ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

{OUTSIDE OF THE TEAR OPEN LEAFLET / 1L BOTTLE or 5L CONTAINER}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Metaxol 20/100 mg/ml solution for use in drinking water.

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:
Active substances:
Trimethoprim 20 mg
Sulfamethoxazole 100 mg

3. PACKAGE SIZE

1 litre, 5 litres

4. TARGET SPECIES

Pigs (fattening pigs) and chickens (broilers).

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

In drinking water use.

7. WITHDRAWAL PERIODS

Withdrawal periods:
Pigs: Meat and offal: 8 days.
Chickens: Meat and offal: 5 days.
Not for use in birds producing or intended to produce eggs for human consumption.

8. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 1 year. Use by __/__/__.
Shelf life after dilution or reconstitution according to directions: 24 hours.

9. SPECIAL STORAGE PRECAUTIONS

Do not freeze.

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

Eurovet Animal Health B.V.

14. MARKETING AUTHORISATION NUMBERS

Vm 16849/3008

15. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET
INSIDE of the TEAR OPEN LEAFLET (1L bottle or 5L container)

1. Name of the veterinary medicinal product

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

2. Composition

Each ml contains:
Active substances:
Trimethoprim 20 mg
Sulfamethoxazole 100 mg

Excipients:
N-methyl pyrrolidone 690,8 mg

Clear, pale yellow to brownish-yellow solution.

3. Target species

Pigs (fattening pigs) and chickens (broilers).

4. Indications for use

Fattening pigs:
Treatment and metaphylaxis of:
- Post-weaning diarrhoea caused by beta-haemolytic K88-positive, K99-positive or 987P *Escherichia coli* strains susceptible to trimethoprim-sulfamethoxazole.
- Secondary bacterial infections caused by *Pasteurella multocida*, *Actinobacillus pleuropneumoniae*, Streptococcus spp. and *Haemophilus parasuis* susceptible to trimethoprim-sulfamethoxazole.

Broilers:
Treatment and metaphylaxis of
- Colibacillosis caused by *Escherichia coli* susceptible to trimethoprim-sulfamethoxazole.
- Coryza caused by *Avibacterium paragallinarum* susceptible to trimethoprim-sulfamethoxazole.

The presence of the disease in the group/flock must be established before the veterinary medicinal product is used.

5. 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.

6. 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 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 regularly, especially in broilers.
In case of insufficient intake of water, pigs should be treated parenterally.

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 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:
Sulphonamides may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to sulphonamides may lead to cross reactions with other antibiotics. Allergic reactions to these substances may occasionally be serious. Do not handle this veterinary medicinal product if you know you are sensitive to sulphonamides.
If you develop symptoms following exposure, such as a skin rash, you should seek medical advice and show the physician this warning.
This veterinary medicinal product may cause skin- and respiratory irritation as well as eye damage.
Personal protective equipment consisting of impermeable gloves, e.g. rubber or latex and protective glasses, should be worn when handling the veterinary medicinal product including when mixing the veterinary medicinal product with drinking water. Avoid inhalation. In the event of eye contact, rinse the eye with large amounts of clean water and, if irritation occurs, seek medical attention. In the event of accidental ingestion, seek medical advice and show the package leaflet or the label to the physician. 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..

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 rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects. Use only according to the benefit-risk assessment by the responsible veterinarian.

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

Overdose:
In chickens an acute overdose will likely 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 litres drinking water). Chronic overdose in chickens will result in a strongly diminished water- and feed intake and retarded growth.

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

7. 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 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 marketing authorisation holder or its local representative using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

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

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.

Fattening pigs:
5 mg trimethoprim and 25 mg sulfamethoxazole per kg body weight a day, for 4-7 days. This corresponds to 1 ml of the veterinary medicinal product per 4.0 kg body weight per day. 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 required should be calculated according to the following formula:

$$\frac{\text{Mean body weight (kg) of pigs to be treate}}{\text{Mean daily water consumption (litre) per pi} \times 4.0} = \text{xx ml veterinary medicinal product per litre drinking water}$$

Broilers:
7.5 mg trimethoprim and 37.5 mg sulfamethoxazole per kg body weight a day, for 3 days. This corresponds to 1 ml of the veterinary medicinal product per 2.67 kg body weight per day. 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:

$$\frac{\text{Mean body weight (kg) of birds to be treated}}{\text{Mean daily water consumption (litre) per bird} \times 2.67} = \text{xx ml veterinary medicinal product per litre drinking water}$$

9. Advice on correct administration

To ensure a correct dosage, the body weight and water consumption should be determined as accurately as possible.
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 water sources other than the medicated water. However, it should be ensured that animals always have sufficient water available. After the end of the medication period, the water supply system should be cleaned appropriately to avoid intake of sub-therapeutic amounts of active substance. 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.

