1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nanotrim 464.2 mg/g + 100 mg/g powder for use in drinking water/milk for chickens, turkeys, pigs and cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Active substances:

464.2 mg sulfachloropyridazine equivalent to 500 mg sulfachloropyridazine sodium
100 mg Trimethoprim

Excipients:

Qualitative composition of excipients and other constituents
Polysorbate 80
Maltodextrin

Light cream to beige powder.

3. CLINICAL INFORMATION

3.1 Target species

Chickens, turkeys, pigs and cattle (pre-ruminant).

3.2 Indications for use for each target species

Chickens and turkeys:
For the treatment and metaphylaxis of:
- *Escherichia coli* infections, including secondary *Escherichia coli* infections in cases of Chronic Respiratory Disease (CRD);
- Pasteurellosis;
- Infectious coryza caused by *Avibacterium paragallinarum;*
- *Staphylococcus* infections.

The presence of the disease in the flock must be established before the veterinary medicinal product is used.

Pigs:
For the treatment and metaphylaxis of:
- Colibacilloses such as gastrointestinal infections caused by *Escherichia coli;*
- Mastitis;
- Polyarthritis caused by *Trueperella pyogenes, Escherichia coli.*

The presence of the disease in the group must be established before the veterinary medicinal product is used.

Cattle (pre-ruminant):
For the treatment and metaphylaxis of:
- Gastroenteritis caused by *Escherichia coli;*
- Colisepticaemia;
- Bronchopneumonia caused by Streptococci, *Trueperella pyogenes*, *Escherichia coli*, *Pasteurella;*

- Polyarthritis caused by Streptococci;
- Diphtheria caused by *Fusobacterium necrophorum.*

The presence of the disease in the group must be established before the veterinary medicinal product is used.

3.3 Contraindications

Do not use in ruminating animals.
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 sulphonamides or trimethoprim or to any of the excipients.

3.4 Special warnings

A high prevalence of resistance has been observed in *E. coli* species.
Cross-resistance has been shown between the different sulfonamides and between sulfachloropyridazine and streptomycin.
Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to other sulfonamides or streptomycin because its effectiveness may be reduced.

In case of insufficient water uptake, pigs and cattle (pre-ruminant) should be treated parenterally instead, using a suitable injectable veterinary medicinal product prescribed by the veterinarian.

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 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 bacteria at farm level, or at local/regional level.

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

To avoid deterioration of the kidneys due to crystalluria during treatment, it should be ensured that the animal receives sufficient amount of drinking water.

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.

Do not use for prophylaxis.

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

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Trimethoprim, sulfachloropyridazine sodium and polysorbate 80 may cause hypersensitivity reactions. In particular, hypersensitivity to sulfonamides may induce cross reactions with other antibiotics. Sensitivity reactions to these substances may occasionally be severe. Persons with known hypersensitivity to these substances should avoid any direct contact with the veterinary medicinal product. To avoid any exposure, wear personal protective equipment consisting of impervious (latex or nitrile) gloves, protective masks, eye protection and suitable protective clothing when handling this veterinary medicinal product.

Do not eat, drink or smoke while handling this veterinary medicinal product.

This veterinary medicinal product may be irritant to the eyes. Avoid contact with the eyes. In case of accidental contact with the eyes, wash the eyes with plenty of water.

If you develop symptoms following exposure, such as skin rash or eye irritation, you should seek medical advice and show the package leaflet or the label to the physician.

Wash hands after use.

Special precautions for the protection of the environment:
In order to prevent any adverse effects on terrestrial plants, the use of the veterinary medicinal product should be limited to:

- In broilers: five cycles of broilers per year
- In weaned piglets: five cycles of weaned piglets per year

3.6 Adverse events

Chickens, turkeys, pigs, cattle (pre-ruminant):

Undetermined frequency (cannot be estimated from the available data):	Thrombocytopenia, Bone marrow disorder[1]

[1] Allergen-specific panmyelopathy, resulting in worsening in general condition

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, lactation or lay.

Use only according to the benefit-risk assessment by the responsible veterinarian.

Laboratory studies in rats and rabbits have shown evidence of teratogenic and foetotoxic effects.

3.8 Interaction with other medicinal products and other forms of interaction

Do not administer concomitantly with veterinary medicinal products containing sulfonamides.

