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, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist 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

Piperacillin Tazobactam contains piperacillin and tazobactam, which belong to the group of medicines known as 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 Piperacillin Tazobactam 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, pharmacist or nurse before receiving 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 another antibiotic called vancomycin at the same time as Piperacillin Tazobactam, this may increase the risk of kidney injury (see also Other medicines and Piperacillin Tazobactam in this leaflet).
- if you are taking certain medicines (called anticoagulants) to avoid an excess of blood clotting (see also 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.

During treatment

- there have been reports about a disease in which the immune system makes too many of otherwise normal white blood cells called histiocytes and lymphocytes, resulting in inflammation (haemophagocytic lymphohistiocytosis). This condition may be life-threatening if not diagnosed and treated early. If you experience multiple symptoms such as fever, swollen glands, feeling weak, feeling lightheaded, shortness of breath, bruising, or skin rash, contact your doctor immediately.
- if you develop serious rash, patches or blisters on your skin; talk to your doctor, as this needs to be checked out; and if your skin condition does not get better, your doctor may decide to stop your treatment with this medicine.
- if you develop fits (convulsions) or if you think you developed a new or worsening infection, talk to 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, pharmacist or other healthcare professional if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription. 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, gentamicin or vancomycin. Tell your doctor if you have kidney problems. Taking Piperacillin Tazobactam and vancomycin at the same time may increase the risk of kidney injury even if you have no 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
This medicine contains 103.3 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 5.2% of the recommended maximum daily dietary intake of sodium for an adult.
This medicine contains 206.6 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 10.3% of the recommended maximum daily dietary intake of sodium for an adult.

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 each individual 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, pharmacist or other healthcare professional.

4. Possible side effects

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

If you notice any of the following side effects, stop taking this medicine and contact your doctor, or other healthcare professional, or go to the nearest hospital casualty department straight away:

Common: may affect up to 1 in 10 people
- reduction in one or more types of blood cells, which may be severe, such as red blood cells, white blood cells that help fight infection, or platelets that help the blood to clot (the signs include: a worsening or increase in infections e.g. sore throat, mouth ulcers, fever and chills, feeling tired, breathless or weak, unusual bruising or bleeding) (agranulocytosis, pancytopenia, leukopenia, neutropenia, thrombocytopenia).
- bruising or bleeding for longer than normal, particularly if you are taking anticoagulants such as warfarin.

Rare: may affect up to 1 in 1,000 people
- serious skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis, dermatitis bullous, dermatitis exfoliative) appearing initially as reddish target-like spots or circular patches often with central blisters on the trunk. Additional signs include ulcers in the mouth, throat, nose, extremities, genitals and red and swollen eyes. The rash may progress to widespread blistering or peeling of the skin and potentially may be life-threatening.
- severe or persistent diarrhoea accompanied by fever or weakness. This may be a sign of a certain form of infection of the colon (pseudomembranous colitis).

Not known: frequency cannot be estimated from the available data
- signs of serious allergic reactions, such as 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
- severe potentially fatal allergic condition (drug reaction with eosinophilia and systemic symptoms) that can involve the skin and most importantly other organs under the skin such as the kidney and the liver.
- skin condition (acute generalised exanthematous pustulosis) accompanied by fever, which consists of numerous tiny fluid filled blisters contained within large areas of swollen and reddened skin
- yellowing of the eyes or skin. This may be a sign of inflammation of the liver (hepatitis)
- damage to blood cells (the signs include: being breathless when you do not expect it, red or brown urine, nosebleeds and bruising) (haemolytic anaemia)
- poor kidney functions and kidney problems (the signs include: passing little or no urine, pain in the back, cloudy urine or blood in the urine).

Other possible side effects:

Very common (may affect more than 1 in 10 people)
- diarrhoea

Common side effects (may affect up to 1 in 10 people)
- yeast infection (candidiasis), such as thrush
- abnormal lab test (positive direct Coombs),
- decrease of the blood protein albumin, decrease of blood total protein
- headache, sleeplessness
- abdominal pain, vomiting, nausea, constipation, indigestion, stomach upset
- increase of certain enzymes in the blood (alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased)
- skin rashes, itching
- increase of muscle metabolism product in the blood (blood creatinine increased), blood urea nitrogen increased
- fever, injection site reaction

Uncommon (may affect up to 1 in 100 people)
- decrease of potassium in the blood (hypokalaemia), decrease of blood sugar (glucose)
- fits (convulsions), seen in patients on high doses or with kidney problems
- low blood pressure, inflammation of the veins (felt as tenderness or redness in the affected area), flushed red skin
- increase of a blood pigments breakdown product (bilirubin)
- nettle rash, skin reactions with redness and formation of skin lesions (rash maculopapular, erythema multiforme)
- joint and muscle pain
- chills

Rare (may affect up to 1 in 1,000 people)
- inflammation of the mucous lining of the mouth
- bleeding of the nose (epistaxis)

Not known: frequency cannot be estimated from the available data
- small spot bruising (purpura), (abnormal) increase of a specific type of white blood cells (eosinophilia), increase of platelets (thrombocythaemia)
- increase of certain enzymes in the blood (gamma-glutamyltransferase increased)
- a form of lung disease where eosinophils (a form of white blood cell) appear in the lung in increased numbers
- acute disorientation and confusion (delirium).

