Package leaflet: information for the Patient

RIIDOR®

(Cefepime hydrochloride powder for solution for injection or infusion 1g)

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 any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

What is in this leaflet?

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1. What Riidor® is and what it is used for

A fourth generation cephalosporin that binds to bacterial cell membranes and inhibits cell wall synthesis; Therapeutic Effect: Bactericidal.

Riidor® is indicated in the treatment of the following infections Cefepime susceptible organisms:

- **Severe and Complicated Urinary Tract Infections** (including those associated with pyelonephritis).
- **Severe pneumonia** including cases associated with concurrent bacteremia due to susceptible strains.
- **Severe Skin and Skin Structure Infections** caused by Staphylococcus aureus (methicillin-susceptible strains only) or Streptococcus pyogenes.
- **Complicated Intra-abdominal Infections** (used in combination with metronidazole) caused by Escherichia coli, viridans group streptococci, Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterobacter species, or Bacteroides fragilis.

2. What you need to know before you are given Riidor®

You must not be given Riidor® if:

You are allergic to any ingredient in Cefepime or to another cephalosporin antibiotic (eg, Cephalexin)

You have had a severe allergic reaction to a penicillin antibiotic (eg, amoxicillin) or another beta-lactam antibiotic (eg, Imipenem)

Contact your doctor or health care provider right away if any of these apply to you.

Warnings and precautions

Tell your doctor if you have ever had an allergic reaction to other Cephalosporins, or to penicillin.

Before therapy with Riidor® is instituted, careful inquiry should be made to determine whether the patient has had previous immediate hypersensitivity reactions to Cefepime, Cephalosporins, penicillins, or other drugs.

Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures including oxygen, corticosteroids, intravenous fluids, intravenous antihistamines, presser amines, and airway management, as clinically indicated.

In patients with creatinine clearance less than or equal to 60 mL/min, the dose of Cefepime (Cefepime hydrochloride) should be adjusted to compensate for the slower rate of renal elimination. Because high and prolonged serum antibiotic concentrations can occur from usual dosages in patients with renal impairment or other conditions that may compromise renal function, the maintenance dosage should be reduced when Cefepime is administered to such patients. Continued dosage should be determined by degree of renal impairment, severity of infection, and susceptibility of the causative organisms.

Prescribing Cefepime in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

As with other antimicrobials, prolonged use of Cefepime may result in overgrowth of non-susceptible microorganisms. Repeated evaluation of the patient's condition is essential. Should superinfection occur during therapy, appropriate measures should be taken.

Many Cephalosporins, including Cefepime, have been associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy. Prothrombin time should be monitored in patients at risk, and exogenous vitamin K administered as indicated.

Cefepime (Cefepime hydrochloride) should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

If you have diabetes, this medicine could affect a urine test for sugar. Clinitest® and similar tests may not work correctly. Ask your doctor how you should do a urine sugar test.

Arginine has been shown to alter glucose metabolism and elevate serum potassium transiently when administered at 33 times the amount provided by the maximum recommended human dose of Cefepime. The effect of lower doses is not presently known.

Make sure your doctor knows if you are pregnant or breastfeeding, or if you have liver disease, kidney disease, or a history of colitis.

If your symptoms do not improve or if they get worse, call your doctor.

Other medicines and Riidor®

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

Aminoglycosides, loop diuretics: Increased risk of nephrotoxicity. Probenecid: May increase Cefepime blood concentration.
Warfarin: May increase response to warfarin

Diagnostic Test Effects: May increase serum alkaline phosphatase, bilirubin, INR, LDH, AST (SGOT) and ALT (SGPT) levels. May cause a positive direct or indirect Coombs' test.

Pregnancy and breast-feeding and fertility

Ask your doctor or pharmacist for advice before taking any medicine.

Pregnancy: Teratogenic Effects: Pregnancy Category B. Cefepime was not teratogenic or embryocidal when administered during the period of organogenesis to rats at doses up to 1000 mg/kg/day (1.6 times the recommended maximum human dose calculated on a mg/m2 basis) or to mice at doses up to 1200 mg/kg (approximately equal to the recommended maximum human dose calculated on a mg/m2 basis) or to rabbits at a dose level of 100 mg/kg (0.3 times the recommended maximum human dose calculated on a mg/m2 basis).

There are, however, no adequate and well-controlled studies of Cefepime use in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only when the anticipated benefit the potential risk.

Labor and delivery: Cefepime has not been studied for use during labor and delivery. Treatment should only be given if clearly indicated. Cefepime should be used when the anticipated benefit the potential risk.

