

## Package leaflet: Information for the user

### Zavicefta ® 2 g/0.5 g powder for concentrate for solution for infusion ceftazidime/avibactam

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

#### **1. What Zavicefta is and what it is used for**

##### **What Zavicefta is**

Zavicefta is an antibiotic medicine that contains two active substances ceftazidime and avibactam.

- Ceftazidime belongs to the group of antibiotics called “cephalosporins”. It can kill many types of bacteria.
- Avibactam is a “beta-lactamase inhibitor” that helps ceftazidime kill some bacteria that it cannot kill on its own.

##### **What Zavicefta is used for**

Zavicefta is used in adults to treat:

- infections of the stomach and gut (abdomen)
- infections of the bladder or kidneys called “urinary tract infections”
- an infection of the lungs called “pneumonia”
- infections caused by bacteria that other antibiotics may not be able to kill

##### **How Zavicefta works**

Zavicefta works by killing certain types of bacteria, which can cause serious infections.

#### **2. What you need to know before you use Zavicefta**

##### **Do not use Zavicefta if:**

- you are allergic to ceftazidime, avibactam or any of the other ingredients of this medicine (listed in section 6)
- you are allergic to other cephalosporin antibiotics
- you have ever had a severe allergic reaction to other antibiotics belonging to the penicillin or carbapenem groups

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

### **Warnings and precautions**

Talk to your doctor or nurse before using Zavicefta if:

- you have ever had any allergic reaction (even if only a skin rash) to other antibiotics belonging to the penicillin or carbapenem groups
- you have kidney problems - your doctor may give you a lower dose to make sure you don't get too much medicine. This could cause symptoms such as fits (see section **If you use more Zavicefta than you should**)

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

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

### Other infections

There is a small possibility that you may get a different infection caused by another bacteria during or after treatment with Zavicefta. These include thrush (fungal infections of the mouth or genital area).

### Lab tests

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

Zavicefta can also affect the results of some urine tests for sugar. Tell the person taking the sample that you have been given Zavicefta.

### **Children and adolescents**

Zavicefta should not be used in children and adolescents. This is because it is not known if the medicine is safe to use in these age groups.

### **Other medicines and Zavicefta**

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

Talk to your doctor before using Zavicefta if you are taking any of the following medicines:

- an antibiotic called chloramphenicol
- a type of antibiotic called an aminoglycoside – such as gentamicin, tobramycin
- a water tablet called furosemide
- a medicine for gout called probenecid

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

### **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.

### **Driving and using machines**

Zavicefta may make you feel dizzy. This may affect you being able to drive, use tools or machines.

### **Zavicefta contains sodium**

The maximum recommended daily dose of this medicinal product contains 444 mg sodium (found in table salt). This is equivalent to 22.2% of the adult recommended maximum daily dietary intake for sodium.

Talk to your pharmacist or doctor if you have been advised to have a low salt diet.

## **3. How to use Zavicefta**

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

### **How much to use**

The recommended dose is one vial (2 g of ceftazidime and 0.5 g of avibactam), every 8 hours.

It is given as a drip into a vein – this will take about 2 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. This is because Zavicefta is removed from your body by the kidneys.

### **If you use more Zavicefta than you should**

Zavicefta will be given to you by a doctor or a nurse, so it is unlikely you will be given the wrong dose. However, if you have side effects or think you have been given too much Zavicefta, tell your doctor or nurse straight away. If you have too much Zavicefta it could have an effect on the brain and cause fits or coma.

### **If you miss a dose of Zavicefta**

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. The following side effects may happen with this medicine:

### **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 – signs include sudden swelling of your lips, face, throat or tongue, a severe rash or other severe skin reactions, difficulty swallowing or breathing. This reaction 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 is stopped with Zavicefta. If this happens do not take medicines that stop or slow bowel movement.

Tell your doctor straight away if you notice any of the serious side effects above.

### **Other side effects**

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

#### **Very common:** (may affect more than 1 in 10 people)

- abnormal result with a test called “DAGT” or “Coombs”. This test looks for antibodies that fight against your red blood cells. It is possible that this could cause anaemia (which may make you feel tired) and jaundice (yellowing of the skin and eyes)

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

- fungal infections, including those of the mouth and vagina
- change in the number of some types of blood cells (called “eosinophils” and “thrombocytes”) – shown in blood tests
- headache
- feeling dizzy
- feeling sick (nausea) or being sick (vomiting)

- stomach pain
- diarrhoea
- increase in the amount of some enzymes produced by your liver - shown in blood tests
- raised itchy skin rash (“hives”)
- itchiness
- redness, pain or swelling where Zavicefta was given into a vein
- fever

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

- increase in the number of a type of blood cell (called “lymphocytes”) – shown in blood tests
- decrease in the number of some types of blood cells (called “leucocytes”) - shown in blood tests
- tingling or numbness
- bad taste in your mouth
- an increase in the level of some types of substances in your blood (called “creatinine” and “urea”). These show how well your kidneys are working.

