Product Information
Company logo

CYTAXIN
CEFOTAXIME POWDER FOR SOLUTION FOR INJECTION 0.5G & 1G

Composition:

Cytaxin 0.5g: Each vial of dry powder contains 524mg cefotaxime sodium, corresponding to 500mg cefotaxime.

Cytaxin 1g: Each vial of dry powder contains 1048mg cefotaxime sodium, corresponding to 1000mg cefotaxime.

Description:

Cytaxin 0.5g: Off-white to pale yellow crystalline powder. After reconstitution, the solution should be pale yellow to light amber colour.

Cytaxin 1g: Off-white to pale yellow crystalline powder. After reconstitution, the solution should be pale yellow to light amber colour.

Properties
Cytaxin is an antibiotic of the cephalosporin group and has a bactericidal effect. Its antibiotic activity against Gram-negative rod-shaped bacteria is many times stronger than that of the traditional cephalosporin and penicillins. In most pathogens, its minimum bactericidal concentration is slightly higher than its minimum inhibitory concentration.
Resistance develops slowly, as with penicillin. In vitro studies of combinations of Cefotaxime with aminoglycoside antibiotics reveal a synergistic or additive effect.
The serum protein binding is 32 – 50%, depending on the method used,
After injection, high Cefotaxime concentrations clearly exceeding the susceptibility of most pathogens are obtained in serum, tissues, and body fluids.
Cefotaxime is excreted mainly through the kidneys in an antibacterially active form.

Indications
Severe infections caused by cefotaxime-susceptible pathogens;
Infections
- of the respiratory tract, including nose and throat
- of the ear
- of the kidneys and urinary tract,
- of the skin and soft tissues
- of the bones and joints,
- of the genital organs including gonorrhoea,
- of the abdominal region

Sepsis, endocartitis, meningitis: for perioperative prophylaxis in patients who are at increased risk from infection, and for the prophylaxis of infections in patients with reduced resistance.
Cefotaxime is generally effective against the following pathogens: Staphylococci, aerobic and anaerobic streptococci, Streptococcus pneumonia, Neisseria spp., Haemophilus influenzae, Eschericha coli, Citrobacter spp., Salmonella spp., Klebsiella spp., Enterobacter areogenes,

Serratia spp., indole-positive and indole-negative Proteus spp., Yersinia entercolitica, Clostridium spp., and Bacteroides spp.
Pathogens with varying susceptibility are: Streptococcus faecalis, Enterobacter colacae, Pseudomonas aeruginosa, and Bacteroides fragilis.
There are not yet sufficient clinical experience with Salmonella typhi and parathyphi A and B infections. Cefotaxime is not effective against Treponema pallidum and Clostridium difficile.

Combination therapy: In severe, life-threatening infections, the combination of Cefotaxime with aminoglycosides is indicated without awaiting the results of sensitivity tests. The two preparations must be administered separately.
Infections with Pseudomonas aeruginosa may require concomitant treatment with other antibiotics effective against Pseudomonas.

Contraindications

- Hypersensitivity to cephalosporins

For pharmaceutical forms containing lidocaine:

- Known history of hypersensitivity to lidocaine or other local anesthetics of the amide type
- Non-paced heart block
- Severe heart failure
- Administration by the intravenous route
- Infants aged less than 30 months of age

