1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Censulfatrim 200 mg/ml + 40 mg/ml solution for injection
Censulfatrim, 200 mg/ml + 40 mg/ml solution for injection (EE)
Neuton, 200 mg/ml + 40 mg/ml solution for injection (DK)
Neuton Vet, 200 mg/ml + 40 mg/ml solution for injection (SE)

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**
Chlorocresol	1 mg
Sodium Formaldehyde Sulfoxylate	1 mg
Disodium Edetate	
Sodium Hydroxide	
N-Methyl Pyrrolidone	466 mg
Water for Injections	

A clear, yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Cattle, pigs, horses, dogs and cats

3.2 Indications for use for each target species

Treatment of systemic 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, to sulphonamides or to any of the excipients.
Do not use by intraperitoneal route.
Do not use in cases of severe liver or kidney damage or blood dyscrasias.
Do not use in cases of reduced water intake or losses of body fluid.
Do not use in horses treated with drugs that can induce cardiac arrhythmias such as certain anaesthetic and sedative agents (e.g. detomidine).

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Use of the product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.

Use of the product should be in accordance with official, national and regional antimicrobial policies.

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.

In order to avoid impairment of the kidneys by crystalluria during the treatment adequate drinking water should be available at all times.

The intravenous route should be used with caution and only if it is therapeutically justified. If this administration route is used, the following precautions will be taken into account:
- Cardiac and respiratory shock in horses has been observed. At the first sign of intolerance the injection should be interrupted and shock treatment initiated.
- The veterinary medicinal product should be warmed to body temperature before administration.
- The veterinary medicinal product should be injected slowly over as long period as is reasonably practical.

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

This veterinary medicinal product may cause an allergic reaction in people sensitised to sulphonamides, trimethoprim or chlorocresol. People with known hypersensitivity to sulphonamides or trimethoprim should avoid contact with the veterinary medicinal product.

Administer the veterinary medicinal product with caution to avoid the accidental self-injection and the skin contact. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

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.

This veterinary medicinal product may produce eye and skin irritation. Avoid the contact with skin and eyes. In case of contact with skin or eyes, rinse immediately with plenty of water.

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.

Wash hands after use.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle, pigs, horses, dogs and cats:

Rare (1 to 10 animals / 10,000 animals treated):	Anaphylactic shock[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Application site swelling and/or tenderness[2] Crystalluria, haematuria, urinary tract obstruction/blockage blood dyscrasia NOS

[1] Particularly after the intravenous route (see section 3.5). At the first sign of intolerance the injection should be interrupted and shock treatment initiated.
[2] These lesions are of a transient nature, resolving within one week after treatment.

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 also section 16 of 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 cattle, pigs, horses, dogs and cats during pregnancy or lactation. Laboratory studies in rabbits and rats with the excipient N-methylpyrrolidone 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

Do not administer with para-aminobenzoic (PABA) acid.

Local anaesthetics from the group of para-aminobenzoic acid esters (procaine, tetracaine) can locally inhibit the effect of sulfonamides.

Do not administer with oral anticoagulants or urinary acidifiers.

Cases of fatal cardiac arrhythmias have been observed due to interaction between sulfonamide- the trimethoprim combination and certain agents for sedating and anesthetizing horses (e.g detomidine).

3.9 Administration routes and dosage

Intramuscular, intravenous or subcutaneous route.

Cattle, pigs and horses: 12.5 mg of sulfadiazine + 2.5 mg of trimethoprim / kg b.w., equivalent to 1 ml of veterinary medicinal product / 16 kg b.w.
- Cattle and pigs: administer by intramuscular or slow intravenous injection. Maximum recommended volume to be administered at a single intramuscular site: 15 ml of product.
- Horses: administration is by slow intravenous injection only.

Dogs and cats: 25 mg of sulfadiazine + 5 mg of trimethoprim / kg b.w., equivalent to 1 ml of veterinary medicinal product / 8 kg b.w. Administration is by subcutaneous injection only.

Treatment may be repeated until two days after the symptoms have been resolved up to a maximum of five days.

To ensure a correct dosage, bodyweight should be determined as accurately as possible.

The cap may be safely punctured up to 30 times. The user should choose the most appropriate vial size according to the target species to be treated.

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

Crystalluria and nerve and hematic disorders may occur.
In case of overdose, suspend the treatment and administer abundant water and folic acid.

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

3.12 Withdrawal periods

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

Pigs:
Meat and offal: 20 days

Horses:
Meat and offal: 28 days
Not authorised for use in horses producing milk for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01EW10

4.2 Pharmacodynamics

Sulfadiazine belongs to the group of sulfonamide chemotherapeutics, trimethoprim belongs to the diaminopyrimidines. Both active substances have an inhibitory effect on the folic acid metabolism of microorganisms at two different stages (sequential effect). Blocking individual steps disrupts the synthesis of nucleic acids and proteins in sensitive bacteria.

Sulfadiazine inhibits the incorporation of p-aminobenzoic (PABA) acid into dihydrofolic acid. Sulfadiazine specifically competes with PABA for the enzyme dihydroproteosynthetase, this selective bacteriostatic effect depends on the difference in the formation of folic acid in bacterial and mammalian cells. Susceptible microorganisms synthesize folic acid, whereas mammalian cells use preformed folic acid.

Trimethoprim selectively inhibits the enzyme dihydrofolate reductase, thus preventing the conversion of dihydrofolic acid to tetradihydrofolic acid.

Sulfonamide resistance genes are linked chromosomally (folP genes) or extrachromosomally, e.g. to integron 1 (sul1 genes) and plasmids (sul2, sul3 genes). The result of the expression of these genes is a change in the structure of the dihydropteroate synthetase enzyme so that sulfonamides lose their ability to bind and the mechanism of their action is disrupted. There is mutual cross-resistance in the sulfonamide group.

Trimethoprim resistance genes (dfr genes) are linked chromosomally or extrachromosomally, e.g. on integrons 1 and 2 or on transposons. Extrachromosomal dfr genes are divided into two subgroups.

More than 30 dfr genes are currently described. Their action is manifested by a change in the structure of the dihydrofolate reductase enzyme and its sensitivity to trimethoprim. Chromosomally linked resistance is manifested either by overproduction of dihydrofolate reductase or loss of function of the thymidylate synthase enzyme.

4.3 Pharmacokinetics

Both active substances of the combination are rapidly absorbed after parenteral administration and distributed throughout the body.

Sulfadiazine is metabolized in the liver to acetylated derivatives (25%) and to a lesser extent to hydroxylated derivatives. Excretion is renal (by glomerular filtration and tubular secretion). 50% of the dose is recovered from the urine within 24 hours.

Trimethoprim is metabolized in the liver by oxidation and subsequent conjugation. Excretion is mostly renal (by glomerular filtration and tubular secretion) and to a lesser extent is excreted by bile, 75% of the dose is recovered from the urine within 24 hours and 85-90% from the urine and faeces within 3 days.

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: 2 years
Shelf life after first opening the immediate packaging: 28 days

5.3 Special precautions for storage

Do not freeze.
Keep the vial in the outer carton in order to protect from light.

Crystallisation of the product, which can occur at low temperatures, can be reversed by gentle warming.

5.4 Nature and composition of immediate packaging

Amber glass vials, with bromobutyl stopper and aluminum cap with FLIP-OFF seal.

Pack sizes:
Cardboard box with 1 vial of 100 ml
Cardboard box with 1 vial of 250 ml
Cardboard box with 10 vials of 100 ml
Cardboard box with 10 vials of 250 ml

Not all pack sizes may be marketed.

5.5 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.

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

CENAVISA S.L.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation:

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

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).