Package leaflet: Information for the user

Emblaveo 1.5 g/0.5 g powder for concentrate for solution for infusion
aztreonam/avibactam

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 Emblaveo is and what it is used for

What Emblaveo is
Emblaveo is an antibiotic medicine that contains two active substances aztreonam and avibactam.
- Aztreonam belongs to the group of antibiotics called "monobactams". It can kill certain types of bacteria (so-called Gram-negative bacteria).
- Avibactam is a "beta-lactamase inhibitor" that helps aztreonam kill some bacteria that it cannot kill on its own.

What Emblaveo is used for
Emblaveo is used in adults to treat:
- complicated bacterial infections of the abdomen (stomach and gut), where the infection has spread into abdominal cavity (space within the abdomen).
- hospital-acquired pneumonia (a bacterial infection of the lungs that is picked up in hospitals), including ventilator-associated pneumonia (pneumonia that develops in patients on a machine called a ventilator to help them breathe).
- complicated (difficult to treat as it has spread to other parts of the body or the patient has other conditions) urinary tract infections, including pyelonephritis (kidney infection).
- infections caused by Gram-negative bacteria that other antibiotics may not be able to kill.

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

You should not be given Emblaveo if:
- you are allergic to aztreonam, avibactam or any of the other ingredients of this medicine (listed in section 6).
- you have ever had a severe allergic reaction (swelling of the face, hands, feet, lips, tongue or throat; or difficulty swallowing or breathing; or a severe skin reaction) to other antibiotics belonging to the penicillin, cephalosporin, or carbapenem groups.

Warnings and precautions
Talk to your doctor or nurse before using Emblaveo if:
- you have ever had any allergic reaction (even if only a skin rash) to other antibiotics. Signs of allergic reaction include itching, a rash on the skin or difficulty in breathing.

- you have kidney problems or if you are taking medicines that affect your kidney function, such as other antibiotics known as aminoglycosides (streptomycin, neomycin, gentamicin). If your kidney function is impaired, your doctor may give you a lower dose of Emblaveo and may want to perform regular blood tests during treatment to check your kidney function. In addition, you may be at higher risk of developing serious side effects that affect the nervous system such as encephalopathy (a disorder of the brain that may be caused by disease, injury, medicines or chemicals) due to increased blood levels of Emblaveo unless the dose is reduced. Symptoms of encephalopathy include confusion, seizures and altered mental function (see Section 3: If you use more Emblaveo than you should).
- you have any liver problems. Your doctor may want to perform regular blood tests during treatment to check your liver since increases in liver enzymes have been observed with Emblaveo.
- you are taking medicines known as anticoagulants (a medicine that prevents the blood from clotting). Emblaveo can affect blood clotting. Your doctor will monitor your blood levels to check if your dose of anticoagulant needs to be changed during treatment with Emblaveo.

Talk to your doctor if after starting treatment with Emblaveo, you experience:
- severe, prolonged, or bloody diarrhoea. This may be a sign of an inflammation of the large bowel. It may be necessary to interrupt the treatment with Emblaveo and start specific treatment for the diarrhoea (see section 4: Possible side effects).
- other infections. There is a small possibility that you may get a different infection caused by another bacteria during or after treatment with Emblaveo.

Lab tests

Tell your doctor that you are taking Emblaveo if you are going to have any tests. This is because you may get an abnormal result with a test called direct or indirect Coombs test. This test looks for antibodies that fight against your red blood cells.

Children and adolescents
Emblaveo should not be used in paediatric or adolescent patients aged under 18 years. This is because it is not known if the medicine is safe to use in this age group.

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

Talk to your doctor before using Emblaveo if you are taking any of the following medicines:
- a medicine for gout called probenecid

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 for advice before using this medicine.

This medicine may harm your unborn child. It should only be used during pregnancy if the doctor considers it necessary and only if the benefit for the mother outweighs the risk for the child.

This medicine may pass into breast milk. If you are breast-feeding a decision must be made whether you should discontinue breast-feeding or abstain from treatment with this medicine, taking into account the benefit of breast-feeding for the child and the benefit of treatment for the woman.

Driving and using machines
Emblaveo may cause side effects, such as dizziness, which can affect your ability to drive and use machines. Do not drive or use tools or machines if you experience side effects such as dizziness (see section 4: Possible side effects).

Emblaveo contains sodium

This medicine contains approximately 44.6 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 2.2% of the recommended maximum daily dietary intake for sodium for an adult.

