**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 the active substances piperacillin and tazobactam.

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.

This medicine 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.
  This medicine may be used to treat bacterial infections in patients with low white blood cell counts (reduced resistance to infections).

- **children aged 2 to 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.
  This medicine 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

**You should not be given 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 you are given Piperacillin/Tazobactam:
- if you have allergies;
- if you had suffered from diarrhoea before;
- 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 this medicine, 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).

Talk to your doctor or nurse **immediately**:
- if you develop diarrhoea during or after your treatment. Do not take any medicine for diarrhoea without asking your doctor first;
- if any unexpected bleeding occurs during the treatment;
- if you develop convulsions during the treatment;
- if you think you have developed a new or worsening of existing infection.

Haemophagocytic lymphohistiocytosis
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.

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

**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 or pharmacist for advice before receiving this medicine.

Piperacillin and tazobactam can pass to a baby in the womb or through breast milk.

If you are pregnant or breast-feeding, your doctor will decide if this medicine is right for you.

**Driving and using machines**
The use of this medicine is not expected to affect the ability to drive or use machines.

**Piperacillin/Tazobactam contains sodium**
Piperacillin/Tazobactam 2 g/0.25 g
This medicine contains 108 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 5.4% of the recommended maximum daily dietary intake of sodium for an adult.

Piperacillin/Tazobactam 4 g/0.5 g
This medicine contains 216 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 10.8% of the recommended maximum daily dietary intake of sodium for an adult.

## 3. How Piperacillin/Tazobactam will be given

Your doctor or nurse will give you this medicine through an infusion (a drip for 30 minutes) into one of your veins.

**Dosage**
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 above 12 years of age**
The usual dose is 4 g/0.5 g of piperacillin/tazobactam given every 6-8 hours into a vein (directly into the blood stream).

**Children aged 2 to 12 years**
The usual dose for children with abdominal infections is 100 mg/12.5 mg/kg of body weight of piperacillin/tazobactam given every 8 hours into a vein. 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 a vein.

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 this medicine until the signs of infection have gone completely (5 to 14 days).

**Patients with kidney problems**
Your doctor may need to reduce the dose of this medicine 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 this medicine from a doctor or nurse, 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 this medicine, tell your doctor or nurse immediately.

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.

If you notice any of these potentially serious side effects, **contact the doctor or nurse immediately**:
- serious skin rashes (Stevens-Johnson syndrome, bullous dermatitis, exfoliative dermatitis (frequency not known), toxic epidermal necrolysis ( frequency rare) 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 conjunctivitis (red and swollen eyes). The rash may progress to widespread blistering or peeling of the skin and potentially may be life-threatening;
- severe potentially fatal allergic condition (called 'drug reaction with eosinophilia and systemic symptoms' (frequency not known) that can involve the skin and most importantly other organs under the skin such as the kidney and the liver;
- a skin condition (called 'acute generalised exanthematous pustulosis' (frequency not known) accompanied by fever, which consists of numerous tiny fluid-filled blisters contained within large areas of swollen and reddened skin;
- swelling of the face, lips, tongue or other parts of the body (frequency not known);
- shortness of breath, wheezing or trouble breathing (frequency not known);
- severe rash or hives (frequency uncommon);
- yellowing of the eyes or skin (frequency not known);
- damage to blood cells (the signs include: being breathless when you do not expect it, red or brown urine, small spot bruising (frequency not known), severe decrease in white blood cells (frequency rare);
- severe or persistent diarrhoea accompanied by a fever or weakness (frequency rare).

If any of **the following** side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or other healthcare professional.

