

Package leaflet: Information for the user

Piperacillin/Tazobactam 2 g/0.25 g powder for solution for infusion

Piperacillin/Tazobactam 4 g/0.5 g powder for solution for infusion

(Piperacillin/Tazobactam)

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

1. What Piperacillin/Tazobactam is and what it is used for

Piperacillin/Tazobactam contains the active substances piperacillin and tazobactam (as piperacillin sodium and tazobactam sodium). This medicine belongs to the pharmacotherapeutic group of combinations of penicillins, including beta-lactamase inhibitors.

Piperacillin belongs to the group of medicines known as “broad-spectrum penicillin antibiotics”. It can kill many kinds of bacteria. Tazobactam can prevent some resistant bacteria from surviving the effects of piperacillin. This means that when piperacillin and tazobactam are given together, more types of bacteria are killed.

Piperacillin/Tazobactam is used in adults and adolescents to treat bacterial infections, such as those affecting the lower respiratory tract (lungs), urinary tract (kidneys and bladder), abdomen, skin or blood. Piperacillin/Tazobactam may be used to treat bacterial infections in patients with low white blood cell counts (reduced resistance to infections).

Piperacillin/Tazobactam is used in children aged 2-12 years to treat infections of the abdomen such as appendicitis, peritonitis (infection of the fluid and lining of the abdominal organs), and gallbladder (biliary) infections. Piperacillin/Tazobactam may be used to treat bacterial infections in patients with low white blood cell counts (reduced resistance to infections).

In certain serious infections, your doctor may consider using this medicine in combination with other antibiotics.

2. What you need to know before you are given Piperacillin/Tazobactam

Do not use Piperacillin/Tazobactam:

- if you are allergic to piperacillin or tazobactam,
- if you are allergic to antibiotics known as penicillins, cephalosporins or other beta-lactamase inhibitors, as you may be allergic to Piperacillin/Tazobactam.

Warnings and precautions

Talk to your doctor or nurse before using Piperacillin/Tazobactam:

- if you have allergies. If you have several allergies, make sure you tell your doctor or other healthcare professional before receiving this product.
- if you are suffering from diarrhoea before, or if you develop diarrhoea during or after your treatment. In this case, make sure you tell your doctor or other healthcare professional immediately. Do not take any medicine for the diarrhoea without first checking with your doctor.
- if you have low levels of potassium in your blood. Your doctor may want to check your kidneys before you take this medicine and may perform regular blood tests during treatment.
- if you have kidney or liver problems, or are receiving haemodialysis. Your doctor may want to check your kidneys before you take this medicine, and may perform regular blood tests during treatment.
- if you are taking certain medicines (called anticoagulants) to avoid an excess of blood clotting (see also section “**Other medicines and Piperacillin/Tazobactam**” in this leaflet) or any unexpected bleeding occurs during the treatment. In this case, you should inform your doctor or other healthcare professional immediately.
- if you develop convulsions during the treatment. In this case, you should inform your doctor or other healthcare professional.
- if you think you developed a new or worsening infection. In this case, you should inform your doctor or other healthcare professional.

Children below 2 years

Piperacillin/tazobactam is not recommended for use in children below the age of 2 years due to insufficient data on safety and effectiveness.

Other medicines and Piperacillin/Tazobactam

Tell your doctor or other healthcare professional if you are taking, have recently taken or might take any other medicines.

Some medicines may interact with piperacillin and tazobactam. These include:

- medicine for gout (probenecid). This can increase the time it takes for piperacillin and tazobactam to leave your body.
- medicines to thin your blood or to treat blood clots (e.g. heparin, warfarin or aspirin).
- medicines used to relax your muscles during surgery. Tell your doctor if you are going to have a general anaesthetic.
- methotrexate (medicine used to treat cancer, arthritis or psoriasis). Piperacillin and tazobactam can increase the time it takes for methotrexate to leave your body.
- medicines that reduce the level of potassium in your blood (e.g. tablets enhancing urination or some medicines for cancer).
- medicines containing the other antibiotics tobramycin or gentamycin. Tell your doctor if you have kidney problems.

