Claforan® 1.0 g

Powder (or powder and solvent) for solution for injection or infusion

cefotaxime sodium

Read all of this leaflet carefully before you start using this medicine.
- keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you personally. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects become serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT CLAFORAN IS AND WHAT IT IS USED FOR

Pharmaceutic group

Claforan (an antibiotic from the group called cephalosporins) is a medicine used to fight bacteria.

Therapeutic indications

It is used to kill the bacteria that cause the following severe, acute and chronic infections:
- respiratory tract infections
- ear, nose and throat infections
- kidney and urinary tract infections
- skin and soft tissue infections
- bone and joint infections
- infections of the genitals, including gonorrhea
- abdominal infections (including peritonitis)
- inflammation of the membranes surrounding the brain and spinal cord (meningitis)
- blood poisoning (sepsis)
- inflammation of the inner layer of the heart (endocarditis)
- Lyme disease (particularly stage II and III) (infection mainly transmitted by tick bites) as well as in prevention of infections in a surgical context in patients with a high risk of infection.

2. BEFORE YOUR USE CLAFORAN

Contraindications

Do not use Claforan in the following situations:
- if you are allergic to cefotaxime or to one of the other ingredients of Claforan.
- if you have known allergy to another cephalosporin.
- if you have ever had an acute or severe allergic reaction to penicillins or other beta lactam antibiotics. There may be cross-reactions between penicillins and cephalosporins.

Claforan mixed with lidocaine for intramuscular injection must not be used in children under the age of 1 year.

Appropriate precautions for use ; special warnings

Special caution is necessary when using Claforan in the following situations:

– if you are allergic to penicillins or other beta lactam antibiotics in any way (for contraindications in patients with known allergic reactions, see "Claforan must not be used in the following situations" above).

– if you are prone to allergic reactions (e.g. hay fever, bronchial asthma, hives) or if you have ever had allergy, you have a high risk of serious (exceptionally even fatal) allergic reactions. If you develop a feeling of tightness in your chest, or if you feel dizzy, unwell or weak, it could be a sign of such an allergic reaction (see Section 4 "Possible side effects").
If you have an allergic reaction, treatment must be stopped.

– if you notice changes in your skin or mucous membranes while using this treatment (see Section 4 "Possible side effects"), inform your doctor immediately, as Claforan can cause serious drug-induced skin reactions that require treatment.

– if you develop severe, persistent diarrhea during or up to several weeks after treatment, inform your doctor immediately, as diarrhea in its most severe form (called pseudomembranous colitis) could in certain circumstances possibly lead to death and must be treated. Do not take any medicines that inhibit bowel function.

– if you know that you have impaired kidney function, inform your doctor, so that he or she can keep this in mind when establishing the dosage, if necessary.

– if you are treated or will subsequently be treated with medicines that could be harmful to the kidneys (such as aminoglycosides), kidney function should be monitored by your doctor, as an increase in effects that could be harmful to the kidneys can occur with these kinds of medicines.

– if you are being treated with high doses, particularly if you also have impaired kidney function, this can lead to brain disturbances, along with, for example, movement disorders, seizures or consciousness disorders. Inform your doctor immediately if you have this kind of reaction.

– if your treatment lasts longer than 7 to 10 days, blood tests should be performed, as changes in the blood may occur (see Section 4 "Possible side effects").

– if you have signs of a new infection (e.g. fungal infection of the mucous membranes with redness and white deposits): Any time antibiotics are used, the number of bacteria that are resistant to the medicine being used can increase. Watch for signs of a new infection and inform your doctor if necessary.

Important information about certain other ingredients of Claforan
1 vial of Claforan 1.0 g contains approximately 2.1 mmol (48 mg) of sodium. You should take this into account if you need to follow a low-salt diet.

Taking other medicines

Please tell your doctor or pharmacist if you are taking/using or have recently taken/used any other medicines, including medicines obtained without a prescription.

Other antibiotics
Using certain other antibiotics at the same time can reduce the effect of Claforan. You should therefore inform your doctor if you are taking or have recently taken another antibiotic.