**Other side effects**
*Very common* (may affect more than 1 in 10 patients)
- diarrhoea

*Common* (may affect up to 1 in 10 patients)
- yeast infection
- decrease in platelets, decrease of red blood cells or blood pigment (haemoglobin)
- sleeplessness
- headache
- abdominal pain, vomiting, constipation, nausea, upset stomach
- rash, itching
- fever, injection site reaction
- changes in blood tests ( decrease in blood protein, increase in blood liver enzymes, abnormal kidney blood tests), abnormal laboratory tests (positive direct Coombs test), prolonged blood clotting time (activated partial thromboplastin time prolonged)

*Uncommon* (may affect up to 1 in 100 patients)
- decrease in white blood cells (leukopenia)
- decreased blood potassium
- 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), reddening of skin (flushing)
- skin reactions with redness, skin lesions, nettle rash
- joint and muscle pain
- chills
- decreased blood sugar, increase of a blood pigment breakdown product (bilirubin), prolonged blood clotting time (prothrombin time prolonged)

*Rare* (may affect up to 1 in 1 000 patients)
- bleeding of the nose
- inflammation of the mucous lining of the mouth

*Not known* (the frequency cannot be estimated from the available data)
- severe decrease of red blood cells, white blood cells and platelets (pancytopenia), decrease in white blood cells (neutropenia), decrease of red blood cells due to premature breakdown or degradation, increase of platelets, increase of a specific type of white blood cells (eosinophilia)
- allergic reactions
- acute disorientation and confusion (delirium)
- a form of lung disease where eosinophils (a form of white blood cell) appear in the lung in increased numbers
- inflammation of the liver, yellow staining of the skin or whites of the eyes
- small spot bruising (purpura)
- poor kidney functions and kidney problems
- changes in blood tests (e.g. bleeding time prolonged, gamma-glutamyl transferase increased)

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 signs of altered brain function (encephalopathy) and convulsions (fits).

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

Do not store above 30 °C.
Keep the vial in the outer carton in order to protect from light.

Shelf life after reconstitution in vial

Chemical and physical in-use stability has been demonstrated for 12 hours at 25 °C and 48 hours at 2 to 8 °C, when reconstituted with one of the compatible solvents for reconstitution.

Shelf life after the dilution of reconstituted solution
Chemical and physical in-use stability of the diluted reconstituted solution has been demonstrated for 12 hours at 25 °C and 48 hours at 2 to 8 °C, when diluted with Ringer's acetate solution, 9 mg/ml (0.9%) sodium chloride, 50 mg/ml (5%) glucose, 50 mg/ml (5%) glucose in 9 mg/ml (0.9%) sodium chloride solution at the suggested dilution volume for further dilution.

For compatible solutions and volume of solutions used for reconstitution and dilution see "The following information is intended for healthcare professionals only" below.

From a microbiological point of view, the diluted 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 12 hours at 2 to 8 °C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

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.

Piperacillin/Tazobactam 2 g/0.25 g
Each vial contains piperacillin sodium equivalent to 2 g piperacillin and tazobactam sodium equivalent to 0.25 g tazobactam.

Piperacillin/Tazobactam 4 g/0.5 g
Each vial contains piperacillin sodium equivalent to 4 g piperacillin and tazobactam sodium equivalent to 0.5 g tazobactam.

There are no other ingredients.

**What Piperacillin/Tazobactam looks like and contents of the pack**
Piperacillin/Tazobactam is white to off-white powder for solution for infusion in glass vials with blue (2 g/0.25 g) or orange (4 g/0.5 g) plastic caps. The vials are placed into outer cartons.

Pack sizes: 1 or 10 vials.

Not all pack sizes may be marketed.

**Marketing Authorisation Holder and Manufacturer**
AS KALCEKS
Krustpils iela 71E, Riga, LV-1057, Latvia
Tel.: +371 67083320
E-mail: kalceks@kalceks.lv

