

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

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.
- 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 belongs to the group of medicines known as “broad spectrum penicillin antibiotics”. It can kill many kinds of bacteria. Tazobactam can prevent some 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 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 or nurse before you are given 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 **Using other medicines** 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.

Always talk to your doctor or nurse before you are given Piperacillin/Tazobactam.

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 if you are using or have recently used or might use 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

Piperacillin and tazobactam can pass to a baby in the womb or through breast milk. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor before getting this product. 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 2g /0.25g contains 4.7 mmol (108 mg) of sodium.

Piperacillin/Tazobactam 4g /0.5g contains 9.4 mmol (216 mg) of sodium.

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

3. How Piperacillin/Tazobactam is given

Your doctor or nurse 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.

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

Adults and adolescents aged 12 years or older

The recommended dose is 4g/0.5 g 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 usual 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.

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 are given 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 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 product, ask your doctor or nurse.

4. Possible side effects

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

If you get any side effects, talk to your doctor or nurse. This includes any side effects not listed in this leaflet.

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 (may affect up to 1 in 10 people)

- diarrhoea, nausea and vomiting

- skin rashes
- Uncommon** (*may affect up to 1 in 100 people*)
- thrush
 - (abnormal) decrease in white blood cells (leucopenia, 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 (*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 (*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 (thrombocythaemia)
- 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 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.

How to store Piperacillin/Tazobactam

Keep this medicine out of the sight and reach of children.

Do not use Piperacillin/Tazobactam after the expiry date which is stated on the vial label and carton after "EXP". The expiry date refers to the last day of that month.

Powder:

Do not store above 25 °C.

Reconstituted/Diluted Product:

For storage conditions for the reconstituted/Diluted product see "The following information is intended for healthcare professionals only:" at the end of the package leaflet.

Do not throw away any medicines via wastewater. 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

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).

There are no other ingredients.

What Piperacillin/Tazobactam looks like and contents of the pack

Piperacillin/Tazobactam is a white to off-white powder for solution for infusion packaged in glass vials, packed in cartons containing 1, 5, 10 or 12 vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Stragen UK Ltd
Castle Court
41 London Road
Surrey
RH2 9RJ

Manufacturer

Mitim S.r.l.
Via Cacciamali 36/38 25125 Brescia
Italy

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The following information is intended for healthcare professionals only:

Piperacillin/Tazobactam Powder for solution for or infusion

This is an extract from the Summary of Product Characteristics to assist in the administration of Piperacillin/Tazobactam. When determining appropriateness of use in a particular patient, the prescriber should be familiar with the SmPC.

Instructions for use

Piperacillin/Tazobactam will be given by intravenous infusion (a drip for 30 minutes).

Incompatibilities with diluents and other medicinal products

- Lactated Ringer's solution is not compatible with Piperacillin/Tazobactam.
- When used concurrently with another antibiotic (e.g. aminoglycosides), Piperacillin/Tazobactam must be administered separately. Mixing with an aminoglycoside in vitro can cause inactivation of the aminoglycoside.
- Piperacillin/Tazobactam should not be mixed with other drugs in a syringe or infusion bottle since compatibility has not been established.
- Piperacillin/Tazobactam should be administered through an infusion set separately from any other drugs unless compatibility is proven.
- Due to chemical instability, Piperacillin/Tazobactam should not be used in solutions that contain sodium bicarbonate.
- Piperacillin/Tazobactam should not be added to blood products or albumin hydrolysates.

Reconstitution directions

The reconstitution and dilution is to be made under aseptic conditions. The solution is to be inspected visually for particulate matter and discolouration prior to administration. The solution should only be used if the solution is clear and free from particles.

Intravenous use

Reconstitute each vial with the volume of solvent shown in the table below, using one of the compatible solvents for reconstitution. To reconstitute, tap lightly the vial to loosen powder from the bottom and sides. Wet all of the internal surface of the vial with solvent whilst shaking continuously. Shake until the powder is dissolved, reconstitution generally occurs within 5 to 10 minutes (for details on handling, please see below).

Content of the vial	Volume of solvent* to be added to 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

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

- Sterile water for injections⁽¹⁾
- 0.9% (9 mg/ml) sodium chloride solution for injection
- Dextrose 5%

For single use only. Discard any unused solution.

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

SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 25° C.

After reconstitution, chemical and physical in-use stability has been demonstrated for 24 hours when stored in a refrigerator at 2-8°C.

After reconstitution and dilution, chemical and physical in-use stability has been demonstrated for 48 hours when stored in a refrigerator at 2-8°C.

From a microbiological point of view, once opened, 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 and would

normally not be longer than 24 hours at 2-8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.