# PT PFIZER INDONESIA
# LOCAL PRODUCT DOCUMENT

Generic Name: Sterile Piperacillin/Tazobactam Sodium
Trade Name: TAZOCIN®
CDS Effective Date: April 02, 2024
Supersedes: September 13, 2021

## PRESENTATION

TAZOCIN, piperacillin/tazobactam parenteral combination, is a white to off-white sterile, cryodesiccated powder consisting of piperacillin and tazobactam as their sodium salts packaged in glass vials. The product does not contain excipients or preservatives.

Each TAZOCIN 4.5 g single-dose vial contains an amount of drug sufficient for withdrawal of piperacillin sodium equivalent to 4 g of piperacillin and tazobactam sodium equivalent to 0.5 g of tazobactam. The product also contains 1 mg edetate disodium (dihydrate) (EDTA) per vial.

## INDICATIONS AND USAGE

TAZOCIN is indicated for the treatment of patients with moderate to severe infections caused by piperacillin resistant, piperacillin/tazobactam susceptible, *β*-lactamase producing strains of the designated microorganisms in the specified conditions listed below:

Appendicitis (complicated by rupture or abscess) and peritonitis caused by piperacillin resistant, *β*-lactamase producing strains of *Escherichia coli* or the following members of the *Bacteroides fragilis* group: *B. fragilis, B. ovatus, B. thetaiotaomicron* or *B. vulgatus*. The individual members of this group were studied in less than 10 cases.

Uncomplicated and complicated skin and skin structure infections, including cellulitis, cutaneous abscesses, and ischemic/diabetic foot infections caused by piperacillin resistant, *β*-lactamase producing strains of *Staphylococcus aureus*.

Postpartum endometritis or pelvic inflammatory disease caused by piperacillin resistant, *β*-lactamase producing strains of *Escherichia coli*.

Community-acquired pneumonia (moderate severity only) caused by piperacillin resistant, *β*-lactamase producing strains of *Haemophilus influenzae*.

As a combination product, TAZOCIN is indicated only for the specified conditions listed above. Infections caused by piperacillin susceptible organisms, for which piperacillin has been shown to be effective are also amenable to TAZOCIN treatment due to its piperacillin content. The tazobactam component of this combination product does not decrease the activity of the piperacillin component against piperacillin susceptible organisms. Therefore, the treatment of mixed infections caused by piperacillin susceptible organisms and piperacillin resistant, *β*-lactamase producing organisms susceptible to TAZOCIN should not require the addition of another antibiotic.

TAZOCIN is useful as presumptive therapy in the indicated conditions prior to the identification of causative organisms because of its broad spectrum of bactericidal activity against gram-positive and gram-negative aerobic and anaerobic organisms. Appropriate cultures should usually be performed before initiating antimicrobial treatment in order to isolate and identify the organisms causing infection and to determine their susceptibility to TAZOCIN. Antimicrobial therapy should be adjusted, if appropriate, once the results of culture(s) and antimicrobial susceptibility testing are known.

**Adults and children:**
Febrile neutropenic infections. Combination treatment with an aminoglycoside is recommended.

## DOSAGE AND ADMINISTRATION

TAZOCIN must be given by slow intravenous infusion (e.g. over 20-30 minutes) or slow intravenous injection (over at least 3-5 minutes).

### Duration of Therapy

The usual duration of TAZOCIN treatment is from seven to ten days.
The duration of therapy should be guided by the severity of the infection and the patient's clinical and bacteriological progress.

### Adults and Children Aged 12 Years and Older

In general, the recommended total daily dosage is 12 g of piperacillin/1.5 g of tazobactam given in divided doses every 6 or 8 hours. Doses as high as 18 g of piperacillin/2.25 g of tazobactam per day in divided doses can be used in severe infections.

In neutropenia, the recommended dose is 4.5 g TAZOCIN (4 g piperacillin/500 mg tazobactam) given every 6 hours in combination with aminoglycoside.

### Pediatric Neutropenia

Febrile neutropenic patients in combination with an aminoglycoside:

For children aged 2-12 years with normal renal function and weighing less than 50 kg, the dose should be adjusted to 80 mg of piperacillin/10 mg of tazobactam per kilogram of body weight every 6 hours, in combination with the appropriate dose of an aminoglycoside.

For children weighing over 50 kg, follow the adult dosing, in combination with the appropriate dose of an aminoglycoside.

### Use in Patients with Renal Impairment

In patients with renal impairment or in hemodialysis patients, intravenous dosages and administration intervals should be adjusted to the degree of renal function impairment as follows.

The recommended daily doses are as follows:

| Creatinine Clearance (mL/min) | Piperacillin/Tazobactam (recommended dose) |
|---|---|
| > 40 | No dose adjustment necessary |
| 20-40 | Maximum dose suggested: 4 g/0.5 g every 8 hours |
| < 20 | Maximum dose suggested: 4 g/0.5 g every 12 hours |

For patients on hemodialysis, the maximum dose is 2.25 g TAZOCIN eight hours. For patients on hemodialysis, one additional dose of piperacillin/tazobactam 2 g/0.25 g should be administered following each dialysis period, because hemodialysis removes 30%-50% of piperacillin in 4 hours.

**Use in Patients with Hepatic Impairment**

No dosage adjustment is necessary in patients with hepatic impairment.

**Co-administration of Piperacillin/Tazobactam with Aminoglycosides**

Due to the *in vitro* inactivation of the aminoglycoside by β-lactam antibiotics, TAZOCIN and the aminoglycoside are recommended for separate administration. TAZOCIN and the aminoglycoside should be reconstituted and diluted separately when concomitant therapy with aminoglycosides is indicated (see Section **COMPATIBILITIES**, **INCOMPATIBILITIES**).

In circumstances where co-administration is preferred, the reformulated TAZOCIN containing EDTA supplied in vials is compatible for simultaneous co-administration via Y-site infusion only with the following aminoglycosides under the following conditions:

| Aminoglycoside | TAZOCIN (g) dose | TAZOCIN Diluent Volume (mL) | Aminoglycoside Concentration Range (mg/mL)‡ | Acceptable Diluents |
|---|---|---|---|---|
| Amikacin | 2.25<br>3.375<br>4.5 | 50<br>100<br>150 | 1.75-7.5 | 0.9% sodium chloride or 5% dextrose |
| Gentamicin | 2.25<br>3.375<br>4.5 | 100<br>150 | 0.7-3.32 | 0.9% sodium chloride or 5% dextrose |

‡ The dose of aminoglycoside should be based on patient weight, status of infection (serious or life threatening) and renal function (creatinine clearance).

Compatibility of TAZOCIN with other aminoglycosides has not been established. Only the concentration and diluents for amikacin and gentamicin with the dosages of TAZOCIN listed in the table above have been established as compatible for co-administration via Y-site infusion. Simultaneous co-administration via Y-site infusion in any manner other than listed above may result in inactivation of the aminoglycoside by TAZOCIN.