3. How to use Emblaveo

Emblaveo will be given to you by a doctor or a nurse.

How much to use
Emblaveo is given as a drip directly into a vein ('intravenous infusion'). The usual dose is one vial (containing 1.5 g aztreonam and 0.5 g avibactam) every 6 hours. The first dose is higher (2 g aztreonam and 0.67 g avibactam). The infusion will last 3 hours. A course of treatment usually lasts from 5 to up to 14 days, depending on the type of infection you have and how you respond to treatment.

People with kidney problems

If you have kidney problems your doctor may lower your dose and increase the time between the doses. This is because Emblaveo is removed from your body by the kidneys. If your kidney function is impaired your blood levels of Emblaveo may be increased.

If you are given more Emblaveo than you should be given
Emblaveo will be given to you by a doctor or a nurse, so it is unlikely you will be given too much of this medicine. However, if you have side effects or think you have been given too much Emblaveo, tell your doctor or nurse straight away. You must tell your doctor if you experience confusion, altered mental function, movement problems, or seizure.

If a dose of Emblaveo has been forgotten
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:

- Swelling of the face, lips, eyes, tongue, and/or throat, hives and with difficulty in swallowing or breathing. These may be signs of an allergic reaction or angioedema which may be life-threatening.
- Severe, persistent, or bloody diarrhoea (which may be associated with stomach pain or fever). This may occur during or after treatment with antibiotics and can be a sign of serious bowel inflammation. If this happens do not take medicines that stop or slow bowel movement.
- Sudden onset of a severe rash or blistering or peeling skin, possibly accompanied by a high fever or joint pain (these may be signs of more serious medical conditions such as toxic epidermal necrolysis, dermatitis exfoliative, erythema multiforme).

These serious side effects are uncommon (may affect up to 1 in 100 people).

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)

- Decrease in the number of red blood cells – shown in blood tests
- Change in the number of some types of blood cells (called "platelets") – shown in blood tests
- Confusion
- Dizziness
- Diarrhoea
- Feeling sick (nausea) or being sick (vomiting)
- Stomach pain
- Increase in certain liver enzymes – shown in blood tests
- Rash
- Inflammation of a vein
- Inflammation of a vein associated with a blood clot
- Pain or swelling at the site of the injection
- Fever

Uncommon: (may affect up to 1 in 100 people)
- Increase in the number of some types of white blood cells (called "eosinophils" and "leucocytes") – shown in blood tests
- Difficulty falling and staying asleep
- Encephalopathy (a condition that affects the brain and causes altered mental state and confusion)
- Headache
- Reduced sensation to touch, pain and temperature in the mouth
- Taste disturbance
- Extra heartbeats
- Bleeding
- Reduced blood pressure
- Reddening of the face
- Excessive contraction of the airway muscles causing breathing difficulty
- Stomach bleeding
- Mouth ulcers
- Increase in the levels of some substances in your blood (gamma-glutamyltransferase, blood alkaline phosphatase, creatinine)
- Itching
- purple patches like bruising, small red spots
- Excessive sweating
- Chest pain
- Weakness

Rare: (may affect up to 1 in 1,000 people)
- Fungal infections of the vagina
- Low levels of blood cells (pancytopenia)
- Significant decrease in the type of white blood cells (called "neutrophils") used to fight infection - shown in blood tests
- Lengthening of the time it takes for a cut to stop bleeding
- Spontaneous bruising
- Abnormal result with a test called direct or indirect Coombs test. This test looks for antibodies that fight against your red blood cells.
- Seizure
- Sensations like numbness, tingling, pins and needles
- Double vision
- A spinning sensation
- Ringing or buzzing in the ears
- Difficulty breathing
- Breath sounds abnormal (wheezing)

- Sneezing
- Blocked nose (nasal congestion)
- Bad breath
- Inflammation of the liver
- Yellowing of the skin and eyes
- Muscle pain
- Breast tenderness
- Feeling generally unwell

Not known: (cannot be estimated from the available data)
- Superinfection (a new infection that occurs after you are treated for your current infection)

Sudden chest pain, which may be a sign of a potentially serious allergic reaction called Kounis syndrome has been noted with other medicines of the same type. If this happens talk to a doctor or nurse immediately.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist, 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 Emblaveo

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

Store in a refrigerator (2 °C – 8 °C).
Store in the original package in order to protect from light.

