SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Methoxasol 20/100 mg/ml solution for use in drinking water for pigs and chickens

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:
Trimethoprim 20.0 mg
Sulfamethoxazole 100.0 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
N-methyl pyrrolidone	690.8 mg
Propylene glycol	
Sodium hydroxide (for pH adjustment)	
Water, purified	

Solution for use in drinking water.
A clear yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Pigs and chickens (broilers).

3.2 Indications for use for each target species

Pigs: Treatment and metaphylaxis of respiratory infections caused by *Actinobacillus pleuropneumoniae* susceptible to trimethoprim and sulfamethoxazole where the disease has been diagnosed in the herd.

Broilers: Treatment and metaphylaxis of respiratory infections caused by *Escherichia coli* susceptible to trimethoprim and sulfamethoxazole where the disease has been diagnosed in the flock.

3.3 Contraindications

Do not use in animals suffering from severe liver or kidney disease, oliguria or anuria.
Do not use in animals with impaired haematopoietic systems.
Do not use in cases of hypersensitivity to sulfonamides or trimethoprim or to any of the excipients.

3.4 Special warnings

Severely diseased animals can have a decreased appetite and water consumption. If necessary the concentration of the veterinary medicinal product in the drinking water may need to be adjusted to make sure that the recommended dosage is being consumed. However if the concentration of the veterinary medicinal product is increased too much, the intake of the medicated drinking water decreases for palatability reasons. Therefore water intake should be monitored regularly, especially in broilers.
In case of insufficient intake of water, pigs should be treated parenterally.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Due to the likely variability (time, geographical) in susceptibility of bacteria for potentiated sulphonamides, occurrence of resistance of bacteria may differ from country to country and even from farm to farm, and therefore bacteriological sampling and susceptibility testing are recommended. Use of the veterinary medicinal product should be based on culture and sensitivity of micro-organisms from diseased cases on farm or from recent previous experience on the farm. Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to sulfamethoxazole and trimethoprim and may also decrease the effectiveness of combinations of trimethoprim with other sulphonamides due to the potential for cross resistance. Official and local antimicrobial policies should be taken into account when the veterinary medicinal product is used.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This veterinary medicinal product contains sulfamethoxazole, which can cause allergic reactions in some people.
People with known hypersensitivity (allergy) to sulphonamides or trimethoprim should avoid contact with the veterinary medicinal product.

During preparation and administration of the medicated drinking water, skin contact with the drug should be avoided. Personal protective equipment consisting of impermeable gloves e.g. rubber or latex should be worn when handling the veterinary medicinal product. Do not handle this veterinary medicinal product if you know you are allergic to trimethoprim or sulphonamides.
Do not smoke, drink or eat when handling the veterinary medicinal product.
If you develop symptoms following exposure to the veterinary medicinal product such as skin rash, you should seek medical advice and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

This veterinary medicinal product can cause eye-irritation.
Personal protective equipment consisting of safety glasses should be worn when mixing the veterinary medicinal product with drinking water. In the event of eye contact, rinse the eye with copious amounts of clean water and if irritation occurs, seek medical advice.

In the event of accidental ingestion, seek medical advice. Wash hands and contaminated skin immediately after handling the veterinary medicinal product.

Laboratory studies in rabbits and rats conducted with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects. The veterinary medicinal product should not be administered by pregnant women and women suspected of being pregnant. Personal

protective equipment consisting of gloves should be worn when handling the veterinary medicinal product by women of childbearing age.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Pigs:

Rare (1 to 10 animals / 10,000 animals treated):	Hypersensitivity reaction.

Chickens:

Rare (1 to 10 animals / 10,000 animals treated):	Hypersensitivity reaction, decreased drinking

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

The safety of the veterinary medicinal product has not been established in pigs and chickens during pregnancy, lactation, lay or in animals intended for breeding.
Laboratory studies in rats conducted with trimethoprim have shown evidence of teratogenicity at higher doses than recommended therapeutic ones.
Laboratory studies in rabbits and rats conducted with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects.
The use of the veterinary medicinal product is not recommended during pregnancy and lactation.

3.8 Interaction with other medicinal products and other forms of interaction

Do not combine with other veterinary medicinal products.

3.9 Administration routes and dosage

Route of administration: in drinking water use.

The veterinary medicinal product can be added directly to the drinking water to prepare a therapeutic solution at the calculated concentration, but can also be used in a concentrated stock solution by adding 200 ml of the veterinary medicinal product per litre of water and diluting this further if required. Do not use this veterinary medicinal product undiluted or in higher concentrated stock solutions.