The concomitant use of sulfonamides with ionophore coccidiostats (e.g. monensin, salinomycin) may increase the risk of toxicosis.

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

Sulfonamides potentiate anticoagulants action.

3.9 Administration routes and dosage

In drinking water/milk (milk replacer) use (see details for each target species).

Chickens and turkeys:
30 mg sulfachloropyridazine sodium and 6 mg trimethoprim per kg body weight per day (corresponding to 60 mg of the veterinary medicinal product per kg body weight per day), for 3–5 days, to be dissolved in drinking water.

Pigs:
10 mg sulfachloropyridazine sodium and 2 mg trimethoprim per kg body weight twice daily (corresponding to 20 mg of the veterinary medicinal product per kg body weight twice daily), for at least 3–5 days, to be dissolved in drinking water.

Cattle (pre-ruminant):
10 mg sulfachloropyridazine sodium and 2 mg trimethoprim per kg body weight twice daily (corresponding to 20 mg of the veterinary medicinal product per kg body weight twice daily), for at least 3–5 days, to be dissolved in milk replacer.

Guidance for preparing veterinary medicinal product solutions:
To ensure a correct dosage, body weight should be determined as accurately as possible.

The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage, the concentration of sulfachloropyridazine and trimethoprim should be adjusted accordingly.

The use of suitably calibrated measuring equipment is recommended.

Based on the recommended dose and the number and weight of animals to be treated, the exact daily concentration of the veterinary medicinal product should be calculated according to the following formula:

$$\frac{\text{mg veterinary medicinal product/kg body weight/day} \times \text{average body weight (kg) of animals to be treated}}{\text{average daily water/milk replacer intake (l/animal)}} = \text{mg veterinary medicinal product per litre of drinking water/milk replacer}$$

Prepare the solution with fresh tap water (or milk replacer for cattle, pre-ruminant) immediately before use. Milk replacer should be prepared prior to the addition of the veterinary medicinal product using water with temperature of at least 20°C or higher. The solution should be vigorously stirred for 5 minutes. Medicated milk replacer should be consumed within 1 hour after preparation.

Water uptake should be monitored at frequent intervals during medication. The medicated drinking water should be the sole source of drinking water for the treatment duration. Any medicated drinking water, which is not consumed within 24 hours, should be discarded. After the end of the medication period, the water supply system should be cleaned appropriately to avoid intake of sub-therapeutic amounts of the active substance.

For water tanks:
The maximum solubility of the veterinary medicinal product is 1 g/L (in worst case condition of hard water and a temperature of 4°C). For stock solutions to be used in water tanks, take care not to exceed the maximum solubility. During dissolution, the solution should be vigorously stirred for at least 5 minutes. Solutions should be checked visually for complete dissolution.

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

In the event of an overdose, no adverse events are known other than those listed in section ‘Adverse events’.

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

Chickens
Meat and offal: 3 days.

Turkeys
Meat and offal: 9 days.

Pigs
Meat and offal: 7 days.

Cattle (pre-ruminant)
Meat and offal: 7 days.

Not for use in birds producing or intended to produce eggs for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code :
QJ01EW12

4.2 Pharmacodynamics

Trimethoprim is an antibacterial diaminopyrimidine derivative that works synergistically with sulphonamides to inhibit bacterial multiplication.
Sulfachloropyridazine is an antibacterial sulphonamide that prevents the multiplication of bacteria. Sulfachloropyridazine inhibits the enzyme synthetase, which converts para-aminobenzoic acid to dihydrofolic acid, a precursor for the formation of folic acid.
Trimethoprim blocks folic acid synthesis at a later stage by inhibiting the reduction of dihydrofolic acid.