Effect on laboratory tests

Tell the doctor or laboratory staff that you are taking Piperacillin/Tazobactam if you have to provide a blood or urine sample.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or other healthcare professional for advice before receiving this medicine. Your doctor will decide if Piperacillin/Tazobactam is right for you.

Piperacillin and tazobactam can pass to a baby in the womb or through breast milk. If you are breast-feeding, your doctor will decide if Piperacillin/Tazobactam is right for you.

Driving and using machines

The use of Piperacillin/Tazobactam is not expected to affect the ability to drive or use machines.

Piperacillin/Tazobactam contains sodium

Piperacillin/Tazobactam 2 g/0.25 g contains 4.5 mmol (or 103.3 mg) sodium per dose.

Piperacillin/Tazobactam 4 g/0.5 g contains 9.0 mmol (or 206.6 mg) sodium per dose.

This should be taken into consideration by patients on a controlled sodium diet.

3. How Piperacillin/Tazobactam is given

Your doctor or other healthcare professional will give you this medicine through an infusion (a drip for 30 minutes) into one of your veins. The dose of medicine given to you depends on what you are being treated for, your age, and whether or not you have kidney problems.

Adults and adolescents aged 12 years or older

The recommended dose is 4 g/0.5 g of piperacillin/tazobactam given every 6-8 hours, which is given into one of your veins (directly into the blood stream).

Children aged 2 to 12 years

The recommended dose for children with abdominal infections is 100 mg/12.5 mg/kg of body weight of piperacillin/tazobactam given every 8 hours into one of your veins (directly into the blood stream). The recommended dose for children with low white blood cell counts is 80 mg/10 mg/kg of body weight of piperacillin/tazobactam given every 6 hours into one of your veins (directly into the blood stream).

Your doctor will calculate the dose depending on your child's weight but the daily dose will not exceed 4 g/0.5 g of Piperacillin/Tazobactam.

You will be given Piperacillin/Tazobactam until the sign of infection has gone completely (5 to 14 days).

Patients with kidney problems

Your doctor may need to reduce the dose of Piperacillin/Tazobactam or how often you are given it. Your doctor may also want to test your blood to make sure that your treatment is at the right dose, especially if you have to take this medicine for a long time.

If you receive more Piperacillin/Tazobactam than you should

As you will receive Piperacillin/Tazobactam from a doctor or other healthcare professional, you are unlikely to be given the wrong dose. However, if you experience side effects, such as convulsions, or think you have been given too much, tell your doctor immediately.

If you miss a dose of Piperacillin/Tazobactam

If you think you have not been given a dose of Piperacillin/Tazobactam, tell your doctor or other healthcare professional immediately.

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

4. Possible side effects

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

The serious side effects of Piperacillin/Tazobactam are:

- swelling of the face, lips, tongue or other parts of the body
- shortness of breath, wheezing or trouble breathing
- severe rash, itching or hives on the skin
- yellowing of the eyes or skin
- damage to blood cells (the signs include: being breathless when you do not expect it, red or brown urine, nosebleeds and bruising).

If you notice any of the above, see a doctor straight away. For frequency of these reactions, refer to the information below.

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

- diarrhoea, vomiting, nausea
- skin rashes.

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

- thrush
- (abnormal) decrease in white blood cells (leukopenia, neutropenia) and platelets (thrombocytopenia)
- allergic reaction
- headache, sleeplessness
- low blood pressure, inflammation of the veins (felt as tenderness or redness in the affected area)
- jaundice (yellow staining of the skin or whites of the eyes), inflammation of the mucous lining of the mouth, constipation, indigestion, stomach upset
- increase of certain enzymes in the blood (alanine aminotransferase increased, aspartate aminotransferase increased)
- itching, nettle rash
- increase of muscle metabolism product in the blood (blood creatinine increased)
- fever, injection site reaction
- yeast infection (candidal superinfection).