**CONTRAINDICATIONS**

Hypersensitivity to any of the β-lactams (including penicillins and cephalosporins) or to β-lactamase inhibitors.

## SPECIAL WARNINGS

Before initiating therapy with TAZOCIN, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, and other allergens. Serious and occasionally fatal hypersensitivity (anaphylactic/anaphylactoid [including shock]) reactions have been reported in patients receiving therapy with penicillins including TAZOCIN.

These reactions are more likely to occur in persons with a history of sensitivity to multiple allergens. Serious hypersensitivity reactions require discontinuation of the antibiotic, and may require administration of epinephrine and other emergency measures.

Piperacillin/tazobactam may cause severe cutaneous adverse reactions, such as Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (see Section **ADVERSE REACTIONS**). If patients develop a skin rash they should be monitored closely and Piperacillin/tazobactam discontinued if lesions progress.

Rare cases of haemophagocytic lymphohistiocytosis (HLH) have been observed following therapy (>10 days) with piperacillin/tazobactam, often as a complication of DRESS. HLH is a pathologic immune activation which leads to excessive systemic inflammation and can be life-threatening and early diagnosis and rapid initiation of immunosuppressive therapy is essential. Characteristic signs and symptoms include fever, hepatosplenomegaly, cytopenias, hyperferritinaemia, hypertriglyceridaemia, hypofibrinogenaemia, and haemophagocytosis. If piperacillin tazobactam is suspected as possible trigger, treatment should be discontinued.

Rhabdomyolysis has been reported with the use of piperacillin/tazobactam. If signs or symptoms of rhabdomyolysis are observed, piperacillin/tazobactam should be discontinued and appropriate therapy initiated.

Antibiotic-induced pseudomembranous colitis may manifest as severe persistent diarrhea which may be life-threatening. The onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment.

## PRECAUTIONS

Bleeding manifestations have occurred in some patients receiving β-lactam antibiotics. These reactions sometimes have been associated with abnormalities of coagulation tests such as clotting time, platelet aggregation and prothrombin time, and are more likely to occur in patients with renal failure (see Section **INTERACTIONS**). If bleeding manifestations occur, the antibiotic should be discontinued and appropriate therapy instituted.

This product contains 2.84 mEq (65 mg) of sodium per gram of piperacillin which may increase a patient's overall sodium intake. Hypokalemia may occur in patients with low potassium reserves or in those who are receiving concomitant medications that may lower potassium levels; periodic electrolyte determinations may be advisable in such patients.

Leukopenia and neutropenia may occur, especially during prolonged therapy. Therefore, periodic assessment of hematopoietic function should be performed.

As with treatment with other penicillins, neurological complications in the form of convulsions

(seizures) may occur when high doses are administered, especially in patients with impaired renal function (see Section **ADVERSE REACTIONS**).

**Use in Patients with Hepatic Impairment**

No dosage adjustment of piperacillin/tazobactam is necessary in patients with hepatic impairment.

**Renal Impairment**

Due to its potential nephrotoxicity (see Section **ADVERSE REACTIONS**), piperacillin/tazobactam should be used with care in patients with renal impairment or in hemodialysis patients. Intravenous dosages and administration intervals should be adjusted to the degree of renal function impairment (see Section **DOSAGE AND ADMINISTRATION**).

In a secondary analysis using data from a large multicenter, randomized-controlled trial when glomerular filtration rate (GFR) was examined after administration of frequently used antibiotics in critically ill patients, the use of piperacillin/tazobactam was associated with a lower rate of reversible GFR improvement compared with the other antibiotics. This secondary analysis concluded that piperacillin/tazobactam was a cause of delayed renal recovery in these patients.

Combined use of piperacillin/tazobactam and vancomycin may be associated with an increased incidence of acute kidney injury (see Section **INTERACTIONS**).

**PREGNANCY**

Studies in mice and rats have not demonstrated any reproductive or embryo-fetal effects with piperacillin-tazobactam combination when administered intravenously. There are no adequate and well-controlled studies with the piperacillin-tazobactam combination or with piperacillin or tazobactam alone in pregnant women. Piperacillin and tazobactam cross the placenta. Pregnant women should be treated only if the expected benefit outweighs the possible risks to the pregnant woman and the fetus.

**LACTATION**

Piperacillin is excreted in low concentrations in human milk; tazobactam concentrations in human milk have not been studied. Women who are breast-feeding should be treated only if the expected benefit outweighs the possible risks to the woman and child.

**GERIATRIC USE**

Patients over 65 years are not at an increased risk of developing adverse effects solely because of age. However, dosage should be adjusted in the presence of renal insufficiency.

**INTERACTIONS**

**Non-Depolarizing Muscle Relaxants**

Piperacillin when used concomitantly with vecuronium has been implicated in prolonging of the neuromuscular blockade of vecuronium. Due to their similar mechanism of action, it is expected that the neuromuscular blockade produced by any of the non-depolarizing muscle relaxants could be

prolonged in the presence of piperacillin.

**Anticoagulants**

During simultaneous administration of heparin, oral anticoagulants and other drugs that may affect the blood coagulation system including thrombocyte function, appropriate coagulation tests should be performed more frequently and monitored regularly (see Section **PRECAUTIONS**).

**Methotrexate**

Piperacillin may reduce the excretion of methotrexate; therefore, serum levels of methotrexate should be monitored in patients to avoid drug toxicity.

**Probenecid**

As with other penicillins, concurrent administration of probenecid and TAZOCIN produces a longer half-life and lower renal clearance for both piperacillin and tazobactam; however, peak plasma concentrations of either drug are unaffected.

**Aminoglycosides**

Piperacillin, either alone or with tazobactam, did not significantly alter the pharmacokinetics of tobramycin in subjects with mild or moderate renal impairment. The pharmacokinetics of piperacillin, tazobactam, and the M1 metabolite were also not significantly altered by tobramycin administration.

TAZOCIN is not compatible with tobramycin for simultaneous co-administration via Y-site infusion.

**Vancomycin**

Studies have detected an increased incidence of acute kidney injury in patients concomitantly administered piperacillin/tazobactam and vancomycin as compared to vancomycin alone (see Section **PRECAUTIONS**). Some of these studies have reported that the interaction is vancomycin dose-dependent. Expert guidelines recommend intensive vancomycin dosing and maintenance of trough levels between 15 mg/L and 20 mg/L which is an increase from previously published recommendations of target trough concentrations of 5-10 mg/L. Attaining these trough concentrations often requires practitioners to prescribe vancomycin doses which exceed manufacturers' recommendations. Therefore, it is possible that in addition to the increased risk of vancomycin-induced nephrotoxicity reported with adherence to these guidelines the risk of nephrotoxicity may also increase due to an interaction with piperacillin/tazobactam.

No pharmacokinetic interactions have been noted between PIPERACILLIN/TAZOBACTAM and vancomycin.

