Package leaflet: Information for the user

Recarbrio® 500 mg/500 mg/250 mg powder for solution for infusion
imipenem/cilastatin/relebactam

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given 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 Recarbrio is and what it is used for

Recarbrio is an antibiotic. It contains the active substances imipenem, cilastatin and relebactam.

Recarbrio is used in adults to treat:
- certain bacterial infections of the lungs (pneumonia)
- infections of the blood associated with the infections of the lung mentioned above
- infections caused by bacteria that other antibiotics may not be able to kill

Recarbrio is used in patients 18 years or older.

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

You should not be given Recarbrio if:
- you are allergic to imipenem, cilastatin, relebactam or any of the other ingredients of this medicine (listed in section 6)
- you are allergic to carbapenem antibiotics
- you ever had a severe allergic reaction to penicillin antibiotics or cephalosporin antibiotics

You should not be given Recarbrio if any of the above apply to you. If you are not sure, talk to your doctor or nurse before being given Recarbrio.

Warnings and precautions
Talk to your doctor or nurse before being given Recarbrio if:
- you are allergic to any medicines - especially antibiotics
- you have ever had convulsions (seizures or fits)
- you have ever had confusion or muscle twitches with a medicine
- you are taking a medicine containing valproic acid

- you have had diarrhoea while taking antibiotics in the past
- you have kidney problems – your doctor may lower your dose

Tell your doctor right away if you have an allergic reaction, convulsions (seizures or fits), diarrhoea, or develop kidney problems while receiving Recarbrio (see section 3).

Children and adolescents
Recarbrio should not be used in children or adolescents who are under 18 years of age. This is because it is not known if the medicine is safe to use in these patients.

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

Tell your doctor about all the medicines you take, especially if you take:
- medicines that contain ganciclovir, used for treating some viral infections
- medicines that contain valproic acid or divalproex sodium, usually used for treating epilepsy, bipolar disorder, or migraine
- medicines to control blood clotting, such as warfarin

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before being given this medicine.

Driving and using machines
Recarbrio may make you feel dizzy, shaky, or cause convulsions or seizures. This may affect your ability to drive or use machines.

Recarbrio contains sodium
This medicine contains approximately 37.5 mg of sodium (main component of cooking/ table salt) in each vial. This is equivalent to about 2 % of the adult recommended maximum amount of sodium you should take daily, and needs to be taken into account if you are on a low-salt diet.

3. How you are given Recarbrio

The usual dose is one vial (containing 500 mg imipenem, 500 mg cilastatin and 250 mg relebactam) every 6 hours. If you have kidney problems, your doctor may lower your dose.

It is given as a drip directly into a vein (‘intravenous infusion’). The infusion will last 30 minutes.

The course of treatment usually lasts from 5 up to 14 days, depending on the type of infection you have and how you respond to treatment.

If you are given more Recarbrio than you should
Recarbrio will be given to you by a doctor or a nurse, so it is unlikely you will be given the wrong dose. If you think you have been given too much Recarbrio, tell your doctor or nurse right away.

If you miss a dose of Recarbrio
Tell your doctor or nurse right away if you think you were not given your dose of Recarbrio.

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.

Serious side effects
Tell your doctor right away if you notice any of the following serious side effects - the medicine must be stopped:
- allergic reactions – the signs may include hives, swelling of the face, lips, tongue or throat, difficulty in breathing or swallowing
- severe skin reactions (e.g., severe rash, skin peeling or blistering)

Other side effects
Common: (may affect up to 1 in 10 people)
- nausea, being sick (vomiting), diarrhoea
- blood test results that may show changes in the liver
- blood test results that may show an increase in the number of some types of blood cells called 'eosinophils'
- blood test results that may show an increase in some white blood cells
- rash
- inflammation and pain caused by a blood clot in the vein

Uncommon: (may affect up to 1 in 100 people)
- hives
- skin itchiness
- convulsions (fits) and nervous system problems like tremor
- confusion
- seeing, hearing or feeling something that is not there (hallucinations)
- dizziness, sleepiness
- low blood pressure
- blood test results that may show changes in the kidney
- blood test results that may show a decrease in the number of red blood cells, white blood cells, and blood cells called platelets
- blood test results that may show an increase in the number of some blood cells called platelets
- abnormal kidney, liver, and blood function detected by blood tests
- pain or redness or formation of a lump where the medicine was injected
- fever
- blood test (called a Coombs test) results showing antibodies that can cause anaemia by destroying red blood cells

Rare: (may affect up to 1 in 1,000 people)
- fungal infection (candidiasis)
- changes in taste
- disease of the brain, tingling sensation (pins and needles), localised tremor
- hearing loss
- staining of the teeth and/or tongue
- inflammation of the colon with severe diarrhoea (colitis)
- low number of white blood cells which may make it difficult for your body to fight infections
- inflammation of the liver
- liver failure
- inability of the kidney to perform normal function
- changes in the amount of urine, changes in urine colour
- swelling of the skin

- painful rash with flu-like symptoms
- redness and scaling of the skin

Very rare: (may affect up to 1 in 10,000 people)
- inflammation of stomach or intestine (gastro-enteritis)
- anaemia due to destruction of red blood cells, leading to symptoms like tiredness, pale skin
- headache
- worsening of a rare disease associated with muscle weakness (aggravation of myasthenia gravis)
- a spinning sensation (vertigo)
- ringing in the ears (tinnitus)
- irregular heartbeat, the heart beating forcefully or rapidly
- chest discomfort, difficulty breathing, abnormally fast and superficial breathing, pain in the upper spine
- pain in the throat
- flushing, bluish discolouration of the face and lips, changes in skin texture, excessive sweating
- increase in the production of saliva
- inflammation of intestine with bloody diarrhoea (haemorrhagic colitis)
- stomach pain
- heartburn
- red swollen tongue, overgrowth of the normal projections on the tongue giving it a hairy appearance
- severe loss of liver function due to inflammation (fulminant hepatitis)
- pain in several joints
- itching of the vulva in women
- weakness, lack of energy

