1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetsultrim 200 mg/ml + 40 mg/ml solution for injection for horses, cattle, goats, sheep and pigs (IE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:
Sulfadoxine 200 mg
Trimethoprim 40 mg

Excipients:

Qualitative composition of excipients and other constituents
Sodium hydroxide
Glycerol formal
Water for injections

Clear, light brown solution, free from visible particles.

3. CLINICAL INFORMATION

3.1 Target species

Horses, cattle, goats, sheep and pigs.

3.2 Indications for use for each target species

Treatment of bacterial respiratory, gastrointestinal and urinary tract infections.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substances (or to any other sulfonamides), or to any of the excipients.
Do not use in animals with impaired hepatic or renal function or blood dyscrasias.
The intravenous route of administration is contraindicated in the case of previous or concurrent administration of central nervous system depressants (e.g. anaesthetics, neuroleptics).
Do not use in horses receiving detomidine or halothane. See also section 3.8.

3.4 Special warnings

High proportion of resistance has been observed across EU notably in *Escherichia coli* in pigs.
Cross-resistance has been shown between sulfadoxine and other sulfonamides. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to combinations of trimethoprim with other sulfonamides because its effectiveness may be reduced.
In horses, life-threatening anaphylactic or anaphylactoid shock reactions may occur following intravenous injection.
In case of infections involving purulent conditions, trimethoprim-sulfonamide combinations are not recommended due to diminished efficacy under such conditions.

3.5 Special precautions for use

Special precautions for safe use in the target species
In order to avoid crystalluria during treatment, adequate drinking water should be available at all times.

Use of the veterinary medicinal 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.

Narrow spectrum antibiotic therapy with a lower risk of antimicrobial resistance selection should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

This antimicrobial combination should only be used where diagnostic testing has indicated the need for simultaneous administration of each of the active substances.

The feeding of waste milk containing residues of sulfadoxine and trimethoprim to calves should be avoided up to the end of the milk withdrawal period (except during the colostral phase), because it could select antimicrobial-resistant bacteria within the intestinal microbiota of the calf and increase the faecal shedding of these bacteria.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Sulfonamides may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to sulfonamides may lead to cross-reactions with other antibiotics and *vice versa*. Allergic reactions to sulfonamides may occasionally be serious.

People with known hypersensitivity to sulfadoxine (or other sulfonamides) or trimethoprim should avoid contact with the veterinary medicinal product. Swelling of the face, lips, or eyes, or difficulty in breathing, are more serious symptoms and require urgent medical attention. If symptoms following exposure, such as skin rash or difficulty in breathing, occur, seek medical advice immediately and show the package leaflet to the physician.

Accidental self-injection may cause gastrointestinal, CNS, haematological, renal or skin effects. Avoid self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet to the physician.

This veterinary medicinal product may cause irritation (pH 9.5-10.5). Avoid contact with skin and eyes. In case of accidental contact, wash immediately with water. If irritation persists, seek medical advice.

The veterinary medicinal product should not be administered by pregnant women and women trying to conceive.

To minimise the possibility of accidental oral ingestion through hand-to-mouth contact, do not eat, drink or smoke while handling this veterinary medicinal product. Wash hands after use.

Special precautions for the protection of the environment
Not applicable.

3.6 Adverse events

Horses, cattle, goats, sheep and pigs:

Undetermined frequency (cannot be estimated from the available data):	Injection site pain [1], injection site swelling[1] Urticaria Unsteady gait[2]

[1]Following intramuscular administration. Therefore, intravenous administration is recommended for horses, cattle, goats and sheep.
[2]In goats and sheep.

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

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

Pregnancy and lactation
Laboratory studies have shown teratogenic effects of sulfonamide/trimethoprim combinations at doses higher than the therapeutic dose, which are characteristic of folic acid antagonists.
In a study in pregnant sows, no foetal malformations were observed when the veterinary medicinal product was administered at the recommended dose on days 8 to 41 of gestation for 5 consecutive treatments.
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 use in horses receiving detomidine or halothane, as this may cause fatal cardiac arrhythmias.
The veterinary medicinal product may potentiate the effects of analgesics, antidiabetics and anticoagulants.

3.9 Administration routes and dosage

Horses, cattle, sheep and goats: Intramuscular or slow intravenous use.
Pigs: Intramuscular use.

For intravenous administration, the solution for injection should be warmed to body temperature and injected slowly into the vein. At the first sign of intolerance, administration must be stopped immediately, and shock treatment initiated.
In horses, cattle, sheep and goats, large doses should be administered intravenously. Death, haemolysis or shock can occur in case the veterinary medicinal product is administered too quickly.
The intravenous route should be used with caution in horses due to the risk of serious adverse events.

The recommended dose is 15 mg (12.5 mg sulfadoxine and 2.5 mg trimethoprim) per kg bodyweight (equivalent to 1 ml of the veterinary medicinal product per 16 kg bodyweight) once daily. In horses, cattle, sheep and goats, intravenous administration is preferred.

