TRIMODIN BOLUS
(Trimethoprim, Sulphadiazine)

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

TRIMODIN BOLUS.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Bolus Contains:
Trimethoprim …….... 200mg
Sulphadiazine …… 1.0gm

3. PHARMACEUTICAL FORM

Bolus.

4. CLINICAL INFORMATION

4.1. Target species

Cattle, Calves Sheep & Horse.

4.2. Indications for use specifying the target species

For the treatment of calves, foals, lambs suffering from bacterial infectious diseases (urinary and genital, respiratory, digestive organs, secondary bacterial diseases after viral diseases, post-traumatic and postoperative infectious diseases).

4.3. Contraindications

Do not use in animals with kidney, liver, hematopoietic organ diseases, hemorrhagic diathesis, dehydration or hypersensitivity to sulfonamides.
Do not use in goats as they are sensitive to sulfonamides

4.4. Special warnings for each target species

None.

4.5. Special precautions for use

Special precautions for safe use in the target species:

If colibacillosis is suspected, it is recommended to perform an antibiogram due to the frequent resistance of E. coli strains to sulfadiazine (SMR) and trimethoprim (TMP).
When treating with this product, attention should be paid to possible folic acid deficiency.
Recommended doses should be followed.

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

People with known hypersensitivity to sulfonamides or trimethoprim should avoid contact with the veterinary medicinal product.
In case of accidental splashing into the eyes, rinse thoroughly with water.
Consult a doctor if skin rash occurs
Consult a doctor immediately if swelling of the face, lips or eyes occurs, or if breathing difficulties occur.

4.6. Adverse reactions (frequency and seriousness)

Adverse reactions occur due to direct toxic effects and may be of immune origin. Adverse reactions include: gastrointestinal disorders due to dysbacteriosis and superinfection - decreased appetite, diarrhea or vomiting; renal failure due to damage to the renal tubules due to the formation of sulfadiazine acetyl compound crystals in the urine (mainly in carnivores); allergic skin reactions (urticaria, rash, redness).

4.7. Use during pregnancy and lactation or lay

Do not use in lactating females.

4.8. Interaction with other veterinary medicinal products and other forms of interaction

Do not use with diuretics (furosemide, hydrochlorothiazide, acetazolamide) as they accelerate the excretion of sulfonamides. Do not use with ionophore coccidiostats (monensin, salinomycin, lasalocid) as they inhibit the absorption of oral sulfonamides. Do not use with sulfonamide antagonists - B vitamins, para-aminobenzoic acid derivatives, local anesthetics (procaine) and penicillin procaine salt, analgesics and antipyretics (phenacetin) and sulfur-containing drugs. Phenylbutazone may displace protein-bound sulfonamides and there is a risk of crystalluria.

4.9. Dosage and administration route

The crushed tablet should be mixed with a small amount of water, milk or milk replacer, or feed. Calves, foals, sheep should be given 1 tablet per 15 kg body weight once daily, once or divided into two doses every 12 hours. Treatment is continued until clinical signs of the disease disappear and for an additional two days.

4.10. Overdose (symptoms, emergency procedures, antidotes), if necessary

There are no animal LD50 data for sulfadiazine. However, LD50s have been established for other sulfonamides. (5,200 mg/kg body weight in mice and 8,000 mg/kg body weight in dogs) indicate that this value for sulfadiazine may be higher. Signs of poisoning in dogs occur at 1 g/kg body weight and 300–500 mg/ kg body weight, respectively. Overdose may cause salivation, vomiting, diarrhea, respiratory distress, agitation, ataxia, and in cattle – ataxia and fainting. Most often, symptoms of poisoning are due to idiosyncrasy or hypersensitivity to sulfadiazine. Trimethoprim is low-toxic (its LD50 value in rats is 1,500 mg/kg body weight and 5,400–7,000 mg/ kg body weight in mice), therefore no symptoms of poisoning were observed.

In case of poisoning, symptomatic treatment should be applied. To accelerate the elimination of sulfonamides excretion, it is necessary to alkalinize the urine using sodium bicarbonate and increase the amount of water consumed or administer fluids parenterally.

