Front

Snare™

(Ceftriaxone)
Injection

سنير

Long acting broad spectrum antibiotic

COMPOSITION:
Snare Injection 250 mg:
Each vial contains:
Ceftriaxone Sodium USP equivalent to
Ceftriaxone ..... 250 mg.

Product Specs.: USP

Snare Injection 500 mg:
Each vial contains:
Ceftriaxone Sodium USP equivalent to
Ceftriaxone ..... 500 mg.

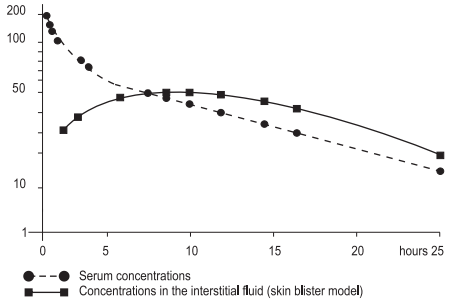
Product Specs.: USP

Snare Injection 1 g:
Each vial contains:
Ceftriaxone Sodium USP equivalent to
Ceftriaxone ..... 1 g.

Product Specs.: USP

DESCRIPTION:
Ceftriaxone:
(6R,7R)-7-{(Z)-2-(2-amino-4-thiazolyl)-2-methoxyimino]acetamido}-3-{[(2,5-dihydro 6-Hydroxy-2-methyl-5-oxo-as-triazin-3-yl)thio]methyl}-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-carboxylic acid in the form of the disodium salt. *Snare* contains approximately 83 mg (3.6 mEq) of sodium per gram of Ceftriaxone. Vials containing dry substance equivalent to 0.25 g 500 mg and 1 g Ceftriaxone.

PHARMACOKINETICS:
Ceftriaxone is characterized by an unusually long elimination half-life of approximately eight hours in healthy adults. The area under the plasma concentration time curves after I.V and I.M administration is identical. This means that the bio-availability of Ceftriaxone administered I.Mis 100%. On intravenous administration, Ceftriaxone diffuses rapidly into the interstitial fluid, where bactericidal concentrations against susceptible organisms are maintained for 24 hours (see figure).
Concentration after 1 g Snare (mg/l)



Elimination:
The elimination half-life in healthy adults is about eight hours. In infants aged less than eight days and in persons over 75 years of age, the average elimination half-life is about twice as long. In adults, 50-60% of Ceftriaxone is excreted unchanged by the kidneys, while 40-50% is excreted unchanged in the bile. The intestinal flora transforms Ceftriaxone into inactive metabolites. In neonates, renal elimination accounts for about 70% of the dose. In patients with *renal impairment* or *hepatic dysfunction*, the *pharmacokinetics* of Ceftriaxone are only minimally altered and the elimination half-life is only slightly increased; If kidney function alone is impaired, biliary elimination of Ceftriaxone is increased; if liver function alone is impaired, renal elimination is increased. Ceftriaxone is reversibly bound to albumin, and the binding decreases with the increase in the concentration, e.g. from 95% binding at plasma concentrations of < 100 mg/l to 85% binding at 300 mg/l. Owing to the lower albumin content, the proportion of free Ceftriaxone in interstitial fluid is correspondingly higher than in plasma.
Penetration into the cerebrospinal fluid:
Ceftriaxone penetrates the inflamed meninges of infants and children. The average extent of diffusion in the cerebrospinal fluid in bacterial meningitis is 17% of the plasma concentration, i.e. approximately four times that in aseptic meningitis. Ceftriaxone concentrations of > 1.4 mg/l have been found in the CSF 24 hours afterI.V Injection of Ceftriaxone in doses of 50-100 mg/kg. In *adult* meningitis patients, administration of 50 mg/kg leads within 2-24 hours of CSF concentrations several times higher than the minimum inhibitory concentrations required for the most common causative organisms of meningitis.
Microbiology:
The bactericidal activity of Ceftriaxone results from inhibition of cell wall synthesis. Ceftriaxone exerts in-vitro activity against a wide range of gram negative and gram positive micro-organisms. Ceftriaxone is highly stable to most b-lactamases, both penicillinases and cephalosporinases, of gram positive and gram negative bacteria.
Ceftriaxone is usually active against the following micro-organisms in-vitro and in clinical infections **(see indications):**
Gram-positive aerobes:
- Staphylococcus aureus (including penicillinase-producing strains)
- Staphylococcus epidermidis
- Streptococcus pneumoniae
- Streptococcus group A (Streptococcus pyogenes)
- Streptococcus group B (Streptococcus agalactiae)
- Streptococcus viridans
- Streptococcus bovis