The maximum duration of treatment is 5 consecutive days. The appropriate treatment duration should be chosen based on the clinical needs and individual recovery of the treated animal and treatment should be continued for 2 consecutive days after the resolution of clinical signs, without exceeding this maximum duration. For infections requiring a treatment duration longer than 5 days, the diagnosis and treatment should be reassessed and alternative therapy should be considered.

To ensure a correct dosage, body weight should be determined as accurately as possible.
Clean the rubber stopper before withdrawing each dose. Use a dry, sterile needle and syringe.
The rubber stopper should not be punctured more than 15 times with a 16G needle and 70 times with a 21G needle.

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

Not 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

Horses, cattle, goats and sheep
Meat and offal: Intravenous use: 10 days. Intramuscular use: 30 days.

Pigs
Meat and offal:
Intramuscular use: 30 days.

Cattle
Milk: 144 hours (6 days).

Goats and sheep
Milk: 216 hours (9 days).

Horses
Not authorised for use in animals producing milk for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01EW13

4.2 Pharmacodynamics

Sulfadoxine (SDX) is used in combination with trimethoprim (TMP) in a ratio of 5 parts sulfadoxine to 1 part trimethoprim. The mechanism of action of the combination is based on a sequential blocking effect exerted by both substances on bacterial folic acid metabolism. The combination exhibits a supra-additive intensity of action, thereby allowing for a significant reduction in the dosage of the individual components.

Trimethoprim-sulfonamide combinations have a broad bactericidal action against many Gram-positive and Gram-negative aerobic bacteria, but a limited bactericidal action against anaerobic bacteria. Certain pathogens, including *Enterococcus faecalis*, *Pseudomonas spp., Erysipelothrix rhusiopathiae*,

Mycoplasmas spp., *Rickettsiae* spp. and *Leptospires* spp., are partially or completely resistant to the combination, and resistance has also been reported in some *E. coli* strains isolated from pigs.

Bacterial resistance to trimethoprim and to sulfonamides can be mediated via five main mechanisms: changes in the permeability barrier and/or efflux pumps, naturally insensitive target enzymes, changes in the target enzymes, mutational or recombinational changes in the target enzymes, and acquired resistance by drug-resistant target enzymes.

Cross-resistance has been shown between combinations of SDX/TMP. Spread of the resistance genes of SDX/TMP is mainly chromosomal-, plasmid- and transposon-encoded.
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.

TMP 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.

Given the current resistance situation, resistance across the entire activity spectrum must be anticipated. Resistance to one component of the combination results in loss of synergistic activity, which is essential for therapeutic efficacy, and resistance to any sulfonamide generally extends to the entire group.

European susceptibility data from 2021–2026 show variability in susceptibility to trimethoprim-sulfonamide combinations according to bacterial species, geographical region and animal population. Resistance has been reported in clinically relevant pathogens of the target animal species, including *Trueperella pyogenes* in cattle, *Actinobacillus pleuropneumoniae* and *Pasteurella multocida* in pigs. Available data do not indicate a uniform increase in resistance across the target animal species in Europe; however, increased resistance or reduced susceptibility has been reported in certain bacterial populations and geographical regions.

Resistance determinants for trimethoprim and sulfonamides may be carried on mobile genetic elements, including plasmids, integrons and transposons, facilitating horizontal dissemination and potential co-selection with other antimicrobial resistance determinants.

For some pathogen–antimicrobial combinations, interpretation of susceptibility data is limited by the absence of veterinary-specific clinical breakpoints.

4.3 Pharmacokinetics

After administration of 10 mg/kg sulfadoxine and 2 mg/kg trimethoprim, plasma concentrations in cattle remain at 2 µg/ml for sulfadoxine up to 24 hours after intravenous administration and at 0.5 µg/ml for trimethoprim up to 5 hours after intravenous administration.
Plasma protein binding is 48–66% for sulfadoxine in cattle and approximately 45% in pigs, and 57% for trimethoprim in cattle and approximately 50% in pigs.
In pigs, the volume of distribution is 0.35 l/kg for sulfadoxine and 1.6 l/kg for trimethoprim.
The plasma half-life of sulfadoxine is 10–15 hours in cattle, 6 hours in pigs and 11 hours in small ruminants.
The plasma half-life of trimethoprim is 2–4 hours in cattle and horses and approximately 2 hours in pigs.
Excretion occurs mainly via the kidneys. The unbound fraction is also excreted in milk.

Environmental properties
Trimethoprim is persistent in soil.

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

Unopened product: this veterinary medicinal product does not require any special storage conditions.
Do not store above 25 °C after the first opening of the immediate packaging.

5.4 Nature and composition of immediate packaging

100 ml amber type II glass vial closed with a bromobutyl rubber stopper and sealed with an aluminium cap or an aluminium/polypropylene flip-off cap.

Pack sizes:
1 × 100 ml vial in a cardboard box.
6 × 100 ml vials 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

Any unused veterinary medicinal product or waste material 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

Interchemie Werken De Adelaar Eesti AS

7. MARKETING AUTHORISATION NUMBER(S)

VPA22812/006/001

8. DATE OF FIRST AUTHORISATION

30/09/2026

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

30/09/2026

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).