PACKAGE LEAFLET

Package leaflet: Information for the user

Zevtera 500 mg Powder for concentrate for Solution for Infusion
ceftobiprole

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

1. What Zevtera is and what it is used for

Zevtera is an antibiotic medicine that contains the active substance ceftobiprole medocaril sodium. It belongs to a group of medicines called 'cephalosporin antibiotics'.

Zevtera is used to treat term neonates, infants, children, adolescents, and adults with infections of the lungs called 'pneumonia'.

Zevtera works by killing certain bacteria, which can cause serious lung infections.

2. What you need to know before you use Zevtera

Do not use Zevtera:
- if you are allergic to ceftobiprole medocaril sodium or any of the other ingredients of this medicine (listed in section 6),
- if you are allergic to other cephalosporin or beta-lactam antibiotics,
- if you have had previous severe allergic reactions to other antibiotics like penicillin or carbapenem.

Do not use Zevtera if any of the above applies to you. If you are not sure, talk to your doctor or nurse before being given Zevtera.

Warnings and precautions
Talk to your doctor or nurse before using Zevtera-:
- if you have kidney problems (your doctor may need to lower your dose of this medicine),
- if you have ever had any allergic reactions to other antibiotics like penicillin or carbapenem,
- if you have ever had fits (seizures or convulsions),
- if you have diarrhea before, during or after your treatment with this medicine (you may have an inflammation of the bowel known as 'colitis'). **Do not take any medicine to treat diarrhea without first checking with your doctor,**
- if you are HIV positive,
- if your immune system is severely weakened,
- if your white blood counts are very low or your bone marrow function is suppressed,
- if your lung infection is developed more than 48 hours after onset of artificial ventilation Zevtera is not suitable for you (your doctor will prescribe a suitable antibiotic for you),

- if you require (or are expected to require) concomitant calcium-containing solutions, except Lactated Ringer's solution for injection, in the same intravenous administration line due to the risk of precipitation.

If your doctor thinks you need more fluids, you may be asked to drink plenty of liquids or you may need to have liquids given as a drip into a vein while you are receiving Zevtera.

If you start taking Zevtera and then require ventilation, your doctor will assess whether Zevtera is still suitable for you.

Lab tests
You may develop an abnormal lab test (called Coombs test) that looks for certain antibodies which may act against your red blood cells. Zevtera may also interact with tests to measure serum creatinine (Jaffé reaction) or with some tests to determine the glucose content in the urine. These tests may provide you with wrong results.

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

Children
No data is available for use of Zevtera in preterm newborns (born prematurely).

Other medicines and Zevtera
Tell your doctor or nurse if you are taking, have recently taken or might take any other 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 for advice before using this medicine.

Driving and using machines
Zevtera may cause side effects such as dizziness.This may impair your ability to drive or operate machinery.

Zevtera contains sodium
This medicine contains approximately 22 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 1.1% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Zevtera

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

The recommended dose for adults is 500 mg ceftobiprole every 8 hours given as a drip into a vein lasting 2 hours.

The recommended dose for term neonates, infants, children and adolescents depends on the age and weight of the child and is given every 8 hours (infants aged 3 months or older, children and adolescents) or every 12 hours (term neonates and infants younger than 3 months) as a drip into a vein lasting 2 hours.

The infusion solution with a ceftobiprole concentration of 2 mg/mL is used for adults and adolescents. For infants and term neonates, the infusion solution with a ceftobiprole concentration of 4 mg/mL is used.

Patients with kidney problems
You may need a lower dose of Zevtera if you have kidney problems.

If you use more Zevtera than you should
If you think you have been given too much Zevtera, talk to your doctor or nurse straight away.

If you forget to use Zevtera
If you think you have missed a dose, talk to 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:

Tell your doctor straight away if you get these symptoms as you may need urgent medical treatment:
- Sudden swelling of your lips, face, throat or tongue; a severe rash; and, swallowing or breathing problems. These may be signs of a severe allergic reaction (anaphylaxis) and may be lifethreatening.
- Diarrhea that becomes severe or does not go away or stool that contains blood or mucus during or after treatment with Zevtera. In this situation, you should not take medicines that stop or slow bowel movement.

Common: may affect up to 1 in 10 people
- Feeling sick (*nausea*)
- Headache, drowsiness (*somnolence)*
- Feeling dizzy
- Rash, itching or hives
- Diarrhea, tell your doctor straight away if you get diarrhea
- Being sick (*vomiting*)
- Stomach pain (*abdominal pain*), indigestion or ′heartburn′ (*dyspepsia*)
- Unusual taste (*dysgeusia*)
- Fungal infections in different parts of your body
- Redness, pain or swelling were the injection was given
- Low levels of the mineral ′sodium′ in your blood
- Increase in the level of some liver enzymes in your blood
- Hypersensitivity including skin reddening

Uncommon: may affect up to 1 in 100 people
- Convulsions, seizures, or fits
- Temporarily decreased or increased numbers of certain types of blood cells
- Blood testing showing decreased levels of potassium
- Sleeplessness and sleep disturbances, maybe including anxiety, panic attacks and nightmares
- Shortness of breath or difficulty breathing, asthma
- Muscle cramps
- Kidney problems
- Swelling, particularly of the ankles and legs
- Blood testing showing temporarily increased levels of triglycerides, blood sugar, or creatinine

Not known: frequency cannot be estimated from the available data
- A more severe decrease in a specific type of white blood cells (*agranulocytosis*)

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 Yellow Card Scheme, website: www.mhra.gov.uk/yellowcard. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Zevtera

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

Store in a refrigerator (2°C–8°C).

