1. NAME OF THE VETERINARY MEDICINAL PRODUCT

TRIMETAZOLE VETERINARY

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substances:
Sulphamethoxazole 10.0% w/v
Trimethoprim 2.0% w/v

Excipients:
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for use in drinking water.

4. CLINICAL PARTICULARS

4.1 Target species

chickens (broilers).

4.2 Indications for use, specifying the target species

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

4.3 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 any of the excipients.

4.4 Special warnings for each target species

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, in broilers.

4.5 Special precautions for use

Special precautions for use in animals

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 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.

4.6 Adverse reactions (frequency and seriousness)

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il/

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established in chickens (broilers) during 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 foetoxic effects. The use of the veterinary medicinal product is not recommended during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

Do not combine with other veterinary medicinal products.

4.9 Amounts to be administered and administration route

Route of administration: in drinking water use.

The 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 water and diluting this further if required. Do not use this veterinary medicinal product undiluted or in higher concentrated stock solutions.

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 amount of the veterinary product can be calculated according to the following formula:

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

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 uptake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of the veterinary medicinal products has to be adjusted accordingly.

4.10 Symptoms of overdose (and where applicable, emergency procedures andantidotes)

In chicken (Broilers) 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.

4.11 Withdrawal period(s)

Meat and offal:
Broilers: 6 days
Eggs:
Not for use in birds producing or intended to produce eggs for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use - Sulfamethoxazole and trimethoprim.
ATC vet code: QJ01EW11.

5.1 Pharmacodynamic properties

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.

5.2 Pharmacokinetic particulars

Following oral administration both active ingredients are rapidly absorbed from the gut. 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 in poultry. Plasma elimination half-life for trimethoprim in poultry is less than 1 hour and that of sulfamethoxazole, approximately 1.5 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
N-Methylpyrrolidone
Monoethanolamine

6.2 Major incompatibilities

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

6.3 Shelf life
The expiry date of the product is indicated on the packaging materials

6.4 Special precautions for storage
Store below 25ºC

6.5 Nature and composition of immediate packaging

1 Liter HDPE bottle

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.
Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. Manufacturer:
BIOVAC LTD., HAILAN STR. 6, POB 300, NORTH INDUSTRIAL ZONE, OR-AKIVA 30600, ISRAEL

8. Registration NUMBER
081 61 92215

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