SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Diatrim 200 mg/ml + 40 mg/ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution contains:
Active substances:
Sulfadiazine 200 mg
Trimethoprim 40 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, greenish yellow to brownish yellow solution, practically free from particles.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle, pigs, dogs and cats.

4.2 Indications for use, specifying the target species

Treatment of infections caused by, or associated with, organisms sensitive to the trimethoprim-sulfadiazine combination.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substances or to any of the excipients.
Do not use in animals with severe liver or renal damage or blood dyscrasias.
Do not use in case of reduced water intake or losses of body fluid.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals
Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the product and may decrease the effectiveness of treatment with other antimicrobials or classes of antimicrobials due to the potential for cross-resistance.
Official, national and regional antimicrobial policies should be taken into account when the product is used.

For intravenous administration the product should be warmed to body temperature and injected slowly over as long a period as is reasonably practical. At the first sign of intolerance the injection should be interrupted and shock treatment initiated. Intravenous administration should be used with extreme caution and only if therapeutically justified.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

- The product may cause an allergic reaction in people sensitised to sulfonamides.
- People with known hypersensitivity to sulfonamides should avoid contact with the veterinary medicinal product.
- The excipient N-methylpyrrolidone (NMP) is a suspected human teratogen; therefore, women of child-bearing age must be very careful to avoid exposure via spillage onto the skin or accidental self-injection when administering the product. If you are pregnant, think you may be pregnant or are attempting to conceive, you should not administer the product.
- If you develop symptoms following exposure such as a skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.
- This product may cause skin and eye irritation.
- Avoid contact with skin or eyes.
- In case of skin or eye contact, wash exposed area with plenty of clean water. If symptoms persist, seek medical advice.
- In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
- Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Anaphylactic shock (potentially fatal) has been observed on rare occasions (more than 1 but less than 10 animals in 10,000 animals treated) following administration of potentiated sulphonamide preparations, mostly after intravenous injection. For intravenous administration, the product should be warmed to body temperature and injected slowly over as long a period as is reasonably practical. At the first sign of intolerance the injection should be interrupted and shock treatment initiated.

4.7 Use during pregnancy, lactation or lay

Can be safely administered to lactating animals. The product contains N-methylpyrrolidone, which is considered to be a reproductive toxicant. As the relevant studies have not been performed, use in pregnant cattle, pigs, dogs, and cats should be avoided.

4.8 Interaction with other medicinal products and other forms of interaction

Local anaesthetics from the group of para-aminobenzoic acid esters (procaine, tetracaine) can locally inhibit the effect of sulfonamides.Do not combine with other veterinary medicinal products.

4.9 Amounts to be administered and administration route

For intramuscular, intravenous or subcutaneous use.
To ensure a correct dosage, the body weight of animals to be treated should be determined as accurately as possible.

Cattle and pigs:
The recommended dose rate is 2.5 mg trimethoprim / 12.5 mg sulfadiazine per kilogram body weight (1 ml product per 16 kg body weight) by intramuscular or slow intravenous injection, once daily until 2 days after symptoms resolve up to a maximum of 5 days. The maximum intramuscular volume of injection per injection site is 5 ml for pigs and 15 ml in cattle. The veterinary medicinal product may be administered by intravenous injection when blood levels of trimethoprim and sulfadiazine are required more rapidly.

Dogs and cats:
The recommended dose rate is 5 mg trimethoprim / 25 mg sulfadiazine per kilogram body weight (1 ml product per 8 kg body weight), by subcutaneous injection only, once daily until 2 days after symptoms resolve up to a maximum of 5 days The recommended injection site in dogs is the loose skin at the top of the neck.

The closures must not be punctured more than 40 times.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

None known.

4.11 Withdrawal periods

Cattle:
Meat and offal: 12 days
Milk: 48 hours

Pig:
Meat and offal: 20 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Combinations of sulphonamides and trimethoprim
ATCvet-code: QJ01EW10

5.1 Pharmacodynamic properties

Sulfadiazine (SDZ) inhibits the incorporation of para-aminobenzoic acid into folic acid and trimethoprim (TMP) inhibits the enzyme dihydrofolate reductase (DHFR) which converts dihydrofolic acid into tetrahydrofolic acid. TMP and SDZ act together

synergistically with a double-blockade mode of action. The combination is bactericidal, inhibiting sequential steps in the synthesis of purines which are required for DNA synthesis. TMP/SDZ combinations have a broad bactericidal action against many Gram-positive and Gram-negative aerobic bacteria and a large proportion of anaerobic bacteria.
Bacterial resistance to trimethoprim and to sulphonamides can be mediated via 5 main mechanisms: (1) changes in the permeability barrier and/or efflux pumps, (2) naturally insensitive target enzymes, (3) changes in the target enzymes, (4) mutational or recombinational changes in the target enzymes, and (5) acquired resistance by drug-resistant target enzymes.

5.2 Pharmacokinetic particulars

Sulfadiazine, is protein bound only to a limited extent and is well distributed. Metabolism occurs in the liver and the major by-products are acetylated derivatives which are excreted mainly by glomerular filtration. The plasma half-lives in cattle, pigs and dogs are 2, 3 and 4 hours respectively Trimethoprim is a weak base with low water solubility. Trimethoprim is about 65% protein bound but, being lipid soluble, readily penetrates cellular barriers to become widely distributed. It is partly oxidised and conjugated in the liver and the metabolites, plus unchanged trimethoprim are excreted in the urine.

The degree of metabolism varies: 80% in the dog and almost 100% in the cow. The half-life is also variable: 2 hours in the pig and 1 hour in the cow.

Given the wide interspecies variability in the half-life of both active substances, it is not possible to attain pharmacokinetic matching of the two compounds, but there is evidence that synergism occurs over a wide range of dose ratios. The combination of 1:5 trimethoprim:sulfadiazine is well documented for veterinary use.

Environmental properties
Trimethoprim is persistent in soils

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide, (for pH adjustment)
Disodium edetate
Sodium formaldehyde sulfoxylate
N-methylpyrrolidone
Water for injections

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

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

Do not store in a refrigerator after broaching

6.5 Nature and composition of immediate packaging

Vials of uncoloured glass type II filled with 50 ml or 100 ml with a fluoropolymer coated chlorobutyl stopper type I secured with an aluminium cap.
1 vial in a cardboard box.

Not all pack sizes may be marketed.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Eurovet Animal Health BV
Handelsweg 25
5531 AE Bladel
The Netherlands

8. MARKETING AUTHORISATION NUMBER

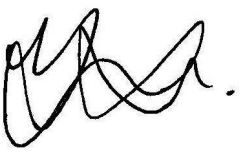
Vm 16849/4059

9. DATE OF FIRST AUTHORISATION

08 February 2018

10. DATE OF REVISION OF THE TEXT

June 2022



Approved: 14 June 2022