NOTE:
Methicillin-resistant *Staphylococcus* spp. are resistant to cephalosporins, including Ceftriaxone. Most strains of Enterococci (e.g. *Streptococcus faecalis*) are resistant.
Gram-negative aerobes:
- Aeromonas spp.
- Alcaligenes spp.
- Branhamella catarrhalis (b-lactamase negative and positive)
- Citrobacter spp.
- Enterobacter spp. (some strains are resistant)
- Escherichia coli
- Haemophilus ducreyl
- Haemophilus influenzae (including penicillinase-producing strains)
- Haemophilus parainfluenzae
- Klebsiella spp. (Including Klebsiella pneumoniae)
- Moraxella spp.
- Morganella morganii
- Neisseria gonorrhoeae (including penicillinase-producing strains)
- Neisseria meningitidis
- Plesiomonas shigelloides
- Proteus mirabilis
- Proteus vulgaris
- Providencia spp.
- Pseudomonas aeruginosa (some strains are resistant).
- Salmonella spp.(including Salmonella typhi)
- Serratia spp. (Including Salmonella marcescens)
- Shigella spp.
- Vibrio spp. (Including Vibrio cholerae)
- Yersinia spp. (Including Yersinia enterocolitica)

NOTE:
Many strains of the above micro-organisms that are multiply resistant to other antibiotics, e.g. penicillins, older cephalosporins and aminoglycosides, are susceptible to Ceftriaxone.
Treponema pallidum is sensitive *in-vitro* and in animal experiments. Clinical investigations indicate that primary and secondary syphilis respond well to Ceftriaxone therapy.
Anaerobic organisms:
- Bacteroides spp. (including some strains of Bacteroides fragilis)
- Clostridium spp. (except Clostridium difficile)
- Fusobacterium spp. (except Fusobacterium mortiferum and Fusobacterium varium)
- Peptococcus spp.
- Peptostreptococcus spp.

NOTE:
Many strains of b-lactamase-producing Bacteroides spp. (notably Bacteroides fragilis) are resistant. Susceptibility to Ceftriaxone can be determined by the disk diffusion test or by the agar or broth dilution test using standardized techniques for susceptibility testing such as thoserecommended by the National Committee for Clinical Laboratory Standards (NCCLS).
The NCCLS issued the following interpretive breakpoints for Ceftriaxone:

	Susceptible	Moderately susceptible	Resistant
Dilution test, inhibitory concentrations in mg/l *Diffusion test* (disk with 30 µg Ceftriaxone)	≤8	16-32	≥64
Inhibition zone diameter in mm	≥21	20-14	≤13

Micro-organisms should be tested with the Ceftriaxone disk since it has been shown by in-vitro tests to be active against certain strains resistant to cephalosporin class disks. Where NCCLS recommendations are not in daily use, alternative, well standardized, susceptibility interpretive guidelines such as those issued by DIN, ICS and others may be substituted.

INDICATIONS:
Infections caused by pathogens sensitive to Ceftriaxone, e.g.:
- Sepsis;
- Meningitis;
- Abdominal infections (peritonitis, infections of the biliary and gastrointestinal tracts);
- Infections of the bones, joints, soft tissue, skin and of wounds;
- Renal and urinary tract infections;
- Respiratory tract infections, particularly pneumonia, and ear, nose and throat infections;
- Genital infections, including gonorrhea;
- Perioperative prophylaxis of infections.

DOSAGE AND ADMINISTRATION:
Adults and children over twelve years:
The usual dosage is 1-2 g of Ceftriaxone administered once daily (every 24 hours). In severe cases or in infections caused by moderately sensitive organisms, the dosage may be raised to 4 g, administered once daily.

