Package leaflet: Information for the user

Ceftriaxone 1 g powder for solution for injection or infusion

Ceftriaxone 2 g powder for solution for injection or infusion

Read all of this leaflet carefully before you start taking this medicine, because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have 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.

The name of your medicine is Ceftriaxone 1 g powder for solution for injection or infusion and Ceftriaxone 2 g powder for solution for injection or infusion. In the rest of this leaflet it is called Ceftriaxone.

What is in this leaflet

1. What Ceftriaxone is and what it is used for

Ceftriaxone is an antibiotic given to adults and children (including newborn babies). It works by killing bacteria that cause infections. It belongs to a group of medicines called cephalosporins.
Ceftriaxone is used to treat infections of
- the brain (meningitis).
- the lungs.
- the middle ear.
- the abdomen and abdominal wall (peritonitis).
- the urinary tract and kidneys.
- bones and joints.
- the skin or soft tissues.
- the blood.
- the heart.

It can be given:
- to treat specific sexually transmitted infections (gonorrhoea and syphilis).
- to treat patients with low white blood cell counts (neutropenia) who have fever due to bacterial infection.
- to treat infections of the chest in adults with chronic bronchitis.
- to treat Lyme disease (caused by tick bites) in adults and children including newborn babies from 15 days of age.
- to prevent infections during surgery.

2. What you need to know before you are given Ceftriaxone

You must not be given Ceftriaxone:

- if you are allergic to Ceftriaxone or any of the other ingredients of this medicine (listed in section 6).
- if you have had a sudden or severe allergic reaction to penicillin or similar antibiotics (such as cephalosporins, carbapenems or monobactams). The signs include sudden swelling of the throat or face which might make it difficult to breath or swallow, sudden swelling of the hands, feet and ankles, chest pain and a severe rash that develops quickly.
- if you are allergic to lidocaine and you are to be given Ceftriaxone as an injection into a muscle.

Ceftriaxone must not be given to babies if:

- The baby is premature.
- The baby is newborn (up to 28 days of age) and has certain blood problems or jaundice (yellowing of the skin or the whites of the eyes) or is to be given a product that contains calcium into their vein.

Warnings and precautions
Talk to your doctor or pharmacist or nurse before you are given Ceftriaxone if:

- You have recently received or are about to receive products that contain calcium.
- You have recently had diarrhoea after having an antibiotic medicine. You have ever had problems with your gut, in particular colitis (inflammation of the bowel).
- You have liver or kidney problems (see section 4).
- You have gall stones or kidney stones.
- You have other illnesses, such as haemolytic anaemia (a reduction in your red blood cells that may make your skin pale yellow and cause weakness or breathlessness).
- You are on a low sodium diet.
- You experience or have previously experienced a combination of any of the following symptoms: rash, red skin, blistering of the lips, eyes and mouth, skin peeling, high fever, flu-like symptoms, increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia) and enlarged lymph nodes (signs of severe skin reactions, see also section 4 “Possible side effects”).

If you need a blood or urine test
If you are given Ceftriaxone for a long time, you may need to have regular blood tests. Ceftriaxone can affect the results of urine tests for sugar and a blood test known as the Coombs test. If you are having tests:

- Tell the person taking the sample that you have been given Ceftriaxone.

If you are diabetic or need to have your blood glucose level monitored you should not use certain blood glucose monitoring systems which may estimate blood glucose incorrectly while you are receiving Ceftriaxone. If you use such systems check the instructions for use and tell your doctor, pharmacist or nurse. Alternative testing methods should be used if necessary.

Children
Talk to your doctor or pharmacist or nurse before your child is administered Ceftriaxone if:

- He/She has recently been given or is to be given a product that contains calcium into their vein.

Other medicines and Ceftriaxone
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

In particular, tell your doctor or pharmacist if you are taking any of the following medicines:
- A type of antibiotic called an aminoglycoside.
- An antibiotic called chloramphenicol (used to treat infections, particularly of the eyes).

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 or pharmacist for advice before taking this medicine.
The doctor will consider the benefit of treating you with Ceftriaxone against the risk to your baby.

