via Portella della Ginestra 9/a
42025 CAVRIAGO (RE)
ITALY
Or
Provet A.E.
Nikiforou Foka & Agíon Anargyron Thesi Vrago
Aspropyrgos
193 00
Greece

Local representatives and contact details to report suspected adverse reactions:
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

België/Belgique/Belgien Ecuphar NV/SA Legeweg 157-I, BE-8020 Oostkamp Tel: +32 50 31 42 69 Email: animal.health@ecuphar.be	**Lietuva** Magnum Veterinarija, UAB Martinavos g. 8, Martinavos k., LT-54463 Kauno r., Lietuva Tel.: +370 688 96944 Email: info@magnumvet.lt
Република България ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND телефон: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Luxembourg/Luxemburg** ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com
Česká republika Sevaron s.r.o. Palackého třída 163a 612 00 Brno Tel: +42 (0) 54 1426 370 Email: info@sevaron.cz	**Magyarország** Dunavet-B ZRt, 7020 Dunaföldvár, Ady E. u. 5. Tel: +36 75 542 940 Email: dunavet-bp@dunavet.hu

Danmark Salfarm Danmark A/S, Nordager 19, 6000 Kolding Tel: +45 75 52 94 13 E-mail: sal@salfarm.dk	**Malta** ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com
Deutschland Ecuphar GmbH Brandteichstrasse 20, 17489 Greifswald, Deutschland, E-mail: info@ecuphar.de Tel: +49 (0)38348 3584 0	**Nederland** Ecuphar BV Verlengde Poolseweg 16 NL-4818 CL Breda Tel : +31 (0)88 033 38 00 Email: info@ecuphar.nl
Eesti AS Magnum Veterinaaria Vae 16, Laagri, Harju mk Tel: +372 6 501 920	**Norge** Salfarm Scandinavia AB Florettgatan 29C, 2. Vån 25 467 Helsingborg Sweden Phone: 0046 767 834 910 Email: Scan@salfarm.com
Ελλάδα DG Nucleus ΕΠΕ Ν.Χαρίτου 11 43100 Καρδιτσα Τηλ:+302441073034 Email: info@vkk.gr	**Österreich** Ecuphar GmbH Brandteichstrasse 20, 17489 Greifswald, Deutschland, E-mail: info@ecuphar.de Tel: +49 (0)38348 3584 0
España Ecuphar Veterinaria S.L.U. C/Cerdanya, 10-12 Planta 6º, 08173 Sant Cugat del Vallés, Barcelona (España). Tel: +34 (0)935 955 000	**Polska** Calier Polska Sp. z o.o. ul. Magazynowa 5, 66-446 Deszczno Tel: +48 95 7214521 E-mail: calierpolska@calier.com.pl HURTOWNIA LEKÓW WETERYNARYJNYCH "AGA-VET" ul. Turkowska 58c 62-720 Brudzew Tel: **+48 (63) 279 70 04** Email: hurtownia@agavet.com.pl

France Laboratoire LCV Z.I. Plessis Beucher 35220 Châteaubourg Tél : +33 (0)2 99 00 92 92	**Portugal** Belphar LDA Sintra Business Park No 7, Edifício 1- Escritório 2K Zona Industrial de Abrunheira 2710-089 Sintra Tel: +35 (0)13088 08321
Hrvatska ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**România** SC MARAVET SA Baia Mare Maravet, Street No 1 Tel: +40 262 211 964 Email: office@maravet.com
Ireland ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Slovenija** ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com
Ísland ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Slovenská republika** Sevaron s.r.o. Palackého třída 163a 612 00 Brno Česká Republika Tel: +42 (0) 54 1426 370 Email: info@sevaron.cz
Italia Ecuphar Italia S.R.L. Viale Francesco Restelli, 3/7, piano 1 20124 Milano Tel: +39 (0)02829 50604	**Suomi/Finland** Vetcare Oy PL 99 24101 Salo Tel: +358 (0)20 144 3360 Email: vetcare@vetcare.fi
Κύπρος Panchris Feeds (Veterinary) Ltd Industrial Area Aradippou, 7100, Larnaca, POB 40261, 6302, Larnaca, Τηλ: + 357 24813333	**Sverige** Salfarm Scandinavia AB Florettgatan 29C, 2. Vån 25 467 Helsingborg Phone: 0046 767 834 910 Email: Scan@salfarm.com

Latvija Magnum Veterinārija SIA Ulbrokas iela 23, Rīga, LV-1021, Tel: +371 671 60091	**United Kingdom (Northern Ireland)** ECO Animal Health Limited The Grange, 100 The High Street London N14 6BN Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

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

2. Composition

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

White granules.

3. Target species

Chickens and turkeys

4. Indications for use

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.

5. Contraindications

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

6. Special warnings

Special warnings:

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

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.

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.

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.

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.

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.

Laying birds:

The product can be used in chickens laying eggs for human consumption and breeding birds producing eggs for hatching broiler stock or replacement layers.
The safety of the veterinary medicinal product has not been established during lay in turkeys.

Overdose:

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.

Major incompatibilities:

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

7. Adverse events

None known.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system:
HPRA Pharmacovigilance
Website: www.hpra.ie
or
Website: https://www.gov.uk/report-veterinary-medicine-problem/animal-reacts-medicine
e-mail: adverse.events@vmd.gov.uk

8. Dosage for each species, routes and method of administration

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 for a total of 1,000 kg of chickens (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 chickens (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 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 tylvalosin-sensitive strains of *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 for 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.

