For Veterinary Use Only.

Primoxal®

Solution for Injection

Veterinary Systemic Antibacterial

COMPOSITION:

Primoxal Solution for Injection is a clear, pale yellow, viscous solution containing 40mg trimethoprim and 200mg sulphamethoxazole per each ml.

PHARMACOLOGICAL PROPERTIES:

Primoxal is a combination of sulphamethoxazole which is a compound from sulphonamide group, and trimethoprim, and it demonstrates a superior effect in terms of mode of action and effect spectrum as a result of the synergism generated. Primoxal Injection for Solution is effective against the majority of Gram-positive and Gram-negative bacteria (including the ones which are resistant to Penicillanase) which are encountered as disease factors Sulphonamides essentially displays bacteriostatic effect. Due to its similarity with PABA (Para-amino benzoic acid) in chemical structure sulphonamide competes on the basis of cell and consequently substitutes PABA and inhibits the normal metabolism of the bacteria. Generally, sulphonamides are used in combination with trimethoprim of other DAP (Diaminopyrimidine) derivatives. As a result of an inhibition performed by trimethoprim at another stage on bacterial basis, the growth of the bacteria is inhibited with double blockage. Bacteria which are sensitive to the combination; Gram positive aerobes: Staphylococcus aureus, Streptococcus sp., Actinomyces sp., Corynebacterium sp., Listeria monocytogenes, Erysipelothrix rhuisiopathie. Gram negative aerobes: Actinobacillus sp., Bordetella sp., Enterobacteriacea (E. coli, Klepsiella sp., Proteus sp., Salmonella sp., Yersinia sp.), Haemophilus sp., Pasteurella sp. Anaerobes: Actinomyces sp., Bacteroides sp., Fusobacterium sp., certain Clostridium sp., Chlamydia sp., certain Mycobacterium sp., and certain Nocardia sp. are moderately sensitive. Ricketsia sp., Leptospira sp., Pseudomonas aeruginosa and Mycoplasma sp. are resistant.

Primoxal Solution for Injection is rapidly absorbed through the administration area. Sulphamethoxazole is mainly metabolized within the body. The main sulphamethoxazole metabolite is acidified form which is excreted via urine. It is excreted from the body through urine, stools, bile, milk, perspiration and tears. It reaches therapeutic blood concentrations within an approximately one hour following parenteral administration. In cattle, pKa value of sulphamethoxazole is 6.0 and its plasma half life is 140 minutes. Volume of distribution is 0.30L/kg and the ratio of binding to proteins is 62%. 60% of trimethoprim and 25-50 of sulphamethoxazole is excreted through urine within the first 24 hours.

AREA OF USE / INDICATIONS:

It is indicated in the treatment of infections in horses, dogs, cattle, sheep and goats caused by the sensitive bacteria. It is used as parenteral support in respiratory infections such as pneumonias, pleuropneumonia and enzootic pneumonia caused by Pasteurella haemolytica and Pasteurella multocida; urogenital system infections; digestive system infections, soft tissue infections; nail infections and other wound infections; and in mastitis and metritis.

USAGE AND DOSAGE:

Primoxal Solution for Injection should be administered intramuscularly (IM) or slow intravenously (IV) to sheep, goats and cattle. It should only be administered intravenously to horses and dogs. Avoid subcutaneous

administration to these species due to local reactions. General dose of Primoxal Solution for Injection is 15mg (sulphamethoxazole + trimethoprim)/kg live weight. Practically, 1ml Primoxal Solution for Injection is adequate for 10-15kg live weight per day. This administration may continue for 3-5 days in accordance with the course of infection.

SPECIFIC CLINICAL PARTICULARS AND SPECIAL WARNINGS FOR TARGET SPECIES:

The animal undergoes a clinical examination on the third day following the initial injection. If required, repeat the injection. Despite the fact that there is not any report concerning the presence in the target species, avoid dehydration of animals during the treatment as sulphonamides may lead to nephrotoxic effects (crystalluria, tubular obturation, haematuria) in case of dehydration and acidic urine media.