Special warnings and precautions
The prescription of cephalosporins necessitates preliminary enquiry with regard to allergic diathesis and particularly with regard to hypersensitivity to beta-lactam antibiotics.
If a hypersensitivity reaction occurs, treatment must be stopped.
The use of cefotaxime is strictly contra-indicated in subjects with a previous history of immediate-type hypersensitivity to cephalosporins. In any doubt, it is essential that a physician be present during the first administration, to treat any possible anaphylactic reaction.
In patients hypersensitive to penicillin or other beta-lactam antibiotics, the possibility of cross-sensitivity exists.
Diarrhoea, particularly if severe and/or persistent, occurring during treatment or in the initial weeks following treatment with various, but especially broad spectrum antibiotics, may be symptomatic of Clostridium difficile-associated disease, the most severe form of which is pseudomembranous colitis. The diagnosis of this rare but possibly fatal condition is confirmed by endoscopy and/or histology. Screening of faeces for this pathogen and above all its cytotoxin, is the best way to diagnose a Clostridium difficile-associate disease.
If a diagnosis of pseudomembranous colitis is suspected, cefotaxime should be stopped immediately and appropriate specific antibiotic therapy should be started without delay (e.g. oral vancomycin or metronidazole). Formulations containing lidocaine: (See Contra-Indications). Do not inject by I.V. route the Cefotaxime I.M. which contains lidocaine. The dosage should be modified according to the creatinine clearance calculated, if necessary on the basis of serum creatinine (see Dosage and Administration). Renal function must be monitored in patients treated concomitantly with aminoglycosides.
Leukopenia, neutropenia and, more rarely, bone marrow failure, pancytopenia, or agranulocytosis may develop during treatment with cefotaxime.
For courses of treatment lasting longer than 10 days, blood counts should therefore be monitored and treatment discontinuation should be considered in case of abnormal results Beta-lactams, including cefotaxime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment.

Administration of antibiotics, especially if prolonged, may lead to the proliferation of resistant micro-organisms. The patient's condition must therefore be checked at regular intervals. If a secondary infection occurs, appropriate measures must be taken.
The sodium content of Cefotaxime (2.09mmol/g cefotaxime) should be taken into consideration.
Some adverse effects (see under 'Adverse effects') may impair the ability to concentrate and react, and, therefore, constitute a risk in situations where these abilities are of particular importance (e.g. operating a vehicle or machinery).
Use in pregnancy and lactation: Although animal experiments did not reveal any malformation or toxic effect on the fetus, Cefotaxime should not be used during pregnancy, especially in the first three months, unless strictly indicated.
As cefotaxime is excreted in breast milk, either breast-feeding or treatment of the mother with Cefotaxime should be discontinued.

Adverse effects

System Organ Class	Very common (≥ 1/10)	Common (≥ 1/100 - < 1/10)	Uncommon (≥ 1/1000 - < 1/100)	Rare (≥ 1/10000 - < 1/1000)	Very rare (< 1/10,000)	Not known (cannot be estimated from available data)*
Infections and infestations						**Superinfection**
Blood and the lymphatic system disorders			**Leukopenia** **Eosinophilia** **Thrombo-cytopenia**			**Bone marrow failure** **Pancytopenia** **Neutropenia** **Agranulocytosis** **Haemolytic anaemia**
Immune system disorders			**Jarisch-Herxheimer reaction**			**Anaphylactic reactions** **Angioedema** **Bronchospasm** **Anaphylactic shock**
Nervous system disorders			**Convulsions**			**Encephalopathy** **Headache** **Dizziness**
Cardiac disorders						**Arrhythmia** following rapid bolus infusion through central venous catheter
Gastro-intestinal disorders			**Diarrhea**			**Nausea** **Vomiting** **Abdominal pain** **Pseudomembranous colitis**
Hepato-bilary disorders			**Increase in liver enzymes (ALAT, ASAT, LDH, gamma-GT and/or alkaline phosphatase) and/or bilirubin**			**Hepatitis** (sometimes with jaundice)

Skin and subcutaneous tissue disorders			**Rash** **Pruritus** **Urticaria**			**Erythema multiforme** **Stevens-Johnson syndrome** **Toxic epidermal necrolysis** **Acute generalized exanthematous pustulosis** (AGEP)
Renal and Urinary disorders			**Decrease in renal function/ increase of creatinine,** particularly when co-prescribed with aminoglycosides			**Acute renal failure** **Interstititial nephritis**
General disorders and administration site conditions	*For IM formulations:* **Pain at the injection site**		**Fever** **Inflammatory reactions at the injection site, including phlebitis/ thrombophlebitis**			*For IM formulations (since the solvent contains lidocaine):* **Systemic reactions to lidocaine**

Hepatobiliary disorders
Increase in liver enzymes (ALAT, ASAT, LDH, gamma-GT and/or alkaline phosphatase) and/or bilirubin have been reported. These laboratory abnormalities, which may also be explained by the infection, may rarely exceed twice the upper limit of the normal range and elicit a pattern of liver injury, usually cholestatic and most often asymptomatic.