**INTERFERENCE WITH LABORATORY AND OTHER DIAGNOSTIC TESTS**

As with other penicillins, the administration of TAZOCIN may result in a false-positive reaction for glucose in urine using a copper-reduction method. It is thus recommended that glucose tests based on enzymatic glucose oxidase reactions be used.

There have been reports of positive test results using the Bio-Rad Laboratories Platelia Aspergillus enzyme immunoassay (EIA) test in patients receiving TAZOCIN injection who were subsequently found to be free of Aspergillus infection. Cross-reactions with non-Aspergillus polysaccharides and polyfuranoses with Bio-Rad Laboratories Platelia Aspergillus EIA test have been reported.

Therefore, positive test results in patients receiving TAZOCIN should be interpreted cautiously and confirmed by other diagnostic methods.

## ADVERSE REACTIONS

**Adverse Drug Reactions (ADRs) by System Organ Class and Council for International Organizations of Medical Science (CIOMS) Frequency Category Listed in Order of Decreasing Medical Seriousness or Clinical Importance Within Each Frequency Category and SOC**

| System Organ Class | Very Common ≥1/10 | Common ≥1/100 to <1/10 | Uncommon ≥1/1,000 to <1/100 | Rare ≥1/10,000 to <1/1,000 | Frequency Not Known (cannot be estimated from available data) |
|---|---|---|---|---|---|
| Infections and infestations | | candida infection* | | pseudomembranous colitis | |
| Blood and lymphatic system disorders | | thrombocytopenia, anaemia* | leukopenia | agranulocytosis | pancytopenia*, neutropenia, haemolytic anaemia*, thrombocytosis*, eosinophilia* |
| Immune system disorders | | | | | anaphylactoid shock*, anaphylactic shock*, anaphylactoid reaction*, anaphylactic reaction*, hypersensitivity* kounis syndrome |
| Metabolism and nutrition disorders | | | hypokalaemia | | |
| Psychiatric disorders | | insomnia | | | delirium* |
| Nervous system disorders | | headache | seizure* | | |
| Vascular disorders | | | hypotension, phlebitis, thrombophlebitis, flushing | | |
| Respiratory, thoracic and mediastinal disorders | | | | epistaxis | eosinophilic pneumonia* |
| Gastrointestinal disorders | diarrhoea | abdominal pain, vomiting, constipation, nausea, dyspepsia | | stomatitis | |
| Hepatobiliary disorders | | | | | hepatitis*, jaundice |

| System Organ Class | Very Common ≥1/10 | Common ≥1/100 to <1/10 | Uncommon ≥1/1,000 to <1/100 | Rare ≥1/10,000 to <1/1,000 | Frequency Not Known (cannot be estimated from available data) |
|---|---|---|---|---|---|
| Skin and subcutaneous tissue disorders | | rash, pruritus | erythema multiforme*, urticaria, rash maculo-papular* | toxic epidermal necrolysis* | Stevens-Johnson syndrome*, drug reaction with eosinophilia and systemic symptoms (DRESS)*, acute generalised exanthematous pustulosis (AGEP)*, dermatitis exfoliative*, dermatitis bullous, linear IgA disease*, purpura |
| Musculoskeletal and connective tissue disorders | | | arthralgia, myalgia | | rhabdomyolysis* |
| Renal and urinary disorders | | | | | renal failure, tubulointerstitial nephritis* |
| General disorders and administration site conditions | | pyrexia, injection site reaction | chills | | |
| Investigations | | alanine aminotransferase increased, aspartate aminotransferase increased, protein total decreased, blood albumin decreased, Coombs direct test positive, blood creatinine increased, blood alkaline phosphatase increased, blood urea increased, activated partial thromboplastin time prolonged | blood glucose decreased, blood bilirubin increased, prothrombin time prolonged | | bleeding time prolonged, gamma-glutamyltransferase increased |

* Adverse Drug Reaction (ADR) identified post-marketing.

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

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

Pusat Farmakovigilans/MESO Nasional
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan
Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079
Website: https://e-meso.pom.go.id/ADR

PT Pfizer Indonesia
Email: IDN.AEReporting@pfizer.com
Website: www.pfizersafetyreporting.com

## OVERDOSAGE

### Symptoms

There have been post-marketing reports of overdose with TAZOCIN. The majority of the adverse events experienced including nausea, vomiting, and diarrhea have also been reported with the usual recommended dosages. Patients may experience neuromuscular excitability or convulsions if higher than recommended doses are given intravenously (particularly in the presence of renal failure).

### Treatment

Treatment should be supportive and symptomatic according to the patient's clinical presentation.

Excessive serum concentrations of either piperacillin or tazobactam may be reduced by hemodialysis.

## PHARMACODYNAMIC PROPERTIES

### Pharmacotherapeutic Group

Antibacterials for systemic use, combinations of penicillins including β-lactamase inhibitors; ATC code: J01C R05.

### Mechanism of Action

TAZOCIN (sterile piperacillin sodium/tazobactam sodium) is an injectable antibacterial combination consisting of the semisynthetic antibiotic piperacillin sodium and the β-lactamase inhibitor tazobactam sodium for intravenous administration. Thus, piperacillin/tazobactam combines the properties of a broad-spectrum antibiotic and a β-lactamase inhibitor.

Piperacillin sodium exerts bactericidal activity by inhibiting septum formation and cell wall synthesis. Piperacillin and other β-lactam antibiotics block the terminal transpeptidation step of cell wall peptidoglycan biosynthesis in susceptible bacteria by interacting with penicillin-binding proteins (PBPs), the bacterial enzymes that carry out this reaction. *In vitro*, piperacillin is active against a variety of gram-positive and gram-negative aerobic and anaerobic bacteria.

Piperacillin has reduced activity against bacteria harboring certain β-lactamase enzymes, which chemically inactivate piperacillin and other β-lactam antibiotics. Tazobactam sodium, which has very little intrinsic antimicrobial activity, due to its low affinity for PBPs, can restore or enhance the activity of piperacillin against many of these resistant organisms. Tazobactam is a potent inhibitor of many class A β-lactamases (penicillinases, cephalosporinases and extended spectrum enzymes). It has variable activity against class A carbapenemases and class D β-lactamases. It is not active against most class C cephalosporinases and inactive against Class B metallo-β-lactamases.

Two features of piperacillin/tazobactam lead to increased activity against some organisms harboring β-lactamases that, when tested as enzyme preparations, are less inhibited by tazobactam and other inhibitors: tazobactam does not induce chromosomally mediated β-lactamases at tazobactam levels achieved with the recommended dosing regimen and piperacillin is relatively refractory to the action of some β-lactamases.

Like other β-lactam antibiotics, piperacillin, with or without tazobactam, demonstrates time-dependent bactericidal activity against susceptible organisms.

**Mechanism of Resistance**

There are three major mechanisms of resistance to β-lactam antibiotics: changes in the target PBPs resulting in reduced affinity for the antibiotics, destruction of the antibiotics by bacterial β-lactamases, and low intracellular antibiotic levels due to reduced uptake or active efflux of the antibiotics.