Driving and using machines
Ceftriaxone may cause dizziness. If you feel dizzy, do not drive or use any tools or machines. Talk to your doctor if you experience these symptoms.

Ceftriaxone contains sodium
This medicine contains 82 mg sodium (main component of cooking/table salt) in each 1 g vial. This is equivalent to 4.1 % of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains 165 mg sodium (main component of cooking/table salt) in each 2 g vial. This is equivalent to 8.3 % of the recommended maximum daily dietary intake of sodium for an adult.

3. How to take Ceftriaxone

Ceftriaxone 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 or
- into a muscle.

Ceftriaxone is made up by the doctor, pharmacist or nurse and will not be mixed with or given to you at the same time as calcium-containing injections.

The recommended dose
Your doctor will decide the correct dose of Ceftriaxone for you. The dose will depend on the severity and type of infection; whether you are on any other antibiotics; your weight and age; how well your kidneys and liver are working. The number of days or weeks that you are given Ceftriaxone depends on what sort of infection you have.

Adults, older people and children aged 12 years and over with a body weight greater than or equal to 50 kilograms (kg):

- 1 to 2 g once a day depending on the severity and type of infection. If you have a severe infection, your doctor will give you a higher dose (up to 4 g once a day). If your daily dose is higher than 2 g, you may receive it as a single dose once a day or as two separate doses.

Newborn babies, infants and children aged 15 days to 12 years with a body weight of less than 50 kg:

- 50-80 mg Ceftriaxone for each kg of the child's body weight once a day depending on the severity and type of infection. If you have a severe infection, your doctor will give you a higher dose up to 100 mg for each kg of body weight to a maximum of 4 g once a day. If your daily dose is higher than 2 g, you may receive it as a single dose once a day or as two separate doses.
- Children with a body weight of 50 kg or more should be given the usual adult dose.

Newborn babies (0-14 days)

- 20 – 50 mg Ceftriaxone for each kg of the child's body weight once a day depending on the severity and type of infection.
- The maximum daily dose is not to be more than 50 mg for each kg of the baby's weight.

People with liver and kidney problems
You may be given a different dose to the usual dose. Your doctor will decide how much Ceftriaxone you will need and will check you closely depending on the severity of the liver and kidney disease.

If you are given more Ceftriaxone than you should
If you accidentally receive more than your prescribed dose, contact your doctor or nearest hospital straight away.

If you forget to use Ceftriaxone
If you miss an injection, you should have it as soon as possible. However, if it is almost time for your next injection, skip the missed injection. Do not take a double dose (two injections at the same time) to make up for a missed dose.

If you stop using Ceftriaxone
Do not stop taking Ceftriaxone unless your doctor tells you to. If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

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

The following side effects may happen with this medicine:

Severe allergic reactions (not known, frequency cannot be estimated from the available data)
If you have a severe allergic reaction, tell a doctor straight away.
The signs may include:

- Sudden swelling of the face, throat, lips or mouth. This can make it difficult to breathe or swallow.
- Sudden swelling of the hands, feet and ankles.

- Chest pain in the context of allergic reactions, which may be a symptom of allergy triggered cardiac infarction (Kounis syndrome).

Severe skin reactions (not known, frequency cannot be estimated from the available data)
If you get a severe skin reaction, tell a doctor straight away.
The signs may include:

- A severe rash that develops quickly, with blisters or peeling of the skin and possibly blisters in the mouth. (Stevens-Johnson syndrome and toxic epidermal necrolysis which are also known as SJS and TEN).
- A combination of any of the following symptoms: widespread rash, high body temperature, liver enzyme elevations, blood abnormalities (eosinophilia), enlarged lymph nodes and other body organs involvement (Drug Reaction with Eosinophilia and Systemic Symptoms which is also known as DRESS or drug hypersensitivity syndrome).
- Jarisch-Herxheimer reaction which causes fever, chills, headache, muscle pain, and skin rash that is usually self-limiting. This occurs shortly after starting Ceftriaxone treatment for infections with spirochete such as Lyme disease.