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 Emblaveo contains
- The active substances are aztreonam and avibactam. Each vial contains 1.5 g aztreonam and avibactam sodium equivalent to 0.5 g avibactam (see section 2: Emblaveo contains sodium).
- The other ingredient is arginine.

What Emblaveo looks like and contents of the pack
Emblaveo is a white to slightly yellow powder for concentrate for solution for infusion in a glass vial with a rubber stopper and aluminium seal with flip-off cap. It is available in packs containing 10 vials.

Marketing Authorisation Holder
Pfizer Limited
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom

Manufacturer
Pfizer Service Company BV

Hoge Wei 10
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For any information about this medicine, please contact:
Medical Information, Pfizer Ltd, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS.
Telephone 01304 616161.

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The following information is intended for healthcare professionals only:

Important: Please refer to the Summary of Product Characteristics before prescribing.

This medicinal product must not be mixed with other medicinal products except sodium chloride (0.9%) solution for injection, glucose (5%) solution for injection, or Lactated Ringer's solution as mentioned below.

The powder must be reconstituted with sterile water for injections and the resulting concentrate must then be immediately diluted prior to use. The reconstituted solution is a clear, colourless to yellow solution and is free of visible particles.

Emblaveo (aztreonam/avibactam) is a combination product; each vial contains 1.5 g of aztreonam and 0.5 g of avibactam in a fixed 3:1 ratio.

Standard aseptic techniques should be used for solution preparation and administration. Doses must be prepared in an appropriately sized infusion bag.

Parenteral medicinal products should be inspected visually for particulate matter prior to administration.

Each vial is for single use only.

The total time interval between starting reconstitution and completing preparation of the intravenous infusion should not exceed 30 minutes.

<u>Instructions for preparing adult doses in an INFUSION BAG:</u>

NOTE: The following procedure describes the steps to prepare an infusion solution with a final concentration of 1.5-40 mg/mL of **aztreonam** and 0.50-13.3 mg/mL of **avibactam**. All calculations should be completed prior to initiating these steps.

1. Prepare the **reconstituted solution** (**131.2 mg/mL** of aztreonam and **43.7 mg/mL** of avibactam):
   a) Insert the needle through the vial closure and inject 10 mL of sterile water for injections.
   b) Withdraw the needle and shake the vial gently to give a clear, colourless to yellow solution free of visible particles.
2. Prepare the **final solution** for infusion (final concentration must be **1.5-40 mg/mL** of aztreonam and **0.50-13.3 mg/mL** of avibactam):
   Infusion bag: Further dilute the reconstituted solution by transferring an appropriately calculated volume of the reconstituted solution to an infusion bag containing any of the following: sodium chloride (0.9%) solution for injection, glucose (5%) solution for injection, or Lactated Ringer's solution.

Refer to Table 1 below.

Table 1. Preparation of Emblaveo for adult doses in an INFUSION BAG

Total dose (aztreonam/avibactam)	Volume to withdraw from reconstituted vial(s)	Final volume after dilution in infusion bag[a,b]
2000 mg/667 mg	15.2 mL	50 mL to 250 mL
1500 mg/500 mg	11.4 mL	50 mL to 250 mL
1350 mg/450 mg	10.3 mL	50 mL to 250 mL
750 mg/250 mg	5.7 mL	50 mL to 250 mL
675 mg/225 mg	5.1 mL	50 mL to 250 mL
All other doses	Volume (mL) calculated based on dose required: **Dose (mg aztreonam) ÷ 131.2 mg/mL aztreonam** **Or** **Dose (mg avibactam) ÷ 43.7 mg/mL avibactam**	Volume (mL) will vary based on infusion bag size availability and preferred final concentration (must be 1.5-40 mg/mL of aztreonam and 0.50-13.3 mg/mL of avibactam)

a Dilute to final aztreonam concentration of 1.5-40 mg/mL (final avibactam concentration of 0.50-13.3 mg/mL) for in-use stability up to 24 hours at 2 °C – 8 °C, followed by up to 12 hours up to 30 °C for infusion bags containing sodium chloride (0.9%) solution for injection or Lactated Ringer's solution.

b Dilute to final aztreonam concentration of 1.5-40 mg/mL (final avibactam concentration of 0.50-13.3 mg/mL) for in-use stability up to 24 hours at 2 °C – 8 °C, followed by up to 6 hours up to 30 °C for infusion bags containing glucose (5%) solution for injection.

From a microbiological point of view, the medicinal product should be used immediately, unless reconstitution and dilution have taken place in controlled and validated aseptic conditions. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and must not exceed those stated above.

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