Package leaflet: Information for the user

Imipenem/cilastatin 500 mg/500 mg powder for solution for infusion

Imipenem/Cilastatin

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 or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

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

Imipenem/cilastatin belongs to a group of medicines called carbapenem antibiotics. It kills a wide range of bacteria (germs) that cause infections in various parts of the body in adults and children one year of age and above.

Treatment

Your doctor has prescribed Imipenem/cilastatin because you have one (or more) of the following types of infection:
- Complicated infections in the abdomen
- Infection affecting the lungs (pneumonia)
- Infections that you can catch during or after the delivery
- Complicated urinary tract infections
- Complicated skin and soft tissue infections

Imipenem/cilastatin may be used in the management of patients with low white blood cell counts, who have fever that is suspected to be due to a bacterial infection.

Imipenem/cilastatin may be used to treat bacterial infection of the blood which might be associated with a type of infection mentioned above.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE IMIPENEM/CILASTATIN

Do not use Imipenem/cilastatin

- if you are allergic to imipenem or cilastatin or any of the other ingredients of this medicine (listed in section 6).
- if you are allergic to other antibiotics such as penicillins, cephalosporins, or carbapenems.

Warnings and precautions

Talk to your doctor or pharmacist before using Imipenem/cilastatin about any medical condition you have or have had including:
- allergies to any medicines including antibiotics (sudden life-threatening allergic reactions require immediate medical treatment)
- colitis or any other gastrointestinal disease
- kidney or urinary problems, including reduced kidney function (Imipenem/cilastatin blood levels increase in patients with reduced kidney function. Central nervous system adverse reactions may occur if the dose is not adjusted to the kidney function)
- any central nervous system disorders such as localized tremors or epileptic seizures (fits)
- liver problems

You may develop a positive test (Coombs test) which indicates the presence of antibodies that may destroy red blood cells. Your doctor will discuss this with you.

Children

Imipenem/cilastatin is not recommended in children less than one year of age or children with kidney problems.

Other medicines and Imipenem/cilastatin

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines.

Tell your doctor if you are taking ganciclovir which is used to treat some viral infections.

Tell your doctor if you are taking valproic acid or sodium valproate (used to treat epilepsy, bipolar disorder, migraine or schizophrenia) or any blood thinners such as warfarin.

Your doctor will decide whether you should use **Imipenem/cilastatin** in combination with these medicines.

Pregnancy and breast-feeding

It is important that you tell your doctor if you are pregnant or are planning to become pregnant before receiving Imipenem/cilastatin. Imipenem/cilastatin has not been studied in pregnant women. Imipenem/cilastatin should not be used during pregnancy unless your doctor decides the potential benefit justifies the potential risk to the foetus.

It is important that you tell your doctor if you are breast-feeding or if you intend to breast-feed before receiving Imipenem/cilastatin. Small amounts of this medicine may pass into breast milk and it may affect the baby. Therefore, your doctor will decide whether you should use Imipenem/cilastatin while breast-feeding.

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

Driving and using machines

There are some side effects associated with this product (such as seeing, hearing, or feeling something that is not there, dizziness, sleepiness, and a spinning sensation) that may affect some patients' ability to drive or operate machinery (see section 4).

Imipenem/cilastatin contains sodium

This medicinal product contains 37.5 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 1.88% of the recommended maximum daily dietary intake of sodium for an adult.

3. HOW TO USE IMIPENEM/CILASTATIN

Imipenem/cilastatin will be prepared and given to you by a doctor or another health care professional. Your doctor will decide how much Imipenem/cilastatin you need.

Use in adults and adolescents

The recommended dose of Imipenem/cilastatin for adults and adolescents is 500 mg/500 mg every 6 hours or 1,000 mg/1,000 mg every 6 or 8 hours. If you have kidney problems, your doctor may lower your dose.

PHARMACODE AREA

Use in children

The recommended dose for children one year of age or older is 15/15 or 25/25 mg/kg/dose every 6 hours. Imipenem/cilastatin is not recommended in children under one year of age and children with kidney problems.

