Package leaflet: Information for the patient

Cefepim MIP 1 g powder for solution for injection / infusion
Cefepim MIP 2 g powder for solution for injection / infusion
Cefepime

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cefepim MIP is and what it is used for
2. What you need to know before you use Cefepim MIP
3. How to use Cefepim MIP
4. Possible side effects
5. How to store Cefepim MIP
6. Contents of the pack and other information

1. What Cefepim MIP is and what it is used for
Cefepim MIP is an antibiotic used in adults and children. It works by killing bacteria that cause infections. It belongs to a group of medicines called *fourth generation cephalosporins*.

In adults and children over 12 years of age, including:
- Infections of the lung (pneumonia)
- Complicated (severe) infections of the urinary tract
- Complicated (severe) infections in the abdominal cavity
- Inflammation of the lining of the abdominal cavity (*peritonitis*) associated with dialysis in patients on continuous ambulatory peritoneal dialysis (CAPD)

In adults:
- Acute infections of the gallbladder

In children aged 2 months up to 12 years and with a body weight below 40 kg including:
- Complicated (severe) infections of the urinary tract
- Infections of the lung (pneumonia)
- Infections of the membranes covering the brain (*bacterial meningitis*)

Cefepime is also used in adults and in children older than 2 months
- in the treatment of attack of fever of unknown reason in patients with diminished resistance (if the fever is suspected to be due to a bacterial infection in patients with medium-severe to severe *neutropenia*). If necessary, a combination with another antibiotic sould be given.
- in the treatment of blood poisoning (*bacteraemia*).

2. What you need to know before you use Cefepim MIP
You must not be given Cefepim MIP if you
- are allergic (*hypersensitive*) to any cephalosporin antibiotics or any of the other ingredients of this medicine (listed in section 6).

- have ever had a severe allergic (*hypersensitive*) reaction to any other type of betalactam antibiotic (penicillins, monobactams and carbapenems)
- have high acidity in your blood (*acidosis*)

→ Tell your doctor before you start on Cefepim MIP if you think that this applies to you. You must not be given Cefepim MIP in that case.

Take special care with Cefepim MIP
Tell your doctor or healthcare professional
- if you have ever had an **allergic reaction** to cefepime or other antibiotics of the beta-lactam type or to any medicinal product. If you develop an allergic reaction during treatment with cefepime, you should contact your doctor **immediately,** this might be serious. In this case the doctor will discontinue the treatment immediately.
- if you have ever had **asthma** or an allergic tendency.
- if you have **kidney problems**, the dosage of cefepime might have to be adjusted.
- if you develop **severe and persistent diarrhoea** during treatment. This may be a sign of an inflammation of the large bowel and needs urgent medical intervention.
- if you suspect to have developed a **new infection** during prolonged use of Cefepim MIP. This may be an infection by micro-organisms which are insensitive to cefepime and may require interruption of treatment.
- if you have any **blood or urine tests,** it is important to tell the doctor you are using Cefepim MIP. This medicine can alter the results of some tests.

Other medicines and Cefepim MIP
Do you use other medicines besides Cefepim MIP, did you do this recently or is it possible that you use other medicines in the near future? Tell your doctor or pharmacist. This is important because some medicines cannot be taken or used together with cefepim.

In particular, tell your doctor if you take the following:
- other antibiotics, in particular aminoglycosides (such as gentamicin) or 'water tablets' (diuretics, such as furosemide); in these cases, your kidney function should be monitored.
- medicines that are used to prevent your blood from clotting (coumarin anticoagulants, such as warfarin); it may be that their effect is enhanced.
- certain types of antibiotics (bacteriostatic antibiotics), as they can affect the functioning of cefepim..

Pregnancy and breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.
There is no information about the use of this medicine during pregnancy, it is preferred to avoid the use of cefepim during pregnancy.
Small amounts of this medicine can pass into breast milk. However, cefepime can be given to you even if you are breast-feeding. You should, however, monitor your suckling child for development of side-effects.

Driving and using machines
Cefepim MIP has no or negligible influence on the ability to drive and use machines. You may get headaches, feel dizzy or have a changed vision while taking this medicine. Don’t drive or use machines if you do not feel well.

3. How to use Cefepim MIP

Administration:
Cefepim MIP is usually given by a doctor or nurse. It can be given as a **drip** (intravenous infusion) or as an **injection** directly into a vein.

The usual dose:
The correct dose of Cefepim MIP for you will be decided by your doctor and depends on: The severity and type of infection, whether you are on any other antibiotics; your weight and age; how well your kidneys are working. The usual duration of therapy is 7 to 10 days.

