Package leaflet: Information for the patient

Vaborem 1 g/1 g powder for concentrate for solution for infusion

meropenem/vaborbactam

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 Vaborem is and what it is used for

What Vaborem is
Vaborem is an antibiotic medicine that contains two active substances: meropenem and vaborbactam.
- Meropenem belongs to group of antibiotics called "carbapenems". It can kill many types of bacteria by preventing them from building the protective walls that surround their cells.
- Vaborbactam is a "beta lactamase inhibitor". It blocks the action of an enzyme that allows some bacteria to resist the action of meropenem. This helps meropenem kill some bacteria that it cannot kill on its own.

What Vaborem is used for
Vaborem is used in adults to treat certain serious bacterial infections:
- of the bladder or kidneys (urinary tract infections)
- of the stomach and gut (intra-abdominal infections)
- of the lungs (pneumonia)

It is also used to treat infections
- of the blood associated with any of the infections mentioned above
- caused by bacteria that other antibiotics may not be able to kill

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

You must not be given Vaborem if
- you are allergic to meropenem, vaborbactam or the other ingredients of this medicine (listed in section 6).
- you are allergic to other carbapenem antibiotics (the group to which meropenem belongs).
- you have ever had a severe allergic reaction to related antibiotics belonging to the beta-lactam group (including penicillins, cephalosporins or monobactams).

Warnings and precautions
Talk to your doctor or nurse before receiving Vaborem if:
- you have ever had any allergic reaction to other antibiotics belonging to the beta-lactam group (including carbapenems, penicillins, cephalosporins, or monobactams)

- you have ever developed severe diarrhoea during or after antibiotic treatment
- you have ever suffered from seizures

If any of the above apply to you or you are not sure, talk to your doctor or nurse before using Vaborem.

You may develop signs and symptoms of severe skin reactions (see section 4). If this happens talk to your doctor or nurse immediately so that they can treat the symptoms.

Talk to your doctor or nurse if you suffer from diarrhoea during your treatment.

This medicine can affect your liver. Your doctor may take some blood to check how well your liver is working while taking the medicine.

New infection
Although Vaborem can fight certain bacteria, there is a possibility that you may get a different infection caused by another organism during or after your treatment. Your doctor will monitor you closely for any new infections and give you another treatment if necessary.

Blood tests
Tell your doctor that you are taking Vaborem if you are going to have any blood tests. This is because you may get an abnormal result with something called a "Coombs test". This test looks for the presence of antibodies that can destroy red blood cells or may be affected by the response of your immune system to Vaborem.

Children or adolescents
Vaborem should not be used in children or adolescents under 18 years of age. This is because it is not known if the medicine is safe to use in these age groups.

Other medicines and Vaborem
Tell your doctor if you are using, have recently used or might use any other medicines.

It is particularly important to tell your doctor if you are taking any of the following medicines:
- medicines used to treat epilepsy called valproic acid, sodium valproate or valpromide because Vaborem may decrease their effect
- a medicine for gout called probenecid
- oral anticoagulant medicines, such as warfarin (used to treat or prevent blood clots)
- hormonal oral contraceptives containing oestrogen and/or progesterone because Vaborem may decrease their effect. Women of childbearing potential should be advised to use alternative effective contraceptive methods during treatment with Vaborem and for a period of 28 days after discontinuation of treatment.
- medicines predominantly metabolised by CYP1A2 (e.g theophylline), CYP3A4 (e.g alprazolam, midazolam, tacrolimus, sirolimus, cyclosporine, simvastatin, omeprazole, nifedipine, quinidine and ethinylestradiol) and/or CYP2C (e.g. warfarin, phenytoin) and/or transported by P-gp (e.g. dabigatran, digoxin) because Vaborem may decrease their effect.

Tell your doctor before using Vaborem if any of the above apply to you.

Pregnancy and breast-feeding
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before receiving this medicine.

As a precautionary measure, you should not be given this medicine during pregancy.

It is important that you tell your doctor if you are breast-feeding or if you intend to breast-feed before receiving Vaborem. Small amounts of this medicine may pass into the breast milk and it may affect the baby. Therefore, you must discontinue breastfeeding before you are given Vaborem.

Driving and using machines
Vaborem may make you feel dizzy, sleepy and sluggish, give you a headache or tingling sensation (like "pins and needles") or, in rare cases, cause a fit or seizure. This may affect your ability to drive, use tools or machines.