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

Beta-lactam antibiotics, including piperacillin tazobactam, may lead to manifestations of encephalopathy and convulsions.

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 HPRA Pharmacovigilance. Website: www.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 after "EXP". The expiry date refers to the last day of that month.

Unopened vials: Do not store above 25°C.

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 contains 2 g piperacillin (as sodium salt) and 0.25 g tazobactam (as sodium salt).
Each vial contains 4 g piperacillin (as sodium salt) and 0.5 g tazobactam (as sodium salt).
See section 2 'Piperacillin Tazobactam contains sodium'.

There are no other ingredients.

What Piperacillin Tazobactam looks like and contents of the pack
Piperacillin Tazobactam is a white to off-white powder supplied in a vial.
Packs containing 1, 5, 10, 12 vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Viatris Limited**,**
Damastown Industrial Park,
Mulhuddart,
Dublin 15,
DUBLIN
Ireland
.

Manufacturer
Mitim S.r.l.,
Via Cacciamali,
34-38, Brescia,
25125, Italy

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

Belgium	Piperacilline/Tazobactam Viatris 2 g/250 mg [4 g/500 mg] poeder voor oplossing voor infusie
Cyprus	Piperacillin+Tazobactam/Viatris Powder for solution for injection/infusion (2g/0.25g) [(4 g/0.5 g)]/vial
Czechia	Piperacillin/Tazobactam Viatris 4 g/ 500 mg, prášek pro infuzní roztok
Greece	Piperacillin + Tazobactam/Viatris Powder solution for infusion (2+0.25) g/vial [4+0.5 g/vial]
Ireland	Piperacillin Tazobactam 2 g/0.25 g [4 g/0.5 g] powder for solution for infusion

Malta	Piperacillin Tazobactam Viatris 2 g/0.25 g [4 g/0.5 g], powder for solution for infusion
The Netherlands	Piperacilline/Tazobactam Viatris 2 g/250 mg [4 g/500 mg], poeder voor oplossing voor infusie
Portugal	Piperacilina + Tazobactam Mylan
Romania	PIPERACILINA/TAZOBACTAM Viatris [4 g/0,5 g], pulbere pentru soluţie perfuzabilă
Slovakia	Piperacillin/Tazobactam Viatris [4 g/0,5 g]
Slovenia	Piperacilin/tazobaktam Viatris 2 g/0,25 g [4 g/0,5 g] prašek za raztopino za infundiranje
United Kingdom	PIPERACILLIN TAZOBACTAM 2g/0.25g [4g/0.5g], powder for solution for infusion

This leaflet was last revised in February 2024

Detailed information on this medicine is available on the website of HPRA (www.hpra.ie).

The following information is intended for healthcare professionals only:

Piperacillin Tazobactam
Powder for solution for infusion

Instructions for use
Piperacillin Tazobactam will be given by intravenous infusion (a drip for 30 minutes) and should only be used if the solution is clear and free from particles.

Intravenous use
Reconstitution and dilution steps are described hereafter.

1) Reconstitution step

Each injection vial of Piperacillin Tazobactam needs to be reconstituted by adding one of the following solutions:

- Sterile water for injection
- 0,9% (9 mg/ml) sodium chloride solution for injection
- Glucose 5%

Add the volume of solution indicated in the table below to each vial:

Content of the vial	**Volume of solution to be added to the vial**
2 g/0.25 g (2 g piperacillin and 0.25 g tazobactam)	10 ml
4 g/0.5 g (4 g piperacillin and 0.5 g tazobactam)	20 ml

Shake strongly during 1 to 2 minutes or until dissolved.

2) Dilution step

The reconstituted solution 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) by adding the withdrawn volume to one of the following solutions:

- Sterile water for injection (maximum recommended volume per dose is 50 ml)

- 0,9% (9 mg/ml) sodium chloride solution for injection
- Glucose 5%

Shake strongly again until it is completely dissolved.

Incompatibilities
Whenever Piperacillin Tazobactam is used concurrently with another antibiotic (e.g. aminoglycosides), the substances must be administered separately. The mixing of beta-lactam antibiotics with aminoglycosides, *in vitro,* can result in substantial inactivation of the aminoglycoside.

Piperacillin Tazobactam should not be mixed with other substances in a syringe or infusion bottle since compatibility has not been established.

Because of chemical instability, Piperacillin Tazobactam should not be used with solutions containing sodium bicarbonate.

Lactated Ringer's (Hartmann's) solution is not compatible with Piperacillin Tazobactam.

Piperacillin Tazobactam should not be added to blood products or albumin hydrolysates.

Co-administration of Piperacillin Tazobactam with aminoglycosides
Due to the *in vitro* inactivation of the aminoglycoside by beta-lactam antibiotics, Piperacillin Tazobactam and the aminoglycoside are recommended for separate administration. Piperacillin Tazobactam and the aminoglycoside should be reconstituted and diluted separately when concomitant therapy with aminoglycosides is indicated.

Piperacillin Tazobactam should be administered through an infusion set separately from any other drugs unless compatibility is proven.

Special precautions for storage
Before first opening:
Do not store above 25°C.

After reconstitution/dilution:
To reduce the risk of microbial contamination, reconstituted/diluted solutions should be used immediately.
If not used immediately, in use storage times and conditions prior to administration are the responsibility of the user.