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

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Diatrim 200 mg/ml + 40 mg/ml solution for injection for cattle, pigs, dogs and cats.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:
Sulfadiazine 200 mg
Trimethoprim 40 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-Methylpyrrolidone	510 mg/ml
Sodium hydroxide (E524)	
Disodium edetate	
Sodium formaldehyde sulfoxylate dihydrate	
Water for injection	

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

3. CLINICAL INFORMATION

3.1 Target species

Cattle, pigs, dogs and cats.

3.2 Indications for use for each target species

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

3.3 Contraindications

Do not use in cases 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.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Use of the veterinary medicinal 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 veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the veterinary medicinal 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 veterinary medicinal product is used.

For intravenous administration the veterinary medicinal 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 veterinary medicinal 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.

Take care to avoid self-injection. In case of accidental self-injection or if you develop symptoms following exposure, such as a skin rash, you should seek medical advice immediately and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.

Wash hands after use.

This veterinary medicinal product may cause skin and eye irritation. Avoid contact with skin or eyes. In case of accidental contact, rinse the affected area immediately with plenty of water. If symptoms persist, seek medical advice.

Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects. Women of childbearing age, pregnant women or women suspected of being pregnant should use the veterinary medicinal product with serious caution to avoid accidental self-injection.

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

3.6 Adverse events

Cattle, pigs, dogs and cats:

Rare (1 to 10 animals / 10,000 animals treated):	Anaphylactic shock [a,b]

[a] Potentially fatal.
[b] Following administration of potentiated sulphonamide preparations, mostly after intravenous injection. For intravenous administration the veterinary medicinal 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.

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

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established in cattle, pigs, dogs and cats during pregnancy, lactation 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.

3.8 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.

3.9 Administration routes and dosage

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 veterinary medicinal 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 veterinary medicinal 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.

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

None known.

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

Cattle:

Meat and offal:	12 days
Milk:	48 hours

Pigs:

Meat and offal:	20 days

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01EW10

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

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 dogs and almost 100% in cows. The half-life is also variable: 2 hours in pigs and 1 hour in cows.

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.

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: 28 days.

5.3 Special precautions for storage

Do not store in a refrigerator after broaching.

5.4 Nature and composition of immediate packaging

Vials of colourless glass type II filled with 50 ml,100 ml or 250 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.

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

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 OUTER PACKAGE

50 ML, 100 ML or 250 ML / CARDBOARD BOX

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

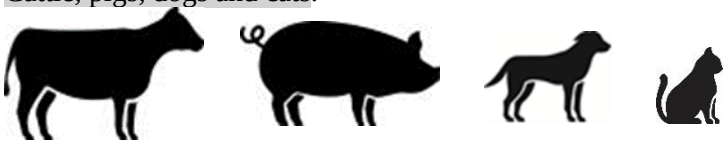
Sulfadiazine	200 mg
Trimethoprim	40 mg

3. PACKAGE SIZE

50 ml, 100 ml, 250 ml

4. TARGET SPECIES

Cattle, pigs, dogs and cats.



5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous (dogs, cats), intramuscular or slow intravenous use (cattle, pigs).

7. WITHDRAWAL PERIODS

Withdrawal periods:

Cattle:

Meat and offal:	12 days
Milk:	48 hours

Pigs:

Meat and offal: 20 days

8. EXPIRY DATE

Exp: {mm/yyyy}

Shelf life after first opening the immediate packaging: 28 days.

Once broached, use by: _____/_____/_____

9. SPECIAL STORAGE PRECAUTIONS

Do not store in a refrigerator after broaching.

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

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

50 ML, 100 ML or 250 ML / GLASS VIAL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

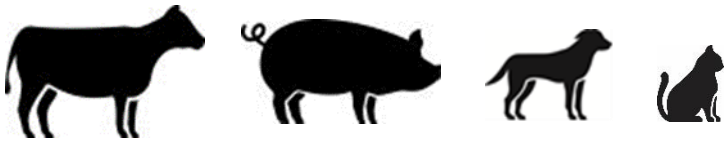
2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

Sulfadiazine	200 mg
Trimethoprim	40 mg

3. TARGET SPECIES

Cattle, pigs, dogs and cats.



4. ROUTES OF ADMINISTRATION

Dogs, cats: s.c.
Cattle, pigs: i.m., i.v. (slow)

5. WITHDRAWAL PERIODS

Withdrawal periods:
Cattle:

Meat and offal:	12 days
Milk:	48 hours

Pigs:
Meat and offal: 20 days

6. EXPIRY DATE

Exp: {mmh/yyyy}
Once broached, use within 28 days. Use by _____/_____/_____

7. SPECIAL STORAGE PRECAUTIONS

Do not store in a refrigerator after broaching.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Diatrim 200 mg/ml + 40 mg/ml, solution for injection for cattle, pigs, dogs and cats.

2. Composition

Each ml contains:

Active substances:

Sulfadiazine	200 mg
Trimethoprim	40 mg

Excipient:

N-methyl pyrrolidone	510 mg

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

3. Target species

Cattle, pigs, dogs and cats.

4. Indications for use

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

5. Contraindications

Do not use in cases 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.

6. Special warnings

Special precautions for safe use in the target species:
Use of the veterinary medicinal 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 veterinary medicinal product deviating from the instructions given in the product leaflet may increase the prevalence of bacteria resistant to the veterinary medicinal 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 veterinary medicinal product is used.

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

Take care to avoid self-injection. In case of accidental self-injection or I-if you develop symptoms following exposure, such as a skin rash, you should seek medical advice immediately and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.

Wash hands after use.

This veterinary medicinal product may cause skin and eye irritation. Avoid contact with skin or eyes. In case of accidental contact, rinse the affected area immediately with plenty of water. If symptoms persist, seek medical advice.

Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects. Women of childbearing age, pregnant women or women suspected of being pregnant should use the veterinary medicinal product with serious caution to avoid accidental self-injection.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established in cattle, pigs, dogs and cats during pregnancy, lactation 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:
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.

Overdose:
None known.

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

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

7. Adverse events

Cattle, pigs, dogs and cats:

Rare (1 to 10 animals / 10,000 animals treated):	Anaphylactic shock [a,b]

[a] Potentially fatal.

[b] Following administration of potentiated sulphonamide preparations, mostly after intravenous injection. For intravenous administration the veterinary medicinal 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.

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 the local representative of the marketing authorisation holder 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

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 veterinary medicinal 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 veterinary medicinal 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.

9. Advice on correct administration

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.

10. Withdrawal periods

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

Pigs:
Meat and offal: 20 days

11. Special storage precautions

Keep out of the sight and reach of children.
Do not store in a refrigerator after broaching Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after Exp. The expiry date refers to the last day of that month.
Shelf life after first opening the immediate packaging: 28 days.

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: 50 ml, 100 ml or 250 ml colourless glass type II vial with fluoropolymer coated chlorobutyl stopper type I stopper secured with an aluminium cap.
1 vial in a cardboard box.

Not all pack sizes may be marketed.

15. Date on which the package leaflet 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).

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:

Manufacturer responsible for batch release:
Eurovet Animal Health B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

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.