Medicines that could potentially harm the kidneys and loop diuretics
Claforan can increase the harmful effects of aminoglycosides and strong diuretics (e.g. furosemide and ethacrynic acid) on the kidneys. Kidney function must be monitored when these medicines are administered at the same time as Claforan, particularly if you have impaired kidney function.

Probenecid
Administration of probenecid at the same time as Claforan can cause elevated cefotaxime concentrations in the blood, and therefore a prolonged effect. This is because probenecid slows the elimination of Claforan by the kidneys.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking/using any medicines.

Sufficient data are not available concerning use of Claforan in pregnant women.
Animal experiments have yielded no evidence that cefotaxime could have harmful effects on the fetus.
Nevertheless, Claforan should only be used during pregnancy after a careful evaluation of the benefit/risk ratio by the treating doctor, particularly during the first trimester.

Only small amounts of cefotaxime pass into breast milk. When Claforan is used during breast-feeding, intestinal flora imbalance with diarrhea, fungal infection and possibly sensitization can occur in the infant.

Driving and using machines

Based on clinical experience to date, Claforan used at low to medium doses has no effect on the ability to concentrate and react.

Very rarely, seizures, consciousness disorders, movement disorders and dizziness have been reported when high doses are used, primarily in patients who also have impaired kidney function. You should therefore not drive cars or operate machines if you notice any such side effects.

3. HOW TO USE CLAFORAN

Claforan should always be used exactly as your doctor has instructed.
The dose, method of administration and interval between injections are based on the effect of the drug on the bacteria, the severity of your infection and your general condition.
Unless your doctor prescribes otherwise, the usual dosage is as follows:

Adults and children over 12 years of age generally receive 1 to 2 g of cefotaxime every 12 hours. In severe cases, the daily dose of cefotaxime can be increased to up to 12 g. Daily doses of up to 6 g of cefotaxime can be divided into at least two separate doses administered at 12 hour intervals. Higher daily doses must be divided into at least 3 to 4 separate doses administered at 8 or 6 hour intervals.

The following table provides guidelines for dosing:

Type of infection	Single dose of cefotaxime	Dosing interval	Daily dose of cefotaxime
Typical infections suspected or shown to be caused by sensitive bacteria	1 g	12 h	2 g
Infections suspected or shown to be caused by various bacteria with high to intermediate sensitivity	2 g	12 h	4 g
Bacterial infections of unknown origin and location, and critical condition of the patient	2-3 g	8 h up to 6 h up to 4 h	6 g up to 8 g up to 12 g

To treat gonorrhea in adults, a single 0.5 g intramuscular dose of cefotaxime is to be administered. A higher dose may be necessary for bacteria that are less sensitive to the drug. Syphilis should be screened for before beginning treatment.

To prevent infections in patients having surgery: 1 to 2 g of cefotaxime should be administered 30 to 60 minutes before the beginning of the operation. The same dose can be administered repeatedly depending on the risk of infection.

To treat Lyme disease, a daily dose of 6 g of cefotaxime (for 14 to 21 days) is to be administered. The daily dose is usually administered in 3 divided doses (2 g of cefotaxime 3 times daily), but in some cases it can be administered in 2 divided doses (3 g of cefotaxime twice daily). These dosage recommendations are based on individual observations and not controlled clinical studies.

Combination treatment with other antibiotics
Claforan in combination with aminoglycosides is indicated in serious, life-threatening infections without an antibiogram. In this case, kidney function must be monitored.
In infections caused by *Pseudomonas aeruginosa*, combination treatment with other antibiotics that are effective against *Pseudomonas* may be indicated. Combined use of Claforan with other suitable antibiotics can also be indicated to prevent infections in patients with weakened immune systems.

Infants and children up to 12 years of age receive 50 to 100 mg (up to 150 mg) of cefotaxime per kg body weight per day, depending on the severity of the infection. The daily dose is to be given as 2 or more equally divided doses, which are to be given at 12 (to 6) hour intervals. In some cases, particularly in life-threatening situations, it may be necessary to increase the daily dose to 200 mg of cefotaxime per kg body weight.

