

N.S. LABORATORY SDN. BHD.

## **NSP3, 500/100 mg/g, Powder for use in drinking water**

### **Active Ingredients:**

Each gram contains  
Sulfachloropyridazine sodium-----500mg  
Trimethoprim-----100mg

### **Product Description:**

White to yellow powder which can be dissolved in water

### **Dosage Form:**

Powder for use in drinking water

### **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.

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. *Sul1* 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.

### **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.

### **Indication:**

#### **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*;

- Coliiseppticaemia;

- 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.

### **Mode of Administration:**

Oral administration via drinking water

### **Recommended Dosage:**

In drinking water/ milk (milk replacer) use.

#### **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:

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

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.

### **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 case of known hypersensitivity to sulphonamides or trimethoprim or any of the excipients.

### **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.

### **Special Warnings for each 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.

N.S. LABORATORY SDN. BHD.

## **NSP3, 500/100 mg/g, Powder for use in drinking 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

### **Interactions with other Medicaments:**

Do not administer concomitantly with coccidiostats or veterinary medicinal products containing sulfonamides.

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

Sulfonamides potentiate anticoagulants action.

### **Usage during Pregnancy and Lactation:**

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.

### **Adverse Effects:**

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

Undetermined frequency (cannot be estimated from the available data):	Thrombocytopenia, Bone marrow disorder <sup>1</sup>
---	---

<sup>1</sup> Allergen-specific panmyelopathy, resulting in worsening in general condition

### **Overdose and Treatment:**

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

### **Withdrawal Periods (Meat and Offal):**

Chickens: 3 days;

Turkeys: 9 days;

Pigs: 7 days;

Cattle (pre-ruminant): 7 days.

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

### **Storage Condition:**

Store in cool, dry place (< 30°C).

### **Shelf Life:**

36 months

### **Shelf Life after Opening:**

Discard any unused powder immediately after opening

### **Shelf Life after Dilution/Reconstitution:**

Drinking water- 24 hours; Milk replacer- 1 hour

### **Packaging Available:**

100g/packet, 100packets/carton, 10kg/carton;

500g/packet, 30packets/carton, 15kg/carton

### **Manufacturer and Registration Holder:**

N.S. Laboratory Sdn. Bhd.

54, Jalan S2C2, Green Technology Park, Seremban 2, 70300 Seremban, Negeri Sembilan, Malaysia.

### **Revised Date:**

02/07/2025