Keep the vial in the outer carton in order to protect from light.

For storage of Zevtera reconstituted and diluted infusion solutions, please see the accompanying information for medical or healthcare professionals.

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 Zevtera contains

- The active substance is ceftobiprole. Each vial contains 500 mg of ceftobiprole(as 666.6 mg of ceftobiprole medocaril sodium). After reconstitution, each mL of concentrate contains 50 mg ceftobiprole, equivalent to 66.7 mg ceftobiprole medocaril sodium.
- The other ingredients are citric acid monohydrate (E330) and sodium hydroxide (E524), see also section 2.

What Zevtera looks like and contents of the pack

Zevtera is a white, yellowish to slightly brownish, cake to broken cake or powder for concentrate for solution for infusion in a 20 mL vial. It is available in packs containing 10 vials.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

Mercury Pharmaceuticals Ltd,
Dashwood House, 69 Old Broad Street,
London, EC2M 1QS, UK

Manufacturer:
ACS Dobfar S.p.A.
Via A. Fleming, 2
37135 Verona (VR)
Italy

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland)under the following names:

Austria:	Zevtera *500 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung*
Denmark:	Zevtera
Finland:	Zevtera *500 mg, kuiva-aine välikonsentraatiksi infuusionestettä varten, liuos*
France:	Mabelio *500 mg, poudre pour solution à diluer pour solution pour perfusion*
Germany:	Zevtera *500 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung*
Ireland:	Adaluzis *500 mg powder for concentrate for solution for infusion*
Italy:	Mabelio *500 mg, polvere per concentrato per soluzione per infusione*

Luxembourg: Mabelio *500 mg, poudre pour solution à diluer pour solution pour perfusion*
Norway: Zevtera *500 mg, pulver til konsentrat til infusjonsvæske, oppløsning*
Poland: Zevtera, *500 mg, proszek do sporządzania koncentratu roztworu do infuzji*
Portugal : Zevtera *500 mg pó para concentrado para solução para perfusão*
Spain: Zevtera *500 mg, polvo para concentrado para solución para perfusión*
Sweden: Zevtera *500 mg pulver till koncentrat till infusionsvätska, lösning*
United Kingdom (Northern Ireland): Zevtera *500mg powder for concentrate for solution for infusion.*

This leaflet was last revised in January 2025.

Detailed information on this medicine is available on the web site of United Kingdom/Medicines and Healthcare Products Regulatory Agency.

<----------->
The following information is intended for healthcare professionals only:

Each vial is for single use only.

Preparation of Zevtera infusion solutions

Zevtera must be reconstituted and then diluted prior to infusion.

Step 1: Reconstitution

For adult and paediatric patients ≥ 12 years who require an infusion solution with a ceftobiprole concentration of 2 mg/mL, the lyophilized powder should be reconstituted with 10 mL of sterile water for injections or dextrose 50 mg/mL (5%) solution for injection.

For paediatric patients < 12 years who require an infusion solution with a ceftobiprole concentration of 4 mg/mL, the lyophilized powder must be reconstituted either with 10 mL dextrose 50 mg/mL (5%) solution for injection if further dilution with the same diluent solution (i.e., dextrose 50 mg/mL (5%) solution for injection) is used, or with 10 mL of water for injection if further dilution with sodium chloride 9 mg/mL (0.9%) solution for injection is used (see tables below).

The vial should be shaken vigorously until complete dissolution, which in some cases may take up to 10 minutes. The volume of the resulting concentrate is approximately 10.6 mL. Any foam should be allowed to dissipate and the reconstituted solution should be inspected visually to ensure the product is in solution and particulate matter is absent. The reconstituted concentrate contains 50 mg/mL of ceftobiprole (as 66.7 mg/mL of ceftobiprole medocaril sodium) and must be further diluted prior to administration. It is recommended that the reconstituted solution be further diluted immediately. However, if this is not possible the reconstituted solution can be stored at room temperature for up to 1 hour, or in a refrigerator for up to 24 hours.

Step 2: Dilution (infusion solution)

Use in adult and paediatric patients ≥ 12 years

Preparation of 500 mg dose of Zevtera solution for infusion (2 mg/mL ceftobiprole)
10 mL of the reconstituted solution should be withdrawn from the vial and injected into a suitable container (e.g. PVC or PE infusion bags, glass bottles) containing 250 mL of sodium chloride 9 mg/mL (0.9%) solution for injection, dextrose 50 mg/mL (5%) solution for injection, or Lactated Ringer's solution for injection. The infusion solution should be gently inverted 5-10 times to form a homogenous solution. Vigorous agitation should be avoided to prevent foaming.

