WEMPITAZ®
injection

(Piperacillin And Tazobactam For Injection IP)
PRESCRIBING INFORMATION

COMPOSITION :
Each vial contains :

Sterile Piperacillin Sodium IP	
Eq. to Piperacillin	4 g
Sterile Tazobactam Sodium IP	
Eq. to Tazobactam	500 mg
Disodium E.D.T.A. IP	1 mg

THERAPEUTIC CLASS: Antibacterials for systemic use, Combinations of penicillins, including beta-lactamase inhibitors.

DESCRIPTION & PHARMACOLOGICAL ACTION: Piperacillin and tazobactam injection is used to treat pneumonia and skin, gynecological, and abdominal (stomach area) infections caused by bacteria. Piperacillin is in a class of medications called penicillin antibiotics.
Pharmacodynamics: Piperacillin is a broad spectrum, semi synthetic penicillin, with bactericidal activity. Penicillins bind to enzymes that are vital for the development of the bacterial cell wall during growth and division, inactivating them and thereby exerting bactericidal activity through inhibition of both septum and cell wall synthesis.
Tazobactam combined with piperacillin enhances and extends the spectrum of the antibacterial activity of piperacillin against beta-lactamase-producing bacteria.
Microbiology: Piperacillin/tazobactam is highly active against piperacillin-sensitive micro-organisms as well as beta-lactamase producing, piperacillin-resistant micro-organisms.
Mechanism of resistance: The two main mechanisms of resistance to piperacillin / tazobactam are:
- Inactivation of the piperacillin component by those beta-lactamases that are not inhibited by tazobactam: beta-lactamases in the Molecular class B, C and D. In addition, tazobactam does not provide protection against extended-spectrum beta-lactamases (ESBLs) in the Molecular class A and D enzyme groups.
- Alteration of penicillin-binding proteins (PBPs), which results in the reduction of the affinity of piperacillin for the molecular target in bacteria.

Pharmacokinetics: Peak piperacillin and tazobactam plasma concentrations are attained after completion of an intravenous infusion or injection. Piperacillin and tazobactam are widely distributed in tissue and body fluids including intestinal mucosa, gallbladder, lung, bile and bone.
Both piperacillin and tazobactam are 20 to 30% bound to plasma proteins. Piperacillin is hepatically metabolised to the microbiologically active desethyl metabolite. Tazobactam is metabolised to a single metabolite which has been found to be microbiologically inactive.
The plasma half-life of piperacillin and tazobactam ranges from 0.7 to 1.2 hours.
Piperacillin, tazobactam, and desethyl piperacillin are also secreted into the bile.

DOSAGE AND ADMINISTRATION:
Route of administration: Piperacillin/Tazobactam 4 g / 0.5 g is administered by intravenous infusion (over 30 minutes).
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 / 0.5 g tazobactam given every eight hours and for nosocomial pneumonia and bacterial infections in neutropenic patients, administered every six hours.
The following table summarises the treatment frequency and the recommended dose for adult and adolescent patients by indication or condition:

Treatment frequency	Piperacillin/Tazobactam 4 g / 0.5 g
Every six hours	Severe pneumonia
	Neutropenic adults with fever suspected to be due to a bacterial infection.
Every eight hours	Complicated urinary tract infections (including pyelonephritis)
	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 (each patient must be monitored closely for signs of substance toxicity; medicinal product dose and interval should be adjusted accordingly):

Creatinine clearance (ml/min)	Piperacillin/Tazobactam (recommended dose)
> 40	No dose adjustment necessary
20-40	Maximum dose suggested: 4 g / 0.5 g every eight hours
< 20	Maximum dose suggested: 4 g / 0.5 g every 12 hours

For patients on haemodialysis, one additional dose of Piperacillin/Tazobactam 2g/0.25g should be administered following each dialysis period, because haemodialysis removes 30%-50% of piperacillin in four hours.
Hepatic Impairment: No dose adjustment is necessary.
Dose in elderly patients: No dose adjustment is required for the elderly with normal renal function or creatinine clearance 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 six hours	Neutropenic children with fever suspected to be due to bacterial infections*
100 mg Piperacillin / 12.5 mg Tazobactam per kg body weight / every eight 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 for signs of substance toxicity; medicinal product dose and interval should be adjusted accordingly):

Creatinine clearance (ml/min)	Piperacillin/Tazobactam (recommended dose)
> 50	No dose adjustment needed.
≤50	70 mg piperacillin / 8.75 mg tazobactam / kg every eight hours.