In gram-positive bacteria, changes in PBPs are a major mechanism of resistance to β-lactam antibiotics, including piperacillin/tazobactam. This mechanism is responsible for methicillin resistance in staphylococci and penicillin resistance in *Streptococcus pneumoniae* as well as viridans group streptococci and enterococci. Resistance caused by changes in PBPs also occurs to a lesser extent in fastidious gram-negative species, such as *Haemophilus influenzae* and *Neisseria gonorrhoeae*. Piperacillin/tazobactam is not active against strains in which resistance to β-lactam antibiotics is determined by altered PBPs. As indicated above, there are some β-lactamases that are not inhibited by tazobactam.

**Methodology for Determining the In Vitro Susceptibility of Bacteria to Piperacillin/Tazobactam:**

Susceptibility testing should be conducted using standardized laboratory methods such as those described by the Clinical and Laboratory Standards Institute (CLSI). These include dilution methods (minimal inhibitory concentration [MIC] determination) and disk susceptibility methods. Both CLSI and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) provide susceptibility interpretive criteria for some bacterial species based on these methods. It should be noted that for the disk diffusion method, CLSI and EUCAST use disks with different drug contents of piperacillin and tazobactam.

The CLSI interpretive criteria for susceptibility testing of piperacillin/tazobactam are listed in the following table:

**CLSI Susceptibility Interpretive Criteria for Piperacillin/Tazobactam**

| Pathogen | Minimal Inhibitory Concentration (mg/L of Piperacillin)[a] | | | | Disk[b] Diffusion Inhibition Zone (mm Diameter) | | | |
|---|---|---|---|---|---|---|---|---|
| | S | SDD | I | R | S | SDD | I | R |
| *Enterobacterales*[c] | ≤8 | 16 | | ≥32 | ≥25 | 21-24 | | ≤20 |
| *Pseudomonas aeruginosa*[d] | ≤16 | | 32-64 | ≥128 | ≥21 | | 15-20 | ≤14 |
| *Acinetobacter spp.* | ≤16 | | 32-64 | ≥128 | ≥21 | | 18-20 | ≤17 |
| Certain other non-Enterobacterales[e] | ≤16 | | 32-64 | ≥128 | | | | |
| *Haemophilus influenzae and Haemophilus parainfluenzae* | ≤1 | | - | ≥2 | ≥21 | | - | - |
| Anaerobes[f] | ≤16 | | 32-64 | ≥128 | - | | - | - |

Source: Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing;* . CLSI document M100:ED32 2022. This document is updated annually and may be accessed at http://clsi-m100.com/.
S = Susceptible. SDD = Susceptible dose-dependent. I = Intermediate. R = Resistant.
[a] MICs are determined using a fixed concentration of 4 mg/L tazobactam and by varying the concentration of piperacillin.
[b] CLSI inhibition zones are based on disks containing 100 µg of piperacillin and 10 µg of tazobactam.
[c] Breakpoints for susceptible are based on a dosage regimen of 3.375- 4.5 g administered every 6 h as a 30- min infusion. Breakpoints for SDD are based on a dosage regimen of 4.5 g administered every 6 h as a 3 h infusion or 4.5 g administered every 8 h as a 4 h infusion.
[d] Breakpoints are based on a dosage regimen of at least 3 g piperacillin administered every 6 h.
[e] Refer to CLSI Document M100 Table 2B-5 for the list of organisms included.
[f] With the exception of *Bacteroides fragilis*, MICs are determined by agar dilution only.
Susceptibility of *Staphylococcus aureus* to piperacillin/tazobactam is determined by the susceptibility to oxacillin (CLSI document M100 Table 2C. *Staphylococcus* spp.).

Standardized susceptibility test procedures require the use of quality control microorganisms to control the technical aspects of the test procedures. Quality control microorganisms are specific strains with intrinsic biological properties relating to resistance mechanisms and their genetic expression within the microorganism; the specific strains used for susceptibility test quality control are not clinically significant.

Organisms and quality control ranges for piperacillin/tazobactam to be utilized with CLSI methodology and susceptibility test interpretive criteria are listed in the following table:

Quality Control Ranges for Piperacillin/Tazobactam to be Used In Conjunction With CLSI Susceptibility Test Interpretive Criteria

| Quality Control Strain | Minimal Inhibitory Concentration (mg/L of piperacillin) | Disk Diffusion Inhibition Zone (mm Diameter) |
|---|---|---|
| *Escherichia coli* ATCC 25922 | 1-4 | 24-30 |
| *Pseudomonas aeruginosa* ATCC 27853 | 1-8 | 25-33 |
| *Staphylococcus aureus* ATCC 29213 | 0.25-2 | - |
| *Staphylococcus aureus* ATCC 25923 | - | 27-36 |
| *Enterococcus faecalis* ATCC 29212 | 1-4 | |
| *Escherichia coli* ATCC 35218 | 0.5-2 | 24-30 |
| *Klebsiella pneumoniae* ATCC 700603 | 8-32 | |
| *Haemophilus influenzae* ATCC 49247 | 0.06-0.5 | 33-38 |
| *Bacteroides fragilis* ATCC 25285 | 0.125-0.5[a] | - |
| *Bacteroides thetaiotaomicron* ATCC 29741 | 4-16[a] | - |
| *Clostridiodes (formerly Clostridium) difficile* ATCC 700057 | 4-16[a] | |
| *Eggerthella lenta (formerly Eubacterium lentum)* ATCC 43055 | 4-16[a] | |

Source: Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing.* CLSI document M100ED32. 2022.
[a] These ranges are for agar dilution only.

**Antibacterial Spectrum**

Piperacillin/tazobactam has been shown to be active against most strains of the following microorganisms, both *in vitro* and in the indicated clinical infections.

Aerobic and facultative gram-positive microorganisms:
*Staphylococcus aureus* (methicillin-susceptible strains only)

Aerobic and facultative gram-negative microorganisms:
*Acinetobacter baumannii*
*Escherichia coli*
*Haemophilus influenzae* (excluding β-lactamase negative, ampicillin-resistant isolates)
*Klebsiella pneumoniae*

*Pseudomonas aeruginosa* (given in combination with an aminoglycoside to which the isolate is susceptible)

Gram-negative anaerobes:
*Bacteroides fragilis* group (*B. fragilis, B. ovatus, B. thetaiotaomicron,* and *B. vulgatus*).

The following *in vitro* data are available, but their clinical significance is unknown.

At least 90% of the following microorganisms exhibit an *in vitro* MIC less than or equal to the susceptible breakpoint for piperacillin/tazobactam. However, the safety and effectiveness of piperacillin/tazobactam in treating clinical infections due to these bacteria have not been established in adequate and well-controlled clinical trials.

