Triaxone

Broad-spectrum, long-acting 3rd generation cephalosporin for parenteral use

Ceftriaxone sodium is a sterile, semisynthetic, broad-spectrum cephalosporin antibiotic for intravenous or intramuscular administration.

Composition

1 vial contains sterile ceftriaxone sodium (USP) equivalent to 0.25g / 0.5g / 1g / 2g of ceftriaxone.

Properties

Microbiology

The bacterial 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 has a long serum half-life and it is highly stable to most ß-lactamases and 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 penicillinases-producing strains)
Staphylococcus epidermidis
Streptococcus pneumoniae
Streptococcus group A (*Str. pyogenes*)
Streptococcus group B (*Str. 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* (ß-lactamase negative and positive), *Citrobacter* spp., *Enterobacter* spp., (some strains are resistant), *Escherichia coli, Haemophilus ducreyi, Haemophilus influenzae* (including penicillinase-producing strains), *Haemophilus parainfluenzae, Klebsiella* spp., (including *Kl.pneumoniae*), *Moraxella* spp., *Morganella morganii, Neisseria gonorrheae* (including penicillinase-producing strains), *Neisseria meningitidis, Plesiomonas shigelloides, Proteus mirabilis, Proteus vulgaris, Providencia* spp., *Pseudomonas aeruginosa* (some strains are resistant), *Salmonella* spp., (including *S. typhi*) *Serratia* spp. (including S. *marcescens*), *Shigella* spp., *Vibrio* spp. (including *V.cholerae*), *Yersinia* spp. (including *Y.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: Bacteriodes spp. (including some strains of *B. fragilis*), *Clostridium* spp. (except *Cl. difficile*), *Fusobacterium* spp. (except *F. mortiferum* and *F. varium*), *Peptococcus* spp., *Peptostreptococcus* spp.

Note: Many strains of ß-lactamase-producing Bacteroides spp. (notably *B. fragilis)* are resistant.

Indications

Infections caused by pathogens sensitive to **Triaxone,** including:

- sepsis
- meningitis
- abdominal infections (peritonitis, infections of the biliary and gastrointestinal tracts)
- infections of the bones, joints, soft tissue, skin and wounds
- infections in patients with impaired defence mechanisms
- 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

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

Neonates, infants, and children up to twelve years old:
The following dosage schedules are recommended for once daily administration.
Neonates (up to two weeks): A daily dose of 20-50mg/kg body weight, not to exceed 50mg/kg, on account of 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 old): A daily dose of 20-80mg/kg.
For children with body weights of 50kg or more, the usual adult dosage should be used.
Intravenous doses of 50mg 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 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 **Triaxone** should be continued for a minimum of 48-72 hours after patient has become afebrile or evidence of bacterial eradication has been obtained.

Combination therapy

Synergy between **Triaxone** 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 100mg/kg (not to exceed 4g) 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 nonpenicillinase-producing strains), a single i.m. dose of 250mg **Triaxone** is recommended.

Perioperative prophylaxis

To prevent postoperative infections in contaminated or potentially contaminated surgery, the recommended approach is a single dose of 1-2g **Triaxone** administered 30-90 minutes prior to surgery. In colorectal surgery, concurrent (but separate) administration of **Triaxone** 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 **Triaxone** provided hepatic function is intact. Only in cases of preterminal renal failure (creatinine clearance <10mL/min.) should the **Triaxone** dosage not exceed 2g daily. In patients with *liver damage*, there is no need for the dosage to be reduced provided renal function intact. In case 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.

Directions for use

Reconstituted solutions retain their physical and chemical stability for six hours at room temperature (25°C) or (24 Hours at 5°C). As a general rule, however, the solutions should be used immediately after preparation. They range in colour from pale yellow to amber, depending on the concentration and the length of storage. This characteristic of the active ingredient is of no significance for the efficacy or tolerance of the drug.

Intramuscular injection

For i.m. injection, **Triaxone** 0.25g or 0.5g is dissolved in 2mL, and **Triaxone** 1g in 3.5mL, of 1% lidocaine solution and administered by deep intragluteal injection. It is recommended that no more than 1g be injected on either side. The lidocaine solution must never be administered intravenously.

Intravenous injection

For i.v. injection, **Triaxone** 0.25g or 0.5g is dissolved in 5mL, and **Triaxone** 1g in 10mL, of sterile water for injection and then administered by i.v. injection lasting two to four minutes.

Intravenous infusion

The infusion should last at least 30 minutes. For i.v. infusion, 2g **Triaxone** are dissolved in 40mL of one of the following calcium-free infusion solutions: sodium chloride 0.9%, sodium chloride 0.45% + dextrose 2.5%, dextrose 5%, dextrose 10%, levulose 5%, dextran 6% in dextrose, or sterile water for injections.

Triaxone solutions should 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.

Contraindications

Ceftriaxone 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 pre-clinical investigations revealed neither mutagenic nor teratogenic effects, ceftriaxone should not be used in pregnancy (parti-cularly 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 countermeasures 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 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 *ceftriaxone* for hyperbilirubinemic neonates, especially prematures.

During prolonged treatment the blood picture should be checked at regular intervals.

No geriartrics-specific problems have been documented to date. However, elderly patients are more likely to have an age-related decrease in renal function, which may require an adjustment of dosage and/or dosing interval.

Ceftriaxone is distributed into breast milk in low concentration. However, no problem has been documented to date.

Side Effects

Ceftriaxone 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, gall bladder 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.

Overdosage

Since there is no specific antidote, treatment of ceftriaxone overdose should be symptomatic.

Drug interactions

No impairment of renal function has so far been observed after concurrent administration of large dose of ceftriaxone and potent diuretics (e.g. furosemide). There is no evidence that ceftriaxone increases renal toxicity of aminoglycosides. No effect similar to that of disulfiram has been demonstrated after ingestion of alcohol subsequent to the administration of ceftriaxone.

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.

Presentation

Triaxone sterile powder for injection is available in vials containing 0.25g, 0.5g, 1g and 2g ceftriaxone.

* *Store at room temperature not exceeding 25°C, away from heat and light.*

THIS IS A MEDICAMENT

- Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of the reach of children.

Council of Arab Health Ministers,
Union of Arab Pharmacists.

Any information ? Call Our Toll Free No. (971) 800-4994

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