Package leaflet: Information for the patient

EXBLIFEP 2 g/0.5 g powder for concentrate for solution for infusion
cefepime/enmetazobactam

▼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 taking 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 EXBLIFEP is and what it is used for

EXBLIFEP is an antibiotic. It contains two active substances:
- cefepime, which belongs to a group of antibiotics called fourth generation cephalosporins and can kill certain bacteria;
- enmetazobactam, which blocks the action of enzymes called beta-lactamases. These enzymes make bacteria resistant to cefepime by breaking down the antibiotic before it can act. By blocking the action of beta-lactamases, enmetazobactam makes cefepime more effective at killing bacteria.

EXBLIFEP is used in adults to treat:
- complicated (severe) infections within the urinary tract (bladder and kidneys)
- certain types of pneumonia (infection of the lungs) that occur during a hospital stay

Exblifep is also used to treat bacteraemia (the presence of bacteria in the blood) due to, or possibly due to, any of the infections listed above.

2. What you need to know before you use EXBLIFEP

Do not use EXBLIFEP
- if you are allergic to cefepime, enmetazobactam or any of the other ingredients of this medicine (listed in section 6).
- if you are allergic to cephalosporins, which are antibiotics used to manage a wide range of infections.
- if you have had a severe allergic reaction (e.g., severe skin peeling; swelling of the face, hands, feet, lips, tongue or throat; or difficulty swallowing or breathing) to so-called beta-lactam antibiotics (antibiotics such as penicillins, carbapenems or monobactams).

Warnings and precautions

Talk to your doctor or pharmacist **before** using EXBLIFEP if:
- you are allergic to cephalosporins, penicillins or other antibiotics (see 'Do not use Exblifep')
- you have or have had asthma or are sensitive to have allergic reactions. Your doctor will check for any signs of allergies the first time you are given this medicine (see section 4).
- you have kidney problems. Your doctor may need to change the dose of this medicine.
- you have any upcoming blood or urine tests scheduled. This medicine can alter the results of some tests (see section 4).

Talk to your doctor or pharmacist **while** using EXBLIFEP if:
- you develop severe and persistent diarrhoea during or right after treatment. This may be a sign of an inflammation of the large bowel and needs urgent medical intervention.
- you suspect to have developed a new infection during prolonged use of EXBLIFEP. This may be caused by micro-organisms which are insensitive to cefepime and may require interruption of EXBLIFEP treatment.

Children and adolescents
This medicine should not be given to children under 18 years old because there is not enough information on its use in this age group.

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

In particular, tell your doctor if you use the following:
- other antibiotics, in particular aminoglycosides (such as gentamicin) or 'water tablets' (diuretics, such as furosemide). If you are using these medicines, your kidney function should be monitored.
- medicines that are used to prevent your blood from clotting (coumarin anticoagulants, such as warfarin). Their effect may be greater when you take Exblifep.
- certain types of antibiotics (bacteriostatic antibiotics). These can affect how well EXBLIFEP works.

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. Your doctor will advise if you should receive EXBLIFEP during pregnancy.

Exblifep may pass into breast milk. If you are breast-feeding, your doctor will advise you on whether you should stop breast-feeding or abstain fromEXBLIFEP therapy, taking into account the benefit of breast-feeding for your child and the benefit of therapy for you.

Driving and using machines
This medicine may cause dizziness, which can affect your ability to drive and use machines. Do not drive or use machines until you no longer feel dizzy.

3. How to use EXBLIFEP

Your doctor or other healthcare professional will give you this medicine as an infusion (drip) into a vein (directly into the bloodstream). Depending on the type of infection that you have and your kidney function the infusion will be given during two or four hours.

The recommended dose is one vial (2 g of cefepime and 0.5 g enmetazobactam) every 8 hours.

Treatment normally lasts between 7 and 14 days, depending on the severity and location of the infection and on how your body responds to the treatment.

If you have kidney problems, your doctor may need to reduce the dose or change how often EXBLIFEP is given to you (see section 2: Warnings and precautions).

