

Piperacillin + Tazobactam

PROPITAZ

4g/500 mg Powder for Injection
Antibacterial

FORMULATION:

Each vial contains Piperacillin (as sodium salt) equivalent to 4g and Tazobactam (as sodium salt) equivalent to 4g/500 mg

INDICATIONS:

Piperacillin/Tazobactam 500 mg powder for solution or infusion is indicated for treatment of the following infections in adults and children over 2 years of age

Adults and adolescents

- Severe pnemonia including hospital-acquired and ventilator-associated pneumonia
- Complicated urinary tract infections (including Pyelonephritis)
- Complicated intra-abdominal infections
- Complicated skin and soft tissue infections (including diabetic foot infections)

Treatment of patients with bacteraemia that occurs in association with, or its suspected to be associated with any of the infections li ted above.

Piperacillin/ Tazobactam maybe used in the management of neutropenic patients with fever suspected to be due to a bacterial infection.

Children aged 2-12 years

- Complicated inta-abdominal infections

Piperacillin/Tazobactam maybe used in the management of neuthropenic children with fever suspected to be due to a bacterial infection.

Consideration should be given to official guidance on the appropriate use of an anti-bacterial agents.

DOSAGE:

The dose and frequency of Piperacillin/Tazobactam depends on the severity and localisation of the infection and expected pathogens.

Adult and Adolescent patients

Infections

The usual dose is 4 g piperacillin / 500 mg tazobactam given every 8 hours

For nosocomial pneumonia and bacterial infections in neutropenic patient: recommended dose is a 4 g piperacillin / 500 mg tazobactam administered every 6 hours. This regimen may also be applicable to treat patie ts with other other indicated infection when particularly severe.

The following table summaries the treatment frequency and the recommended dos for adult and adolescent patients by indication or condition:

Treatment frequency	Piperacillin/Tazobactam 4g/500 mg
Every 6 hours	Severe pnemonia
	Neutropenic adults with fever suspected to be due to a bacterial infection
Every 8 hours	Complicated urinary tract infections (including yyelonephritis)
	Complicated intra-abdominal infections
	Skin and soft tissue infections (including diabetic foot infections)

Renal impairment

The intravenous dose should be adjusted to the degree of actual renal impairment as follows (each patient must be monitored closely signs of substance toxicity; medicinal product dose and interval should be adjusted accordingly).

Creatinine cleaance (ml/min)	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 haemodialysis, one additional dose of pipacillin / tazobactam 2g/250mg should be administered following each dialysis period because haemodialysis removes 30%-50% of piperacillin in 4 hours.

Hepatic impairment

No dose adjustment is necessary

Dose in elderly patie ts

No dose adjustment is required for the elderly with normal renal function or creatinine cleaance values above 40 ml/min.

Paediatric population (2-12 years of age)

Infections

The following table summarises the treatment frequency and the dose per body weight for paediatric patients 2-12 years of age by indication or condition:

Dose per weight and treatment frequency	Indication / condition
80 mg Piperacillin / 10 mg Tazobactam per kg body weight / every 8 hours	Neutropenic children with fever suspected to be due to bacterial infections*
100 mg Piperacillin / 12.5 mg Tazobactam per kg body weight/ every 8 hours	Complicated intra-abdominal infections*

* Not to exceed the maximum 4 g / 0.5 g per dose over 30 minutes

Renal impairment

The intravenous dose should be adjusted to the degree of actual renal impairment as follows (each patient must be monitored closely signs of substance toxicity; medicinal product dose and interval should be adjusted accordingly).

Creatinine clearance (ml/min)	Recommended dose
> 50	No dose adjustment necessary
≤ 50	70 mg piperacillin / 8.75 mg azobactam / kg every 8 hours

For children on haemodialysis, one additional dose of 40 mg piperacillin / 5mg tazobactam /kg should be administered following each dialysis period.