**Very rare:** (may affect up to 1 in 10,000 people)

- swelling in a part of the kidney that causes a reduction in its normal working function

**Not known:** (frequency cannot be estimated from the available data)

- significant decrease in the type of white blood cells used to fight infection - shown in blood tests
- decrease in the number of red blood cells (haemolytic anaemia) – shown in blood tests
- severe allergic reaction (see **Serious side effects**, above)
- yellowing of the whites of the eyes or skin
- 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, Stevens-Johnson syndrome, erythema multiforme or a condition known as DRESS, Drug Reaction with Eosinophilia and Systemic Symptoms)
- swelling under the skin, particularly lips and around the eyes

Tell your doctor or nurse if you notice any of the side effects listed above.

### **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 (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

### **United Kingdom**

Yellow Card Scheme

Website: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

### **Ireland**

HPRa Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

### **Malta**

ADR Reporting

Website: [www.medicinesauthority.gov.mt/adrportal](http://www.medicinesauthority.gov.mt/adrportal)

## **5. How to store Zavicefta**

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.

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 require. These measures will help to protect the environment.

## **6. Contents of the pack and other information**

### **What Zavicefta contains**

- The active substances are ceftazidime and avibactam. Each vial contains ceftazidime pentahydrate equivalent to 2 g ceftazidime and avibactam sodium equivalent to 0.5 g avibactam.
- The other ingredient is sodium carbonate (anhydrous).

### **What Zavicefta looks like and contents of the pack**

Zavicefta is a white to yellow powder for concentrate for solution for infusion in a vial. It is available in packs containing 10 vials.

### **Marketing Authorisation Holder**

Pfizer Ireland Pharmaceuticals  
Operations Support Group  
Ringaskiddy, County Cork  
Ireland

### **Manufacturer**

GlaxoSmithKline Manufacturing S.p.A. Via Alessandro Fleming 2  
Verona 37135  
Italy

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

### **Ireland**

Pfizer Healthcare Ireland  
Tel: +1800 633 363 (toll free)  
+44 (0)1304 616161

### **Malta**

Vivian Corporation Ltd.  
Tel: +35621 344610

### **United Kingdom**

Pfizer Limited  
Tel: +44 (0) 1304 616161

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### **Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site:  
<http://www.ema.europa.eu>.

**The following information is intended for healthcare professionals only:**

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

Aseptic technique must be followed in preparing the infusion solution. The contents of Zavicefta vial should be reconstituted with 10 mL of sterile water for injections. Instructions for the reconstitution of Zavicefta vial are summarized below:

| <b>Dosage strength<br/>ceftazidime/avibactam<br/>(mg)</b> | <b>Volume of diluent<br/>to be added<br/>(mL)</b> | <b>Approximate<br/>ceftazidime/avibactam<br/>concentration<br/>(mg/mL)</b> | <b>Amount to be<br/>withdrawn</b> |
|---|---|--|-----------------------------------|
| 2000/500  | 10  | 167.3/41.8   | Total volume                      |

1. Introduce the syringe needle through the vial closure and inject 10 mL of sterile water for injections.
2. Withdraw the needle and shake the vial to give a clear solution.
3. Do not insert a gas relief needle until the product has dissolved. Insert a gas relief needle through the vial closure to relieve the internal pressure.
4. Transfer the entire contents (approximately 12.0 mL) of the resultant solution to an infusion bag immediately. Reduced doses may be achieved by transfer of an appropriate volume of the resultant solution to an infusion bag, based upon ceftazidime and avibactam content of 167.3 mg/mL and 41.8 mg/mL, respectively. A dose of 1000 mg/250 mg or 750 mg/187.5 mg is achieved with 6.0 mL or 4.5 mL aliquots, respectively.

Note: to preserve product sterility, it is important that the gas relief needle is not inserted through the vial closure before the product is dissolved.

The reconstituted solution must be further diluted to produce Zavicefta solution for infusion. A 100 mL infusion bag can be used to prepare the infusion, based on the patient's volume requirements. Appropriate infusion diluents include: sodium chloride 9 mg/mL (0.9%) solution for injection, dextrose 50 mg/mL (5%) solution for injection, sodium chloride 4.5 mg/mL and dextrose 25 mg/mL solution for injection (0.45% sodium chloride and 2.5% dextrose) or Lactated Ringer's solution. The resulting solution should be administered over 120 minutes.

Reconstitution time is less than 2 minutes. Mix gently to reconstitute and check to see that the contents have dissolved completely. The total time interval between starting reconstitution and completing preparation of the intravenous infusion should not exceed 30 minutes. Parenteral medicinal products should be inspected visually for particulate matter prior to administration.

The colour of Zavicefta infusion solution is pale yellow and free of particles.

Studies have shown that Zavicefta solutions for infusion are stable for up to 12 hours at room temperature. Alternatively they are stable for up to 24 hours under refrigerated storage. Once removed from refrigeration to room temperature, the diluted product must be used within 12 hours. The total in-use stability from reconstitution to administration should not exceed 36 hours (24 hours at 2-8°C plus 12 hours room temperature).

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

The compatibility of Zavicefta with other medicines has not been established. Zavicefta should not be mixed with or physically added to solutions containing other medicinal products.

Each vial is for single use only.

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