Superinfection:
As with other antibiotics, the use of cefotaxime, especially if prolonged, may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Jarisch-Herxheimer
As reported with other antibiotics for the treatment of borreliosis a Jarisch-Herxheimer reaction may develop during the first days of treatment.
The occurrence of one or more of the following symptoms has been reported after several week's treatment of borreliosis: skin rash, itching, fever, leucopenia, increase in liver enzymes, difficulty of breathing, joint discomfort. To some extent, these manifestations are consistent with the symptoms of the underlying disease for which the patient is being treated.
For IM formulations:

If the solvent contains lidocaine, systemic reactions to lidocaine may occur, especially in the event of inadvertent intravenous injection or injection into highly vascularized tissue or in the event of an overdose

Interactions
By delaying renal excretion, the concurrent administration of probenecid increases the concentration of cefotaxime in serum and prolongs its duration of action.

Patients under concurrent of subsequent medication with potentially nephrotoxic drugs such as furosemide and aminoglycosides should be closely monitored for renal function.
Interference with laboratory tests: a false-positive result for the Coombs' test may be obtained in rare cases during treatment with Cefotaxime. Non-enzymatic methods for the determination of glycosuria may also give a false-positive result. Glycosuria should therefore be determined by enzymatic methods during Cytaxin treatment.

Dosage
Dosage, mode, and frequency of administration depend on the severity of the infection, susceptibility of the pathogen, and condition of the patient.
Cytaxin is an injectable antibiotic administered by the IM or IV rout (given by slow injection or infusion).

Dosage in infants and children up to 12 years old, unless otherwise prescribed, are given daily doses of 50 – 100 mg/kg body weight, divided into equal doses at intervals of 12-6 hours. In individual cases, patients with life-threatening infections were treated with daily amounts of 150 – 200 mg/kg body weight: these doses were well tolerated. Since renal clearance is not yet fully developed in premature infants, daily doses of 50 mg/kg body weight should not be exceeded.
For the perioperative prophylaxis of infections, one of the above single doses is administered 30 – 60 minutes before the start of the surgery. Depending on the risk of infection, the same dose may be repeated.
Dosage in adults and children over 12 years old

Indications	Unit dose	Dose interval	Route	Daily Dose
- Gonorrhoea uncomplicated	0.5 or 1 g	Single dose	IM	0.5 or 1 g
- Uncomplicated/ moderate infections	1 to 2 g	8h or 12 h	IM or IV	2 to 6 g
- Severe infections	2 – 3 g	6h or 8 h	IV	6 to 12 g

Where infection is caused by strains that are not usually sensitive, antibiotic sensitivity testing is the only means of confirming the efficacy of cefotaxime.
For perioperative prophylaxis of infections, the administration of 1 – 2g Cefotaxime 30 – 60 minutes before the start of surgery is recommended. Depending on the risk of infection, the same dose may be repeated.
In patients with a creatinine clearance less than 10 ml/minute, after an initial normal dose, the maintenance doses have to be reduced to one half of the normal dose, without change of the dose interval

Dosage in patients with impaired renal function
Haemodialysis: 1 to 2 g daily, depending on the severity of the infection; on dialysis days, Cefotaxime must be given after dialysis.
In patients undergoing peritoneal dialysis: 1 to 2 g daily, depending on the severity of the infection; cefotaxime is not removed by peritoneal dialysis.
***Duration of treatment*:** The duration of treatment depends on the patient's response. It should be continued for at least three days after the body temperature has returned to normal.