Use in children aged below 2 years

The safety and efficacy of Piperacillin/Tazobactam in children 0-2 years of age has been established. No data from controlled clinical studies are available

Treatment duration

The usual duration of treatment for most indications is in the range of 5-14 days. However the duration of treatment should be guided by the severity of the infection, the pathogen (s) and the patient's clinical and bacteriological progress/

Method of administration

Piperacillin/Tazobactam 4 g . 0.5g is administered by intravenous infusion (over 30 minutes)

CONTRAINDICATIONS

Hypersensitivity to the active substances or any other penicillin-antibacterial agent. History of acute severe allergic reaction to any other beta-lactam active substances (e.g. cephalosporin, monobactam or carbapenem).

ADVERSE EFFECTS:

Frequencies are defined as follows:

Very common (≥1/10)

Common (>1/100 to <1/10)

Uncommon (≥/1/1,000 to <1/1.000)

Rare (>1/10,000 to <1/1.000)

Very rare (,1/10,000)

Not known (cannot be estimated from the available data).

In the following table, adverse reactions are listed by system organ class and MedRA-preferred term. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

MedRA System Organ Class	Frequency	Undesirable Effects
Infections and infestations	Uncommon	Candidal superinfection
Blood and lymphatic system disorders	Uncommon	Leukopenia, neutropenia, thrombocytopenia
	Rare	Anaemia, haemolytic anaemia, purpura, epistaxis, bleeding time prolonged, eosinophilia
	Very Rare	Agranulocytosis, pancytopenia, activated partial thromboplastin time prolonged, Coombs' direct test positive, pancytopenia, thrombocytopenia
Immune system disorder	Uncommon	Hypersensitivity
	Rare	Anaphylactic / Anaphylactoid reaction (including shock)
Metabolism and nutrition disorders	Very Rare	Hypokalaemia, blood glucose decreased, blood albumin decreased, blood protein total decreased
Nervous system disorders	Uncommon	Headache, Insomnia
Vascular disorders	Uncommon	Hypotension, thrombophlebitis, phlebitis
	Rare	Flushing
Gastrointestinal disorders	Common	Diarrhea, nausea, vomiting
	Uncommon	Jaundice, constipation, dyspepsia, stomatitis
	Rare	Abdominal pain, pseudomembranous colitis
Hepatobiliary disorders	Uncommon	Alanine aminotransferase increased, aspartate aminotransferase increased
	Rare	Hepatitis, blood bilirubin increased, blood alkaline phosphatase+ increased, gamma-glutamyltransferase increased

Skin and subcutaneous tissue disorders	Common	Rash including maculopapular rash
	Uncommon	Pruritus, urticarial
	Rare	Erytema multiforme, dermatitis bullous, exantema
	Very rare	Steven-Johnson-Syndrome, toxic epidermal necrolysis
Musulo-skeletal and connective tissue disorders	Rare	Arthralgia, myalgia
Renal and urinary disorders	Uncommon	Blood creatinine inceased
	Rare	Tubolonterstitial nephritis renal failure
	Very rare	Blood urea increased
General disorders and administration sie conditions	Uncommon	Pyrexia, injection site reactions
	Rare	Chills

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

SPECIAL PRECAUTIONS:

The factors such as the severity of the infection and pevalence of resistance to other suitable antibacterial agents.

Before initiating treatment with Piperacilllin/Tazobactam careful inquiry should be made concerning previous hypersensitivity reaction to penicillins, other beta-lactam agents (e.g cephalosporins, monobactam or carbapenem) and other allergens. Serious and occasionally fatal hypersensitivity (anaphylactic / anaphylactoid [including shock]) reactionshave been reported in patie ts receiving treatment with penicillins, including Piperacillin/Tazobactam. These reactions ae more likely to occur in persons with a historry of sensitivity to multiple allergens. Serious hypersensitivity reactions require the discontinuation of the antibiotic, and may require administration of epinephrine equire the disconntinuation of the antibiotic,

Serious skin reaction, such as Seven-Johnson syndrome and toxic epidermal to multiple have been reported in patie ts receiving piperacillin tazobactam. If patients develop a skin rash they should be monitored closely and Piperacillin Tazobactam. If patients develop a skin progress.