4.11. Restrictions and special conditions of use, including restrictions on the use of antimicrobial and antiparasitic veterinary drugs, in order to reduce the risk of resistance development

Medication administered under the control or supervision of the veterinarian

4.12. Withdrawal period:

Meat: 15 days.
Horse: Not Applicable

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antimicrobials for systemic use, sulfonamides with trimethoprim.
ATCvet code: **QJ01EW18.**

5.1. Pharmacodynamics properties

The mechanism of action of sulfadiazine is related to competitive antagonism with para-aminobenzoic acid (PABR). Due to structural similarity, the sulfonamide, which has replaced PABR, inhibits the synthesis of folic acid and its further conversion to dihydrofolic acid. Trimethoprim (TMP) blocks dihydrofolic acid reductase and prevents the conversion of dihydrofolic acid to tetrahydrofolic acid, a derivative necessary for the synthesis of purines and nucleic acids. The synergistic action of the two derivatives significantly enhances the antibacterial effect and reduces the possibility of the emergence of resistant strains. The preparation is not effective against mycobacteria, viruses, fungi.

5.2. Pharmacokinetic information

Absorption The active substances of the preparation, trimethoprim and sulfadiazine, are well and rapidly absorbed from the gastrointestinal tract after oral administration and reach therapeutic concentrations in sheep and horses after 2 hours, and in cattle after 6 hours, which persist for 12 hours. The absorption and distribution of sulfonamides occurs by passive diffusion. In calves with diarrhea, the absorption process is faster than in healthy ones. The absorption of oral sulfonamides in different species of animals is different: in dogs and very young calves – very good, horses – good, cattle – very slow.

Distribution The absorbed active substances of the drug quickly enter the tissues and organs of the body. SMR, unlike TMP, does not accumulate in tissues. In the respiratory, gastrointestinal, urinary and circulatory systems, in the joint fluid and in the central nervous system, the concentration reaches 50-80% of the blood plasma concentration. High concentrations are found in milk and fetal tissues. Plasma protein binding is 44-57% for SMR in cattle, 44.7% for horses, and 48% for TMP.

Biotransformation Trimethoprim is biotransformed in the liver. It involves oxidative demethylation of the methyl group or oxidation of the so-called parent nitrogen atom in the ring, followed by conjugation with glucuronic or sulfuric acid. SMR is also biotransformed in the liver, and the metabolites formed retain antibacterial activity. The course of the biotransformation processes depends on the species and age of the animal. SMR can be biotransformed by acetylation or hydroxylation of the amino group. The metabolites formed after hydroxylation, it can be oxidized to carboxy derivatives. Each of these metabolites is subsequently conjugated with glucuronic acid or acetic acid (acetylation).

Excretion The main route of excretion of sulfadiazine and its metabolites is via the kidneys (glomerular filtration). It is also excreted in sweat, tears, feces, bile and milk. The half-life in very young animals is generally longer than in adults. Metabolites are eliminated much more rapidly than the parent compound, but are present in small amounts. TMP is also excreted by the kidneys. 77% of trimethoprim is excreted in the urine within 24 hours after administration 9% in the feces. 16% of the metabolites excreted in the urine are in the form of conjugates.

5.3 Ecotoxicity

TMP and SMP metabolites are excreted in the urine and biodegrade in the environment. The active parent substances of SMR and TMP, which may have an impact on the environment, constitute a very small amount of the animal excretions. Sulfonamides, so the product used to treat animals does not pose a real threat to the environment.

6. PHARMACEUTICAL INFORMATION

6.1 Incompatibilities

Sulfur compounds should not be used during sulfonamide treatment, as the hydrogen sulfide formed combines with hemoglobin to form sulfhemoglobin.

6.2. Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the container: use immediately in 28 days, do not store.

6.2. Special precautions for storage

Do not store above 25°C.
Store in a dry place
Protect from light and moisture.
Keep out of the reach of children.
To be used as directed by the registered veterinary practitioner only.

6.3. Nature and composition of primary conditioning

Alu/PVC blister in carton (20's, 50's & 100's)

SPECIAL PRECAUTIONS FOR THE DISPOSAL OF WASTE MATERIALS
UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS

Any unused veterinary medicinal products or waste materials derived from such medicinal products should be disposed of in accordance with local requirements and placed in appropriate collection and disposal systems for unused or expired medicinal products.

7. MARKETING AUTHORISATION HOLDER

Nawan Laboratories (Pvt.) Ltd.
Plots No. 136-138, Sector-15,
Korangi Industrial Area, Karachi-74900, Pakistan.

8. MARKETING AUTHORISATION NUMBER

Reg. No. 017130

9. DATE OF FIRST AUTHORISATION

Date of Reg.: 31.03.1998

10. DATE OF REVISION OF THE TEXT

20-03-2025

MANUFACTURED BY:

NAWAN LABORATORIES (PVT) LTD.
136, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan.