For The use of a registered veterinary Practitioner or a Hospital only

FARMTAZO

(Cefoperazone & Tazobactam for Injection 4500 mg)

COMPOSITION:
Each vial contains:
Cefoperazone Sodium (Sterile) IP Eq. to Anhydrous Cefoperazone 4000 mg
Tazobactam Sodium (Sterile) IP
Eq. to Anhydrous Tazobactam 500 mg

PHARMACEUTICAL FORM
Powder for injection.
PHARMACOTHERAPEUTIC GROUP:
Cefoperazone, combinations.
ATC code: J01DD62.

DESCRIPTION
Cefoperazone:
Cefoperazone is a semisynthetic broad-spectrum cephalosporin proposed to be effective against Pseudomonas infections. It is a third-generation antibiotic agent and it is used in the treatment of various bacterial infections caused by susceptible organisms in the body, including respiratory tract infections, peritonitis, skin infections, endometritis, and bacterial septicemia. its chemical formula is CH,N,O,S,. Its chemical structure is as follows:

Tazobactam sodium:
Tazobactam is a compound which inhibit the action of bacterial beta-lactamase. It is added to extend spectrum of B- lactam

antibiotic. Tazobactam sodium is a derivative of penicillin nucleus, is a penicillanic acid sulfone. The chemical formula is C, H, N.NaO, S and the chemical structure is as follows:

MECHANISM OF ACTION
Cefoperazone is bactericidal in action. The antibacterial activity of the drug results from inhibition of nucleopeptide synthesis in the bacterial cell wall. Tazobactam has little, clinically relevant activity against bacteria due to its reduced affinity to penicillin binding proteins. It is a å-lactamase inhibitor of the Richmond-Sykes class III penicillinases and

cephalosporinases. It does not induce chromosomally mediated à-lactamases.

PHARMACOKINETICS AND DISTRIBUTION
The plasma disposition of Cefoperazone by intravenous (IV) and intramuscular (IM) administrations of 20 mg/kg as a single dose in six camels (Camelus dromedarius).
After IV administration, elimination half-life (11/28), volume of distribution at steady state (Vdss), total body clearance (Citot) and mean residence time (MRT) of Cefoperazone were 1.95 h, 0.38 L/kg, 0.17 L/h/kg and 2.16 h, respectively. After IM administration of Cefoperazone, peak plasma concentration (Cmax) was 21.95 µg/ml, and it was obtained at (tmax) 1.23 h. Absorption half-life (t1/2ab), elimination half-life and mean absorption time were 0.45 h, 2.84 h and 2.07 h, respectively. The bioavailability of Cefoperazone was 89.42%. In camels, no local reaction or any other adverse effects were observed and very good bioavailability following IM administration was observed. It indicates that Cefoperazone might be a promising alternative treatment for a variety of infectious diseases in camels.
In sheep, following single dose intravenous administration at the dose rate of 20 mg/kg body weight; the apparent volume of distribution, area under the curve, elimination half-life and total body clearance were 1.06 ±0.13 L/kg (mean and standard error), 86.43 ±5.15 µg.h/mL,

3.80 ± 0.60 h and 5.16 ± 0.32 mL/min/kg, respectively. Following intramuscular administration at the dose rate of 20 mg/kg body weight, the peak plasma drug concentration was 25.67±3.02 µg/ml, at 0.5 h and the drug was detected for up to 12 h. The area under curve and limination half-life were 60.99 ± 4.27 µg.h/ml, and 3.32 ± 0.68 h, respectively. Bioavailability after intramuscular administration of cefoperazone was 71.83 ± 5.96%. Cefoperazone has favorable pharmacokinetics with good bioavailability in sheep indicating that the drug can be used for susceptible infections via intramuscular administration in sheep at the dose of 20 mg/kg.

The pharmacokinetics and bioavailability of cefoperazone (CPZ) following intravenous (IV) and intramuscular (IM) administration of single doses (30 mg/kg) to horses, Concentrations in serum, urine and synovial fluid samples were measured following IV administration. CPZ concentrations in serum, synovial fluid and spongy bone samples were measured following IM administration. After IV administration a rapid distribution phase (11/2 (alpha): 4.22 +/- 2.73 min) was followed by a slower elimination phase (t1/2(beta) 0.77 +/- 0.19 h). The apparent volume of distribution was 0.68 +/- 0.10 L/kg. Mean synovial fluid peak concentration was 5.76 +/- 0.74 microgram/mliter. After IM administration a bioavailability of 42.00 +/- 5.33% was obtained. Half-life of absorption was 2.51 +/-0.72 min and t1/2(beta) was 1.52 +/- 0.15 h. The mean synovial fluid and spongy bone peak concentrations at 2 h after IM administration were 2.91 +/-0.85 microgram/mliter and 5.56 +/- 0.70 microgram/mliter, respectively. Similar studies in Cattle are limited or not available.

Metabolism and Excretion

Cefoperazone is excreted mainly in the bile where it rapidly achieves high concentrations. Up to 20% of tazobactam is also found to be excreted through bile. About 60% to 80% of tazobactam is excreted unchanged in the urine by glomerular filtration and tubular secretion within 24 hours. Up to 30% of cefoperazone is excreted unchanged in the urine within 12 to 24 hours; this proportion may be increased in patients with hepatic or biliary disease. Cefoperazone A, a degradation product less active than cefoperazone, has been found in vivo, rarely. Plasma concentrations of tazobactam are enhanced by probenecid. Tazobactam can be removed by hemodialysis.

CLINICAL PARTICULARS

Therapeutic Indications

The first-generation cephalosporins represented by the oral drugs cephalexin and cefadroxil, and the injectable drug cefazolin have a spectrum of activity that includes *staphylococci*, *streptococci,* and many of the enteric gram- negative bacilli. However, resistance among gram-negative bacteria develops easily, primarily from synthesis of B- lactamase enzymes that can hydrolyze these drugs. Extended-spectrum cephalosporins include those from the 2nd, 3rd, and 4th generation have been used in resistant infections caused by *Escherichia coli*, *Klebsiella pneumoniae, Enterobacter* species*, Proteus* species (especially indole-positive), and *Pseudomonas aeruginosa*. Treatment of Bacterial infections caused by Cefoperazone sensitive Gram-positive, Gram-negative bacteria, Mastitis, pneumonia, metritis & other soft tissues infection associated with septicemia, Genito-urinary tract infections, Respiratory tract infections, etc.

POSOLOGY AND METHOD OF ADMINISTRATION

Cefoperazone and tazobactam are

preferably administered by IV infusion but may also be given by deep IM injection. An IV infusion should be given slowly over 15 to 30 minutes. 5-10 mg/kg body weight by IM or IV route.

WITHDRAWAL PERIOD:
Milk: 7 days | Meat: 28 days

DIRECTIONS FOR USE
Constitute with requisite quantity from the Sterile Water for Injections IP 20 ml provided with this pack. The constituted solution should be used immediately after preparation. Do not allow to freeze.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Warnings hypersensitivity reaction to cefoperazone, cephalosporins, penicillins, or other drugs before therapy with cefoperazone and tazobactam is instituted. Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics)

SIDE EFFECTS
The following is a list of possible side effects that may occur from all constituting ingredients of Cefoperazone & Tazobactum Injection. This is not a comprehensive list. These side effects are possible, but do not always occur. Some of the side effects may be rare but serious

- Decrease In White Blood Cells
- Decrease In Hemoglobin
- Increased creatinine Levels in Blood

SHELF LIFE
24 months.

STORAGE
Store in a dry place at a temperature not exceeding 30°C. Protect from light.

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