Breast-feeding: Cefepime is excreted in human breast milk in very low concentrations (0.5mcg/mL). Caution should be exercised when Cefepime is administered to a nursing woman.

Driving and using machines

Although there were not reported effects on the ability to drive or use machines, the possibility of dizziness should be taken in account.

3. How Riidor® is given

The recommended adult and pediatric dosages and routes of administration are outlined in the following table Riidor® should be administered intravenously over approximately 30 minutes. Before administration ensure that the powder has been fully dissolved in the solution. Administration duration should be within 10 days.

Adults

Indication	Dose	Frequency
Pneumonia (moderate to severe)	1-2 g, IV	Every 12h
Uncomplicated and complicated Urinary Tract Infection	Mild to moderate	Every 12h
Uncomplicated and complicated skin and skin structure Tract infection	2 g, IV	Every 12h
Complicated Intra-abdominal Infections	2 g, IV	Every 12h

- including cases associated with concurrent bacteremia or until resolution of neutropenia. In patients whose fever resolves but who remain neutropenic for more than 7 days, the need for continued antimicrobial therapy should be re-evaluated frequently.
- IM route of administration is indicated only for mild to moderate, uncomplicated or complicated UTIs due to E. coli when the IM route is considered to be a more appropriate route of drug administration.

Pediatric patients

For the treatment of uncomplicated and complicated urinary tract infections (including pyelonephritis), uncomplicated skin and skin structure infections, or pneumonia, recommends that pediatric patients weighing less than 40 kg receive cefepime in a dosage of 50 mg/kg given IV every 12 hours.1 Pediatric dosage should not exceed the recommended adult dosage.

The American Academy of Pediatrics (AAP) recommends that pediatric patients 2 months of age or older receive IM or IV cefepime in a dosage of 100-150 mg/kg daily in 3 equally divided doses for the treatment of mild to moderate infections or a dosage of 150 mg/kg daily in 3 equally divided doses for the treatment of severe infections.

Patients with Renal Impairment

In patients with creatinine clearance less than or equal to 60 ml/min, the dose of Riidor® should be adjusted to compensate for the slower rate of renal elimination. The recommended initial dose of Riidor® should be the same as in patients with normal renal function except in patients undergoing hemodialysis. The recommended doses of Riidor® in patients with renal impairment are presented in below.
When only serum creatinine is available, the following formula (Cockcroft and Gault equation) may be used to estimate creatinine clearance. The serum creatinine should represent a steady state of renal function:

$$\text{Males:} \quad \frac{\text{(weight in kg) x (140-age)}}{\text{(72) x serum creatinine (mg/100mL)}}$$

Females: (0,85) x (above value)

(Where age is year, weight is in kg and serum creatinine is in mg/mL).

Dosage of cefepime should be modified in renal impairment. After a normal first dose the maintenance dosage should be adjusted according to the patient's creatinine clearance (CC) and the severity of the infection:

- CC 30 to 60 mL/minute: 0.5 to 2 g every 24 hours (2 g every 12 hours for febrile neutropenia)
- CC 11 to 29 mL/minute: 0.5 to 1 g every 24 hours (2 g every 24 hours for febrile neutropenia)
- CC 10 mL/minute or less: 250 to 500 mg every 24 hours (1 g every 24 hours for febrile neutropenia)

Patients undergoing haemodialysis should be given a dose of 1 g on the first day of treatment, followed by 500 mg daily; the dose should be given after haemodialysis on those days. A dose of 1 g daily should be used for febrile neutropenia. Patients undergoing continuous ambulatory peritoneal dialysis should receive normal recommended doses at intervals of 48 hours. A dose of 2 g every 48 hours is used for febrile neutropenia.

Riidor® should be administered at the same time each day and following the completion of hemodialysis on hemodialysis days.

Geriatric: Of the more than 6400 adults treated with Cefepime in clinical studies, 35% were 65 years or older while 16% were 75 years or older. When geriatric patients received the usual recommended adult dose, clinical efficacy and safety were comparable to clinical efficacy and safety in nongeriatric adult patients.

Serious adverse events have occurred in geriatric patients with renal insufficiency given unadjusted doses of Cefepime, including life-threatening or fatal occurrences of the following: encephalopathy, myoclonus, andseizures.

Administration

***Intermittent IV Infusion*:** For intermittent IV infusion, vials labeled as containing 500 mg or 1.0 g, of cefepime should be reconstituted with 5, or 10 mL, respectively, of a compatible IV solution to provide solutions containing approximately 100 or 100 mg/mL of the drug, respectively. The appropriate dose of the drug should then be added to a compatible IV solution.