Rare side effects (may affect up to 1 in 1,000 people):

- (abnormal) decrease of red blood cells or blood pigment/haemoglobin, (abnormal) decrease of red blood cells due to premature breakdown (degradation) (haemolytic anaemia), small spot bruising (purpura), bleeding of the nose (epistaxis) and bleeding time prolonged, (abnormal) increase of a specific type of white blood cells (eosinophilia)
- severe allergic reaction (anaphylactic/anaphylactoid reaction, including shock)
- flushed red skin
- a certain form of infection of the colon (pseudomembranous colitis), abdominal pain
- inflammation of the liver (hepatitis), increase of a blood pigments breakdown product (bilirubin), increase of certain enzymes in the blood (blood alkaline phosphatase increased, gamma-glutamyltransferase increased)
- skin reactions with redness and formation of skin lesions (exanthema, erythema multiforme), skin reactions with blistering (bullous dermatitis)
- joint and muscle pain
- poor kidney functions and kidney problems
- rigors chill/rigidity.

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

- severe decrease of granular white blood cells (agranulocytosis), severe decrease of red blood cells, white blood cells and platelets (pancytopenia)

- prolonged time for blood clot formation (prolonged partial thromboplastin time, prothrombin time prolonged), abnormal lab test (positive direct Coombs), increase of platelets (thrombocytosis)
- decrease of potassium in the blood (hypokalaemia), decrease of blood sugar (glucose), decrease of the blood protein albumin, decrease of blood total protein
- detachment of the top layer of the skin all over the body (toxic epidermal necrolysis), serious bodywide allergic reaction with skin and mucous lining rashes and various skin eruptions (Stevens-Johnson Syndrome)
- blood urea nitrogen increased.

Piperacillin therapy has been associated with an increased incidence of fever and rash in cystic fibrosis patients.

Reporting of side effects

If you get any side effects, talk to your doctor or other healthcare professional. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

HPRA Pharmacovigilance,
Kevin O'Malley House,
Earlsfort Centre, Earlsfort Terrace,
IRL-Dublin 2.

Tel: +353 1 6764971

Fax: +353 1 6762517

Website: www.hpra.ie

e-mail: medsafety@hpra.ie.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Piperacillin/Tazobactam

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 label after EXP. The expiry date refers to the last day of that month.

Unopened vials: Do not store above 30°C.

Reconstituted solution in vial:

The reconstituted solution should be further diluted immediately without delay.

Diluted solution for infusion:

The diluted solution for infusion should be used immediately without delay.

Do not use this medicine if you notice particulate matter and discoloration prior to administration. The solution should only be used if the solution is clear and free from particles.

For single use only. Discard any unused solution.

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 Piperacillin/Tazobactam contains

- The active substances are piperacillin and tazobactam.
 - Each vial of Piperacillin/Tazobactam 2 g/0.25 g contains 2 g piperacillin (as sodium salt) and 0.25 g tazobactam (as sodium salt).
 - Each vial of Piperacillin/Tazobactam 4 g/0.5 g contains 4 g piperacillin (as sodium salt) and 0.5 g tazobactam (as sodium salt).

What Piperacillin/Tazobactam looks like and contents of the pack

Piperacillin/Tazobactam 2 g/0.25 g is a white to off-white powder supplied in a 30 ml type I flint glass vial sealed with a dark grey bromobutyl rubber stopper and an electric blue coloured flip off aluminium seal. Pack sizes: 1, 5, 12, 25 and 50 vials.

Piperacillin/Tazobactam 4 g/0.5 g is a white to off-white powder supplied in a 50 ml type I flint glass vial sealed with a dark grey bromobutyl rubber stopper and a red coloured flip off aluminium seal. Pack sizes: 1, 5, and 12 vials.

Not all packs sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

Pfizer Healthcare Ireland,
9, Riverwalk,
National Digital Park,
Citywest Business Campus,
Dublin 24,
Ireland.

Manufacturer:

Pfizer Service Company BVBA,
Hoge Wei 10, B-1930 Zaventem,
Belgium.