Vaborem contains sodium
This medicine contains 250 mg of sodium (main component of cooking salt) in each vial. This is equivalent to 12,5% of the recommended maximum daily dietary intake of sodium salt for an adult.

3. How you will be given Vaborem

The recommended dose is 2 vials (a total of 2 g meropenem and 2 g vaborbactam), given every 8 hours. Your doctor will decide how many days of treatment are needed, depending on the type of infection.

Vaborem will be given to you by a doctor or nurse by infusion (a drip) into a vein, lasting 3 hours.

Patients with kidney problems
If you have kidney problems, your doctor may lower your dose. Your doctor may also want to do some blood tests to see how well your kidneys are working.

If you are given more Vaborem than you should
Vaborem 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 Vaborem, tell your doctor or nurse straight away.

If you miss a dose of Vaborem
If you think you have missed a dose, tell your doctor or nurse straight away.

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 straight away if you notice any of the following serious side effects – you may need urgent medical treatment:
- Severe allergic reactions that could include sudden swelling of your lips, face, throat or tongue, difficulty swallowing or breathing or a severe rash or other severe skin reactions, or a decrease in blood pressure (which could make you feel faint or dizzy). Such reactions may be life-threatening.
- Diarrhoea that keeps getting worse or does not go away, or stools that contains blood or mucus – this may happen during or after treatment with Vaborem is stopped. It may be due to bacteria called *Clostridium difficile*. If this happens, do not take medicines that stop or slow bowel movement.

Other side effects
Tell your doctor or nurse if you notice any of the following side effects:

Common: (may affect up to 1 in 10 people)

- Increase in the number of platelets (a type of blood cell) – shown in blood tests
- Decrease in the amount of potassium or sugar- seen in blood tests
- Headache
- Low blood pressure
- Diarrhoea
- Feeling sick (nausea) or being sick (vomiting)
- Swelling, redness and/or pain around the needle where the medicine is given into a vein
- Fever
- Increase in the amount of enzymes produced by your liver called alanine aminotransferase or aspartate aminotransferase – shown in blood tests
- Increase in the level of an enzyme called alkaline phosphatase that may be a sign of your liver, gallbladder or bones working less well – shown in blood tests
- Increase in the level of an enzyme called lactate dehydrogenase that may be a sign of damage to some of your body organs – shown in blood tests

Uncommon: (may affect up to 1 in 100 people)

- Swelling and irritation in the large intestine or colon – this can cause diarrhoea, fever and stomach cramps and is due to another colon infection
- Fungal infections, including those of the vagina or mouth
- Decrease in the number of white blood cells or some types of white blood cells called neutrophils and a decrease of platelets – shown in blood tests
- Increase in a type of white blood cell called eosinophils – shown in blood tests
- Sudden and serious allergic reaction that needs urgent medical treatment and may include itching, skin color change, abdominal cramps, swelling, difficulty breathing, fainting and drop in blood pressure
- Less severe allergic reaction that may include redness, red bumps, flaking of the skin, itching, generally feeling unwell
- A feeling of being less hungry
- Increase in the amount of potassium or sugar – shown in blood tests
- Inability to sleep
- Seeing, hearing or sensing things that are not there
- Feeling dizzy
- Tremor or shaking
- A tingling feeling (pins and needles)
- A feeling of being sleepy and sluggish
- Swollen and red and irritated veins
- Painful veins
- Difficulty breathing
- Bloating or a feeling of fullness in your abdomen
- Stomach pain
- Itchy skin
- Rash
- Raised itchy skin rash (“hives”)
- Difficulty to control the bladder
- Reduction in the way your kidneys work
- Abnormal feeling in the chest
- The following reactions may develop, alone or in combination, where Vaborem is given into a vein: reddened skin (erythema); hot, tender and swollen vein around the needle (phlebitis); a blood clot in the vein where the needle was put through your skin (infusion site thrombosis)
- Pain
- Increase in the level of a substance in the blood called creatine phosphokinase that is a sign of possible damage to certain tissues such as your muscles and/or other organs – shown in blood tests
- Increase in the level of a substance in the blood called bilirubin that is a sign of possible damage to your red blood cells or that your liver is working less well – shown in blood tests