**This medicine is authorised in the Member States of the European Economic Area under the following names:**

| | |
|---|---|
| Denmark | Piperacillin/Tazobactam Kalceks |
| Austria, Germany | Piperacillin/Tazobactam Kalceks 2 g/0,25 g Pulver zur Herstellung einer Infusionslösung |

| | |
|---|---|
| | Piperacillin/Tazobactam Kalceks 4 g/0,5 g Pulver zur Herstellung einer Infusionslösung |
| Czech Republic, Norway, Sweden | Piperacillin/Tazobactam Kalceks |
| Belgium | Piperacilline/Tazobactam Kalceks 2 g/0,25 g, 4 g/0,5 g poeder voor oplossing voor infusie<br>Piperacilline/Tazobactam Kalceks 2 g/0,25 g, 4 g/0,5 g poudre pour solution pour perfusion<br>Piperacilline/Tazobactam Kalceks 2 g/0,25 g, 4 g/0,5 g Pulver zur Herstellung einer Infusionslösung |
| Croatia | Piperacilin/tazobaktam Kalceks 2 g/0,25 g, 4 g/0,5 g prašak za otopinu za infuziju |
| Finland | Piperacillin/Tazobactam Kalceks 2 g/0,25 g, 4 g/0,5 g infuusiokuiva-aine, liuosta varten |
| France | PIPERACILLINE/TAZOBACTAM KALCEKS 2 g/0,25 g poudre pour solution pour perfusion<br>PIPERACILLINE/TAZOBACTAM KALCEKS 4 g/0,5 g poudre pour solution pour perfusion |
| Hungary | Piperacillin/Tazobactam Kalceks 2 g/0,25 g, 4 g/0,5 g por oldatos infúzióhoz |
| Ireland | Piperacillin/Tazobactam 2 g/0.25 g, 4 g/0.5 g powder for solution for infusion |
| Italy | Piperacillina/Tazobactam Kalceks |
| Latvia | Piperacillin/Tazobactam Kalceks 2 g/0,25 g, 4 g/0,5 g pulveris infūziju šķīduma pagatavošanai |
| Lithuania | Piperacillin/Tazobactam Kalceks 2000 mg/250 mg, 4000 mg/500 mg milteliai infuziniam tirpalui |
| The Netherlands | Piperacilline/Tazobactam Kalceks 2 g/0,25 g, 4 g/0,5 g poeder voor oplossing voor infusie |
| Poland | Piperacillin + Tazobactam Kalceks |
| Slovenia | Piperacilin/tazobaktam Kalceks 2 g/0,25 g, 4 g/0,5 g prašek za raztopino za infundiranje |
| Spain | Piperacilina/Tazobactam Kalceks 2 g/0,25 g, 4 g/0,5 g polvo para solución para perfusión EFG |

**This leaflet was last revised in 12/2022**

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The following information is intended for healthcare professionals only:

Please refer to the Summary of Product Characteristics for full prescribing information.

**Incompatibilities**
This medicinal product must not be mixed with other medicinal products except those mentioned below.

Whenever piperacillin/tazobactam is used concomitantly with another antibiotic (e.g. aminoglycosides), the substances must be administered separately. The mixing of beta-lactam antibiotics with an aminoglycoside *in vitro* can result in substantial inactivation of the aminoglycoside.

Due to chemical instability, piperacillin/tazobactam should not be used in solutions containing only 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.

**Instructions for use and other handling**
For single use only.

The reconstitution and dilution should be performed under aseptic conditions. Discard any unused solution.

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 2 minutes (for details on handling, see below). The reconstituted solution is colourless to yellowish.

| **Content of 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:
– 9 mg/ml (0.9%) sodium chloride solution
– 50 mg/ml (5%) glucose solution
– 50 mg/ml (5%) glucose in 9 mg/ml (0.9%) sodium chloride solution
– water for injections(1)

(1) Maximum recommended volume of sterile water for injections 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 diluted to the desired volume (e.g. 50 ml to 150 ml) with one of the following compatible solutions:
– 9 mg/ml (0.9%) sodium chloride solution
– 50 mg/ml (5%) glucose solution
– 50 mg/ml (5%) glucose in 9 mg/ml (0.9%) sodium chloride solution
– Ringer's acetate solution

The solution should be visually inspected prior to use. Only clear solutions free from particles should be used.

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