PACKAGE LEAFLET: INFORMATION FOR THE USER

Imipenem/Cilastatin 500 mg/500 mg Powder for Solution for Infusion

Read all of this leaflet carefully before you start using this medicine.

- 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.

In this leaflet:

1. WHAT IMIPENEM/CILASTATIN IS AND WHAT IT IS USED FOR

Imipenem/Cilastatin contains two different medicines called imipenem and cilastatin. Imipenem belongs to a group of medicines called carbapenem antibiotics and is able to kill a wide range of bacteria that may cause infection. Imipenem is inactivated by a reaction that occurs in the kidneys. Cilastatin stops this reaction by inhibiting the enzyme that inactivates imipenem. This allows the levels of imipenem in the blood and urine to be higher to kill bacteria.

Like all antibiotics, Imipenem/Cilastatin is only effective against some types of bacteria. So, it is suitable for treating some types of infections. The treatment may sometimes need to be started before knowing the bacteria causing the infection.

This medicine can be used to treat infections in different parts of the body including the:

- abdomen
- lungs
- urinary system
- skin and soft tissue

Imipenem/Cilastatin is not recommended for the treatment of meningitis, which is an infection of the membranes surrounding the brain and spinal cord.

2. BEFORE YOU USE IMIPENEM/CILASTATIN

Do not use Imipenem/Cilastatin if you are:

- allergic (hypersensitive) to imipenem, cilastatin or to sodium hydrogen carbonate.

Take special care with Imipenem/Cilastatin if:

- you have ever had an allergic reaction to carbapenem antibiotics, penicillins, cephalosporins and other beta-lactam antibiotics.
- you experience severe or persistent diarrhoea with stomach pain or cramps during or shortly after treatment. You should stop receiving treatment with this medicine and contact your doctor immediately because you may have an infection of the large bowel (called pseudomembranous colitis) that needs special treatment.
- you have ever had inflammation of your bowel, called colitis or any other severe disease affecting your gut.
- the treatment is for your child and your child is less than 3 years of age or has kidney problems. This medicine is not recommended for use in these children.
- you have nervous system problems such as brain disorders or fits (seizures).
- you have ever been told that your kidneys do not work very well. Also, if you are receiving any treatment like dialysis for kidney failure. You may still receive treatment with this medicine but you may need a lower dose.
- You have myasthenia gravis (a nerve disease which causes muscle weakness).

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before using Imipenem/Cilastatin.

Taking other medicines

Special care should be taken if you are taking other medicines as some could interact with Imipenem/Cilastatin. In particular, tell your doctor or pharmacist if you are taking:

- Ganciclovir (a medicine used in the treatment of certain viral infections). This medicine may lead to an increased risk of fits when used with Imipenem/Cilastatin.
- Probenecid (a medicine used in the treatment of gout or hyperuricemia).
- Valproic acid. (a medicine used in the treatment of convulsions).

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

Taking Imipenem/Cilastatin with food and drink

Food/meals have no influence on the effectiveness of Imipenem/Cilastatin as it is given into a vein.

Pregnancy and breast-feeding

Before starting treatment, you must tell your doctor if you are pregnant or if you intend to become pregnant. It is not known whether this medicine may harm the unborn child. It will only be given to pregnant women if it is absolutely necessary.

Mothers who wish to breast-feed should discuss this with their doctor. Small amounts of this medicine are known to enter the milk. Breast feeding is to be avoided by mothers who receive Imipenem/Cilastatin.

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

Driving and using machines

This medicine can cause confusional states, fits and hallucinations. You should not drive or operate dangerous machinery until it is known how this medicine affects you.

Important information about one of the ingredients of Imipenem/Cilastatin

A 500 mg dose of this medicinal product contains 1.6 mmol (or 37.5 mg) sodium. To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO USE IMIPENEM/CILASTATIN

This medicine is supplied as a powder, so it must be made into a solution before it can be given. Only some types of solutions can be used to mix with the powder to make it ready for use. Your doctor or nurse will use one of the right solutions to prepare a fresh solution of this medicine for administration.

Imipenem/Cilastatin will be given to you by a doctor or a nurse as a slow injection (infusion) via a drip into a vein.

For doses up to 500 mg the infusion time for each dose is between 20 and 30 minutes. For doses more than 500 mg the infusion time is 40 to 60 minutes.

Dosage

Your doctor will decide on the right dose for you. The dose will depend on the type of infection that you have, where the infection is in the body, how serious the infection is, your kidney function and your body weight.