For children on haemodialysis, one additional dose of 40 mg piperacillin / 5 mg 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 not been established.
Reconstitution:
Each vial is for single use only.
A solution for bolus injection is prepared by dissolving the drug product meropenem in sterile water for injection to a final concentration of 50 mg/ml.
The solution should be shaken before use. The solutions should be inspected visually for particles and discolouration prior to administration. Only clear colourless to yellow solution, free from particles should be used.
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.

INDICATIONS: PRA-PIPTAZ is indicated for treatment of the following systemic and/or local bacterial infections in which susceptible organisms have been detected or are suspected:
Adults
Bacterial infections in neutropenic patients, in combination with an aminoglycoside.
Community acquired pneumonia caused by Haemophilus influenzae.
Intra-abdominal infections caused by piperacillin-resistant beta-lactamase producing strains of Escherichia coli and Bacteroides fragilis.
Gynaecological infections, including endometritis caused by piperacillin-resistant beta-lactamase producing strains of Escherichia coli.
Skin and soft tissue infections caused by piperacillin-resistant beta-lactamase producing strains of Staphylococcus aureus.
Children
Bacterial infections in neutropenic patients, in combination with an aminoglycoside.
Serious intra-abdominal infections, caused by E.coli or Bacteriodes species, in hospitalised children aged 2-12 years. TAPIAZ has not been evaluated for this condition in younger children.

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

WARNINGS AND PRECAUTIONS: The selection of Piperacillin/Tazobactam to treat an individual patient should take into account the appropriateness of using a broad-spectrum semi-synthetic penicillin based on factors such as the severity of the infection and the prevalence of resistance to other suitable antibacterial agents.
Before initiating therapy with Piperacillin/Tazobactam, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, other beta-lactam agents (e.g. cephalosporin, monobactam or carbapenem) and other allergens. Serious and occasionally fatal hypersensitivity (anaphylactic/anaphylactoid [including shock]),
Serious skin reactions, have been reported in patients receiving Piperacillin/Tazobactam.
Antibiotic-induced pseudomembranous colitis may be manifested by severe, persistent diarrhoea which may be life-threatening. The onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment. In these cases Piperacillin/Tazobactam, should be discontinued.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION: Non-depolarising muscle relaxants
Piperacillin when used concomitantly with vecuronium has been implicated in the prolongation of the neuromuscular blockade of vecuronium.
Oral anticoagulants: During simultaneous administration of heparin, oral anticoagulants and other drugs that may affect the blood coagulation system including thrombocyte function.
Methotrexate: Piperacillin may reduce the excretion of methotrexate.
Probenecid: As with other penicillins, concurrent administration of probenecid and Piperacillin/Tazobactam produces a longer half-life and lower renal clearance for both piperacillin and tazobactam; however, peak plasma concentrations of either substances are unaffected.
Aminoglycosides: Piperacillin, either alone or with tazobactam, did not significantly alter the pharmacokinetics of tobramycin in subjects with normal renal function and with mild or moderate renal impairment.
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.

ADVERSE EFFECTS:
Common: Headache, insomnia, abdominal pain, vomiting, nausea, constipation, dispepsia, rash, pruritus, blood creatinine increased, blood urea increased, pyrexia, injection site reaction, blood albumin decreased, protein total decreased, candidiasis.
Uncommon: Leukopenia, prothrombin time prolonged, hypotension, thrombophlebitis, phlebitis, flushing, erythema multiforme, urticaria, rash maculopapular, chills.
Rare: Agranulocytosis, epistaxis, pseudo-membranous colitis, stomatitis, toxic epidermal necrolysis.

PREGNANCY, LACTATION & FERTILITY:
Pregnancy: There are no or a limited amount of data 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 risks to the pregnant woman and foetus.
Lactation: Piperacillin is excreted in low concentrations in breast 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.
Fertility: A fertility study in rats showed no effect on fertility and mating after intraperitoneal administration of tazobactam or the combination Piperacillin/ Tazobactam.

OVERDOSAGE:
Symptoms: The majority of those events experienced including nausea, vomiting, and diarrhoea have also been reported with the usual recommended dose. Patients may experience neuromuscular excitability or convulsions if higher than recommended doses are given intravenously (particularly in the presence of renal failure).
Treatment: In the event of an overdose, Piperacillin/Tazobactam treatment should be discontinued. No specific antidote is known.
Excessive serum concentrations of either piperacillin or tazobactam may be reduced by haemodialysis.

SHELF LIFE: 24 months from the date of manufacturing

STORAGE : Store protect from light at a temperature not exceeding 25°C.

PRESCRIPTION :
30 ml clear glass vial, sealed with butly rubber stopper and flip off and packed in a printed carton along with 20 ml sterile water for injection IP and package insert.

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