Aerobic and facultative gram-positive microorganisms:
*Enterococcus faecalis* (ampicillin- or penicillin-susceptible isolates only)
*Staphylococcus epidermidis* (methicillin-susceptible isolates only)
*Streptococcus agalactiae*†
*Streptococcus pneumoniae*† (penicillin-susceptible isolates only)
*Streptococcus pyogenes*†
Viridans group streptococci†

Aerobic and facultative gram-negative microorganisms:
*Citrobacter koseri*
*Moraxella catarrhalis*
*Morganella morganii*
*Neisseria gonorrhoeae*
*Proteus mirabilis*
*Proteus vulgaris*
*Serratia marcescens*
*Providencia stuartii*
*Providencia rettgeri*
*Salmonella enterica*

**†These are not β-lactamase producing bacteria and, therefore, are susceptible to piperacillin alone**.

**Pharmacokinetic Properties**

**Distribution**

Both piperacillin and tazobactam are approximately 30% bound to plasma proteins.
The protein binding of either piperacillin or tazobactam is unaffected by the presence of the other compound. Protein binding of the tazobactam metabolite is negligible.

Piperacillin/tazobactam is widely distributed in tissues and body fluids including intestinal mucosa, gallbladder, lung, bile, and bone. Mean tissue concentrations are generally 50% to 100% of those in plasma.

**Metabolism**

Piperacillin is metabolized to a minor microbiologically active desethyl metabolite. Tazobactam is metabolized to a single metabolite that has been found to be microbiologically inactive.

**Elimination**

Piperacillin and tazobactam are eliminated via the kidney by glomerular filtration and tubular secretion.

Piperacillin is excreted rapidly as unchanged drug with 68% of the administered dose appearing in the urine. Tazobactam and its metabolite are eliminated primarily by renal excretion with 80% of the administered dose appearing as unchanged drug and the remainder as the single metabolite. Piperacillin, tazobactam, and desethyl piperacillin are also secreted into the bile.

Following administration of single or multiple doses of piperacillin/tazobactam to healthy subjects, the plasma half-life of piperacillin and tazobactam ranged from 0.7 to 1.2 hours and was unaffected by dose or duration of infusion. The elimination half-lives of both piperacillin and tazobactam are increased with decreasing renal clearance.

There are no significant changes in the pharmacokinetics of piperacillin due to tazobactam. Piperacillin appears to reduce the rate of elimination of tazobactam.

**Special Populations**

The half-lives of piperacillin and of tazobactam increase by approximately 25% and 18%, respectively, in patients with hepatic cirrhosis compared to healthy subjects.

The half-lives of piperacillin and tazobactam increase with decreasing creatinine clearance. The increase in half-life is two-fold and four-fold for piperacillin and tazobactam, respectively, at creatinine clearance below 20 mL/min compared to patients with normal renal function.

Hemodialysis removes 30% to 50% of piperacillin/tazobactam with an additional 5% of the tazobactam dose removed as the tazobactam metabolite. Peritoneal dialysis removes approximately 6% and 21% of the piperacillin and tazobactam doses, respectively, with up to 18% of the tazobactam dose removed as the tazobactam metabolite.

**Preclinical Safety Data**

**Reproductive Toxicity**

In embryo-fetal development studies, there was no evidence of teratogenicity following intravenous administration of tazobactam or the piperacillin/tazobactam combination; however, in rats there were slight reductions in fetal body weight at maternally toxic doses.

Intraperitoneal administration of piperacillin/tazobactam was associated with slight reductions in litter size and an increased incidence of minor skeletal anomalies (delays in bone ossification) at doses that produced maternal toxicity. Peri/post-natal development was impaired (reduced pup weights, increase in still birth, increase in pup mortality), concurrent with maternal toxicity.

**Impairment of Fertility**

Reproduction studies in rats revealed no evidence of impaired fertility due to tazobactam or piperacillin/tazobactam when administered intraperitoneally.

**COMPATIBILITIES, INCOMPATIBILITIES**

Solutions known to be compatible with TAZOCIN containing EDTA for reconstitution are:

- 0.9% Sodium chloride for injection
- Sterile water for injection
- Dextrose 5%
- Bacteriostatic saline/parabens
- Bacteriostatic water/parabens
- Bacteriostatic saline/benzyl alcohol
- Bacteriostatic water/benzyl alcohol

The reconstituted solution of TAZOCIN containing EDTA may be further diluted to the desired volume (e.g. 50 mL to 150 mL) with one of the compatible solvents for intravenous use listed below:

- 0.9% Sodium chloride for injection
- Sterile water for injection†
- Dextrose 5%
- Dextran 6% in saline
- Lactated Ringer's Injection
- Hartmann's solution
- Ringer's acetate
- Ringer's acetate/malate

†Maximum recommended volume of sterile water for injection per dose is 50 mL.

Whenever TAZOCIN is used concurrently with another antibiotic (e.g. aminoglycosides), the drugs must be administered separately. The mixing of TAZOCIN with an aminoglycoside *in vitro* can result in substantial inactivation of the aminoglycoside.

The mixing of β-lactam antibiotics with aminoglycosides *in vitro* can result in substantial inactivation of the aminoglycoside. However, amikacin and gentamicin were determined to be compatible with TAZOCIN *in vitro* in certain diluents at specific concentrations (see Section **DOSAGE AND ADMINISTRATION**).

TAZOCIN should not be mixed with other drugs in a syringe or infusion bottle since compatibility has not been established.

Because of chemical instability, TAZOCIN should not be used with solutions containing only sodium bicarbonate.

TAZOCIN should not be added to blood products or albumin hydrolysates.

## HANDLING

Directions for Reconstitution and Dilution for Use

Intravenous use only: 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.

| Vial Size (Piperacillin/Tazobactam) | Volume of Compatible Solvent to be Added to Vial |
|---|---|
| 4.50 g | 20 mL |

## HOW SUPPLIED

TAZOCIN (sterile piperacillin sodium and tazobactam sodium) is supplied in the following sizes: Each TAZOCIN 4.5 g vial provides piperacillin sodium equivalent to 4 g of piperacillin and tazobactam sodium equivalent to 0.5 g of tazobactam. Each vial contains 11.17 mEq (256 mg) of sodium.

Before reconstitution, store TAZOCIN vials below 25°C. TAZOCIN vials should be used immediately after reconstitution. For vials not used immediately after reconstitution, please follow these guidelines:

- Discard any unused portion after 24 hours if stored below 25°C, but outside of the refrigerator.
- Discard any unused portion after 7 days, if refrigerated (between 2°C to 8°C)
- Vials should not be frozen after reconstitution.

