Package leaflet: Information for the user
Imipenem/Cilastatin 250 mg/250 mg Powder for Solution for Infusion
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 nurse.
- If you get any side effects, talk to your doctor or nurse. 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

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 of your baby
- 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, 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 nurse before using Imipenem/Cilastatin

- if you have allergies to any medicines including antibiotics (sudden life-threatening allergic reactions require immediate medical treatment)
- if you have colitis or any other gastrointestinal disease
- if you have 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)
- if you have any central nervous system disorders such as localized tremors or epileptic seizures (fits)
- if you have 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, have recently taken or might take any other medicines.

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

Also, 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

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.

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 developing baby.

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.

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

Imipenem/Cilastatin 250 mg/250 mg contains 0.8 mmol (18.8 mg) sodium per dose and Imipenem/Cilastatin 500 mg/500 mg contains 1.6 mmol (37.5 mg) sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

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 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.

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 does 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 are concerned that you may have been given too much Imipenem/Cilastatin, contact your doctor or another healthcare professional immediately.

If you forget to use Imipenem/Cilastatin

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

Do not take a double dose to make up for a forgotten dose.

If you stop using Imipenem/Cilastatin

Do not stop using Imipenem/Cilastatin until 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 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)

Other possible side effects:
Common (may affect up to 1 in 10 people)

- Nausea, vomiting, diarrhoea. Nausea and vomiting appear to occur more frequently in patients with low number of white blood cells
- Swelling and redness along a vein which is extremely tender when touched
- Rash
- Abnormal liver function detected by blood tests
- Increase in some white blood cells

Uncommon (may affect up to 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 swollen tongue, overgrowth of the normal projections on the tongue giving it a hairy appearance, heartburn, 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 nurse. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly to:

United Kingdom:
Yellow Card Scheme www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store
Ireland:
HPRA Pharmacovigilance www.hpra.ie

By reporting side effects you can help provide more information on the safety of this medicine.

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

Before opening:
Do not store above 25ºC.

After first opening/reconstitution:
Reconstituted/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 the 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 either:

- 250 mg imipenem (as 265mg imipenem monohydrate) and 250 mg cilastatin (as 265mg cilastatin sodium salt)

or

- 500 mg imipenem (as 530mg imipenem monohydrate) and 500 mg cilastatin (as 530mg cilastatin sodium salt)

The other ingredient is sodium hydrogen carbonate

What Imipenem/Cilastatin looks like and contents of the pack

Imipenem/Cilastatin 250 mg imipenem and 250 mg cilastatin is a white to almost white or yellow powder delivered in 20 ml glass vials.
Imipenem/Cilastatin 500 mg imipenem and 500 mg cilastatin is a white to almost white or yellow powder delivered in 20 ml glass vials and 100 ml glass bottles.

Imipenem/Cilastatin 250 mg/250 mg and 500 mg/500 mg comes in packs containing 10 glass vials or 10 glass bottles of powder, closed with a rubber stopper, aluminium cap and flip-off cap.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorization Holder:
For UK
Fresenius Kabi Ltd
Cestrian Court
Eastgate Way, Manor Park
Runcorn, Cheshire, WA7 1NT
United Kingdom

For IE
Fresenius Kabi Deutschland GmbH
Else-Kröner-Straße 1,
61352 Bad Homburg v.d.Höhe
Germany

Manufacturer:
ACS Dobfar S.p.A., Nucleo Industriale S. atto, S. Nicolo a Tordino, Teramo, 64100 Teramo, Italy

For further information about this medicinal product, please contact the Marketing Authorization Holder.

This leaflet was last revised in November 2020

The following information is intended for healthcare professionals only:

Each vial is for single use only.

Reconstitution

Contents of each container must be transferred to 50 mL (for 250mg strength) and 100 mL (for 500mg strength) 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 from the appropriate infusion solution to the container. 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 container contents to the infusion solution. The resulting mixture should be agitated until a clear solution is obtained.

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.

Incompatibility

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

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

After reconstitution

Reconstituted/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 medicinal product or waste material should be disposed of in accordance with local requirements.