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Neonates, infants and children up to twelve years:
The following dosage schedules are recommended for once daily administration
Neonates (up to two weeks):
A daily dose of 20-50 mg/kg body weight, not to exceed 50 mg/kg, on account of the immaturity of the infant's enzyme systems. It is not necessary to differentiate between premature and infants born at term.
Infants and children (three weeks to twelve years:
A daily dose of 20-80 mg/kg. For children with body weights of 50kg or more, the usual adult dosage should be used. Intravenous doses of 50 mg or more per kg should be given by infusion over at least 30 minutes.
Elderly patients:
The dosages recommended for adults require no modification in the case of geriatric patients.
Duration of therapy:
The duration of therapy varies according to the course of the disease. As with antibiotic therapy in general, administration of Ceftriaxone should be continued for a minimum of 48-72 hours after the patient has become afebrile or evidence of bacterial eradication has been obtained.
Combination therapy:
Synergy between Ceftriaxone and aminoglycosides has been demonstrated with many gram-negative bacilli under experimental conditions. Although enhanced activity of such combinations is not always predictable, it should be considered in severe, life-threatening infections due to micro-organisms such as *Pseudomonas aeruginosa.* Because of physical incompatibility the two drugs must be administered separately at the recommended dosages.

SPECIAL DOSAGE INSTRUCTIONS:
Meningitis:
In *bacterial meningitis in infants and children, treatment begins with doses of 100 mg/kg (not to exceed 4 g) once daily. As soon as the causative organism has been identified and its sensitivity determined, the dosage can be reduced accordingly.*
The best results have been found with the following duration of therapy:

Neisseria meningitidis	4 days	Streptococcus pneumoniae	7 days
Haemophilus influenzae	6 days	Susceptible Enterobacteriaceae	10-14 days

Gonorrhea:
For the treatment of gonorrhea (penicillinase-producing and non-penicillinase-producing strains), a single I.M dose of 250 mg of *Snare* is recommended.
Perioperative prophylaxis:
To prevent post-operative infection in contaminated or potentially contaminated surgery, the recommended approach depending on the risk of infection-is a single dose of 1-2 g Snare administered 30-90 minutes prior to surgery. In colorectal surgery, concurrent (but separate) administration of Snare and a 5-nitroimidazole, e.g. ornidazole, has proven effective.
Impaired renal and hepatic function:
In patients with impaired renal function, there is no need to reduce the dosage of Snare provided hepatic function is intact. Only in cases of preterminal renal failure (creatinine clearance <10 ml/min) the Snare dosage should not exceed 2 g daily. In patients with liver damage, there is no need for the dosage to be reduced provided renal function is intact. In cases of concomitant severe renal and hepatic dysfunction, the plasma concentrations of Ceftriaxone should be determined at regular intervals. In patients undergoing dialysis no additional supplementary dosing is required following the dialysis. Serum concentrations should be monitored, however, to determine whether dosage adjustments are necessary, since the elimination rate in these patients may be reduced.
Direction For Use:
As a general rule the solutions should be used immediately after preparation. Reconstituted solutions retain their physical and chemical stability for 6 hours at room temperature (or 24 hours in the refrigerator at 2-8°C). The solution's range in color from pale yellow to amber, depending on the concentration and length of storage. The coloration of the solutions is of no significance for the efficacy or tolerance of the drug.
Intramuscular injection:
For I.M injection,Snare 250 mg or 500 mg is dissolved in 2 ml and Snare 1 g in 3.5 ml of 1% lidocaine hydrochloride solution and injected well within the body of a relatively large muscle. It is recommended that not more than 1 g be injected at one site. The lidocaine solution should not be administered intravenously.
Intravenous injection:
For I.V injection,Snare 250 mg or 500 mg is dissolved in 5ml and Snare 1 g in 10 ml sterile water for injection. The intravenous administration should be given over 2-4 minutes.
Intravenous infusion:
The infusion should be given over at least 30 minutes. For I.V infusion, 2 g Snare is dissolved in 40 ml of one of the following calcium-free infusion solutions: sodium chloride 0.9%, sodium chloride 0.45% + dextrose 2.5%, dextrose 5%,dextrose 10%, dextran 6% in dextrose 5%, hydroxyl ethyl starch 6-10%, water for injection. Snare solution should be not be mixed with or piggybacked into solutions containing other antimicrobial drugs or into diluent solutions other than those listed above, owing to possible incompatibility.
Restrictions On Use:
Snare is contraindicated in patients with known hypersensitivity to the cephalosporin class of antibiotics. In patients hypersensitive to penicillin, the possibility of allergic cross-reactions should be borne in mind. Although the relevant preclinical investigations revealed neither mutagenic nor teratogenic effects, Snare should not be used in pregnancy (particularly in the first trimester) unless absolutely indicated.