Method of administration

Imipenem/cilastatin is given intravenously (into a vein) over 20-30 minutes for a dose of ≤ 500 mg/500 mg or 40-60 minutes for a dose of > 500 mg/500 mg. The rate of infusion may be slowed if you feel sick.

If you use more Imipenem/cilastatin than you should

Symptoms of overdose may include seizures, confusion, tremors, nausea, vomiting, low blood pressure and slow heart rate. If you think you have been given too much medicine you should notify your doctor or another healthcare professional immediately.

PHARMACODE AREA

If you forget to take Imipenem/cilastatin

If you are concerned that you may have missed a dose, contact your doctor or another healthcare professional immediately.

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

4. POSSIBLE SIDE EFFECTS

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

The following side-effects occur rarely, however if they do occur, while receiving or after receiving Imipenem/cilastatin, the medicine must be stopped and your doctor contacted immediately.
- Allergic reactions including rash, swelling of the face, lips, tongue and/or throat (with difficulty in breathing or swallowing), and/or low blood pressure.
- Skin peeling (toxic epidermal necrolysis)
- Severe skin reactions (Stevens-Johnson syndrome and erythema multiforme)
- Severe skin rash with loss of skin and hair (exfoliative dermatitis)

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

Each vial is for single use only.

Reconstitution

Contents of the vials must and transferred to 100 mL of an appropriate infusion solution (see **Incompatibility** and **After reconstitution**): 0.9% sodium chloride. In exceptional circumstances where 0.9% sodium chloride cannot be used for clinical reasons, 5% glucose may be used instead. A suggested procedure is to add approximately 10 mL of the appropriate infusion solution to the vial. Shake well and transfer the resulting mixture to the infusion solution container.

CAUTION: THE MIXTURE IS NOT FOR DIRECT INFUSION.

Repeat with an additional 10 mL of infusion solution to ensure complete transfer of vial contents to the infusion solution. The resulting mixture should be agitated until clear. The concentration of the reconstituted solution following the above procedure is approximately 5 mg/ml for both imipenem and cilastatin.
Variations of colour, from colourless to yellow, do not affect the potency of the product.

Compatibility and stability

In keeping with good clinical and pharmaceutical practice, **Imipenem/cilastatin** should be administered as a freshly prepared solution with the following diluent: 0.9% Sodium Chloride Injection.

Incompatibility

This medicinal product is chemically incompatible with lactate and should not be reconstituted with diluents containing lactate, however, can be administered into an IV system through which a lactate solution is being infused.

This medicinal product must not be mixed with other medicinal products except those mentioned under **Reconstitution**.

After reconstitution

Diluted solutions should be used immediately. The time interval between the beginning of reconstitution and the end of intravenous infusion should not exceed two hours.

Any unused product or waste material should be disposed of in accordance with local requirements.

Other possible side effects:

Common (may affect up to 1 in 10 people)
- Increased numbers of specific white blood cells
- Swelling and redness along a vein which is extremely tender when touched
- Rash
- Abnormal liver function detected by blood tests
- Nausea, vomiting, diarrhoea. Nausea and vomiting appear to occur more frequently in patients with low number of white blood cells

Uncommon (may affect up yo 1 in 100 people)
- Local skin redness
- Local pain and formation of a firm lump at the injection site
- Skin itchiness
- Hives
- Fever
- Blood disorders affecting the cell components of the blood and usually detected by blood tests (symptoms may be tiredness, paleness of skin, and prolonged bruising after injury)
- Abnormal kidney, liver and blood function detected by blood tests
- Tremors and uncontrolled twitching of muscles
- Seizures (fits)
- Psychic disturbances (such as mood swings and impaired judgment)
- Seeing, hearing or feeling something that is not there (hallucinations)
- Confusion
- Dizziness, sleepiness
- Low blood pressure

Rare (may affect up to 1 in 1,000 people)
- Fungal infection (candidiasis)
- Staining of the teeth and/or tongue
- Inflammation of the colon with severe diarrhoea
- Disturbances in taste
- Inability of the liver to perform normal function
- Inflammation of the liver
- Inability of the kidney to perform normal function
- Changes in the amount of urine, changes in urine colour
- Disease of the brain, tingling sensation (pins and needles), localised tremor
- Hearing loss