This medicinal product is authorised in the Member States of the EEA under the following names:

| | |
|---------|---|
| Austria | Piperacillin/Tazobactam Pfizer 4 g/0.5 g Pulver zur Herstellung einer Infusionslösung |
| Belgium | Piperacillin/Tazobactam Pfizer 2 g/0.25 g & 4 g/0.5 g Poudre pour solution pour perfusion Piperacillin/Tazobactam Pfizer 2 g/0.25 g & 4 g/0.5 g poeder voor oplossing voor infusie Piperacillin/Tazobactam Pfizer 2 g/0.25 g & 4 g/0.5 g Pulver zur Herstellung einer Infusionslösung |
| Germany | Piperacillin/Tazobactam 2 g/0.25 g (4 g/0.5 g) Pulver zur Herstellung einer Infusionslösung |
| Denmark | Piperacillin/Tazobactam Pfizer |
| Greece | Piperacillin + Tazobactam/Pfizer |
| Finland | Piperacillin/Tazobactam Pfizer |

| | |
|------------|--|
| Ireland | Piperacillin/Tazobactam 2 g/0.25 g & 4 g/0.5 g powder for solution for infusion |
| Luxembourg | Piperacilline/Tazobactam Pfizer 2 g/0.25 g & 4 g/0.5 g poudre pour solution pour perfusion |
| Norway | Piperacillin/Tazobactam Pfizer |
| Portugal | Piperacilina + Tazobactam Pfizer |

This leaflet was last revised in 07/2014.

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The following information is intended for healthcare professionals only:

Instructions for use

This medicine will be given by intravenous infusion (a drip for 30 minutes).

Intravenous use

Reconstitute each vial with the volume of solvent shown in the table below, using one of the compatible solvents for reconstitution. Swirl until dissolved. When swirled constantly, reconstitution generally occurs within 5 to 10 minutes (for details on handling, please see below).

| Content of vial | Volume of solvent* to be added to vial | Displacement Volume | Approximate concentration per ml |
|---|--|---------------------|---|
| 2 g / 0.25 g (2 g piperacillin and 0.25 g Tazobactam) | 10 ml | 1.2 ml | Piperacillin: 178.6 mg/ml Tazobactam: 22.3 mg/ml |
| 4 g / 0.50 g (4 g piperacillin and 0.5 g tazobactam) | 20 ml | 3.4 ml | Piperacillin: 170.9 mg/ml Tazobactam: 21.4 mg/ml |

*Compatible solvents for reconstitution:

- 0.9% (9 mg/ml) sodium chloride solution for injection
- Sterile water for injections⁽¹⁾.

⁽¹⁾Maximum recommended volume of sterile water for injection per dose is 50 ml.

The reconstituted solutions should be withdrawn from the vial by syringe. When reconstituted as directed, the vial contents withdrawn by syringe will provide the labelled amount of piperacillin and tazobactam.

The reconstituted solutions may be further diluted to the desired volume (e.g. 50 ml to 150 ml) with one of the following compatible solvents:

- 0.9% (9 mg/ml) sodium chloride solution for injection
- Glucose 5%
- Dextran 6% in 0.9% sodium chloride.

Do not use this medicine if you notice particulate matter and discoloration prior to administration. The solution should only be used if the solution is clear and free from particles.

The diluted solution for infusion has a pH of between 5.0 and 7.0 and an osmolarity of 600-700 mOsmol/kg.

Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned above.

This medicinal product must **not** be mixed or co-administered with any aminoglycosides. Whenever Piperacillin/Tazobactam is used concurrently with another antibiotic (e.g. aminoglycosides), the substances must be administered separately. The mixing of piperacillin/tazobactam with an aminoglycoside in vitro can result in substantial inactivation of the aminoglycoside.

This medicinal product should not be mixed with other substances in a syringe or infusion bottle since compatibility has not been established.

This medicinal product should be administered through an infusion set separately from any other drugs unless compatibility is proven.

Due to chemical instability, this medicinal product should not be used with solutions containing sodium bicarbonate.

This medicinal product is **not** compatible with lactated Ringer's (Hartmann's) solution

This medicinal product should not be added to blood products or albumin hydrolysates.

For storage conditions and disposal instructions, please refer to section 5.