Not known: (frequency cannot be estimated from the available data)
- agitation
- abnormal movements
- jaundice (yellowing of your skin and eyes)
- blood tests showing an increase in a substance called lactic dehydrogenase (LDH) which may be a sign of tissue damage

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 via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Recarbrio

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 container. The expiry date refers to the last day of that month.

Keep this medicine in the outer carton to protect from light.

Do not throw away any medicines via wastewater. 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 Recarbrio contains

- The active substances are imipenem, cilastatin, and relebactam. Each vial contains 500 mg imipenem, 500 mg cilastatin, and 250 mg relebactam.
- The other ingredient is sodium hydrogen carbonate.

What Recarbrio looks like and contents of the pack

Recarbrio is a white to light yellow powder supplied for solution for infusion in glass vials. Pack size is 25 vials.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

Merck Sharp & Dohme (UK) Limited, 120 Moorgate, London EC2M 6UR, UK

Manufacturer

FAREVA Mirabel, Route de Marsat, Riom, 63963, Clermont-Ferrand Cedex 9, France

For any information about this medicine, please contact:

Merck Sharp & Dohme Limited
Tel: +44 (0) 208 154 8000
Email: medicalinformationuk@msd.com

This leaflet was last revised in June 2022.

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PIL.RCB.22.GB.8185.Art61(3).RCN023678

The following information is intended for healthcare professionals only:

Recarbrio is supplied as a dry powder in a single-dose vial that must be constituted and further diluted using aseptic technique prior to intravenous infusion as outlined below:

- To prepare the infusion solution, contents of the vial must be transferred to 100 mL of an appropriate infusion solution: 9 mg/mL (0.9 %) sodium chloride. In exceptional circumstances where 9 mg/mL (0.9 %) sodium chloride cannot be used for clinical reasons 5 % glucose may be used instead.
- Withdraw 20 mL (10 mL times 2) of diluent from the appropriate infusion bag and constitute the vial with 10 mL of the diluent. The constituted suspension must not be administered by direct intravenous infusion.
- After constitution, shake vial well and transfer resulting suspension into the remaining 80 mL of the infusion bag.
- Add the additional 10 mL of infusion diluent to the vial and shake well to ensure complete transfer of vial contents; repeat transfer of the resulting suspension to the infusion solution before administering. Agitate the resulting mixture until clear.
- Constituted solutions of Recarbrio range from colourless to yellow. Variations of colour within this range do not affect the potency of the product.
- For patients with renal insufficiency, a reduced dose of Recarbrio will be administered according to the patient's CrCl, as determined from the table below. Prepare 100 mL of infusion solution as directed above. Select the volume (mL) of the final infusion solution needed for the appropriate dose of Recarbrio as shown in the table below.

Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration, whenever solution and container permit. Discard if discolouration or visible particles are observed.

Preparation of Recarbrio Doses

Creatinine Clearance (mL/min)	**Dosage of Recarbrio (imipenem/cilastatin/relebactam) (mg)**	**Volume (mL) of Solution to be Removed and Discarded from Preparation**	**Volume (mL) of Final Infusion Solution Needed for Dosage**
Greater than or equal to 90	500/500/250	N/A	100
Less than 90 to greater than or equal to 60	400/400/200	20	80
Less than 60 to greater than or equal to 30	300/300/150	40	60
Less than 30 to greater than or equal to 15 or ESRD on haemodialysis	200/200/100	60	40

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

Compatible medicinal products

The physical compatibility of Recarbrio with selected injectable medicinal products was evaluated in two commonly available diluents at a Y-infusion site. Compatible medicinal products with the corresponding compatible diluent (i.e., 5 % Dextrose Injection or 0.9 % Sodium chloride Injection)

are listed below. Recarbrio should not be co-administered through the same intravenous line (or cannula), with other medicinal products not listed below, as no compatibility data are available. Refer to the respective prescribing information of the co-administered medicinal product(s) to confirm compatibility of simultaneous co-administration. This medicinal product must not be mixed with other medicinal products except those mentioned below.

List of Compatible Injectable Medicinal Products for use with 5 % Dextrose or 0.9 % Sodium chloride Injection as Diluents

- dexmedetomidine
- dopamine
- epinephrine
- fentanyl
- heparin
- midazolam
- norepinephrine
- phenylephrine

Compatible intravenous bags and infusion set materials

Recarbrio is compatible with the following intravenous container bags and infusion set materials. Any intravenous bags or infusion set materials not listed below should not be used.

Intravenous Container Bag Materials
Polyvinyl chloride (PVC) and polyolefin (polypropylene and polyethylene)

Intravenous Infusion Set Materials (with tubing)
PVC + Di-(2-ethylhexyl)phthalate (DEHP) and polyethylene (PE)-lined PVC

Incompatible medicinal products

Recarbrio for solution for infusion is physically incompatible with propofol in 5 % Dextrose (also named Glucose) or 0.9 % Sodium chloride.

After constitution and dilution

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.

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PIL.RCB.22.GB.8185.Art61(3).RCN023678