In adults, the entire contents of the infusion bag should be infused to administer a 500 mg dose of ceftobiprole.

In paediatric patients ≥ 12 years the volume to be administeredshould be calculated based on the patient body weight and must not exceed a maximum of 250 mL (500 mg dose).

Preparation of 250 mg dose of Zevtera solution for infusion for adult patients with severe renal impairment

5 mL of the reconstituted solution should be withdrawn from the vial and injected into a suitable container (e.g. PVC or PE infusion bags, glass bottles) containing 125 mL of sodium chloride 9 mg/mL (0.9%) solution for injection, dextrose 50 mg/mL (5%)solution for injection, or Lactated Ringer's solution for injection. The infusion solution should be gently inverted 5-10 times to form a homogenous solution. Vigorous agitation should be avoided to prevent foaming. The entire contents of the infusion bag should be infused to administer a 250 mg dose of ceftobiprole.

Use in paediatric patients < 12 years

Preparation of Zevtera solution for infusion at a concentration of 4 mg/mL of ceftobiprole
Administration via infusion bags, bottles or syringes:
The reconstituted solution prepared with 10 mL dextrose 50 mg/mL (5%)solution for injection must be diluted with the same diluent solution (i.e., dextrose 50 mg/mL (5%)solution for injection). The reconstituted solution prepared with 10 mL water for injection solution must be diluted with sodium chloride 9 mg/mL (0.9%) solution for injection.

10 mL should be withdrawn from an infusion container (e.g. PVC or PE infusion bags, glass bottles) containing 125 mL of diluent solution and replaced with 10 mL of the reconstituted solution withdrawn from the vial. The infusion solution should be gently inverted 5–10 times to form a homogenous solution. Vigorous agitation should be avoided to prevent foaming. The volume to be administered should be calculated based on the patient body weight and must not exceed a maximum of 125 mL (500 mg dose).

For administration via a 50 mL syringe if the calculated dose does not exceed 200 mg, 4 mL of the reconstituted solution (equivalent to 200 mg ceftobiprole) prepared with dextrose 50 mg/mL (5%) solution for injection or water for injection should be withdrawn from the vial and diluted with 46 mL of the appropriate infusion solution diluent (see table below). The infusion solution should be gently inverted 5–10 times to form a homogenous solution. Vigorous agitation should be avoided to prevent foaming. The volume to be administered should be calculated based on the patient body weight and must not exceed 50 mL (200 mg dose).

Appearance of diluted solution
The solution for infusion should be clear to slightly opalescent and yellowish in colour. The solution for infusion should be inspected visually for particulate matter prior to administration, and discarded if particulate matter is visible.

See also section 3 for further information.

Storage of Zevtera reconstituted and diluted infusion solutions

Chemical and physical in-use stability of the reconstituted solution has been demonstrated for 1 hour at 25°C and up to 24 hours at 2°C–8°C.

Chemical and physical in-use stability data support the total times for reconstitution and infusion of 2 mg/mL or 4 mg/mL ceftobiprole dilution solutions described in the tables below:

Use in adults and adolescents ≥ 12 years (2 mg/mL ceftobiprole): Total time by which reconstitution and infusion (including the period of infusion) must be completed

Reconstitution solution diluent	Infusion solution diluent	Infusion solutions stored at 25°C		Infusion solutions stored at 2°C to 8°C
		Protected from light	NOT protected from light	Protected from light
Dextrose 50 mg/mL (5%) solution for injection or Water for injection	Sodium chloride 9 mg/mL (0.9%) solution for injection	24 hours	8 hours	96 hours
	Dextrose 50 mg/mL (5%) solution for injection	12 hours	8 hours	96 hours
	Lactated Ringer's solution for injection	24 hours	8 hours	Do not refrigerate

Use in children, infants, and neonates (< 12 years) (4 mg/mL ceftobiprole): Total time by which reconstitution and infusion (including the period of infusion) must be completed

Reconstitution solution diluent	Infusion solution diluent	Infusion solutions stored at 25°C	Infusion solutions stored at 2°C to 8°C
		NOT protected from light	Protected from light
Dextrose 50 mg/mL (5%) solution for injection	Dextrose 50 mg/mL (5%) solution for injection	12 hours	24 hours
Water for injection	Sodium chloride 9 mg/mL (0.9%) solution for injection	8 hours	8 hours

From a microbiological point of view, unless the method of reconstitution/dilution precludes the risk of microbiological contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

The reconstituted and infusion solutions should not be frozen or exposed to direct sunlight.

If the infusion solution is stored in the refrigerator, it should be equilibrated to room temperature prior to administration. The infusion solution does not need to be protected from light during administration.

See also section 5 for further information.