10. Withdrawal periods

Pigs: Meat and offal: 8 days.
Chickens: Meat and offal: 5 days.
Not for use in birds producing or intended to produce eggs for human consumption.

11. 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.

Shelf life after first opening the immediate packaging: 1 year.
Shelf life after dilution or reconstitution according to directions: 24 hours.

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

Pack sizes:
HDPE bottle of 1 litre, closed with a tamper proof HDPE screw cap.
HDPE container of 5 litres, closed with tamper proof HDPE screw cap.

Not all pack sizes may be marketed.

15. PID LINK (Do not print heading)

[The following statement must be included where reference to the European Union Product Database is included on the product information. This statement is relevant to both UK(GB) and UK(NI) products:]

Find more product information by searching for the 'Product Information Database' on www.gov.uk.

16. 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

BE: Dechra Regulatory 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.

17. Other information

Environmental properties:
Trimethoprim is persistent in soils.

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

{1L bottle or 5L container}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. COMPOSITION

Each ml contains:
Active substances:
Trimethoprim 20 mg
Sulfamethoxazole 100 mg

Excipients:
N-methyl pyrrolidone 690,8 mg

Clear, pale yellow to brownish-yellow solution.

3. PACKAGE SIZE

1 litre, 5 litres

4. TARGET SPECIES

Pigs (fattening pigs) and chickens (broilers).

5. INDICATIONS FOR USE

Indications for use

Fattening pigs:
Treatment and metaphylaxis of
- Post-weaning diarrhoea caused by beta-haemolytic K88-positive, K99-positive or 987P *Escherichia coli* strains susceptible to trimethoprim-sulfamethoxazole.
- Secondary bacterial infections caused by *Pasteurella multocida, Actinobacillus pleuropneumoniae, Streptococcus* spp. and *Haemophilus parasuis* susceptible to trimethoprim-sulfamethoxazole.

Broilers:
Treatment and metaphylaxis of
- Colibacillosis caused by *Escherichia coli* susceptible to trimethoprim-sulfamethoxazole.
- Coryza caused by *Avibacterium paragallinarum* susceptible to trimethoprim-sulfamethoxazole.

The presence of the disease in the group/flock must be established before the veterinary medicinal product is used.

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 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 regularly, especially in broilers.
In case of insufficient intake of water, pigs should be treated parenterally.

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 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:
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Do not handle this veterinary medicinal product if you know you are sensitive to sulphonamides.
If you develop symptoms following exposure, such as a skin rash, you should seek medical advice and show the physician this warning.
This veterinary medicinal product may cause skin- and respiratory irritation as well as eye damage.
Personal protective equipment consisting of impermeable gloves, e.g. rubber or latex and protective glasses, should be worn when handling the veterinary medicinal product including when mixing the veterinary medicinal product with drinking water. Avoid

inhalation. In the event of eye contact, rinse the eye with large amounts of clean water and, if irritation occurs, seek medical attention. In the event of accidental ingestion, seek medical advice and show the package leaflet or the label to the physician. 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.

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 rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects. Use only according to the benefit-risk assessment by the responsible veterinarian.

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

Overdose:
In chickens an acute overdose will likely 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 litres drinking water). Chronic overdose in chickens will result in a strongly diminished water- and feed intake and retarded growth.

Major incompatibilities:
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.
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.

Fattening pigs:
5 mg trimethoprim and 25 mg sulfamethoxazole per kg body weight a day, for 4-7 days. This corresponds to 1 ml of the veterinary medicinal product per 4.0 kg body weight per day. 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:

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Broilers:
7.5 mg trimethoprim and 37.5 mg sulfamethoxazole per kg body weight a day, for 3 days. This corresponds to 1 ml of the veterinary medicinal product per 2.67 kg body weight per day. 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:

$$\frac{\text{Mean body weight (kg) of birds to be treated}}{\text{Mean daily water consumption (litre) per bird} \times 2.67} = \text{xx ml veterinary medicinal product per litre drinking water}$$

10. ADVICE ON CORRECT ADMINISTRATION

Advice on correct administration

To ensure a correct dosage, the body weight and water consumption should be determined as accurately as possible.
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 water sources other than the medicated water. However, it should be ensured that animals always have sufficient water available. After the end of the medication period, the water supply system should be cleaned appropriately to avoid intake of sub-therapeutic amounts

of active substance. 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: Meat and offal: 8 days.
Chickens: Meat and offal: 5 days.
Not for use in birds producing or intending to produce 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
Pack sizes: 1 litre and 5 litres.
HDPE bottle of 1 litre, closed with a tamper proof HDPE screw cap.
HDPE container of 5 litres, closed with 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

12 October 2023

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

BE: Dechra Regulatory 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}

Approved 14 May 2024