If you use more EXBLIFEP than you should
As this product is given by a doctor or other healthcare professional, it is unlikely that you will be given too much EXBLIFEP. However, let your doctor or nurse know immediately if you have any concerns.

If you forget to use EXBLIFEP
If you think you have not been given a dose of EXBLIFEP, tell your doctor or other healthcare professional immediately.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor straight away if you experience the following side effects, as you may need urgent medical treatment:

Rare: may affect up to 1 in 1 000 people
- anaphylactic (allergic) reaction and angioedema. This may be life-threatening. Signs and symptoms may be a sudden swelling of your lips, face, throat or tongue; a severe rash; and, swallowing or breathing problems.

Not known: frequency cannot be estimated from the available data
- Stevens-Johnson syndrome and toxic epidermal necrolysis. Extremely intense and serious skin reactions. The adverse reaction of the skin may appear as rashes with or without blisters. Skin irritation, sores or swelling in the mouth, throat, eyes, nose and around the genitals and fever and flulike symptoms may occur. The skin rashes may develop into serious widespread skin damage (peeling of the epidermis and superficial mucous membranes) with life-threatening consequences.

Other side effects
Other side effects which may occur after Exblifeb treatment include those listed below

Very common : may affect more than 1 in 10 people
Side effect seen in blood tests:
- positive Coombs test (a blood test checking for antibodies that attack your body’s red blood cells)

Common: may affect up to 1 in 10 people
- infusion site phlebitis (inflammation at the site of infusion, causing pain, swelling and redness along a vein)
- reaction, pain and inflammation at the infusion site
- diarrhoea
- skin rash
- headache

Side effects seen in blood tests:
- increased liver enzyme levels in the blood
- increased levels of bilirubin (a substance produced by the liver) in the blood
- increased levels of amylase (an enzyme that helps the body digest carbohydrates) in the blood
- increased levels of lipase (an enzyme that helps the body digest fat) in the blood

- increased levels of lactate dehydrogenase (a marker indicating cell and tissue damage in the body) in the blood
- changes in your white blood cell count (*eosinophilia*)
- low levels of red blood cells (*anaemia*)
- blood coagulation delayed (increased time for blood to clot)

Uncommon: may affect up to 1 in 100 people
- *clostridioides difficile*-associated diarrhoea (CDAD), painful, severe diarrhoea caused by a bacteria called clostridioides difficile
- fungal infection in the mouth
- vaginal infection
- inflammation of the large intestine, causing diarrhoea, usually with blood and mucus
- dizziness, nausea, vomiting
- reddening of the skin, hives, iching
- fever
- infusion site inflammation

Side effects seen in blood tests:
- low levels of certain blood cells (*leucopenia, neutropenia, thrombocytopenia*)
- increased levels of urea and creatinine (measures indicating reduced kidney function) in the blood

Rare: may affect up to 1 in 1 000 people
- shortness of breath
- stomach pain, constipation
- fungal infection
- convulsion (fits)
- distortion of the sense of taste
- sensation of pricking or numbness of your skin, pins and needles
- itching in and around the vaginal area
- allergic dermatitis
- chills
- widening of blood vessels in the body

Not known: frequency cannot be estimated from the available data
- coma
- reduced consciousness
- encephalopathy (a brain disorder caused by harmful substance or infection)
- altered state of consciousness
- muscle jerks
- confusion, hallucinations
- false positive urinary glucose tests
- kidney problems (failure or any other structural changes or dysfunction)
- bleeding
- erythema multiforme (a skin rash, which may blister, and looks like small targets (central dark spot surrounded by a paler area, with a dark ring around the edge).

Side effects seen in blood tests:
- very low levels of granulocytes, a type of white blood cells (*agranulocytosis*)
- red blood cells destroyed too quickly (*haemolytic anaemia*)
- low levels of red blood cells caused by the inability of your bone marrow to make enough new cells *(aplastic anaemia)*

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly 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.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store EXBLIFEP

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.