Adults and adolescents over 40 kg (approx. over 12 years)
The usual adult dose is 4 g per day divided into two doses (2 g every12 hours). In very severe infections the dose may go up to 6 g daily (2 g every 8 hours).

Babies (from 2 months) and children up to 40 kg (approx. 12 years)
For every 1 kg the baby or child weighs, they'll be given 50 mg of cefepime every 12 hours. In case of very severe infections and e.g. for meningitis, this dose will be given every 8 hours.

Babies (1 - less than 2 months)
For every 1 kg the baby weighs, it will be given 30 mg of cefepime every 12 hours (or every 8 hours in case of very severe infections).

Patients with kidney problems
If you have a kidney problem, your doctor may change your dose.
→ **Talk to your doctor** if this applies to you.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects
Like all medicines, this medicine can cause side effects, although not everybody gets them.

Conditions you need to look out for
A small number of people using Cefepim MIP get an allergic reaction or potentially serious skin reaction. Symptoms of these reactions include:
- **Severe allergic reaction**. Signs include **raised and itchy rash, swelling**, sometimes of the face or mouth causing **difficulty in breathing**.
- **Skin rash**, which may **blister**, and looks like **small targets** (central dark spot surrounded by a paler area, with a dark ring around the edge).
- **A widespread rash** with **blisters** and **peeling skin**. (These may be signs of *Stevens-Johnson* syndrome or *toxic epidermal necrolysis*).
- **Fungal infections**: On rare occasions, medicines like Cefepim MIP can cause an overgrowth of yeast (*Candida*) in the body which can lead to fungal infections (such as thrush). This side effect is more likely if you take Cefepim MIP for a long time.

→ **Contact a doctor or nurse immediately if you get any of these symptoms.**

Very common side effects that may show up in blood tests:
These may affect **more than 1 in 10 people**:
- positive Coombs test

Common side effects
These may affect **up to 1 in 10 people**:
- injection site pain, swelling and redness along a vein
- diarrhoea
- skin rash

→ **Tell your doctor** if any of these are troubling you.

Common side effects that may show up in blood tests:
- increases in substances (*enzymes*) produced by the liver
- increase in bilirubin (a substance produced by the liver)

- changes in your white blood cell count (*eosinophilia*)
- low levels of red blood cells (*anaemia*)

Uncommon side effects
These may affect **up to 1 in 100 people**:
- inflammation of the colon (large intestine), causing diarrhoea, usually with blood and mucus, stomach pain
- fungal infections in the mouth, vaginal infections
- high temperature (fever)
- redness of the skin, nettle rash (*urticaria*), itching (*pruritus*)
- feeling sick (nausea), vomiting
- headache

→ **Tell your doctor** if you get any of these.

Uncommon side effects that may show up in blood tests:
- low levels of certain blood cells (*leucopenia, neutropenia, thrombocytopenia*)
- increase in levels of urea nitrogen and serum creatinine in the blood.

Rare side effects
These may affect **up to 1 in 1000 people**:
- allergic reactions
- fungal infections (*candidiasis*)
- fits, dizziness, distortion of the sense of taste, sensation of pricking or numbness of your skin.
- shortness of breath
- abdominal pain, constipation
- shivering
- swelling of the deeper layes of the skin

Other side effects of unknown frequency (also single case reports)
- severe allergic reactions
- coma, reduced consciousness or difficulty in thinking, confusion and hallucinations
- false positive urinary glucose tests
- digestion problems
- kidney problems
- bleeding

Side effects that may show up in blood tests:
- changes in your blood cell count (*agranulocytosis*)
- red blood cells destroyed too quickly (*haemolytic anaemia*)

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via www.xxx.xx. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cefepim MIP

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 label and carton after 'EXP'. The expiry date refers to the last day of that month.

Store below 30°C. Keep the vial in the outer carton in order to protect from light.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Cefepim MIP contains

- The active substance is cefepime. Each vial contains cefepime dihydrochloride monohydrate corresponding to 1g 2g cefepime.
- The other ingredient is arginine.

What Cefepim MIP looks like and contents of the pack

Cefepim MIP 1 g is available in 15 ml glass vials with a rubber stopper and a flip-off cap.
Cefepim MIP 2 g is available in 50 ml lass vials with a rubber stopper and a flip-off cap.
Pack sizes: Packages with 1, 5 or 10 glass vials. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

MIP Pharma GmbH
Kirkeler Str. 41
66440 Blieskastel, Germany
tel 0049 (0) 6842 9609 0
fax 0049 (0) 6842 9609 355

<This medicinal product is authorised in the Member States of the EEA under the following names:>
<{Name of the Member State}> <{Name of the medicinal product}>
[to be completed nationally]

This leaflet was last revised in May 2019.