- Increase in the level of some types of substances in the blood called urea and creatinine that are signs that your kidneys are working less well – shown in blood tests
- Reaction that occurs during or shortly after Vaborem is given that presents as a malaise (generally feeling unwell) possibly with any of the following: reduced blood pressure, nausea, vomiting, abdominal cramps, fever, flushing, rapid heart beats or difficulty to breathe, headache

Rare (may affect up to 1 in 1000 people)
- Seizures (fits)

Unknown: (frequency cannot be estimated from the available data)
- A severe and very low white blood cell count – shown in blood tests
- Haemolytic anaemia (a condition where red blood cells are damaged and reduced in number), which may make you feel tired and turn your skin and eyes yellow
- Swelling of the tongue, face, lips or throat
- Sudden onset of a severe rash with bullseye-like spots or blistering or peeling skin, possibly with a high fever, joint pain, abnormal function of your liver, kidney or lung (these may be signs of more serious medical conditions called toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, acute generalised exanthematous pustulosis, or a condition known as drug reaction with eosinophilia and systemic symptoms (DRESS))
- A positive result from a test called"Coombs"used to identify haemolytic anemia (see above) or reaction of your immune system to Vaborem
- Acute disorientation and confusion (delirium)

Reporting of side effects
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme, website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

5. How to store Vaborem

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.

Do not store above 25 °C.

6. Contents of the pack and other information

What Vaborem contains
- The active substances are meropenem and vaborbactam. Each vial contains 1 g meropenem (as meropenem trihydrate) and 1 g vaborbactam.
- The other ingredient is sodium carbonate.

What Vaborem looks like and contents of the pack
Vaborem is a white to light yellow powder for concentrate for solution for infusion supplied in a vial.

Vaborem is available in packs containing 6 vials.

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This leaflet was last revised in May 2024.

The following information is intended for healthcare professionals only:

Vaborem is intended for intravenous (IV) administration, only after reconstitution and dilution.
Standard aseptic techniques must be used for solution preparation and administration.

The number of vials used for a single dose will depend on the creatinine clearance (CrCl) of the patient.

Reconstitution:
20 ml of sodium chloride 9 mg/ml (0.9%) solution for injection (normal saline) should be withdrawn from a 250 ml infusion bag of sodium chloride 9 mg/ml (0.9%) solution for injection for each vial and reconstituted with the appropriate number of vials of meropenem/vaborbactam for the corresponding Vaborem dosage:

- Reconstitute 2 vials for the Vaborem 2 g/2 g dose
- Reconstitute 1 vial for the Vaborem 1 g/1 g and Vaborem 0.5 g/0.5 g doses

After mixing gently to dissolve, the reconstituted meropenem/vaborbactam solution will have an approximate meropenem concentration of 0.05 g/ml and an approximate vaborbactam concentration of 0.05 g/ml. The final volume is approximately 21.3 ml. The reconstituted solution is not for direct injection. The reconstituted solution must be diluted before intravenous infusion.

Dilution:
To prepare the Vaborem 2 g/2 g for intravenous infusion: Immediately after reconstitution of two vials, the entire reconstituted vial contents should be withdrawn from each of the two vials and added back into the 250 ml infusion bag of sodium chloride 9 mg/ml (0.9%) solution for injection (normal saline). The final infusion concentration of meropenem and vaborbactam will be about 8 mg/ml each.

To prepare the Vaborem 1 g/1 g for intravenous infusion: Immediately after reconstitution of one vial, the entire reconstituted vial contents should be withdrawn from the vial and added back into the 250 ml infusion bag of sodium chloride 9 mg/ml (0.9%) solution for injection (normal saline). The final infusion concentration of meropenem and vaborbactam will be about 4 mg/ml each.

To prepare the Vaborem 0.5 g/0.5 g for intravenous infusion: Immediately after reconstitution of one vial, 10.5 ml of the reconstituted vial contents should be withdrawn from the vial and added back into the 250 ml infusion bag of sodium chloride 9 mg/ml (0.9%) solution for injection (normal saline). The final infusion concentration of meropenem and vaborbactam will be 2 mg/ml each.

The diluted solution should be inspected visually for particulate matter. The colour of the diluted solution is clear to light yellow.

Following dilution, the infusion should be completed within 4 hours when stored at 25 °C, or within 22 hours when refrigerated at 2 – 8 °C.

From a microbiological point of view, the medicinal product should be used immediately upon reconstitution and dilution.

Vaborem is not chemically compatible with glucose-containing solutions. This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6 of the SmPC.