Very rare (may affect up to 1 in 10,000 people)
- Severe loss of liver function due to inflammation (fulminant hepatitis)
- Inflammation of stomach or intestine (gastro-enteritis)
- Inflammation of intestine with bloody diarrhoea (haemorrhagic colitis)
- Red sowllen tongue, overgrowth of the normal projections on the tongue giving it a hairy appearance, heatburn, sore throat, increase in the production of saliva
- Stomach pain
- A spinning sensation (vertigo), headache
- Ringing in the ears (tinnitus)
- Pain in several joints, weakness
- Irregular heartbeat, the heart beating forcefully or rapidly
- Chest discomfort, difficulty breathing, abnormally fast and superficial breathing, pain in the upper spine
- Flushing, bluish discoloration of the face and lips, skin texture changes, excessive sweating
- Itching of the vulva in women
- Changes in the amounts of blood cells
- Worsening of a rare disease associated with muscle weakness (aggravation of myasthenia gravis)

Not known (frequency cannot be estimated from the available data)
- Abnormal movements
- Agitation

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system in: Yellow Card Scheme,
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store; or HPRA Pharmacovigilance, Website: www.hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine.

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5. HOW TO STORE IMIPENEM/CILASTATIN

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 carton and on the vials after EXP. The expiry date refers to the last day of that month.

Do not store above 25 °C.
Keep the vials in the outer carton.

After reconstitution:
Diluted solutions should be used immediately. The time interval between the beginning of reconstitution and the end of intravenous infusion should not exceed two hours.

Do not freeze reconstituted solution.

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 Imipenem/cilastatin contains

- The active substances are imipenem and cilastatin. Each vial of Imipenem/cilastatin 500 mg/500 mg contains 530 mg imipenem monohydrate equivalent to 500 mg imipenem and 530 mg cilastatin sodium salt equivalent to 500mg cilastatin.
- The other ingredient is 20 mg sodium hydrogen carbonate.

What Imipenem/cilastatin looks like and contents of the pack

Imipenem/cilastatin 500 mg/500 mg is a white to almost white or light (pale) yellow powder for solution for infusion available in uncoloured 20 ml glass vials type III, stoppered with bromobutyl rubber stoppers having a diameter of 20 mm.

Pack sizes:

1 vial / carton (20 ml vial)
10 vials / carton (20 ml vial)

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Hikma Farmacêutica (Portugal) S.A.
Estrada do Rio da Mó, nº8, 8A e 8B, Fervença
2705-906 Terrugem SNT
Portugal
Tel.: 351-21-960 84 10 / Fax: 351-21-961 51 02
E-mail: portugalgeral@hikma.com

Manufacturer
ACS Dobfar S.p.A.
Nucleo Industriale S. Atto
S. Nicolò a Tordino
64020 TERAMO
Italy

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria:	*Imipenem/Cilastatin Hikma 500 mg/500 mg Pulver zur Herstellung einer Infusionslösung*
Germany:	*Imipenem/Cilastatin Hikma 500 mg/500 mg Pulver zur Herstellung einer Infusionslösung*
Ireland:	*Imipenem/Cilastatin 500 mg/500 mg Powder for solution for infusion*
Italy:	*Imipenem/Cilastatina Hikma 500 mg/500 mg Polvere per soluzione infusione*
Netherlands:	*Imipenem/Cilastatin Hikma 500 mg/500 mg*
Portugal:	*Imipenem/Cilastatina Hikma 500 mg + 500 mg Pó para solução para perfusão*
United Kingdom:	*Imipenem/cilastatin 500 mg/500 mg Powder for solution for infusion*
France:	*Imipenem/Cilastatine Hikma 500 mg/500 mg Poudre pour solution pour perfusion*
Spain:	*Imipenem /Cilastatina Hikma 500 mg/500 mg Polvo para solución para perfusión*

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