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.

Cefazolin 2 g

powder for solution for injection / infusion

Cefazolin

What is in this leaflet:

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 cefazolin-susceptible bacteria, e.g:
- Infections of skin and soft tissue
- Infections of bones 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 betalactam 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 (e.g. penicillins), 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, reduction in blood platelets which increases risk of bleeding or bruising (thrombocytopenia), administration of medicines that prevent blood clotting (anticoagulants like heparin)).
- suffer from diseases which can cause bleedings (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 a prescription.
Your doctor will take special care if you are using any of the following medicines:
- **Anticoagulants (medicines that prevent blood clotting):** Cefazolin may very rarely lead to disorders of blood clotting. Therefore, if you simultaneously receive cefazolin and medicines 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 kidney:** Cefazolin may intensify 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 this medicine.
Cefazolin crosses the placenta and can affect the unborn child. Therefore, if you are pregnant, your doctor should only give you cefazolin if clearly necessary and after careful consideration of benefits and risks.
Cefazolin passes in small amounts into breast milk. Therefore, 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 inform you about the necessary duration and frequency of administration of Cefazolin 2 g.

The recommended doses are:

Adult patients with normal kidney function

- Infections caused by bacteria susceptible to this medicine:
  1-2 g daily, divided into 2-3 doses.
- Infections caused by bacteria less susceptible to this medicine:
  3-4 g daily, divided into 3-4 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 infants 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
1 g cefazolin 30 - 60 minutes before surgery.
In case of long surgical procedures (2 hours or more), additional 0.5 g - 1 g cefazolin during the operation.

Patients with impaired kidney function
In patients with impairment of the kidney function, the elimination of cefazolin is slower. For this reason, your doctor will adjust the dosage according to the severity of the kidney impairment by reducing the maintenance dose or prolongation of the dosage intervals.

Duration of treatment

The treatment duration depends on the severity of the infection as well as on your recovery from your illness.

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 are headache, dizziness (vertigo), sensation of pricking or tingling on the skin (paraesthesia), restlessness (agitation), involuntary twitching of a muscle or a group of muscles (myoclonia) and cramps (convulsions). Contact your physician if these symptoms occur!
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 dosage, 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 everybody 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) are:
- redness of the skin (erythema), widespread skin rash (erythema multiforme or exanthema), hives (red, itchy, 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 and breathing difficulties (interstitial pneumonia or pneumonitis), as these side effects may indicate an allergic reaction to this medicine.

Rare (occurring in 1 to 10 out of 10,000 treated patients)
- jaundice (yellow colour in the skin and whites of the eyes)
- 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 out of 10,000 treated patients)
- a severe allergic reaction (anaphylactic shock) with breathing difficulty , swelling of the throat, face, eyelids or lips, increased heart rate and falling blood pressure. This reaction may start soon after you first take the medicine, or it might start later.

The following side effect has been reported but its frequency of occurrence is unknown:
- severe and frequent diarrhoea, sometimes containing blood, as this may indicate a more serious condition (pseudomembranous colitis).

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

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 after a few days.
- injection into the muscle may cause pain at the location of the injection which may sometimes include hardening of the skin and soft tissue at the same site.

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

- oral thrush (thick white or cream-coloured deposits in the mouth and tongue).
- fits/convulsions in patients with kidney problems.
- swelling of a vein 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 candidasis, monoliasis, vaginitis).
- increase or decrease in blood glucose concentration (hyperglycemia or hypoglycemia).
- reversible blood abnormalities including the reduction or increase in the number of red and white blood cells (leukopenia, granulocytopenia, neutropenia, thrombocytopenia, leukocytosis, granulocytosis, monocytosis, lymphocytopenia, basophilia and eosinophilia) which may cause bleeding, easy bruising and/or skin discolouration (confirmed by blood test).
- feelings of dizziness, tiredness and a general feeling of being unwell.
- chest pain, excess fluid in the lungs, shortness of breath, cough, stuffy nose (rhinitis).
- liver problems (such as alkaline phosphatise or transient hepatitis) with symptoms such as an increase in liver enzymes (alanine transaminase (ALT), aspartate transaminase (AST), gamma-glutamyl transpeptidase (gamma GT) and lactate dehydrogenase (LDH)) and bilrubin (a product of the breakdown of blood cells) in bile or urine (diagnosed by blood test).
- 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 resolved by increasing vitamin K intake and should be confirmed by blood test (see section 2).

Side effects with unknown frequency

- long-term or repeated treatment with Cefazolin may lead to further infection by Cefazolin resistant fungi or bacteria (superinfection).
- sleep disorders including nightmares and being unable to sleep (insomnia).
- feelings of nervousness or anxiety, drowsiness, weakness, hot flushes, disturbed colour vision, vertigo and epileptic seizures (involuntary rapid and repeated muscle contraction and relaxation).

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any side 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 you can help provide more information on the safety of this medicine.

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

Do not store above 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 Cefazolin 2 g contains

- The active substance is cefazolin. Each vial contains 2 g 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 (15 or 100 ml) with a chlorobutyl rubber stopper and a flip-off cap. Not all pack sizes may be marketed.

