[Version 9,03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Methoxasol-T 20/100 mg/ml solution for use in drinking water for pigs and broilers

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
Sodium hydroxide (for pH adjustment)	
Propylene glycol	
Water, purified	

Solution for use in drinking water.
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 sulphonamides or trimethoprim or 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 should 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, especially in broilers.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Due to the likely variability (time, geographical) in the occurrence of resistance of bacteria for trimethoprim/sulfamethoxazole bacteriological sampling and susceptibility testing are recommended. Resistance against potentiated sulphonamides may vary. Therefore the 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

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
During preparation and administration of the medicated drinking water, skin contact with the drug should be avoided. Therefore it is recommended to wear impermeable gloves e.g. rubber or latex when applying the veterinary medicinal product. In case of allergy to trimethoprim or sulfonamides, special care should be taken when handling this veterinary medicinal product or the medicated solution. In the event of eye contact, rinse the eye with copious amounts of clean water and if irritation occurs, seek medical attention. 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 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 the 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.

Pigs: 25 mg TMPS/kg bodyweight, corresponding to approximately 1 litre of the veterinary medicinal product in 500 L drinking water, for 3-4 days.
Broilers: 33 mg TMPS/kg bodyweight, corresponding to approximately 1 litre of the veterinary medicinal product in 750 L drinking water, for 3-4 days.

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)

A 2 ½ fold overdose is well tolerated by pigs.
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

Pigs: 5 days
Broilers: 6 days
Not authorised for use in laying birds producing 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 TMP and SMX is not very high.
The drug is 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

Solubility and stability of the veterinary medicinal product in drinking water are pH-dependent.
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 is closed with a tamper-proof HDPE screw-cap.
5000 ml HDPE can is 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.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}.

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

{DD/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 III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE - COMBINED LABEL AND PACKAGE LEAFLET

{White HDPE bottle / can: 1L or 5L}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Methoxasol-T 20/100 mg/ml solution for use in drinking water for pigs and broilers.

2. COMPOSITION

Each ml contains**:**

Active substances:
Trimethoprim 20.0 mg
Sulfamethoxazole 100.0 mg

Excipients:
N-methyl-pyrrolidone 690,8 mg
Clear yellow solution.

3. PACKAGE SIZE

1 litre, 5 litres
Not all pack sizes may be marketed.

4. TARGET SPECIES

Pigs and chickens (broilers).

5. INDICATIONS FOR USE

Indications for use
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.

6. CONTRAINDICATIONS

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 sulphonamides or trimethoprim or any of the excipients.

7. SPECIAL WARNINGS

Special warnings

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, especially in broilers.

Special precautions for safe use in the target species:
Due to the likely variability (time, geographical) in the occurrence of resistance of bacteria for trimethoprim / sulfamethoxazole bacteriological sampling and susceptibility testing are recommended. Resistance against potentiated sulphonamides may vary. Therefore the 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.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
During preparation and administration of the medicated drinking water, skin contact with the drug should be avoided. Therefore it is recommended to wear impermeable gloves e.g. rubber or latex when applying the product. In case of allergy to trimethoprim or sulfonamides, special care should be taken when handling this veterinary medicinal product or the medicated solution. In the event of eye contact, rinse the eye with copious amounts of clean water and if irritation occurs, seek medical attention. 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.

Pregnancy and 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 the 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.

Interaction with other medicinal products and other forms of interaction:
Do not combine with other veterinary medicinal products.

Overdose:
A 2 ½ fold overdose is well tolerated by pigs.
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.

Special restrictions for use and special conditions for use:
Not applicable.

Major incompatibilities:
Solubility and stability of the veterinary medicinal product in drinking water are pH-dependent.
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

8. ADVERSE EVENTS

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 product. If you notice any side effects, even those not already listed on this label, 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 marketing authorisation holder or its local representative using the contact details on this label, or via your national reporting system {national system details}.

9. DOSAGE FOR EACH TARGET SPECIES, ROUTES AND METHOD OF ADMINISTRATION

Dosage for each species, routes and method of administration
Route of administration: in drinking water use.
Pigs: 25 mg TMPS/kg bodyweight, corresponding to approximately 1 litre of the veterinary medicinal product in 500 L drinking water, for 3-4 days.
Broilers: 33 mg TMPS/kg bodyweight, corresponding to approximately 1 litre of the veterinary medicinal product in 750 L drinking water, for 3-4 days.

10. ADVICE ON CORRECT ADMINISTRATION

Advice on correct administration
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.

11. WITHDRAWAL PERIODS

Withdrawal periods
Pigs: 5 days
Broilers: 6 days
Not authorised for use in laying birds producing eggs for human consumption

12. SPECIAL STORAGE PRECAUTIONS

Special storage precautions

Keep out of the sight and reach of children.

Do not freeze.
Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp
The expiry date refers to the last day of that month.

13. SPECIAL PRECAUTIONS FOR DISPOSAL

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.

14. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Classification of veterinary medicinal products
Veterinary medicinal product subject to prescription.

15. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

Pack sizes
1000 ml HDPE bottle is closed with a tamper proof HDPE screw cap.
5000 ml HDPE can is closed with a tamper proof HDPE screw cap.
Not all pack sizes may be marketed.

16. DATE ON WHICH THE LABEL WAS LAST REVISED

Date on which the label was last revised
{DD/MM/YYYY}

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

17. CONTACT DETAILS

Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
Eurovet Animal Health B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands
Tel: +31 348 563434

Manufacturer responsible for batch release:
Genera Inc.
Svetonedeljska cesta 2
Kalinovica
10436 Rakov Potok
Croatia

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 listed below.

18. OTHER INFORMATION

Other information

Environmental properties:
Trimethoprim is persistent in soils

19. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

20. EXPIRY DATE

Exp {mm/yyyy}

Once opened use by: __/__/__.
Shelf life after first opening the immediate packaging: 1 year.
Shelf life after dilution or reconstitution according to directions: 24 hours.

21. BATCH NUMBER

Lot {number}