PRECAUTIONS:
As with other cephalosporins, anaphylactic shock cannot be ruled out even if a thorough patient history is taken. Anaphylactic shock requires immediate counter measures such as intravenous epinephrine followed by a glucocorticoid. In rare cases, shadows suggesting sludge have been detected by sonograms of the gallbladder.
This condition was reversible on discontinuation or completion of Snare therapy. Even if such findings are associated with pain, conservative nonsurgical management is recommended. In-vitro studies have shown that Ceftriaxone, like some other cephalosporins, can displace bilirubin from serum albumin. Caution should be exercised when considering *Snare* for hyperbilirubinemic neonates, especially prematures. During prolonged treatment the blood picture should be checked at regular intervals.

UNDESIRABLE EFFECTS: Snare is generally well tolerated.
During the use of Ceftriaxone, the following side effects, which were reversible either spontaneously or after withdrawal of the drug, have been observed:
Systemic side effects:
Gastrointestinal complaints (about 2% of cases):
Loose stools or diarrhea, nausea, vomiting, stomatitis and glossitis.
Hematological changes (about 2%):
Eosinophilia, leukopenia, granulocytopenia, hemolytic anemia, thrombocytopenia.
Skin reactions (about 1%):
Exanthema, allergic dermatitis, pruritus, urticaria, edema, erythema multiforme.
Other rare side effects:
Headache and dizziness, increase in liver enzymes, gallbladder sludge, oliguria, increase in serum creatinine, mycosis of the genital tract, shivering and anaphylactic or anaphylactoid reactions. Pseudomembranous enterocolitis and coagulation disorders have been reported as very rare side effects.
Local side effects:
In rare cases phlebitic reactions occurred after I.V administration.
These may be prevented by slow (two to four minutes) injection of the substance.
Intramuscular injection without lidocaine solution is painful.

INTERACTIONS:
No impairment of renal function has so far been observed after concurrent administration of large doses of Snare and potent diuretics (e.g. Furosemide). There is no evidence that Snare increases renal toxicity of aminoglycosides. No effect similar to that of disulfiram has been demonstrated after ingestion of alcohol subsequent to the administration of Snare. Ceftriaxone does not contain an N-methylthiotetrazole moiety associated with possible ethanol intolerance and bleeding problems of certain other cephalosporins. The elimination of Ceftriaxone is not altered by probenecid.

INSTRUCTIONS:
Store below 30°C. Protect from heat, sunlight & moisture. Use immediately after reconstitution. Keep out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

NOTE:
For intravenous application, the injection time is 2 to 4 minutes. Use only freshly prepared solutions.

PRESENTATION:

Snare Injection I.M 250 mg	:	Vial with 2 ml of 1% lidocaine solution ampoule.
Snare Injection I.M 500 mg	:	Vial with 2 ml of 1% lidocaine solution ampoule.
Snare Injection I.M 1 gm	:	Vial with 3.5 ml of 1% lidocaine solution ampoule.
Snare Injection I.V 250 mg	:	Vial with 5 ml of water for injection.
Snare Injection I.V 500 mg	:	Vial with 5 ml of water for injection.
Snare Injection I.V 1 gm	:	Vial with 10 ml of water for injection.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
تیار کرنے کے بعد فوراً استعمال کریں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

نوٹ:
وریدی انجکشن کے لیے وقت ۲ تا ۴ منٹ ہے۔
انجکشن کے لیے تازہ تیار کردہ محلول استعمال کریں۔

Manufactured by:
Pharmasol (Pvt.) Ltd.
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Lahore, Pakistan.

FOR FURTHER INFORMATION PLEASE CONTACT:

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