## LIST OF EXCIPIENTS

Sodium Bicarbonate
Citric Acid Monohydrate
Disodium Edetate Dihydrate
Water for Injection

## PRODUCT LICENCE NUMBERS

TAZOCIN; Box, 12 vials @ 4.5 g, Reg. No. DKI1134400144A1

HARUS DENGAN RESEP DOKTER

Manufactured and packaged by:
Wyeth Lederle S.r.l
Via Franco Gorgone Zona Industriale
I-95100 Catania CT, Italy

Imported by:
PT. Pfizer Indonesia

**Leaflet kemasan: Informasi bagi pengguna**

# TAZOCIN® 4 g/0,5 g serbuk untuk larutan infus
# Piperasilin/Tazobaktam Natrium Steril

**Baca semua bagian leaflet ini dengan cermat sebelum mulai menggunakan obat ini karena berisi informasi penting untuk Anda.**
- Simpan leaflet ini. Anda mungkin perlu membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker, atau perawat Anda.
- Obat ini telah diresepkan hanya untuk Anda. Jangan berikan kepada orang lain. Obat ini dapat membahayakan mereka, sekali pun tanda-tanda penyakit mereka sama dengan Anda.
- Jika Anda mengalami efek samping apa pun, berkonsultasilah dengan dokter, apoteker, atau perawat Anda. Ini termasuk segala kemungkinan efek samping yang tidak tercantum di dalam leaflet ini. Lihat bagian 8.

**Apa isi leaflet ini?**


## 1. Nama produk
TAZOCIN® 4 g/0,5 g serbuk untuk larutan infus

## 2. Keterangan produk
Piperasilin termasuk ke dalam golongan obat-obatan yang dikenal dengan istilah “antibiotik penisilin berspektrum luas”. Bahan ini dapat membunuh banyak jenis bakteri. Tazobaktam dapat mencegah bertahannya beberapa jenis bakteri resistan terhadap pengaruh piperasilin. Artinya ketika piperasilin dan tazobaktam diberikan secara bersamaan, maka akan lebih banyak jenis bakteri yang mati.

## 3. Apa kandungan di dalam obat ini?
TAZOCIN, kombinasi parenteral piperasilin/tazobaktam, adalah serbuk kering beku yang steril dengan warna putih hingga hampir putih yang mengandung piperasilin dan tazobaktam dalam bentuk garam natrium yang dikemas dalam vial kaca. Produk ini tidak mengandung eksipien atau bahan pengawet.

Produk juga mengandung 1 mg dinatrium edetat (dihidrat) (EDTA) per vial.

## 4. Kekuatan obat
TAZOCIN (piperasilin natrium dan tazobaktam natrium steril) disediakan dalam ukuran berikut ini:

Setiap vial TAZOCIN 4,5 g memberikan piperasilin natrium yang setara dengan 4 g piperasilin dan tazobaktam natrium yang setara dengan 0,5 g tazobaktam. Setiap vial berisi 11,17 mEq (256 mg) natrium.

**5. Apa kegunaan obat ini?**
TAZOCIN digunakan untuk mengobati infeksi bakteri, seperti infeksi yang menyerang saluran pernapasan bawah (paru-paru), abdomen, kulit, atau darah. TAZOCIN dapat digunakan pada orang dewasa dan anak-anak untuk mengobati infeksi bakteri pada pasien dengan jumlah sel darah putih yang rendah (penurunan resistansi terhadap infeksi).

Dalam infeksi serius tertentu, dokter mungkin akan mempertimbangkan penggunaan TAZOCIN dalam kombinasi dengan antibiotik lainnya.

**6. Berapa banyak dan seberapa sering Anda seharusnya menggunakan obat ini?**
Dokter Anda atau petugas kesehatan lainnya akan memberikan obat ini kepada Anda melalui infus (tetesan selama 20–30 menit) atau injeksi lambat (selama setidaknya 3–5 menit) ke dalam salah satu pembuluh vena Anda.

**Dosis**
Dosis obat yang diberikan kepada Anda bergantung pada penyakit apa yang sedang diobati, usia Anda, dan apakah Anda memiliki masalah ginjal atau tidak.

**Orang dewasa dan remaja berusia di atas 12 tahun**
Dosis yang umum adalah 12 g/1,5 g piperasilin/tazobaktam yang diberikan setiap 6 atau 8 jam, yang diberikan ke dalam salah satu pembuluh vena Anda (langsung ke dalam aliran darah). Dosis sebanyak 18 g piperasilin/2,25 g tazobaktam per hari dalam dosis terbagi dapat digunakan untuk mengobati infeksi yang berat.

Dalam kasus neutropenia, dosis yang dianjurkan adalah 4,5 g TAZOCIN (4 g piperasilin/500 mg tazobaktam) yang diberikan setiap 6 jam dalam kombinasi dengan aminoglikosida.

**Anak-anak berusia antara 2 hingga 12 tahun**
Dosis yang umum untuk anak-anak dengan jumlah sel darah putih yang rendah adalah 80 mg/10 mg/kg berat badan piperasilin/tazobaktam yang diberikan setiap 6 jam ke dalam salah satu pembuluh vena Anda (langsung ke dalam aliran darah), dalam kombinasi dengan dosis aminoglikosida yang sesuai.

Untuk anak-anak dengan berat badan lebih dari 50 kg, ikuti dosis orang dewasa, dalam kombinasi dengan dosis aminoglikosida yang sesuai.

Anda akan diberikan TAZOCIN hingga tanda-tanda infeksi mereda sepenuhnya (7 hingga 10 hari).

**Pasien dengan masalah ginjal**
Dokter Anda mungkin perlu menurunkan dosis TAZOCIN atau kekerapan pemberiannya. Dokter mungkin juga akan melakukan tes darah terhadap Anda untuk memastikan bahwa dosis pengobatan Anda sudah tepat, khususnya jika Anda harus menggunakan obat ini untuk waktu yang lama.

**Jika Anda melewatkan satu dosis TAZOCIN**
Jika Anda merasa tidak diberikan satu dosis TAZOCIN pada waktu yang seharusnya, segera beri tahu dokter Anda atau petugas kesehatan lainnya.

Jika Anda memiliki pertanyaan lebih lanjut seputar penggunaan obat ini, tanyakan kepada dokter atau perawat Anda.

## 7. Kapan seharusnya Anda tidak menggunakan obat ini?

**Jangan gunakan TAZOCIN**
- jika Anda alergi terhadap piperasilin atau tazobaktam atau bahan lain yang terkandung dalam obat ini (lihat daftar pada bagian 3).
- jika Anda alergi terhadap antibiotik seperti penisilin, sefalosporin, atau penghambat beta-laktamase lainnya, karena ada kemungkinan Anda alergi terhadap TAZOCIN.

**Kehamilan dan menyusui**

Jika Anda sedang hamil atau menyusui, atau mungkin sedang hamil atau berencana untuk hamil, konsultasikan dengan dokter atau petugas kesehatan lainnya sebelum menerima obat ini.

Dokter akan memutuskan apakah TAZOCIN sudah tepat bagi Anda.

Piperasilin dan tazobaktam dapat diteruskan kepada bayi di dalam kandungan atau melalui ASI. Jika Anda sedang menyusui, dokter akan memutuskan apakah TAZOCIN tepat diberikan kepada Anda.