Rate of Administration. The cefepime dose may be administered by IV infusion over approximately 30 minutes.

***IM Injection*:** IM injections of cefepime are prepared by adding 1.3 or 2.4 mL of an appropriate diluent (i.e., sterile water for injection, 0.9% sodium chloride, 5% dextrose) to a vial labeled as containing 500 mg or 1.0 g of cefepime, respectively, to provide a solution containing approximately 280 mg/mL.

If you are given more Riidor®

As Riidor® is given to you under the supervision of your doctor, it is very unlikely that you will receive too much. However, if you experience any unexpected or worrying side effects after being given Riidor® accidentally use more than your prescribed dose, contact your doctor or nearest hospital straight away
You may need urgent medical attention.

If you forget to use Riidor®

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. Don't take a double dose (two injections at the same time) to make up for a missed dose.

4. Possible side effects

Undesirable effects are classified into the following categories, according to system organ class, MedDRA terminology and MedDRA frequencies: Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to ≤1/100), rare (≥1/10,000 to ≤1/1,000), very rare (≤ 1/10,000) and not known (frequency cannot be estimated from the available data).
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System Organ Class	Frequency	MedDRA Term
Infections and infestations	Uncommon	Oral candidiasis, vaginal infection
	Rare	Candidiasis
Blood and lymphatic system disorders	Very common	Coombs test positive
	Common	Prothrombin time prolonged, partial thromboplastin time prolonged, anaemia, eosinophilia
	Uncommon	Thrombocytopenia, leukopenia, neutropenia
	Not known	Aplastic anaemia, haemolytic anaemia, agranulocytosis
Immune system disorders	Rare	Anaphylactic reaction, angioedema
	Not known	Anaphylactic shock
Metabolism and nutrition disorders	Not known	Urine glucose false positive
Psychiatric disorders	Not known	Confusional state, hallucination
Nervous system disorders	Uncommon	Headache
	Rare	Convulsion, paraesthesia, dysgeusia, dizziness
	Not known	Coma, stupor, encephalopathy, altered state of consciousness, myoclonus
Vascular disorders	Common	Infusion site phlebitis
	Rare	Vasodilation
	Not known	Haemorrhagea
Respiratory, thoracic and mediastinal disorders	Rare	Dyspnoea
Gastrointestinal disorders	Common	Diarrhoea
	Uncommon	Pseudomembranous colitis, colitis, nausea, vomiting
	Rare	Abdominal pain, constipation

	Not known	Gastrointestinal disorder
Hepatobiliary disorders	Common	Alanine aminotransferase increased, Aspartate aminotransferase increased, Blood bilirubin increased
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Erythema, urticaria, pruritus
	Not known	Toxic epidermal necrolysisa , Stevens-Johnson syndrome, erythema multiformea
Renal and urinary disorders	Uncommon	Blood urea increased, blood creatinine increased
	Not known	Renal failure, nephropathy toxica
Reproductive system and breast disorders	Rare	Pruritus genital
General disorders and administration site condition	Common	Infusion site reaction, injection site pain, injection site inflammation
	Uncommon	Pyrexia, infusion site inflammation
	Rare	Chills
Investigations	Common	Alkaline phosphatase increased

Paediatric population

The safety profile of cefepime in infants and children is similar to that seen in adults. The most frequently reported adverse event considered related to cefepime in clinical trials was rash.
If you notice other side effects that you think are caused by this medicine, tell your doctor.

5. How to store Riidor®

Preserve the tightly closed containers. Do not store above 25°C. Protect from light. Keep out of reach of children.

Do not use Riidor® after the expiry date printed on the carton. The expiry date refers to the last day of that month.

Reconstituted solution are stable for 24 hours when kept at room temperature (not exceeding 25°C), or when kept in a refrigerator (2~8°C). From a microbiological point of view, once opened, the production should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Riidor® contains:

The active substance is Cefepime Hydrochloride. One vial with powder for solution for injection or infusion contains 1.0 g Cefepime as Cefepime Hydrochloride. The other ingredients are L-Arginine (contains approximate 725mg per gram of Cefepime. It is added to control the pH of the reconstituted solution at 4-6)

What Riidor® looks like and contents of the pack.

White to pale yellow powder

Size of packing:

Box with 1 or 50 colorless glass vials containing powder for solution for injection or infusion.

Name and Address of the Marketing Authorization Holder/ Manufacturer

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Date of Revision of the Text

12.06.2018