Use during pregnancy: Sulphonamide and diaminopyrimidine combinations pass placenta. No side effect of treatment doses has been observed in pregnant dogs. The drug safety has not been studied in pregnant horses. No considerable change has been observed on spermatogenesis in horses at recommended doses. It has been determined to have teratogenic effects in pregnant rats and mice at very high doses.

UNDESIRED/SIDE EFFECTS

Treatment safety is narrowed down in case of folic acid deficiency in patients. In this case, reduction is observed in the number of platelets and erythrocytes whereas an enhancement in the number of megablasts. They may cause deterioration in blood table, non-septic polyarthritis and idiosyncratic intoxication characterized by skin eruption in all dog types, particularly in Doberman-Pinscher. Sulphonamide and DAB (diaminopyrimidine) combinations may result in diarrhoea, vomiting, skin rash, Stevens-Johnson syndrome, hepatitis, phantasmata, anaemia, impaired blood clotting, sulphemoglobinemia and reduction in granulocyte number especially in long-term administration. Albeit rare, respiratory and cardiac shock may occur in horses following intravenous administration. Therefore, the product should have the same temperature with the body and should be administered as slow as possible. The possibility of sensitivity to sulphonamides, and the cross hypersensibility between sulphonamides should be taken into consideration.

DRUG INTERACTIONS:

Avoid using sulphonamides with para-aminobenzoic acid (PABA), which is their structural analogue; and with local anaesthetics including procaine and butocaine which contain PABA nucleus in their structure, due to the possibility of antagonism formation. Procaine should not be used with Penicillin G as it may create an antagonist effect. Ammonium may cause crystalluria in urinary system when given with chloride and urine acidizers. B complex vitamins as nicotinamide, folic acid and choline; and amino acids including glutamic acid and methionine which are the presubstances of those may cause a sulphonamide antagonist effect. Avoid using with diuretics since they may result in the reduction of thrombocyte number. This is particularly important for the patients with coronary failure and may lead to mortality. Ancillary enzymes, glucose and sublimates should not be used with sulphonamides as they have an antagonist effect. In case of use with alpha-2 receptor agonists, a fatal cardiac arrhythmia may be developed. Therefore, it should not be intravenously administered to horses whose sedation has been provided with Alpha-2 agonists.

SYMPTOMS OF OVERDOSE, PRECAUTIONS AND ANTIDOTE:

Although trimethoprim is better tolerated in overdose, the administration of sulphonamides in overdoses for long periods, the insufficient level of fluid intake or dehydration state catalyzes crystalluria formation. The primary toxic effects of sulphonamides in kidneys are anorexia and depression. In more serious cases certain symptoms are seen such as haematuria, the presence of sulphonamide crystals in the urine, whitish hardening of the urethra

hole, albuminuria, enhancement of urea and nitrogen values in the blood, renal colic, anuria and hydronephrosis. In case of crystallization formation in kidneys, infuse bicarbonate or Ringer lactate solution, develop alkalosis and ensure its excretion through kidneys, and induce drinking plenty of water.

WARNINGS ON DRUG RESIDUES IN FOOD:

Withholding Period (WHP): Cattle, sheep and goats should not be sent for slaughtering during treatment and before 14 days following the final drug administration. Cow, sheep and goat's milk produced should not be offered for human consumption during the treatment and 5 days (10 milkings) following the final administration.

CONTRAINDICATIONS:

Avoid administration to sulphonamide-sensitive animals; animals with severe liver and renal failure; with hemopoietic system disorder and highly dehydrated animals.

GENERAL WARNINGS:

Consult your veterinary surgeon before using and in case an unexpected effect is observed. It is sold with Veterinary Surgeon prescription. Keep out of reach of children. Protect from light.

STORAGE CONDITIONS AND SHELF LIFE:

Store at room temperature of (15-25℃) away from sun light. The shelf life is 4 years. Opened vials should be used within 28 days.

COMMERCIAL PRESENTATION FORM:

Offered for sale in 20, 50, 100ml amber vials in cardboard box packages and in 250ml amber vials in plastic boxes.

PLACE AND CONDITIONS OF SALE:

Sold with Veterinary Surgeon's prescription in pharmacies and veterinary surgeries (VSP).

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NAME AND ADDRESS OF MARKETING AUTHORIZATION OWNER:

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