The usual adult dose is 1.5 to 2 g per day, given in 3-4 divided doses. The dose for children is normally determined on bodyweight; the usual dose is 15 mg for each kilogram (kg) of bodyweight every 6 hours. The maximum daily dosage in children should not be more than 2 g.

The following information is intended for medical or healthcare professionals only:

Imipenem/Cilastatin 500 mg/500 mg Powder for Solution for Infusion

The product is chemically incompatible with lactate and must not be reconstituted in solutions that contain it. However, it can be administered into an IV tubing, through which a lactate solution is to be infused.

The product must not be mixed or physically added to other antibiotics

Method of administration

Each dose of 250 mg or 500 mg should be given by intravenous infusion over 20-30 minutes. Each dose of 1000 mg should be infused over 40-60 minutes. In patients who develop nausea during infusion, the infusion rate may be slowed.

Preparation instructions

Reconstitution of the intravenous solution

The product is supplied as dry sterile powder in vials containing the equivalent of 500 mg of imipenem and 500 mg of cilastatin.

The product is buffered with sodium hydrogen carbonate, in order to obtain pH solutions between 6.5 and 8.5. There is no significant modification of the pH when the solutions are prepared and used as indicated. The product contains 37.5 mg of sodium (1.6 mmol).

For single use only. Discard any unused solution.

Q70316
M.L. No. 763

Component Specification

Item number:	Q70316
Request number:	AS0177
Country:	UK
Inventory code(s):	E1034AUK1 E1035AUK1
OI template:	88S119
Amalia version:	4
Mulgrave version:	4
Dimensions:	118 x 570 mm (20 panels)
Container(s):	vial
Supplier:	Orchid
Stock:	n/a
Folded dimensions:	28.5 x 118 mm
Printed both sides:	Yes
Perforated:	No
Pharma code:	n/a
Pharma code length:	n/a
Supplier Code:	n/a

Colours

Black: ■

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Version 1		**Version 2**	
Technician:	DY	Technician:	KN
Date:	14-Jun-10	Date:	14/Jun/10
Version 3		**Version 4**	
Technician:	JH	Technician:	gdw
Date:	26/Jul/10	Date:	19/Aug/10
Version 5		**Version 6**	
Technician:	XX	Technician:	XX
Date:	dd/mmm/yy	Date:	dd/mmm/yy
Version 7		**Version 8**	
Technician:	XX	Technician:	XX
Date:	dd/mmm/yy	Date:	dd/mmm/yy
Version 9		**Version 10**	
Technician:	XX	Technician:	XX
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If you have kidney problems, you may be given a lower dose of this medicine.

As Imipenem/Cilastatin is most likely to be given to you under the supervision of a doctor, it is unlikely that you will receive an incorrect dose. However, if you have any concerns about the dose you receive, please tell your doctor or nurse.

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, Imipenem/Cilastatin can have side effects, although not everybody gets them.

If you experience any of the following side effects, tell your doctor immediately as these are all serious and you may require urgent medical attention:

- severe allergic reaction (rare, affects 1 to 10 users in 10,000); you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), and you may feel you are going to faint

If any of the following happen, tell your doctor immediately:

- severe abdominal pain with diarrhoea and fever (rare, affects 1 to 10 users in 10,000)
- blistering or peeling skin (rare, affects 1 to 10 users in 10,000)

If any of the following happen, tell your doctor as soon as possible:

Common side effects (affect 1 to 10 users in 100):

- pain and hardening of tissue at the injection site
- vein inflammation related to a blood clot
- increases in the amounts of different blood cells (platelets and eosinophils). Your doctor may do blood tests from time to time
- changes in blood tests that show how well your liver is working
- redness of the skin, skin rash, skin irritation, itchy skin, hives

Uncommon side effects (affect 1 to 10 users in 1,000):

- decreases in the amount of white blood cells and haemoglobin. You may bleed for longer. Your doctor may do blood tests from time to time
- changes in result of a specific blood test (called Coombs' test)
- psychiatric disturbances including hallucinations and confusion
- seizures
- drowsiness, dizziness and vertigo
- headache
- diarrhoea, feeling sick (nausea) or being sick (vomiting)
- staining of the teeth or tongue
- kidney problems (detected by blood tests)

Rare side effects (affect 1 to 10 users in 10,000):

