Piperacillin and tazobactam for injection is an injectable antibacterial combination containing 2 grams of piperacillin and 1 gram of tazobactam. It is available as a sterile powder for reconstitution with sterile water for injection. The chemical structure of piperacillin is:

\[
\text{Clo} [3.2.0] \text{heptane-2-carboxylate.}
\]

The chemical structure of tazobactam is:

\[
\text{ Piperacillin is metabolized to a minor microbiologically active desethyl metabolite.}
\]

Both piperacillin and tazobactam are approximately 30% bound to plasma proteins. Tazobactam is minimally bound to plasma proteins. Piperacillin is metabolized to a minor microbiologically active desethyl metabolite. Piperacillin and tazobactam are minimally bound to plasma proteins. Piperacillin is metabolized to a minor microbiologically active desethyl metabolite.

The pharmacokinetics of piperacillin and tazobactam are essentially similar after oral and parenteral administration. Piperacillin is minimally bound to plasma proteins. Piperacillin is metabolized to a minor microbiologically active desethyl metabolite. Piperacillin is minimally bound to plasma proteins.

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Pregnancy: Teratogenic Effects—Pregnancy Category B

Rats, tazobactam crosses the placenta. Concentrations in the fetus are less than or equal to those in the mother at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy in the latter. There are no adequate and well-controlled studies in pregnant women. Because of the potential for adverse effects in the human fetus, piperacillin/tazobactam should be given to a pregnant woman only if clearly needed.

Adverse Events From Clinical Trials

Alcohol intolerance was noted in one patient administered piperacillin/tazobactam for 1 day in a 1991 study. No other intolerance was noted with piperacillin/tazobactam in clinical trials. There have been postmarketing reports of overdose with piperacillin/tazobactam.

Piperacillin therapy has been associated with an increased incidence of fever and hypothermia.

Stability of piperacillin and tazobactam for injection is not affected when administered intravenously using infusion pumps. Infusions may be given in normal saline or 5% dextrose and are compatible with the following diluents: 0.9% Sodium Chloride for Injection, Dextran 70, 20% Mannitol for Injection, 4% Albumin (Human) Injection, 5% Dextrose in Water for Injection, and 5% Dextrose in Water for Injection with 0.01 N Sodium Hydroxide to adjust the pH to 6.0 to 7.0. Compatibility of the combination with other parenteral solutions or medicines has not been established.

In clinical trials, adverse events that occurred in more than 1% of patients and were reported to be related to the combination were: frequency of nausea, vomiting, diarrhea, or pharyngitis; one episode of severe neutropenia; two episodes of urticaria; and one episode of angioedema.

In patients with renal insufficiency (Creatinine Clearance < 20 mL/min) or patients with hepatic insufficiency, the antibiotic dose should be adjusted to the patient's renal or hepatic function, respectively.

In the 12-month multiple-dose clinical experience, piperacillin/tazobactam has been used for treatment of infections in a broad spectrum of patients in diverse hospital settings. In this experience, adverse events that occurred in more than 1% of patients and were related to piperacillin/tazobactam therapy were: pharyngitis, pulmonary edema, bronchospasm, coughing, and taste perversion.

Toxicity and Overdose

There have been reports of toxic effects occurring in patients who were given simultaneous therapy with an aminoglycoside and piperacillin/tazobactam. In this setting, the onset of ototoxicity may be masked by the antibiotic effect of the aminoglycoside, and the clinical appearance of certain symptoms may be difficult to interpret. It is recommended that the dose of an aminoglycoside be adjusted according to the recommendations of the manufacturer. The occurrence of toxic effects during therapy with piperacillin/tazobactam should be monitored by appropriate laboratory tests. The use of piperacillin/tazobactam with inactivated vaccines has not been studied.

In vivo synergy testing often failed to predict clinical response and treatment failure was noted in some cases; however, the clinical significance of this observation is uncertain.

Piperacillin/tazobactam is compatible in clinical settings where the use of a combination of one or more antimicrobial agents is indicated.

The following abbreviations and acronyms are used in this monograph:

VC—vein
BC—branchial cleft
ICDR—International Committee for Drug Resistant Bacteria
NCCOS—National Committee for Clinical Lab Standards
NCCLS—National Committee for Clinical Laboratory Standards