	Minimum inhibitory concentration breakpoints for Trimethoprim/Sulfamethoxazole (1:19) (µg/ml)[1,2,3]			
Clinical condition	**Organism**	**Susceptible**	**Intermediate**	**Resistant**
Mastitis	*Staphylococcus spp*	≤2	No breakpoints	≥4
Enteric swine/cattle	*Enterobacterales*	≤2/38	No breakpoints	≥4/76
Lameness/footrot or metritis	*Anaerobic pathogens*	No breakpoints	No breakpoints	No breakpoints
Respiratory isolates cattle/swine	*Diverse pathogens*	No breakpoints	No breakpoints	No breakpoints
Septicaemia cattle/swine/ poultry	*Enterobacterales*	≤2/38	No breakpoints	≥4/76
MMA/PPDS swine	*Staphylococcus spp*	≤2	No breakpoints	≥4
UTI isolates swine	*Enterobacterales*	≤2/38	No breakpoints	≥4/76
Respiratory isolates chicken/turkey	*Enterobacterales*	≤2/38	No breakpoints	≥4/76

[1]Stephen Hawser (2022). European Collection of Veterinary Pathogens (VetPath V) – Minimal Inhibitory Concentration (MIC) Testing. IHMA Europe Sarl. Report study 3638.

[2.] Ian Morrissey (2019). European Collection of Veterinary Pathogens (VetPath IV) – Minimal Inhibitory Concentration (MIC) Testing. IHMA Europe Sarl. Report study 2420.

[3.] Ed Siegwart (2015) MIC determination of the VetPath III collection of veterinary bacterial pathogens in Europe. Quotient Bio Analytical Sciences. Project number IV 102277.

Resistance to sulfonamides and trimethoprim can be chromosomal due to mutational modifications in the genes encoding the target enzymes (dihydropteroate synthase; dihydrofolate reductase). Plasmid-mediated resistance to sulfonamide and trimethoprim is instead caused by nonallelic and drug-resistant variants of the chromosomal target enzymes dihydropteroate synthase and dihydrofolate reductase, encoded by *dfr* and *sul* genes respectively.

In *Escherichia coli,* sulfonamide resistance is mediated by three *sul* genes (*sul1, sul2* or *sul3). Sul1* is widespread in *E.coli* isolates from healthy and diseased animals. *Sul2* and *sul3* were found in *E. coli* pig isolates. *Sul 1* and *sul2* are often found on plasmids that harbour other antimicrobial resistance genes. *Sul2* gene is often linked to the streptomycin resistance genes *strA-strB.* The *sul3* gene is linked to other resistance genes such as macrolide resistance gene *mef(B).*

In Enterobacteriaceae and other gram-negative bacteria, *dfr genes* have been found encoding dihydrofolate reductases that are insensitive to trimethoprim.

There is a complete cross-resistance between the different sulfonamides. The plasmid-mediated resistance of streptomycin is commonly linked with sulfonamide, ampicillin and tetracycline resistance genes and well known since many years.

4.3 Pharmacokinetics

After oral administration via feeding tube, drinking water or formula milk, sulfachloropyridazine and trimethoprim are rapidly absorbed and steady-state plasma concentration is quickly achieved. The active ingredients do not accumulate after long-term treatment, and are instead quickly eliminated. Sulfachloropyridazine and trimethoprim are both short-acting, and their half-lives in the blood after oral administration are roughly equal.

Environmental properties
Sulfachloropyridazine is very persistent in soils and toxic for terrestrial plants.
Trimethoprim is persistent in soils.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

This veterinary medicinal product must not be administered using drinking water containing chlorine or hydrogen peroxide as the active substance, sulfachloropyridazine sodium, degrades in the presence of these biocidal active substances.
No information is available on potential interactions or incompatibilities of this veterinary medicinal product administered orally by mixing into drinking water containing biocidal products other than chlorine or hydrogen peroxide, feed additives or other substances used in drinking water.

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: 22 months.
Shelf life after first opening the immediate packaging: 3 months.
Shelf life after dissolution in drinking water according to directions: 24 hours.
Shelf life after dissolution in milk replacer according to directions: 1 hour.

5.3 Special precautions for storage

This veterinary medicinal product does not require any special temperature storage conditions.
Store in the original container in order to protect from moisture. Store in a dry place. Keep the sachet tightly closed.

5.4 Nature and composition of immediate packaging

100 g pillow sachet and 1 kg resealable block-bottom zipped sachet made of polyethylene/aluminium/polyethylene terephthalate laminate.

Package sizes:
Pillow sachet with 100 g
Resealable block-bottom zipped sachet with 1 kg

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

Huvepharma NV

7. MARKETING AUTHORISATION NUMBER(S)

VPA10782/046/001

8. DATE OF FIRST AUTHORISATION

10/01/2025

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

17/07/2025

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).