In premature infants, doses of 50 mg of cefotaxime per kg body weight per day should not be exceeded, as kidney function is not fully developed.

In patients with severely impaired kidney function (creatinine clearance of 10 ml/min or less), the initial dose (the first dose at the beginning of treatment) is to be the same as in patients with healthy kidneys. The maintenance dose is to be reduced to half the usual dose. In patients with creatinine clearance (excretion of creatinine from the blood) of 5 ml/min or less, a reduction in the maintenance dose to 1 g of cefotaxime (administered as 2 divided doses at 12 hour intervals) appears to be adequate. These recommendations are based on experience in adults.

As cefotaxime is eliminated to a large extent by hemodialysis, an additional dose should be administered after the dialysis session in patients undergoing dialysis.

Claforan is administered intravenously (in a vein). It can also be administered intramuscularly.

Elderly patients
In elderly patients, kidney function must be monitored carefully and the dose adjusted if necessary.

Intravenous injection
For intravenous injection, 1 g of cefotaxime is dissolved in at least 4 ml of water for injection, and then injected directly into the vein for 3 to 5 minutes.

Infusion
For a rapid infusion, 1 or 2 g of cefotaxime are dissolved in 40 to 50 ml of water for injection or an appropriate infusion solution, and then infused intravenously for approximately 20 minutes.
For an IV drip infusion, 2 g of cefotaxime are dissolved in 100 ml of isotonic sodium chloride or glucose solution and then infused intravenously for 50 to 60 minutes. Another appropriate infusion solution can also be used for dissolution.

Intramuscular injection
For intramuscular injection, 1.0 g of cefotaxime is dissolved in 4 ml of water for injection then given by deep injection in the gluteal muscle. Pain during the intramuscular injection can be avoided by dissolving 1.0 g of cefotaxime in 4 ml of 1% lidocaine solution. Intravascular injection (injection into a blood vessel) is to be avoided in this case, as lidocaine administered into a blood vessel can lead to restlessness, rapid heart rate, cardiac conduction disorders (disruption of the electrical activity of the heart) as well as vomiting and spasms. Claforan mixed with lidocaine should not be used in children under 1 year of age.
No more than 4 ml should be injected on one side. Intravenous injection is recommended if the daily dose of 2 g of cefotaxime is exceeded or if the drug is injected more than twice daily.

Mixing of the solution with other substances
Unless chemical and physical compatibility with other solutions for infusion has been proven, cefotaxime solution should generally be administered separately.

Major incompatibilities
Claforan is not compatible with the following:
– sodium bicarbonate solution,
– solutions for infusion with a pH higher than 7,
– aminoglycosides.

Claforan should generally not be injected in the same syringe as other antibiotics or medicines. Claforan must not be mixed with aminoglycoside antibiotics in an infusion set or syringe.

Compatibility with infusion solutions
Claforan can also be dissolved in sodium lactate solution or Ringer's solution.

Treatment duration is based on the course of the disease.

If you use more Claforan than you should

In very rare cases, and generally only in patients who also have kidney failure, very high doses of cephalosporins can cause seizures (as in epilepsy), excitation (central nervous system disorder) and twitching.
If Claforan is injected too quickly via a central venous catheter (CVC) (in less than 1 minute), it can cause severe heart rhythm disorders.
If you think you have used too much Claforan, tell your doctor or medical staff immediately.

If you forget to take Claforan

You should make up for a missed dose, unless it is time for the next regular dose.

If you have any other questions about using this medicine, please consult your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Claforan can cause side effects, although not everybody gets them.

If you notice the following serious side effects, you must inform a doctor or nurse immediately and stop using Claforan, as you need urgent medical treatment:

Uncommon (1 to 10 in 1000 treated patients)
– seizures.

Unknown frequency (frequency cannot be determined based on available data)
– severe acute allergic reactions including life-threatening shock, as well as swelling (angioedema) and constriction of the airways (bronchospasm). If you develop a feeling of tightness in your chest, or if you feel dizzy, unwell or weak, it could be a sign of such an allergic reaction.
– skin reactions with blisters (erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis).
– severe, persistent diarrhea or bloody stools resulting from possibly life-threatening bowel inflammation.
– destruction of red blood cells (hemolytic anemia), causing urine to be a brown-red color.