**Mengemudi dan menggunakan mesin**
Penggunaan TAZOCIN diperkirakan tidak memengaruhi kemampuan untuk mengemudi atau menggunakan mesin.

## 8. Efek yang tidak diinginkan
Seperti semua obat-obatan yang ada, obat ini bisa menimbulkan efek samping, meskipun tidak semua orang mengalaminya.

**Segera kunjungi dokter** jika Anda mengalami efek samping TAZOCIN yang berpotensi serius berikut ini:

Efek samping serius (dengan frekuensi tertera di dalam tanda kurung) TAZOCIN adalah:
- ruam kulit serius [sindrom Stevens-Johnson, dermatitis bulosa (Tidak diketahui), dermatitis eksfoliatif (Tidak diketahui), nekrolisis epidermal toksik (Jarang)] yang muncul awalnya dalam bentuk bintik-bintik kemerahan menyerupai target atau bercak-bercak melingkar seringkali dengan lepuh pada bagian tengah di badan. Tanda-tanda tambahan meliputi ulkus di mulut, tenggorokan, hidung, ekstremitas, alat kelamin, dan konjungtivitis (mata merah dan bengkak). Ruam dapat berkembang menjadi lepuh yang menyebar luas atau pengelupasan kulit dan berpotensi mengancam jiwa.
- kondisi alergi berat yang berpotensi fatal (reaksi obat dengan gejala-gejala eosinofilia dan sistemik) yang dapat melibatkan kulit dan yang terpenting organ-organ lainnya di bawah kulit seperti ginjal dan hati.
- gangguan kulit (pustulosis eksantematosa generalisata akut) disertai dengan demam, berupa lepuh kecil berisi cairan dalam jumlah banyak yang muncul pada area kulit yang membengkak dan memerah.
- pembengkakan wajah, bibir, lidah, atau bagian tubuh lainnya (Tidak diketahui)
- napas pendek, mengi, atau kesulitan bernapas (Tidak diketahui)
- nyeri dada tiba-tiba yang dapat terjadi bersama reaksi alergi yang disebut sebagai sindrom Kounis (Tidak diketahui)
- ruam atau kaligata berat (Tidak umum), gatal-gatal atau ruam pada kulit (Umum)
- mata atau kulit menguning (Tidak diketahui)
- kerusakan sel darah [tanda-tandanya meliputi: sesak napas ketika Anda tidak mengharapkannya, urine merah atau coklat (Tidak diketahui), mimisan (Jarang), dan lebam bintik kecil (Tidak diketahui)], penurunan drastis sel darah putih (Jarang)
- diare berat atau terus-menerus yang disertai dengan demam atau rasa lemah (Jarang)
- nyeri, nyeri tekan, atau kelemahan pada otot tanpa penyebab yang jelas dan/atau urine berwarna gelap (Tidak diketahui)

Jika ada efek samping **berikut** yang menjadi serius, atau jika Anda menjumpai efek samping yang tidak tercantum pada leaflet ini, silakan beri tahu dokter Anda atau petugas kesehatan lainnya.

**Efek samping yang sangat umum** (mungkin terjadi pada lebih dari 1 di antara 10 orang)**:**
- diare

**Efek samping yang umum** (mungkin terjadi pada 1 di antara 10 orang)**:**
- infeksi jamur
- penurunan trombosit, penurunan sel darah merah atau pigmen darah/hemoglobin, tes lab abnormal (Coombs langsung positif), waktu pembekuan darah memanjang (waktu tromboplastin parsial yang diaktifkan memanjang)
- penurunan protein darah
- sakit kepala, insomnia
- nyeri abdomen, muntah, mual, konstipasi, sakit perut
- peningkatan enzim hati dalam darah
- ruam kulit, gatal
- hasil tes darah ginjal abnormal
- demam, reaksi di lokasi injeksi

**Efek samping yang tidak umum** (mungkin terjadi pada 1 di antara 100 orang)**:**
- penurunan sel darah putih (leukopenia), waktu pembekuan darah memanjang (waktu protrombin memanjang)
- penurunan kalium darah, penurunan gula darah
- kejang (konvulsi), teramati pada pasien yang mendapatkan dosis tinggi atau dengan masalah ginjal
- tekanan darah rendah, peradangan pembuluh vena (terasa seperti nyeri tekan atau kemerahan pada area yang terpengaruh), kulit memerah
- peningkatan produk penguraian pigmen darah (bilirubin)
- reaksi kulit dengan kemerahan, pembentukan lesi kulit, kaligata
- nyeri sendi dan otot
- menggigil

**Efek samping yang jarang** (mungkin terjadi pada 1 di antara 1000 orang)**:**
- penurunan drastis sel darah putih (agranulositosis), mimisan
- infeksi serius pada usus besar, peradangan lapisan mukosa mulut
- terlepasnya lapisan atas kulit di seluruh tubuh (nekrolisis epidermal toksik)

**Efek samping tidak diketahui** (tidak dapat diperkirakan dari data yang tersedia)**:**
- penurunan drastis sel darah merah, sel darah putih, dan trombosit (pansitopenia), penurunan sel darah putih (neutropenia), penurunan sel darah merah dikarenakan penguraian atau degradasi dini, lebam bintik kecil, waktu perdarahan memanjang, peningkatan trombosit, peningkatan jenis sel darah putih spesifik (eosinofilia)
- reaksi alergi dan reaksi alergi berat
- peradangan hati, bercak kekuningan pada kulit atau pada bagian putih mata
- reaksi alergi seluruh tubuh yang serius dengan ruam pada kulit dan lapisan mukosa, muncul lepuh dan berbagai erupsi kulit (Sindrom Stevens-Johnson), kondisi alergi berat yang melibatkan kulit dan organ-organ lain seperti ginjal dan hati (reaksi obat dengan gejala eosinofilia dan sistemik), banyak lepuh kecil berisi cairan yang terdapat di dalam area kulit yang membengkak dan memerah yang disertai dengan demam (pustulosis eksantematosa generalisata akut), reaksi kulit disertai lepuh (dermatitis bulosa), penyakit melepuh yang membuat terbentuknya lepuh di kulit dan membran mukosa (penyakit IgA linear).
- fungsi ginjal buruk dan masalah ginjal

- sejenis penyakit paru dengan kemunculan eosinofil (salah satu bentuk sel darah putih) di dalam paru-paru dalam jumlah yang meningkat.
- disorientasi akut dan kebingungan (delirium).

Terapi piperasilin telah dikaitkan dengan peningkatan insiden demam dan ruam pada pasien dengan fibrosis kistik.

**Melaporkan efek samping**

Jika Anda mengalami efek samping, konsultasikan dengan dokter atau apoteker Anda. Ini termasuk segala kemungkinan efek samping yang tidak tercantum di dalam leaflet ini. Dengan melaporkan efek samping, Anda dapat membantu memberikan lebih banyak informasi perihal keamanan obat ini.

Untuk melaporkan efek samping, hubungi www.pfizersafetyreporting.com atau email di IDN.AEReporting@pfizer.com.