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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 route of administration see the table for addition volumes and solution concentrations, which may be useful when fractional doses are required.

Intravenous injection:
2 g dry powder are dissolved in at least 10 ml water for injection or a compatible solvent (see below).

Reconstitution table for intravenous injection

Content per vial	Minimum amount of diluent to be added	Approximate concentration
2 g	10 ml	200 mg/ml

Cefazolin is to be injected slowly over three to five minutes. In no case should the solution be injected in less than 3 minutes. This should be done directly into the vein or into the tube from which the patient receives intravenous solution.
Single doses exceeding 1 g should be given as intravenous infusion over 30 to 60 minutes.

Intravenous infusion
2 g dry powder is dissolved in 8 ml water for injections and diluted to 50-100 ml with a compatible diluent.

Dilution table for intravenous infusion

Content per vial	Reconstitution	Dilution	Approximate concentration
	Minimum amount of diluent to be added	Amount of diluent to be added	
2 g	8 ml	50 ml - 100 ml	34 mg/ml - 19 mg/ml

If smaller doses are needed, it is recommended to use half of the reconstituted solution (about 4 ml with 1 g cefazolin; i.e. half of the vial content) and to add a compatible diluent to a final volume of 100 ml (resulting concentration about 10 mg/ml). The required amount of this diluted solution can then be administered to the patient over the prescribed time.

Compatibility with intravenous liquids
The following solvents are suitable for preparation of the solution:
- water for injections
- 9 mg/ml (0.9 %) sodium chloride solution
- 50 mg/ml (5%) glucose solution

The reconstituted solution is clear, pale yellow and should be protected from light.
Only clear solutions, free from particles, must be used.

Storage after reconstitution

Shelf-life of the prepared infusion solution
The chemical and physical stability of the prepared solution is 12 hours at 25°C and 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 are the responsibility of the user.

The reconstituted product is for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Adult patients with renal impairment

Creatinine clearance [ml/min]	Serum creatinine [mg/dl]	Dosage
≥ 55	≤ 1.5	Normal dose and normal dosage interval
35 - 54	1.6 - 3.0	Normal dose, every 8 hours
11 - 34	3.1 - 4.5	Half of the normal dose every 12 hours
≤ 10	≥ 4.6	Half of the normal dose every 18-24 hours

Guidelines for paediatric dosage

The content of 1 vial (2000 mg cefazolin) is dissolved in 10 ml of a compatible solvent (i.e. concentration approx. 200 mg/ml). The respective volume of this solution to be used is indicated in the following table in addition to the dose in mg.
Alternatively, the dosage can be given as intravenous infusion, using the diluted solution (10 mg/ml) described above.

Body weight	5 kg	10 kg	15 kg	20 kg	25 kg
Divided dose every 12 hours at 25 mg / kg body weight per day	63 mg; 0.3 ml	125 mg; 0,65 ml	188 mg; 0.95 ml	250 mg; 1.3 ml	313 mg; 1.55 ml
Divided dose every 8 hours at 25 mg / kg body weight per day	42 mg; 0.2 ml	85 mg; 0.4 ml	125 mg; 0.65 ml	167 mg; 0.85 ml	208 mg; 1.05 ml
Divided dose every 6 hours at 25 mg / kg body weight per day	31 mg; 0.15 ml	62 mg; 0.3 ml	94 mg; 0.45 ml	125 mg; 0.65 ml	156 mg; 0.8 ml
Divided dose every 12 hours at 50 mg / kg body weight per day	125 mg; 0.65 ml	250 mg; 1.3 ml	375 mg; 1.9 ml	500 mg; 2.5 ml	625 mg; 3.15 ml
Divided dose every 8 hours at 50 mg / kg body weight per day	83 mg; 0.4 ml	166 mg; 0.85 ml	250 mg; 1.3 ml	333 mg; 1.65 ml	417 mg; 2.1 ml
Divided dose every 6 hours at 50 mg / kg body weight per day	63 mg; 0.3 ml	125 mg; 0.65 ml	188 mg; 0.95 ml	250 mg; 1.3 ml	313 mg; 1.55 ml
Divided dose every 8 hours at 100 mg / kg body weight per day	167 mg; 0.85 ml	333 mg; 1.7 ml	500 mg; 2.5 ml	667 mg; 3.5 ml	833 mg; 4.15 ml
Divided dose every 6 hours at 100 mg / kg body weight per day	125 mg; 0.65 ml	250 mg; 1.3 ml	375 mg; 1.9 ml	500 mg; 2.5 ml	625 mg; 3.15 ml

Paediatric patients with renal impairment

Children with renal impairment (like adults) may need a lower dose to avoid overlapping.
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 40-20 ml / min), 25% of the normal daily dose, divided into doses every 12 hours are sufficient.
In children with severe impairment (creatinine 20-5 ml / min) will be 10% of normal daily dose, given every 24 hours are sufficient.
All these guidelines are valid after an initial starting dose.

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