Treatment with Ceftriaxone, particularly in elderly patients with serious kidney or nervous system problems may rarely cause decreased consciousness, abnormal movements, agitation and convulsions.

Other possible side effects:

Common (may affect up to 1 in 10 people)

- Abnormalities with your white blood cells (such as a decrease of leucocytes and an increase of eosinophils) and platelets (decrease of thrombocytes).
- Loose stools or diarrhoea.
- Changes in the results of blood tests for liver functions.
- Rash.

Uncommon (may affect up to 1 in 100 people)

- Fungal infections (for example, thrush).
- A decrease in the number of white blood cells (granulocytopenia).
- Reduction in number of red blood cells (anaemia).
- Problems with the way your blood clots. The signs may include bruising easily and pain and swelling of your joints.
- Headache.
- Dizziness.
- Feeling sick or being sick.
- Pruritis (itching).
- Pain or a burning feeling along the vein where Ceftriaxone has been given. Pain where the injection was given.
- A high temperature (fever).
- Abnormal kidney function test (blood creatinine increased).

Rare (may affect up to 1 in 1,000 people)

- Inflammation of the large bowel (colon). The signs include diarrhoea, usually with blood and mucus, stomach pain and fever.
- Difficulty in breathing (bronchospasm).
- A lumpy rash (hives) that may cover a lot of your body, feeling itchy and swelling.
- Blood or sugar in your urine.
- Oedema (fluid build-up).
- Shivering.

Not known (Frequency cannot be estimated from the available data)

- A secondary infection that may not respond to the antibiotic previously prescribed
- Form of anaemia where red blood cells are destroyed (haemolytic anaemia).
- Severe decrease in white blood cells (agranulocytosis).
- Convulsions.

- Vertigo (spinning sensation).
- Inflammation of the pancreas (pancreatitis). The signs include severe pain in the stomach which spreads to your back.
- Inflammation of the mucus lining of the mouth (stomatitis).
- Inflammation of the tongue (glossitis). The signs include swelling, redness and soreness of the tongue.
- Problems with your gallbladder and/or liver, which may cause pain, nausea, vomiting, yellowing of the skin, itching, unusually dark urine and clay-coloured stools.
- A neurological condition that may occur in neonates with severe jaundice (kernicterus).
- Kidney problems caused by deposits of calcium Ceftriaxone. There may be pain when passing water (urine) or low output of urine.
- A false positive result in a Coombs' test (a test for some blood problems).
- A false positive result for galactosaemia (an abnormal build up of the sugar galactose).
- Ceftriaxone may interfere with some types of blood glucose tests - please check with your doctor.

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

5. How to store Ceftriaxone

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. The expiry date refers to the last day of that month
- The vials and bottles should not be stored above 25^{o}C
- Keep the vial or bottle in the outer carton in order to protect from light
- From a microbiological point of view, the product should be used immediately. In use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2^{o}C to 8^{o}C, unless reconstitution has taken place in controlled and validated aseptic conditions. Once reconstituted, any unused portion of solution should be discarded.

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 Ceftriaxone contains
- The active substance is Ceftriaxone sodium. Each container contains the equivalent of 1 g or 2 g of Ceftriaxone. The sodium content is approximately 82 mg (3.6 mmol) for the 1 g vial and 165 mg (7.2 mmol) for the 2 g bottle.

What Ceftriaxone looks like and contents of the pack
Ceftriaxone is a white to pale yellow powder, which must be made into a solution before injection or infusion.
Ceftriaxone 1 g is available in packs of 1, 5, 10, 25 or 50 vials. Not all pack sizes are marketed.
Ceftriaxone 2 g is available in packs of 1 or 10 bottles. Not all pack sizes are marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder: Pinewood Laboratories Ltd., Ballymacarbry, Clonmel, Co. Tipperary, Ireland.
Manufacturer: Labesfal - Laboratorios Almiro, S.A, Zona Industrial do Lagedo, Santiago de Besteiros, 3465-157, Portugal.

