Cefazolin 2 g powder for solution for injection / infusion

1. What Cefazolin 2 g is and what it is used for

This medicine contains the active substance cefazolin, which is an antibiotic. Cefazolin 2 g is used to treat bacterial infections caused by susceptible bacteria, e.g.: • Infections of skin and soft tissue • Infections of tones and joints

Cefazolin can also be used before, during and after surgery to prevent possible infections.

2. What you need to know before you use Cefazolin 2 g

Do not use Cefazolin 2 g if you • are allergic (hypersensitive) to any cephalosporin antibiotics • have ever had a severe allergic (hypersensitive) reaction to any other type of beta-lactam antibiotic (penicillins, monobactams and carbapenems).

Warnings and precautions

Talk to your doctor before using Cefazolin 2 g if you • are prone to allergic reactions (e.g. hay fever or bronchial asthma), since then the risk of severe allergic reactions to Cefazolin 2 g is increased • have had previously an allergic reaction to other beta-lactam antibiotics or a penicillin, since then there is an increased risk of being allergic to Cefazolin 2 g as well • suffer from an impaired kidney or liver function • suffer from disorders of blood clotting (e.g. haemophilia) or your present condition can lead to such defects (parenteral feeding, malnutrition, liver or kidney diseases). Cefazolin can reduce in blood platelets which increases risk of bleeding or bruising (thrombocytopenia). • you have or have previously had aseptic meningitis or heart block (anticoagulants like heparin). • suffer from certain conditions or if you have certain types of bowel problems (e.g. gastrointestinal ulcers). • suffer from severe persistent diarrhoea during or after treatment with Cefazolin 2 g. In this case contact your doctor immediately. Do not take any anti-diarrhoea medicine without consulting your doctor.

Children

Cefazolin may not be used in newborn infants and infants below the age of 1 month as the safety of use has not yet been established in this group.

Other medicines and Cefazolin 2 g

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

Your doctor or take special care if you are using any of the following medicines:

• Anticonvulsants (medicines that prevent blood clotting): Cefazolin may very rarely lead to disorders of blood clotting. Therefore, if you are already taking these medicines and that prevent blood clotting (e.g. heparin), a careful and regular control of the coagulation factors is necessary.

• Probenecid (medicine for the treatment of joint disease and gout). Medicines potentially harmful to the kidney: Cefazolin may increase the harmful effect of certain antibiotics (aminoglycosides) and of medicines that cause increase in urination (diuretics, e.g. furosemide) on the kidney. Using Cefazolin 2 g and one of these medicines at the same time requires regular monitoring of the kidney function, especially in patients with kidney disease.

Pregnancy, 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 Cefazolin. Cefazolin crosses the placenta and can affect the unborn child. Therefore, it is not possible to say whether Cefazolin is clearly necessary and after careful consideration of benefits and risks. Cefazolin passes in small amounts into breast milk. If you are breastfeeding, breast-feeding should be discontinued during treatment with Cefazolin 2 g.

Driving and using machines

Cefazolin 2 g has no or negligible influence on the ability to drive and use machines.

3. How to use Cefazolin 2 g

Administration:

Cefazolin 2 g is always administered by healthcare personnel. It will be given as an injection or infusion (into a vein) after being dissolved. Your doctor will decide on the necessary duration and frequency of administration of Cefazolin 2 g.

The recommended doses are:

Adult patients with normal kidney function

Infections caused by susceptible bacteria to this medicine: 1.25 g daily, divided into 2-3 doses.

Infections caused by bacteria less susceptible to this medicine: 3.4 g daily, divided into 2-3 doses.

An increase of the daily dose up to 6 g in three or four equal doses is possible.

Use in children and adolescents

Newborn infants and children below the age of one month:

The safety in infants below the age of one month has not been determined.

Children over the age of one month:

• Infections caused by bacteria susceptible to this medicine: 25 - 50 mg per kg body weight per day divided in 2-4 single doses, every 6, 8 or 12 hours.

• Infections caused by bacteria less susceptible to this medicine: Up to 100 mg cefazolin/kg body weight/day divided in 3-4 single doses, every 6-8 hours.

This product is not recommended for children under 1 month of life.

Elderly patients

No dosage adjustment is required for elderly patients with normal renal function.

Special dosage recommendations

Prevention of infections during surgical procedures

If a dose of Cefazolin 2 g has been forgotten

A double dose must not be given to make up for a forgotten dose. A forgotten dose should only be given before the next regular dose if the time until the next regular dose is long enough.

If too much of Cefazolin 2 g has been used:

Symptoms of overdose and headache, dizziness (vertigo), sensation of losing or distorting of the vision, a twitching or trembling of a muscle (tremor), pricking or tingling on the skin (paraesthesia), restlessness (agitation), involuntary twitching of a muscle or a group of muscles (myoclonia) or problems with swallowing or breathing (dysphagia or dyspnoea)

In emergencies, your physician must take the necessary measures for the treatment of symptoms of overdose.