The following information is intended for healthcare professionals only:

Preparation of the solution for i.v. injection

The vial contents are dissolved in 10 ml solvent as indicated in the table below. The prepared solution is injected slowly over a 3 to 5-minute period - either directly into a vein or directly into the cannula of an infusion system whilst the patient is receiving an infusion with a compatible i.v. solution.

Preparation of the solution for i.v. infusion

For intravenous infusion, reconstitute the 1 g or 2 g cefepime solution, as noted above for direct intravenous administration; and add the required quantity of the resulting solution to a container with one of the compatible i.v. fluids (recommended final volume: about 40-50 ml). The prepared solution should be administered over a period of approximately 30 minutes.

The following table contains instructions for reconstitution:

Dosage and route of administration	Solvent added [ml]	Resulting volume [ml]	Concentration (approx., in mg/ml)
1 g i.v.	10.0	11.4	90
2 g i.v.	10.0	12.8	160

Compatibility with intravenous liquids

The following solvents are suitable for preparation of the solution:

- water for injections
- Glucose solution 50 mg/ml (5%)
- Sodium chloride solution 9 mg/ml (0.9%)

The reconstitution/dilution is to be made under aseptic conditions. Add the recommended volume of reconstitution solution and shake gently until the contents of the vial have dissolved completely.
Like other cephalosporins, cefepime solutions can develop a yellow to amber colour, depending on storage conditions. However, this has no negative influence on the effect of the product.
Inspect the vial before use. It must only be used if the solution is free from particles. Use only clear solutions.

For single use only. Any remaining solution should be discarded. Any unused product or waste material should be disposed of in accordance with local requirements.

Storage after reconstitution
Shelf-life of the prepared solution
The chemical and physical stability of the prepared solution has been demonstrated for 2 hours at 25°C and for 24 hours at 2-8°C. From a microbiological point of view, the prepared solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

Dosage in patients with impaired renal function*:*

Adults and adolescents over 40 kg:
The recommended starting dose for patients with renal impairment is the same as for patients with normal renal function. The following table gives the maintenance dose:

Creatinine clearance [ml/min]	**Recommended maintenance dosage:** single doses and interval of administration	
	*Severe infections:*Bacteraemia, pneumonia, urinary tract infections, acute biliary tract infections	*Very severe infections:* Complicated intra-abdominal infections, empirical treatment of patients with febrile neutropenia
> 50 (usual dose, no adjustment required)	2 g every 12 h	2 g every 8 h
30-50	2 g every 24 h	2 g every 12 h
11-29	1 g every 24 h	2 g every 24 h
≤ 10	0.5 g every 24 h	1 g every 24 h

Dialysis patients:
One loading dose of 1 g on the first day of treatment with cefepime followed by 500 mg per day thereafter except for febrile neutropenia, for which indication the recommended dose is 1 g per day.
On days of dialysis, cefepime should be administered after the course of dialysis. If possible, cefepime should be administered at the same time each day.
In patients undergoing CAPD the following dosage is recommended: 1 g every 48 hours in case of severe infections or 2 g every 48 hours in case of very severe infections.

Impaired renal function in children:
A starting dose of 30 mg/kg for infants aged 1 to less than 2 months or 50 mg/kg for patients between 2 months and 12 years is recommended. The following table gives the maintenance dose:

Single doses (mg/kg body weight) and dosage interval				
Creatinine clearance [ml/min]	*Severe infections:* Pneumonia, complicated urinary tract infections		*Very severe infections:* Bacteraemia, bacterial meningitis, empirical treatment of patients with febrile neutropenia	
	Infants 1 to less than 2 months	2 months - 12 years	Infants 1 to less than 2 months	2 months - 12 years
> 50 (usual dose, no	30 mg/kg / 12 h	50 mg/kg / 12 h	30 mg/kg / 8 h	50 mg/kg / 8 h

adjustment required)				
30-50	30 mg/kg / 24 h	50 mg/kg / 24 h	30 mg/kg / 12 h	50 mg/kg / 12 h
11-29	15 mg/kg / 24 h	25 mg/kg / 24 h	30 mg/kg / 24 h	50 mg/kg / 24 h
≤ 10	7.5 mg/kg / 24 h	12.5 mg/kg / 24 h	15 mg/kg / 24 h	25 mg/kg / 24 h