Package leaflet: Information for the patient

Kefadim 1 g powder for solution for injection
(ceftazidime)

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.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leflet

1. What Kefadim is and what it is used for

Kefadim is an antibiotic which killing bacteria that cause infections. It works by suppressing the synthesis of their cell wall.

Kefadim is used to treat various types of infections including:
- Respiratory infections, incl. lung infections in patients with cystic fibrosis;
- Infections of the urinary system, such as cystitis and kidney infections;
- Infections of the skin and soft tissues;
- Infections of the bones and joints;
- Gastro-intestinal, biliary and abdominal infections;
- Infections related to hemodialysis and peritoneal dialysis;
- Sepsis, bacteremia (blood infections);
- Peritonitis (infection of the lining of the abdomen);
- Bacterial meningitis (infection of the meninges);

Kefadim can be used alone as a first-line treatment until the results of the microbiological test.

If necessary, Kefadim may be used in combination with an aminoglycoside or other beta-lactam antibiotic or an antibiotic active against anaerobes when the presence of *Bacteroides fragilis* is suspected.

2. What do you need to know before you are given Kefadim

Do not use Kefadim
- if you are allergic to ceftazidime, cephalosporines, penicillin or any of the other ingredients of this medicine (listed in section 6).

In patients with allergy to penicillin or other β-lactam antibiotics, the product should be used with caution and should not be used in case of hypersensitivity. In case of severe hypersensitivity reactions, adrenaline, hydrocortisone, antihistamines and, if necessary, other emergency measures should be used.

Warnings and precautions

Talk to your doctor or pharmacist before using Kefadim.

As with other broad-spectrum antibiotics, prolonged use of the product may lead to the development of resistant microorganisms or fungi. This may require discontinuation of treatment and additional measures.

During treatment, some strains of *Enterobacter* and *Serratia* may acquire resistance to the product. Therefore, sensitivity should be monitored periodically.

Cases of pseudomembranous colitis have been reported with all broad-spectrum antibiotics, incl. in cephalosporins. This should be taken into account in patients who develop diarrhea during treatment. When the diagnosis of pseudomembranous colitis is confirmed, treatment with the product should be discontinued and other appropriate treatment instituted.
In case of renal impairment, lower doses should be administered as shown in the tables.

Other medicines and Kefadim
Tell you doctor or pharmaciest, if you are taking, have recently taken or might take any other medicines.

The product should be used with caution in patients taking medicines that are toxic to the kidneys, such as aminoglycosides or diuretics (furosemide), as the combination may adversely affect renal function.
Co-administration of ceftazidime with chloramphenicol should anticipate the possibility of antagonism.

Kefadim with food and drinks
Kefadim intake is not affected by food and drink.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmaciest for advice before taking this medicine.
There is no evidence of an effect of ceftazidime on the fetus, but like all medicines, Kefadim should be used with caution during pregnancy only at the discretion of the treating physician.
Ceftazidime is excreted in human milk in low concentrations and should therefore be used with caution in breast-feeding women.

Driving and using machines
There are no data on the effect of Kefadim on the ability to drive and use machines.

3. How Kefadim is given

Always take Kefadim exactly as your doctor has told you. If you are not sure, talk to your doctor or pharmacist.
The dosage depends on the susceptibility, type, location and severity of the infection, as well as the age and renal function of the patient.
The recommended dose is 1 to 6 g daily for 8 or 12 hours, by intravenous (i.v.) or intramuscular (i.m.) injection; for most infections, 1 g is given every 8 hours or 2 g every 12 hours.

In urinary tract infections and uncomplicated infections: 500 mg to 1 g every 12 hours.
In very severe infections, especially in immunocompromised patients, including those with neutropenia: 2 g every 8 or 12 hours, or 3 g every 8 hours.
Adults with cystic fibrosis in Pseudomonas lung infections: doses of 100 to 150 mg/kg/24 hours in three doses.
In adults with preserved renal function, a dose of 9 g per day was used without the development of side effects.
When used for prophylaxis in prostate surgery, a dose of 1 g is given during induction of anesthesia. A second dose when removing the catheter may be considered.

Use in children and adolescents

- Babies and children over 2 months of age: 30 to 100 mg/kg/24 hours in three doses. Doses of 150 mg/kg/24 hours (max 6 g daily) in three doses can be given to immunocompromised or children with cystic fibrosis and infections, as well as children with meningitis
- Newborns and children up to 2 months of age: Doses of 25 to 60 mg/kg/24 hours in two doses. Ceftazidime may be three to four times the plasma half-life of neonates in adults.

If the child is being treated for meningitis, bladder fibrosis or if there are problems with the immune system, a higher dose of Kefadim may be needed, but it should not exceed 6 g per day.

Elderly patients:
Due to the reduced clearance of ceftazidime in severely ill elderly patients, the daily dose should not exceed 3 g, especially in patients over 80 years of age.

Patients with renal insufficiency:
Ceftazidime is excreted unchanged by the kidneys. It is recommended that the dose shpuld be reduced in patients with renal insufficiency.
An initial dose of 1 g of ceftazidime may be given. The maintenance dose should be determined after evaluation of glomerular filtration. Recommended maintenance doses of ceftazidime in renal failure:

Creatinine clearance ml/min	Serum creatinine approximate values (μmol/l) (mg/dl)	Recommended dose Ceftazidime to take (g)	Dosing interval (hours)
>50	< 150 (< 1,7)	Standard dosage	
50 – 31	150 – 200 (1,7 – 2,3)	1,0	12
30 – 16	200 – 350 (2,3 – 4,0)	1,0	24
15 – 6	350 – 500 (4,0 – 5,6)	0,5	24
<5	>500 (>5,6)	0,5	48

In patients with severe infections, the single dose given in the table above may be increased by 50% or the frequency of administration may be increased accordingly. Serum ceftazidime levels should be monitored in these patients and the minimum levels should not exceed 40 mg/l.
In children, creatinine clearance should be calculated according to body surface area or body weight.