If you notice the following serious side effects, you must inform a doctor or nurse immediately, as you probably need medical treatment:

Unknown frequency (frequency cannot be determined based on available data)
– jaundice, which may be a sign of liver inflammation.
– severe drop in the number of certain white blood cells (agranulocytosis). This is noticeable because of acute signs of infection.

Inform your doctor, particularly if one of the side effects listed below becomes serious or lasts longer than a couple of days:

Very common (more than 1 in 10 treated patients):
– pain at the injection site, or hardening at the injection site following intramuscular administration.

Common (more than 1 in 100 treated patients):
– allergic reactions such as skin rash, itching or hives.
– impaired kidney function, e.g. increase in creatinine and urea concentrations in the blood.
– fever.
– inflammatory reactions at the injection site including inflammation of the vein (phlebitis/thrombophlebitis).
– joint disorders (e.g. swelling).

Uncommon (1 to 10 in 1000 treated patients)
– increase in the number of eosinophil white blood cells (eosinophilia).
– decrease in the number of platelets (thrombocytopenia) and certain white blood cells (leukopenia, granulocytopenia).
– Jarisch-Herxheimer reaction (see explanation below).
– diarrhea.
– loss of appetite, nausea, vomiting, abdominal pain.
– increase in bilirubin (bile pigment in the blood) and/or liver enzyme levels in the blood (ALT, AST, gamma-GT, alkaline phosphatase, LDH).
– kidney inflammation (interstitial nephritis).
– secondary infection caused by bacteria or fungi (e.g. in the mouth or vagina).

Unknown frequency (frequency cannot be determined based on available data)
– decrease in the number of certain white blood cells (neutropenia).
– rapid heart rate, heart rhythm disorders (following rapid intravenous administration).
– excitation (central nervous system disorder), consciousness disorders, movement disorders, muscle twitching (particularly in patients with impaired kidney function).
– headache.
– dizziness.
– intolerance reactions such as a feeling of hotness or sickness during rapid intravenous administration.

Jarisch-Herxheimer reaction: Jarisch-Herxheimer reaction can develop at the beginning of treatment for spirochete infections (e.g. Lyme disease) and occur along with fever, shivering, headache and joint disorders.
In patients treated for Lyme disease for several weeks with Claforan, one or more of the following symptoms has been reported: skin rash, itching, fever, decrease in number of white blood cells, increase in liver enzymes, respiratory disorders, joint disorders. To some extent, these symptoms are consistent with the symptoms of the underlying disease, for which the patient is being treated.

If you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE CLAFORAN

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the box and vials after "EXP".

Store the vials in the original package to protect from light, at a temperature no higher than 30°C.

The solution is chemically and physically stable for 12 hours at 30°C after preparation. To avoid contamination with bacteria or other agents, the solution should be used immediately. If the solution is not used immediately, the user is responsible for the storage time and conditions until it is used. Even if the solution is prepared under controlled and proven aseptic conditions, the storage time should generally not exceed 24 hours at 2 to 8°C.

6. FURTHER INFORMATION

What Claforan contains:
The active substance is: cefotaxime sodium.
1 vial contains 1.048 g of cefotaxime sodium (equivalent to 1.0 g of cefotaxime).
The other ingredients are: water for injection as solvent (note: packs without solvent are also available).

What Claforan looks like and contents of the pack:
White to yellowish-white powder (or powder and solvent) for preparation of a solution for injection or infusion.
Pack sizes: 1 vial and 1 ampoule containing 4 ml of water for injection.

Marketing Authorization Holder
Sanofi-Aventis Deutschland GmbH
65926 Frankfurt am Main, Germany

Manufacturer
S.C. Zentiva S.A.
B-dul Theodor Pallady nr. 50, sector 3, Bucureşti, cod 032266, Romania

This leaflet was last revised in October 2012.