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Information for Health Care Professionals
Ceftriaxone 1 g Powder for solution for injection/infusion
Ceftriaxone 2 g Powder for solution for injection/infusion

Dosage and Administration Information Only
Please refer to the Summary of Product Characteristics for further information.

- **Posology and method of administration**

Posology

The dose depends on the severity, susceptibility, site and type of infection and on the age and hepato-renal function of the patient.

The doses recommended in section 4.2 of the SmPC are the generally recommended doses in these indications. In particularly severe cases, doses at the higher end of the recommended range should be considered.
Please refer to section 4.2 of the SmPC for further information.

Duration of therapy
The duration of therapy varies according to the course of the disease. As with antibiotic therapy in general, administration of Ceftriaxone should be continued for 48 - 72 hours after the patient has become afebrile or evidence of bacterial eradication has been achieved.

Older people
The dosages recommended for adults require no modification in older people provided that renal and hepatic function is satisfactory.

Patients with hepatic impairment
Available data do not indicate the need for dose adjustment in mild or moderate liver function impairment provided renal function is not impaired.
There are no study data in patients with severe hepatic impairment (see section 5.2).

Patients with renal impairment:
In patients with impaired renal function, there is no need to reduce the dosage of Ceftriaxone provided hepatic function is not impaired. Only in cases of preterminal renal failure (creatinine clearance < 10 ml/min) should the Ceftriaxone dosage not exceed 2 g daily.
In patients undergoing dialysis no additional supplementary dosing is required following the dialysis. Ceftriaxone is not removed by peritoneal- or haemodialysis. Close clinical monitoring for safety and efficacy is advised.

Patients with severe hepatic and renal impairment
In patients with both severe renal and hepatic dysfunction, close clinical monitoring for safety and efficacy is advised.

Method of Administration

Intramuscular administration

1 g Ceftriaxone should be dissolved in 3.5 ml of 1 % Lidocaine Injection BP.
2 g Ceftriaxone should be dissolved in 7.0 ml of 1 % Lidocaine Injection BP.

The solution should be administered by deep intramuscular injection.
Intramuscular injections should be injected well within the bulk of a relatively large muscle and not more than 1 g should be injected at one site.
Dosages greater than 1 g should be divided and injected at more than one site.

As the solvent used is lidocaine, the resulting solution should never be administered intravenously (see section 4.3). The information in the Summary of Product Characteristics of lidocaine should be considered.

Intravenous administration

Ceftriaxone 1 g powder for solution for injection or infusion

For IV injection 1 g Ceftriaxone is dissolved in 10 ml of water for injections PhEur. The injection should be administered over 5 minutes, directly into the vein or via the tubing of an intravenous infusion.

Ceftriaxone 2 g powder for solution for injection or infusion

Ceftriaxone can be administered by intravenous infusion over at least 30 minutes (preferred route) or by slow intravenous injection over 5 minutes. Intravenous intermittent injection should be given over 5 minutes preferably in larger veins. Intravenous doses of 50 mg/kg or more in infants and children up to 12 years of age should be given by infusion. In neonates, intravenous doses should be given over 60 minutes to reduce the potential risk of bilirubin encephalopathy (see section 4.3 and 4.4 of the SmPC). Intramuscular administration should be considered when the intravenous route is not possible or less appropriate for the patient. For doses greater than 2 g intravenous administration should be used.

Ceftriaxone is contraindicated in neonates (≤ 28 days) if they require (or are expected to require) treatment with calcium-containing intravenous solutions, including continuous calcium-containing infusions such as parenteral nutrition, because of the risk of precipitation of Ceftriaxone-calcium (see section 4.3).

Diluents containing calcium, (e.g. Ringer's solution or Hartmann's solution), should not be used to reconstitute Ceftriaxone vials or to further dilute a reconstituted vial for IV administration because a precipitate can form. Precipitation of Ceftriaxone-calcium can also occur when Ceftriaxone is mixed with calcium-containing solutions in the same IV administration line. Therefore, Ceftriaxone and calcium-containing solutions must not be mixed or administered simultaneously (see sections 4.3, 4.4 and 6.2).