Administration
Intravenous injection: For intravenous injection, the contents of one vial of Cytaxin 500mg are dissolved in at least 2 ml water for injections: Cytaxin 1 g are dissolved in at least 4 ml water for injections and Cefotaxime 2 g are dissolved in at least 10 ml water for injection and best use immediately. The solution is then injected over a period of 3 to 5 minutes. During post-marketing

surveillance, potentially life-threatening arrhythmia has been reported in a very few patients who received rapid intravenous administration of cefotaxime through a central venous catheter.
Intravenous infusion: If higher doses are required, they may be administered by intravenous infusion:
For short infusion, 2 g Cefotaxime are dissolved in 40 ml water for injections or one of the usual infusion solutions (0.9% Sodium Chloride Injection, 5% Dextrose Injection, 5% Dextrose and 0.9% Sodium Chloride injection, Lactated Ringer's Injection) and then administered over approximately 20 minutes.
For continuous drip infusion, 2 g Cefotaxime are dissolved in 100 ml of one of the above-mentioned infusion solutions and then administered over 50 – 60 minutes.
Cefotaxime should not be mixed with other antibiotics in the same syringe or with other infusion solution; this applies above all to aminoglycosides.
Sodium bicarbonate solutions must not be mixed with Cefotaxime.
Intramuscular administration: The contents of one vial of Cytaxin 1 g are dissolved in 4 ml water for injections; the solution is then injected deep into the gluteus muscle.
It is advisable not to inject more than 4 ml into either side. Intravenous injection is recommended if the daily dose exceeds 2 g or if Cefotaxime 1 g is administer more than twice daily.

Pain resulting from the i.m. injection can be prevented by dissolving Cytaxin 1 g in the corresponding amount of 1% lidocaine solution, but in this case intravascular injection must be strictly avoided.

The solution should be used immediately after reconstitution. Aseptic handling is particularly important if the solution is not intended for immediate use.

1. *For intramuscular and intravenous injection*
Cefotaxime sterile powder after reconstitution in water for injection is chemically stable:
- up to 12 hours at room temperature (not exceeding 25ºC)
- up to 12 hours under refrigerated conditions (5 ºC ± 3 ºC)
2. *For infusion in infusion fluids*
Cefotaxime sterile powder is chemically stable at room temperature (not exceeding 25ºC) and at refrigerated conditions (5 ºC ± 3 ºC)
- up to 12 hours after reconstitution in the usual infusion solution (0.9% Sodium Chloride Injection, 5% Dextrose Injection, 5% Dextrose and 0.9% Sodium Chloride injection, Lactated Ringer's Injection).

Storage
Store at or below 30 ºC. Protect from light.

Expiry date
Do not use later than date of expiry.

Keep medicines out of reach of children.
Emergency measures to be taken in the event of anaphylactic shock
Generally, the following emergency procedure is recommended: At the first signs (sweating, nausea, cyanosis), interrupt the injection immediately, but leave the venous cannula in place or perform venous cannulation. In addition to the usual emergency measures, ensure that the patient remains lying down, with the legs raised and airways patent.
Emergency drug therapy
Immediately epinephrine (adrenaline) i.v. : In the first instance, slowly inject 1 ml of a solution containing 0.1 mg epinephrine per ml while monitoring pulse and blood pressure (watch for disturbances in cardiac rhythm). Repeat as required.

Then volume substitution i.v., e.g. plasma expanders, human albumin, balanced electrolyte solution.
Subsequently glucocorticoids i.v., e.g. 250 – 1000 mg methylprednisolone. Repeat as required.
The dosage recommendations refer to adults of normal weight. In children, the reduction of dose should be in relation to body weight.
Other therapeutic measures, e.g. artificial respiration, oxygen inhalation, antihistaminics.

Presentations
1g: Powder for Solution for Injection is filled in 15 mL clear moulded Type-II glass vials stoppered with 20 mm bromobutyl rubber stoppers sealed with 20 mm flip-off aluminium seals and labeled, packed in printed carton with package insert. 1 vial packed in carton.

0.5g: Powder for Solution for Injection is filled in 15 mL clear moulded Type-II glass vials stoppered with 20 mm bromobutyl rubber stoppers sealed with 20 mm flip-off aluminium seals and labeled, packed in printed carton with package insert. 1 vial packed in carton.

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