- infections caused by yeast (Candida) or *Xanthomas maltophilia*
- severe decrease in the amount of white blood cells (agranulocytosis), decrease in the amount of neutrophils (a type of white blood cell), decrease in the amount of platelets (a type of blood cell) and haemolytic anaemia (abnormal breakdown of red blood cells). Your doctor may do blood tests from time to time
- erythema multiforme (a severe allergic reaction of the skin, mouth or eyes), serious allergic reaction (anaphylaxis), severe allergic reactions (swelling of the face, lips and tongue and throat) toxic epidermal necrolysis and Stevens-Johnson Syndrome (both life-threatening skin conditions where the top layer of skin detaches from the lower layers)
- encephalopathy (disorder of the structure of the brain)
- impaired hearing
- low blood pressure
- infection of the large bowel (pseudomembranous colitis), impaired taste
- a disease of the liver (hepatitis), liver failure
- change in the colour of the urine, change in the quantity of urine
- physical weakness

Very rare side effects (affect less than 1 user in 10,000):

- decrease in the number of blood cells (bone marrow suppression)
- rapid breathing, shortness of breath
- acute liver failure (fulminant hepatitis)
- physical weakness including exacerbation of a pre-existing condition called myasthenia gravis
- rapid loss of kidney function (acute renal failuire), increased blood levels of creatinine and urea, harmless discoloration of the urine in children

Not known (frequency cannot be estimated from the available data):

- rapid heart rate (tachycardia), abnormal awareness of the beating of the heart (palpitations)
- abdominal cramps and bloody diarrhoea (haemorrhagic colitis), gastric flu, abdominal pain, swollen and discolored tongue, inflammation of the tongue, heartburn, sore throat, increased salivation
- flushing of the skin, blue coloration of the skin and mucous membranes, increased perspiration, change in skin texture, vaginal itching
- joint pain, chest pain
- fever including drug fever

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE IMIPENEM/CILASTATIN

Keep out of the reach and sight of children

Expiry

Do not use after the expiry date which is stated on the vial label and carton. The expiry date refers to the last day of that month.

Storage

Prior to reconstitution, this medicinal product does not require any special storage conditions.

Prepared solutions should be used immediately. Prepared solutions should not be frozen.

Disposal

Unused medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines that are no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Imipenem/Cilastatin contains

The active substances are imipenem and cilastatin. Each vial contains 530 mg of Imipenem monohydrate and 530 mg of Cilastatin sodium corresponding to 500 mg of Imipenem and 500 mg of Cilastatin.

The other ingredient is sodium hydrogen carbonate.

What Imipenem/Cilastatin looks like and contents of the pack

This medicine is an off white to yellowish white hygroscopic powder for solution for infusion, which comes in glass containers called vials. The powder is made into a colourless to yellow solution, which is further diluted and given as an infusion via a drip. When reconstituting the sterile powder, allow 3-4 minutes for the contents of the vials to dissolve. It is supplied in packs containing either 20 ml or 100 ml vials, each containing 500 mg of imipenem and 500 mg of cilastatin.

Packs of the 20 ml vials contain 5 vials per carton. Packs of the 100 ml vials contain 1 vial per carton.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

The Marketing Authorisation Holder and manufacturer (responsible for batch release of the product in the EEA) is Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, UK.

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The reconstitution of powder is to be made under aseptic conditions using the diluents mentioned below. The solution is to be inspected visually for particulate matter and discoloration prior to administration. The solution should only be used if it is clear and free from particles.

Reconstituted solution stability has been established for 0.9% sodium chloride injection and sterile Water for Injections.

Reconstituted and diluted solutions should be used immediately.

Reconstitution of the 100 ml vial

The sterile powder must be reconstituted as directed below. It must be shaken until a clear solution is obtained allowing 3-4 minutes to reconstitute the powder. The variations in colour, from colourless to yellow, do not affect the potency of the product.

Dose (imipenem in mg)	Volume of solvent to be added (ml)	Mean approximate concentration of product (mg/ml of imipenem)
500	100	5

Reconstitution of the 20 ml vial

The contents of the vial must be suspended and transferred to 100 ml of an appropriate solution for infusion. A suggested procedure is to add approximately 10 ml of appropriate infusion solution to the vial. Shake well and transfer the resulting suspension to the infusion solution container.

Caution: The suspension is not for direct infusion.

Repeat with an additional 10 ml of infusion solution to ensure complete transfer of the vial contents to the infusion solution. The resulting mixture must be shaken until clear.

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Amalia version:	4
Mulgrave version:	4
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Container(s):	vial
Supplier:	Orchid
Stock:	n/a
Folded dimensions:	28.5 x 118 mm
Printed both sides:	Yes
Perforated:	No
Pharma code:	n/a
Pharma code length:	n/a
Supplier Code:	n/a

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Hospira

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