• If the treatment with Cefazolin 2 g is interrupted or discontinued too early

Low dose, irregular administration or stopping the treatment too early can compromise the outcome of the therapy or lead to a relapse, that is more difficult to treat. Please follow the instructions of your doctor.

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 everyone gets them.

You must stop taking the medicine and speak to your doctor straight away if you notice any of these symptoms:

Uncommon side effects (occurring in 1 to 10 out of 1,000 treated patients)

• Redness of the skin (erythema), widespread skin rash (erythema multiforme or exanthemat), fever, itch, lump, bumpy skin rash on the surface of the skin (urticaria, fever, swelling beneath the skin (angioedema) and/or swelling of the lung tissue possibly with a cough (angioedema with pulmonary oedema).

Rare (occurring in less than 10 out of 1,000 treated patients)

• Severe skin rash with flushing, fever, blisters or ulcers (Stevens–Johnson syndrome) or a severe rash with reddening, peeling and swelling of the skin that looks like a burn (toxic epidermal necrolysis).

Very rare (occurring in less than 1 in 10,000 treated patients)

• A severe allergic reaction (anaphylactic shock) with breathing difficulty, swelling of the throat, face, eyes or lips, increased heart rate and falling blood pressure. This reaction may start soon after you take the medicine, or it may start later. The following side effect is has been reported but its frequency of occurrence is not known.

• Severe and frequent diarrhoea, sometimes containing blood. This may indicate a more serious condition (pseudomembranous colitis).

The following side effects may also occur during the use of cefazolin:

• Skin rash and itching

Common side effects, occurring in 1 to 10 out of 100 treated patients:

• Mild gastrointestinal disturbances (loss of appetite, diarrhoea, nausea, vomiting, severe and frequent diarrhoea). These side effects usually resolve if you stop taking the medicine.

• Injection into the muscle may cause pain at the location of the injection. The following side effects include hardening of the skin and soft tissue at the same site.

What is in this leaflet:

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

Package leaflet: Information for the user

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.
Uncommon side effects, occurring in 1 to 10 out of 1,000 treated patients:

- oral thrush white or cream-coloured deposits in the mouth and tongue
- fits/convulsions in patients with kidney problems
- swelling of the local area
- burning sensation caused by a blood clot forming following injection into the muscle (thrombophlebitis).

Rare side effects, occurring in 1 to 10 out of 10,000 treated patients:

- bacterial infection of male or female genitals with symptoms such as itching, redness, swelling and female discharge (genital candidiasis, mononiasis, vaginitis)
- increased tendency to develop in blood glucose concentration (hyperglycaemia or hypoglycaemia)
- reversible blood abnormalities including the reduction or increase in the number of red and white blood cells (leukopenia, granulocytopenia, neutropenia, thrombocytopenia, leukocytosis, granulocytosis, monocytosis, lymphocytosis, basophilia and eosinopenia) which may cause bleeding, easy bruising and skin discoloration (confirmed by blood tests).
- feelings of anxiety, nervousness, drowsiness, weakness, hot flushes, sweating, vertigo and epileptic seizures (irreversible and rapid muscle contraction and relaxation).
- kidney problems (nephrotoxicity, interstitial nephritis, undefined nephropathy, proteinuria) with symptoms such as kidney swelling and an increase of nitrogen in the body that may be diagnosed by urine tests, usually only occurring in patients taking cefazolin at the same time as other medicines that can cause kidney problems.

Very rare side effects, occurring in less than 1 out of 10,000 treated patients:

- itching of the anus or genitalia (pruritus)
- blood not clotting properly which may result in increased bleeding. This may be caused by a deficiency of coagulation K and should be confirmed by blood test (see section 2).

Side effects with uncommon frequency

- long-term or repeated treatment with Cefazolin may lead to further infections caused by resistant fungi or bacteria (superinfection)
- sleep disorders including nightmares and being unable to sleep (somnolence)
- feelings of nervousness or anxiety, drowsiness, weakness, hot flushes, sweating, vertigo and epileptic seizures (irreversible and rapid muscle contraction and relaxation).

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any effects not listed in this leaflet.

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.mhra.gov.uk/yellowcard. By reporting side effects, it helps to ensure that the benefits of medicines are balanced against their risks and it allows timely withdrawal of medicines if required.

5. How to store Cefazolin 2 g

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

Do not use this medicine after the expiry date that is stated on the outer carton.

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any effects not listed in this leaflet.

6. Contents of the pack and other information

What Cefazolin 2 g contains

- The active substance is cefazolin. Each vial contains 2 g of cefazolin (as cefazolin sodium).
- There are no other ingredients.

What Cefazolin 2 g looks like and contents of the pack

White or almost white powder: Cefazolin 2 g is available in packages with 1, 5 or 10 colourless glass vials (10 ml) with a chlorobutyl rubber stopper and a flip-off cap. Not all pack sizes may be marketed.