## 9. Apa saja obat lain atau makanan yang harus dihindari selama menggunakan obat ini?

Harap beri tahu dokter atau petugas kesehatan lainnya jika Anda sedang menggunakan atau baru-baru ini telah menggunakan obat-obatan lain, termasuk obat-obatan yang diperoleh tanpa resep dokter. Beberapa jenis obat dapat berinteraksi dengan piperasilin dan tazobaktam.
Di antaranya:

- obat untuk asam urat (probenesid). Obat ini dapat meningkatkan durasi bagi piperasilin dan tazobaktam untuk keluar dari tubuh Anda.
- obat-obatan untuk mengencerkan darah atau mengobati bekuan darah (misalnya heparin, warfarin, atau aspirin).
- obat-obatan yang digunakan untuk melemaskan otot selama pembedahan. Beri tahu dokter jika Anda akan menjalani pembiusan total.
- metotreksat (obat yang digunakan untuk mengobati kanker, artritis, atau psoriasis). Piperasilin dan tazobaktam dapat meningkatkan durasi bagi metotreksat untuk keluar dari tubuh Anda.
- obat-obatan yang menurunkan kadar kalium dalam darah Anda (misalnya tablet untuk membantu berkemih atau beberapa jenis obat untuk kanker).
- obat-obatan yang mengandung antibiotik lain seperti tobramisin, gentamisin, atau vankomisin. Beri tahu dokter Anda jika Anda memiliki masalah ginjal.

*Efek terhadap tes laboratorium*
Beri tahu dokter atau staf laboratorium bahwa Anda sedang menggunakan TAZOCIN jika Anda harus memberikan sampel darah atau urine.

## 10. Apa yang harus dilakukan jika ada dosis terlewat?

Jika Anda merasa tidak diberikan satu dosis TAZOCIN pada waktu yang seharusnya, segera beri tahu dokter Anda atau petugas kesehatan lainnya.

## 11. Bagaimana cara menyimpan obat ini?

Jauhkan obat ini dari pandangan dan jangkauan anak-anak.

Jangan gunakan obat ini jika sudah melewati tanggal kedaluwarsanya. Tanggal kedaluwarsa mengacu pada hari terakhir dari bulan yang tertera.

Simpan pada suhu di bawah 25 °C.

Jangan buang obat melalui saluran pembuangan air atau bersama sampah rumah tangga. Tanyakan kepada apoteker cara membuang obat yang sudah tidak digunakan lagi. Langkah-langkah ini akan membantu melindungi lingkungan.

**12. Tanda-tanda dan gejala-gejala overdosis**
Gejala-gejala kemungkinan overdosis dapat meliputi eksitabilitas neuromuskular atau konvulsi, mual, muntah, dan diare.

**13. Apa yang harus dilakukan jika Anda menggunakan lebih dari dosis yang dianjurkan?**
Karena Anda akan menerima TAZOCIN dari dokter atau petugas kesehatan lainnya, maka kemungkinan Anda tidak akan menerima dosis yang salah. Namun demikian, jika Anda merasakan efek samping, seperti konvulsi, atau Anda merasa bahwa dosis yang diberikan terlalu banyak, segera beri tahu dokter Anda.

**14. Apa saja yang perlu diperhatikan saat menggunakan obat ini?**

**Peringatan dan tindakan pencegahan**
Konsultasikan dengan dokter, apoteker, atau perawat Anda sebelum menggunakan TAZOCIN
- jika Anda menderita alergi. Jika Anda menderita beberapa jenis alergi, pastikan Anda memberi tahu dokter Anda atau petugas kesehatan lainnya sebelum menerima produk ini.
- jika Anda atau keluarga Anda memiliki limfohistiositosis hemofagositik (HLH), beri tahu dokter Anda atau tenaga kesehatan lainnya sebelum menerima produk ini.
- jika Anda menderita diare sebelum, atau jika Anda mengalami diare selama atau setelah menjalani pengobatan. Dalam kasus ini, pastikan Anda melaporkannya kepada dokter atau petugas kesehatan lainnya dengan segera. Jangan meminum obat apa pun untuk mengobati diare tanpa berkonsultasi dengan dokter Anda.
- jika kadar kalium dalam darah Anda tergolong rendah. Dokter Anda mungkin akan memeriksa ginjal Anda sebelum memberikan obat ini kepada Anda dan akan melakukan tes darah rutin selama pengobatan berlangsung.
- jika Anda memiliki masalah pada ginjal atau hati, atau Anda sedang menjalani hemodialisis. Dokter Anda mungkin akan memeriksa ginjal Anda sebelum memberikan obat ini kepada Anda dan akan melakukan tes darah rutin selama pengobatan berlangsung.
- jika Anda sedang meminum obat-obatan tertentu (yang disebut antikoagulan) untuk menghindari pembekuan darah berlebihan (lihat juga **9. Apa saja obat lain atau makanan yang harus dihindari selama menggunakan obat ini?** dalam leaflet ini) atau perdarahan yang tidak diharapkan yang terjadi selama pengobatan berlangsung. Dalam kasus ini, Anda harus segera memberi tahu dokter Anda atau petugas kesehatan lainnya.
- jika Anda mengalami konvulsi selama pengobatan berlangsung. Dalam kasus ini, Anda harus memberi tahu dokter Anda atau petugas kesehatan lainnya.
- jika Anda merasa bahwa Anda mengalami infeksi baru atau infeksi yang memburuk. Dalam kasus ini, Anda harus memberi tahu dokter Anda atau petugas kesehatan lainnya.

Jika Anda mengalami nyeri, nyeri tekan, atau kelemahan pada otot tanpa penyebab yang jelas dan/atau urine berwarna gelap, segera beri tahu dokter Anda. Ini bisa jadi merupakan tanda-tanda kerusakan otot (disebut rabdomiolisis) yang dapat menyebabkan masalah ginjal.

**Anak-anak**
Piperasilin/tazobaktam tidak dianjurkan untuk digunakan pada anak-anak berusia di bawah 2 tahun dikarenakan kurangnya data mengenai keamanan dan keefektifannya.

**15. Kapan sebaiknya Anda berkonsultasi dengan dokter?**
Jika Anda memiliki pertanyaan lebih lanjut atau Anda mengalami situasi yang sama seperti yang tercantum dalam leaflet ini, konsultasikan dengan dokter, apoteker, atau perawat Anda.

**16. Nama/logo produsen/importir/Pemegang Hak Pemasaran**
TAZOCIN; Dus, 12 vial @ 4,5 g, No. Reg. DKI1134400144A1

HARUS DENGAN RESEP DOKTER

Diproduksi dan dikemas oleh:
Wyeth Lederle S.r.l
Via Franco Gorgone Zona Industriale
I-95100 Catania CT, Italia

Diimpor oleh:
PT. Pfizer Indonesia
Jakarta, Indonesia

**17. Tanggal revisi PIL**
Februari 2025