9. Advice on correct administration

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 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.

10. 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.

11. Special storage precautions

Keep out of the sight and reach of children.
Do not store above 25 ºC

Do not use this veterinary medicinal product after the expiry date which is stated on the label after "Exp".
Shelf life after first opening the immediate packaging: 5 weeks.
Shelf life of the medicated drinking water: 24 hours

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription

14. Marketing authorisation numbers and pack sizes

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

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

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

16. Contact details

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

Manufacturer responsible for batch release:
Acme Drugs s.r.l.
Via Portella della Ginestra 9/a
42025 CAVRIAGO (RE)
ITALY
Or
Provet A.E.
Nikiforou Foka & Agíon Anargyron Thesi Vrago
Aspropyrgos
193 00
Greece

Local representatives and contact details to report suspected adverse reactions:
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

België/Belgique/Belgien Vaccifar BVBA Sint Damiaanstraat 18 B-2160 Wommelgem BELGIUM Tel : +32 3 355 29 50 Email : info@vaccifar.com	**Lietuva** Magnum Veterinarija, UAB Martinavos g. 8, Martinavos k., LT-54463 Kauno r., Lietuva Tel.: +370 688 96944 Email: info@magnumvet.lt
Република България ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND телефон: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Luxembourg/Luxemburg** Vaccifar BVBA Sint Damiaanstraat 18 B-2160 Wommelgem BELGIUM Tel : +32 3 355 29 50 Email : info@vaccifar.com
Česká republika Sevaron s.r.o. Palackého třída 163a 612 00 Brno Tel: +42 (0) 54 1426 370 Email: info@sevaron.cz	**Magyarország** Dunavet-B ZRt, 7020 Dunaföldvár, Ady E. u. 5. Tel: +36 75 542 940 Email: dunavet-bp@dunavet.hu
Danmark Salfarm Danmark A/S, Nordager 19, 6000 Kolding Tel: +45 75 52 94 13 E-mail: sal@salfarm.dk	**Malta** ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com
Deutschland Gallicare GbR Leopoldstraße 116, D-06366 Köthen, Deutschland	**Nederland** Vaccifar BVBA Sint Damiaanstraat 18 B-2160 Wommelgem BELGIUM Tel : +32 3 355 29 50 Email : info@vaccifar.com
Eesti AS Magnum Veterinaaria Vae 16, Laagri, Harju mk Tel: +372 6 501 920	**Norge** Salfarm Scandinavia AB Florettgatan 29C, 2. Vån 25 467 Helsingborg Sweden Phone: 0046 767 834 910 Email: Scan@salfarm.com
Ελλάδα DG Nucleus ΕΠΕ Ν.Χαρίτου 11 43100 Καρδιτσα Τηλ:+302441073034 Email: info@vkk.gr	**Österreich** Gallicare GbR Leopoldstraße 116, D-06366 Köthen, Deutschland

España Ecuphar Veterinaria S.L.U. C/Cerdanya, 10-12 Planta 6º, 08173 Sant Cugat del Vallés, Barcelona (España). Tel: +34 (0)935 955 000	**Polska** Calier Polska Sp. z o.o. ul. Magazynowa 5, 66-446 Deszczno Tel: +48 95 7214521 E-mail: calierpolska@calier.com.pl HURTOWNIA LEKÓW WETERYNARYJNYCH "AGA-VET" ul. Turkowska 58c 62-720 Brudzew Tel: **+48 (63) 279 70 04** Email: hurtownia@agavet.com.pl
France Laboratoire LCV Z.I. Plessis Beucher 35220 Châteaubourg Tél : +33 (0)2 99 00 92 92	**Portugal** Belphar LDA Sintra Business Park No 7, Edifício 1- Escritório 2K Zona Industrial de Abrunheira 2710-089 Sintra Tel: +35 (0)13088 08321
Hrvatska ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**România** SC MARAVET SA Baia Mare Maravet, Street No 1 Tel: +40 262 211 964 Email: office@maravet.com
Ireland ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Slovenija** ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com
Ísland ECO Animal Health Europe Limited 6th Floor, South Bank House Barrow Street Dublin 4 D04 TR29 IRELAND Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com	**Slovenská republika** Sevaron s.r.o. Palackého třída 163a 612 00 Brno Česká Republika Tel: +42 (0) 54 1426 370 Email: info@sevaron.cz

Italia Ecuphar Italia S.R.L. Viale Francesco Restelli, 3/7, piano 1 20124 Milano Tel: +39 (0)02829 50604	**Suomi/Finland** Vetcare Oy PL 99 24101 Salo Tel: +358 (0)20 144 3360 Email: vetcare@vetcare.fi
Κύπρος Panchris Feeds (Veterinary) Ltd Industrial Area Aradippou, 7100, Larnaca, POB 40261, 6302, Larnaca, Τηλ: + 357 24813333	**Sverige** Salfarm Scandinavia AB Florettgatan 29C, 2. Vån 25 467 Helsingborg Phone: 0046 767 834 910 Email: Scan@salfarm.com
Latvija Magnum Veterinārija SIA Ulbrokas iela 23, Rīga, LV-1021, Tel: +371 671 60091	**United Kingdom (Northern Ireland)** ECO Animal Health Limited The Grange, 100 The High Street London N14 6BN Tel: +44 (0) 20 8447 8899 Email: sales@ecoanimalhealth.com