Marketing authorisation holder

MIP Pharma GmbH
Kirkeler Straße 41
66440 Blieskastel
Germany
Tel. +49 (0) 6843 9600 0
Fax +49 (0) 6843 9600 355

Manufacturer

MIP Pharma GmbH
Kirkeler Straße
66440 Blieskastel
Germany

This leaflet was last revised 21/02/2014.

The following information is intended for healthcare professionals only.

Mode of application

Cefazolin 2 g for injection or infusion may be administered by slow intravenous injection or by intravenous infusion after dilution. For each indication, there are tables for the vial content, minimum volume to be added, and the diluent to be used, according to the following guidelines:

-***Children with moderate impairment (creatinine clearance 40-50 ml/min):***
-***20% of the normal daily dose, divided into doses every 12 hours is sufficient.***
-***Children with severe impairment (creatinine 20-5 ml/min) will be 10% of the normal daily dose, given every 24 hours are sufficient.***

All these guidelines are valid after an initial starting dose.

Intravenous injection

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>Volume to be added (ml)</th>
<th>Diluent (ml)</th>
<th>Concentration (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.25-12.5</td>
<td>1.25-2.5</td>
<td>0.9% sodium chloride</td>
<td>500 mg/ml</td>
</tr>
<tr>
<td>12.5-25</td>
<td>2.5-5</td>
<td>0.9% sodium chloride</td>
<td>250 mg/ml</td>
</tr>
<tr>
<td>25-50</td>
<td>5-10</td>
<td>0.9% sodium chloride</td>
<td>125 mg/ml</td>
</tr>
</tbody>
</table>

Intravenous infusion

<table>
<thead>
<tr>
<th>Body weight (kg)</th>
<th>Minimum amount of diluent to be added per vial</th>
<th>Approximate concentration (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>12.5</td>
<td>80 mg/ml</td>
</tr>
<tr>
<td>20</td>
<td>16.5</td>
<td>62.5 mg/ml</td>
</tr>
<tr>
<td>25</td>
<td>20.5</td>
<td>50 mg/ml</td>
</tr>
<tr>
<td>30</td>
<td>24</td>
<td>41.67 mg/ml</td>
</tr>
<tr>
<td>35</td>
<td>27.5</td>
<td>33.33 mg/ml</td>
</tr>
<tr>
<td>40</td>
<td>31</td>
<td>29.17 mg/ml</td>
</tr>
<tr>
<td>45</td>
<td>34.5</td>
<td>25 mg/ml</td>
</tr>
<tr>
<td>50</td>
<td>38</td>
<td>20 mg/ml</td>
</tr>
</tbody>
</table>

Guidelines for paediatric dosage

<table>
<thead>
<tr>
<th>Body weight (kg)</th>
<th>Minimum amount of diluent to be added per vial</th>
<th>Approximate concentration (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>2.5</td>
<td>19 mg/ml</td>
</tr>
<tr>
<td>10</td>
<td>5</td>
<td>9.5 mg/ml</td>
</tr>
<tr>
<td>15</td>
<td>7.5</td>
<td>7 mg/ml</td>
</tr>
<tr>
<td>20</td>
<td>10</td>
<td>5 mg/ml</td>
</tr>
</tbody>
</table>

Dilution table for intravenous injection

<table>
<thead>
<tr>
<th>Volume of diluent</th>
<th>Concentration of solution</th>
<th>Amount of diluent to be added</th>
<th>Approximate concentration (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 ml</td>
<td>0.1% sodium chloride</td>
<td>0.1 ml</td>
<td>190 mg/ml</td>
</tr>
<tr>
<td>20 ml</td>
<td>0.1% sodium chloride</td>
<td>0.2 ml</td>
<td>380 mg/ml</td>
</tr>
<tr>
<td>30 ml</td>
<td>0.1% sodium chloride</td>
<td>0.3 ml</td>
<td>570 mg/ml</td>
</tr>
<tr>
<td>40 ml</td>
<td>0.1% sodium chloride</td>
<td>0.4 ml</td>
<td>760 mg/ml</td>
</tr>
<tr>
<td>50 ml</td>
<td>0.1% sodium chloride</td>
<td>0.5 ml</td>
<td>950 mg/ml</td>
</tr>
</tbody>
</table>

Dilution table for intravenous infusion

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</tr>
</tbody>
</table>

Paeediatric patients with renal impairment

Children with renal impairment. Like adults may need a lower dose to avoid overloading.

This lower dose may be guided by determining blood levels. If not possible, the dosage of creatinine clearance may be determined according to the following guidelines:

In children with moderate impairment (creatinine clearance 40-50 ml/min), 20% of the normal daily dose, divided into doses every 12 hours is sufficient.

In children with severe impairment (creatinine 20-5 ml/min) will be 10% of the normal daily dose, given every 24 hours are sufficient. All these guidelines are valid after an initial starting dose.