Hemodialysis:
The serum half-life of ceftazidime during hemodialysis is 3 to 5 hours. The appropriate maintenance dose of ceftazidime should be re-administered after each dialysis session.

Peritoneal dialysis:
Ceftazidime can be used in peritoneal dialysis and in long-term outpatient peritoneal dialysis.
Ceftazidime is for parenteral administration. It can be administered in dialysis fluid (usually 125 to 250 mg per 2 l of dialysis fluid).
In patients with severe renal insufficiency on prolonged arteriovenous hemodialysis or high-speed haemofiltration in intensive care, 1 g daily or once divided doses is recommended. When using low-speed haemofiltration, the usual dose for renal insufficiency is used.

Administration:
Kefadim 1 g powder for solution for injection/infusion can be administered intravenously or by deep intramuscular injection into a voluminous muscle mass, such as the upper quadrant of the gluteal muscle or the lateral thigh.
Ceftazidime may be administered intravenously or administered to patients receiving parenteral solutions..

Physico-chemical incompatibilities
Dissolved in sodium bicarbonate for injection, ceftazidime is more unstable than other solutions for intravenous administration. Therefore, the use of sodium bicarbonate for dilution is not recommended. Do not mix aminoglycosides and ceftazidime in one syringe or system. Precipitation of the solution by adding vancomycin to dissolved ceftazidime has been described. The systems or venous catheters should be checked when using both drugs in succession.

If you are given more Kefadim than you should
Overdose can lead to neurological consequences, including encephalopathy (brain damage), seizures and coma. Peritoneal or hemodialysis may be used to lower serum ceftazidime levels. As Kefadim is used in hospital and administered by medical professionals, no cases of overdose are expected..

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
In most cases, the side effects are mild and transient.
Below are presented the observed adverse effects, depending on their frequency (very common (≥1/10), common (≥1/100 до <1/10), uncommon (≥1/1 000 до <1/100), rare (≥1/10 000 до <1/1 000), very rare (<1/10 000) and not known (frequency cannot be estimated from the available data)).

Infections and infestations
Uncommon: candidiasis (incl. vaginitis)

Disorders of the blood and lymphatic system
Common: eosinophilia and thrombocytosis;
Uncommon: leukopenia, neutropenia, thrombocytopenia (low white blood cell and platelet counts);
Very rare: lymphocytosis (increased number of lymphocytes), hemolytic anemia, agranulocytosis (increased number of granulocytes)

Vascular disorders
Common: phlebitis or thrombophlebitis when administered intravenously

Gastro-intestinal disorders
Common: diarrhoea
Very rare: unpleasant taste in the mouth;
As with other cephalosporins, pseudomembranous colitis may develop.

Immune system disorders
Very rare: anaphylaxis (including bronchospasm and/or hypotension)

Nervous system disorders
Uncommon: headache and dizziness;
Very rare: paresthesia (tingling)

Hepato-biliary disorders
Common: an increase in liver enzymes (SGTP, SGOT and alkaline phosphatase)
Very rare: jaundice

Skin and subcutaneous tissue disorders
Common: maculopapular and urticarial rash;
Uncommon: persistent itching;
Very rare: severe changes such as angioedema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis

General disorders and administration site conditions:

Common: pain and/or inflammation at the application site;
Uncommon: fever

Changes in laboratory tests:
Common: positive Coombs test;
Uncommon: increased urea and serum creatinine.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via national reporting system of Bulgarian Drug Agency. By reporting side effects, you can help provide more information on the safety of this medicine.

Contacts:
Bulgarian Drug Agency.
Bulgaria
8 Damyan Gruev Str.,
1303 Sofia
Tel.: +35 928903417
website: www.bda.bg

5. How to store Kefadim

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 carton box. The expiry date refers to the last day of that month.
Store below 25 °C.
After reconstitution, Kefadim should be stored in a refrigerator for no more than 24 hours.

Self life
3 years.

Shelf life after reconstitution: up to 24 hours at 2-8 ºC.
Do not throw away any medicines via wastewater. Ask your pharmacist to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Kefadim contains:
- The active substance is ceftazidime pentahydrate.
- The only other ingredient is sodium carbonate.

What Kefadim looks like and contents of the pack
Kefadim is a white to off-white powder, in single-dose glass vials type I, with rubber stopper and aluminum cap.
Kefadim is available in a carton box of one, ten or one hundred vials, accompanied by a patient leaflet..

Marketing Authorisation Holder and Manufacturer
Tchaikapharma High Quality Medicines Inc.
1 G. M. Dimitrov Blvd, Sofia 1172, Bulgaria
Tel.: +359 2 962 54 54
FAX: +359 2 9603 703
e-mail: info@tchaikapharma.com

For any information about this medicine, please contact the Marketing Authorization Holder:
Tchaikapharma High Quality Medicines Inc.
1 G. M. Dimitrov Blvd, Sofia 1172, Bulgaria
Tel.: +359 2 962 54 54
FAX: +359 2 9603 703
e-mail: info@tchaikapharma.com

Date of last revision of the leaflet
August, 2019