Pigs: 25 mg TMPS per kg bodyweight per day for 3-4 days, corresponding to 1 ml of the veterinary medicinal product per 4,8 kg bodyweight per day. This corresponds to approximately 1 litre of the veterinary medicinal product in 500 L drinking water.
Based on the recommended dose, daily water consumption, and the number and weight of the pigs to be treated, the exact daily concentration of the veterinary medicinal product should be calculated according to the following formula:

$$\frac{\text{Mean body weight (kg) of pigs to be treated}}{\text{Mean daily water consumption (l) per pig} \times 4.8} = \text{xx ml veterinary medicinal product per l drinking water}$$

Broilers: 33 mg TMPS per kg bodyweight per day for 3-4 days, corresponding to 1 ml of the veterinary medicinal product per 3,64 kg bodyweight per day. This corresponds to approximately 1 litre of the veterinary medicinal product in 750 L drinking water.
Based on the recommended dose, daily water consumption, and the number and weight of the birds to be treated, the exact daily concentration of the veterinary medicinal product should be calculated according to the following formula:

$$\frac{\text{Mean body weight (kg) of broilers to be treated}}{\text{Mean daily water consumption (l) per bird} \times 3.64} = \text{xx ml veterinary medicinal product per l drinking water}$$

One litre of the veterinary medicinal product weighs 1079 gram; therefore weight can also be used to measure the veterinary medicinal product quantity to be added in drinking water, according to the following formula:

Amount to be added in drinking water (g/L) = calculated ml/L x 1.079.

The daily amount is to be added to the drinking water such that all medication will be consumed in 24 hours. Medicated drinking water and stock solutions should be freshly prepared every 24 hours. During the treatment period animals should not have access to other water sources than the medicated water the dilution of which should be calculated to ensure that animals always have sufficient water available. To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing. The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of the veterinary medicinal product may need to be adjusted accordingly.

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

In pigs, a 2 ½ fold overdose induces no adverse reactions.
In chicken an acute overdose will not occur because the birds will be reluctant to drink the strongly concentrated drinking water (too bitter taste if above 2 litres of the veterinary medicinal product per 1000 litre drinking water). Chronic overdose in chicken will result in a strongly diminished water- and feed intake and retarded growth.

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:
Pigs: 5 days
Broilers: 6 days
Eggs:
Not for use in birds producing or intended to produce eggs for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01EW11

4.2 Pharmacodynamics

In vitro trimethoprim is generally bacteriostatic and has a broad spectrum of activity against both gram-positive and gram-negative bacteria. A synergistic and bactericidal effect occurs when trimethoprim is combined with sulfamethoxazole, because trimethoprim and sulfamethoxazole inhibit sequential steps in the synthesis of tetrahydrofolic acid, an essential metabolic cofactor in bacterial synthesis of purine and, subsequently, DNA.

4.3 Pharmacokinetics

Following oral administration both active ingredients are rapidly absorbed from the gut. The C_{max} of sulfamethoxazole in pigs is approximately 6.2 µg/g. The C_{max} of trimethoprim is 0.29 µg/g. The C_{max} of sulfamethoxazole in chickens is approximately 9.0 µg/g, whereas that of trimethoprim is 0.12 µg/g.
High trimethoprim concentrations are found in the kidneys, the liver and the lungs. With the exception of the kidneys, sulfamethoxazole concentrations in the tissues are significantly lower than in the plasma. Protein binding for trimethoprim and sulfamethoxazole is not very high.
The drugs are primarily excreted through the kidneys (both actively and passively), but elimination also occurs through the faeces. Elimination is relatively fast both in poultry and pigs. Plasma elimination half-life for trimethoprim in poultry is less than 1 hour and that of sulfamethoxazole, approximately 1.5 hours. In pigs, elimination half-life for both substances is approximately 2.5 hours. Within 48 hours after the last medication trimethoprim, sulfamethoxazole and their metabolites are undetectable in urine and faeces.

Environmental properties
Trimethoprim is persistent in soils.

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: 1 year.
Shelf life after dilution or reconstitution according to directions: 24 hours.

5.3 Special precautions for storage

Do not freeze.

5.4 Nature and composition of immediate packaging

1000 ml HDPE bottle closed with a tamper-proof HDPE screw-cap.
5000 ml HDPE can closed with a tamper-proof HDPE screw-cap
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

Eurovet Animal Health B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

7. MARKETING AUTHORISATION NUMBER

Vm 16849/3007

8. DATE OF FIRST AUTHORISATION

04 September 2012

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

December 2023

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).

Approved 15 December 2023