For pre-operative prophylaxis of surgical site infections, Ceftriaxone should be administered 30-90 minutes prior to surgery.

For instructions on reconstitution of the medicinal product before administration, see section 6.6 of the SmPC.

- **Incompatibilities**

Based on literature reports, Ceftriaxone is not compatible with amsacrine, vancomycin, fluconazole and aminoglycosides and labetalol.
Solutions containing Ceftriaxone should not be mixed with or added to other agents except those mentioned in section 6.6 of the SmPC.
In particular, diluents containing calcium, (e.g. Ringer's solution, Hartmann's solution) should not be used to reconstitute Ceftriaxone vials or to further dilute a reconstituted vial for IV administration because a precipitate can form.
Ceftriaxone must not be mixed or administered simultaneously with calcium containing solutions including total parenteral nutrition (refer to the Summary of Product Characteristics, sections 4.2, 4.3, 4.4 and 4.8).

If treatment with a combination of another antibiotic with Ceftriaxone is intended, administration should not occur in the same syringe or in the same infusion solution.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

- **Shelf life and special precautions for storage**

Unopened – Three years. Do not store above 25^{o}C. Keep the vials or bottles in the outer carton.

For reconstituted solution, chemical and physical in-use stability has been demonstrated for 24 hours at 25^{o}C and for four days at 2-8^{o}C. From a microbiological point of view, once opened, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to the use are the responsibility of the user and would normally not be longer than 24 hours at 2-8^{o}C, unless reconstitution has taken place in controlled and validated aseptic conditions.

- **Instructions for use/handling**

1 g vial - Concentrations for the intravenous injection: approximately 100 mg/ml,
1 g vial - Concentrations for the intravenous infusion: approximately 50 mg/ml
2 g vial – Concentrations for the intravenous injection or intravenous infusion: approximately 50 mg/ml
(Please refer to section 4.2 of the SmPC for further information).

Reconstitution Table

Strength	Administration route	Diluent	Volume of diluent to be added (ml)	Approximate available volume (ml)	Approximate displacement volume (ml)
1 g	Intravenous injection[1]	Water for injections	10 ml	10.8 ml	0.8 ml
1 g	Intramuscular injection	1 % lidocaine	3.5 ml	4.1 ml	0.6 ml
2 g	Intramuscular injection[2]	1 % lidocaine	7 ml	8.4 ml	1.4 ml
2 g	Intravenous injection or infusion	See list of compatible diluents below*	40 ml	41.5 ml[#]	1.5 ml[#]

[1] For Intravenous injection, 1 g Ceftriaxone is dissolved in 10 ml of Water for Injections. The injection should be administered over 5 minutes, directly into the vein or via the tubing of an intravenous infusion.
[2] Dosages greater than 1 g should be divided and injected at more than one site.
[#] These approximate available volume and approximate displacement volume values are when reconstituted using Water for Injections.

The use of freshly prepared solutions is recommended. For storage conditions of the reconstituted medicinal product, see section 6.3 of the SmPC.

Ceftriaxone should not be mixed in the same syringe with any drug other than 1 % Lidocaine Injection BP (for intramuscular injection only).

*Ceftriaxone is compatible with several commonly used intravenous infusion fluids e.g. Sodium Chloride Intravenous Infusion BP, 5 % or 10 % Glucose Intravenous Infusion BP, Sodium Chloride and Glucose Intravenous Infusion BP (0.45 % sodium chloride and 2.5 % glucose), Dextran 6 % in Glucose Intravenous Infusion BP 5 %, isotonic hydroxyethylstarch 6-10 % infusions and Water for Injections.

The reconstituted solution should be clear. Do not use if particles are present.

Ceftriaxone sodium when dissolved in Water for Injections Ph Eur forms a pale yellow to amber solution. Variations in the intensity of colour of the freshly prepared solutions do not indicate a change in potency or safety.

For single use only. Discard any unused contents.

This leaflet was last revised in 04/2024

The information in this leaflet applies only to Ceftriaxone 1 g Powder for solution for injection/infusion and Ceftriaxone 2 g Powder for solution for injection/infusion.