Antibiotic-induced pseudomembranous colitis may be manifested by severe, persitent diarrhoea which may be life-threatening. The onset of pseudomembranous colitis symptoms may occur during of after antibacterial treatment. In these cases Piperacillin / Tazobactam, should be discontinued.

Therapy with Piperacillin/Tazobactam my result in the emergence of resistant organisms, which might cause superinfections.

Bleeding manifestations have occured in some patients receiving beta-lactam an antibiotics. These reactions some mess have been associated with abnormalities of coagulation tests,

such as clotting time, platelet aggregation and proprothrombin time, and more likely to occur in patients with renal failiure. If bleeding manifestation occur, the antibiotic should be discontinued and appopriate therapy instituted,

Leukopenia and neutropenia may occur, especially during prolonged therapy, therefore periodic assesment of haematopoietic function should be pe rformed.

As with treatment with other penicillins, neurological complications in the form of convulsions may occur when high doses are administered, especiallly in patie ts with impaired renal function.

Hypokalaemia may occur in patients with low potasssium reserves or those receiving concomitant medicinal products that may be lower potassium levels: periodic electrolyte determinations should be perormed in such paati ts.

USE IN PREGNANCY AND LACTATION:

Pregnancy

There are no or a limited amount of date from the use of piperacillin / tazobactam in pregnant women.

Studies in animals have shown developmental toxicity, but no evidence of teratogenicity. at doses that are maternally toxic.

Piperacillin and tazobactam cross the placenta. Piperacillin/Tazobactam should only be used during pregnancy if clearly indicated i.e. only if the expected benefit outweighs the possible risk to the pregnant woman and foetus.

Breast-feeding.

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

DRUG INTERACTIONS AND OTHERS:

Non-depolarizing muscle relaxants: Piperacillin when used concomitantly with vecuronium has been implicated in the prolongation of the neuomuscular blockade of vecuronium. Due to their similar mechanisms of action, it is xpected that the neuromuscular blockade produced by any of the non-depolarising muscle relaxants could be prolonged in the presence of piperacillin.

Oral anti oagulants: During simultaneous administration of heparin, oral anticoagulants and other substances that may effect the blood coagulaation system including thrombocyte function, appopriate coagulaation test should be performed more frequently and monitored regularly.

Methotrexate: Piperacillin may reduce the excretion of methotrexate; therefore, serum levels of methotrexate should be monitored in patie ts to avoids substance toxicity.

Probenecid: As with other penicillins, concurrent administration of probenecid and piperacillin/tazobactam produce a longer half-life and lower renal clearance of piperacillin



and tazobactam; however peak plasma concentration of either active substance the pharmacokinetics of tobramycin in subjects with normal renal function and with mild or are unaffected.

Aminoglycosides: Piperacillin either alone or with tazobactam did not significantly alter

moderate renal impairment. The pharmacokinetics of piperacillin, tazobactam, and the M1 metabolite were also not significantly altered by tobramycin administration.

Vancomycin: No pharmacokinetic interactions have been noted between piperacillin/tazobactam and vancomycin.

Effects on laboratory tests

Non-enzymatic methods of measuring urinary glucose may lead to false-positive results, as with other penicillins. Therefore, enzymatic urinary glucose measurement is required under piperacillin / tazobactam therapy.

A number of chemical urine protein measurement methods may lead to false-positive result. Protein measurement with dip stick is not affected.

The direct Coombs test may be positive.

Positive test results for the essays listed above in patients receiving piperacillin / tazobactam should be confirmed by other diagnostic methods.

CAUTION:

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription

For suspected adverse drug reaction, report to the **FDA: www.fda.gov.ph** and **BIOCARE: pv@biocarelifesciences.com**

STORAGE:

Store at temperatures not exceeding 30°C.

SHELF-LIFE:

36 months

AVAILABILITY:

Single 30-ml USP type III flint glass vial is packed inside a carton along with a package insert.

REG. NO: DRP-11191

Date of First Authorization: 11 February 2022

Date of Revision of Package Insert: 4 May 2023

Imported and Distributed by:

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