Unopened vials: Store in a refrigerator (2 ºC – 8 ºC). Keep the vial in the outer carton in order to protect from light.

After reconstitution and dilution: Store in a refrigerator (2 ºC – 8 ºC) for not more than 6 hours before use.

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

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 EXBLIFEP contains
- The active substances are cefepime and enmetazobactam.
  Each vial contains cefepime dihydrochloride monohydrate equivalent to 2 g cefepime and 0.5 g enmetazobactam.
- The other ingredient is L-arginine.

What EXBLIFEP looks like and contents of the pack
EXBLIFEP is a white to yellowish powder for concentrate for solution for infusion (powder for concentrate) supplied in a 20 mL glass vial with a bromobutyl rubber stopper and flip-off seal.

Pack size of 10 vials.

Marketing Authorisation Holder
Advanz Pharma Limited
Unit 17 Northwood House
Northwood Crescent
Dublin 9
D09 V504
Ireland
+44 (0)208 588 9131
medicalinformation@advanzpharma.com

Manufacturer
Infosaúde - Instituto De Formação E Inovação Em Saúde S.A.
Rua Das Ferrarias Del Rei,
nº6 - Urbanização da Fábrica da Pólvora,
Barcarena,

2730-269,
Portugal

This leaflet was last revised in January 2024.

The following information is intended for healthcare professionals only:

Preparation of solution

This medicinal product is for intravenous infusion and each vial is for single use only.

Aseptic technique must be followed in preparing the infusion solution.

Preparation of doses

Cefepime-enmetazobactam is compatible with sodium chloride 9 mg/ml (0.9%) solution for injection, 5% glucose injection solution and a combination of glucose injection solution and sodium chloride injection solution (containing 2.5% glucose and 0.45% sodium chloride).

EXBLIFEP is supplied as a dry powder in a single-dose vial that must be reconstituted and further diluted prior to intravenous infusion as outlined below.

To prepare the required dose for intravenous infusion, reconstitute the vial as determined from **Table 1** below:

1. Withdraw 10 mL from an infusion bag of 250 mL (compatible injection solution) and reconstitute the cefepime-enmetazobactam vial.
2. Mix gently to dissolve. The reconstituted cefepime-enmetazobactam solution will have an approximate cefepime concentration of 0.20 g/mL and an approximate enmetazobactam concentration of 0.05 g/mL. The final volume is approximately 10 mL.
   CAUTION: THE RECONSTITUTED SOLUTION IS NOT FOR DIRECT INJECTION.

The reconstituted solution must be diluted further, **immediately**, in an infusion bag of 250 mL (compatible injection solution) before intravenous infusion. To dilute the reconstituted solution, withdraw the full or partial reconstituted vial content and add it back into the infusion bag according to **Table 1** below.

3. The intravenous infusion of the diluted solution must be completed within 8 hours, if stored under refrigerated conditions (i.e., at 2 °C to 8 °C; where it has been refrigerated for less than 6 hours, prior to being allowed to reach room temperature and then administered at room temperature over a period of 2 or 4 hours).

Table 1: Preparation of cefepime-enmetazobactam doses

Cefepime/enmetazobactam dose	Number of vials to reconstitute	Volume to withdraw from each reconstituted vial for further dilution	Final volume of infusion bag
2.5 g (2 g / 0.5 g)	1	Entire content (approximately 10 mL)	250 mL
1.25 g (1 g / 0.25 g)	1	5.0 mL (discard unused portion)	245 mL
0.625 g (0.5 g / 0.125 g)	1	2.5 mL (discard unused portion)	242.5 mL

Inspect the vial before use. It must only be used if the solution is free from particles. Use only clear solutions.

Like other cephalosporins, cefepime-enmetazobactam solutions can develop a yellow to amber colour, depending on storage conditions. However, this has no negative influence on the effect of the product.

The prepared solution should be administered via intravenous infusion.

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