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Pharmacokinetics

Piperacillin is not absorbed from the gastrointestinal tract. It is well absorbed after intramuscular use, with peak plasma concentrations of 30 to 40 micrograms/mL 30 to 50 minutes after a dose of 2 g. The pharmacokinetics of piperacillin are reported to be nonlinear and dose-dependent. The plasma half-life is about 1 hour, but is prolonged in neonates. In patients with severe renal impairment there may be a threefold increase in half-life; in those with end-stage renal failure half-lives of 4 to 6 hours have been reported, and in those with both renal and hepatic impairment much longer half-lives may result. About 20% of piperacillin in the circulation is bound to plasma proteins.

Piperacillin is widely distributed in body tissues and fluids. It crosses the placenta into the fetal circulation and small amounts are distributed into breast milk. There is little diffusion into the CSF except when the meninges are inflamed.

About 60 to 80% of a dose is excreted unchanged in the urine by glomerular filtration and tubular secretion within 24 hours, achieving high concentrations. High concentrations are also found in the bile and up to 20% of a dose may be excreted by this route.

Plasma concentrations are enhanced by probenecid.

Piperacillin is removed by haemodialysis.

Piperacillin with tazobactam. The pharmacokinetics of piperacillin do not appear to be altered by tazobactam, but piperacillin reduces the renal clearance of tazobactam.

◊ References.
1. Heikkilä A, Erkkola R. Pharmacokinetics of piperacillin during pregnancy. *J Antimicrob Chemother* 1991; **28:** 419–23.
2. Wise R, *et al.* Pharmacokinetics and tissue penetration of tazobactam administered alone and with piperacillin. *Antimicrob Agents Chemother* 1991; **35:** 1081–4.
3. Johnson CA, *et al.* Single-dose pharmacokinetics of piperacillin and tazobactam in patients with renal disease. *Clin Pharmacol Ther* 1992; **51:** 32–41.
4. Dupon M, *et al.* Plasma levels of piperacillin and vancomycin used as prophylaxis in liver transplant patients. *Eur J Clin Pharmacol* 1993; **45:** 529–34.
5. Sörgel F, Kinzig M. The chemistry, pharmacokinetics and tissue distribution of piperacillin/tazobactam. *J Antimicrob Chemother* 1993; **31** (suppl A): 39–60.
6. Reed MD, *et al.* Single-dose pharmacokinetics of piperacillin and tazobactam in infants and children. *Antimicrob Agents Chemother* 1994; **38:** 2817–26.
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Uses and Administration

Piperacillin is a ureidopenicillin that is used similarly to ticarcillin (p.353) for the treatment of infections caused by *Pseudomonas aeruginosa*, and also infections due to other susceptible bacteria. It has been used particularly in immunocompromised patients (neutropenic patients) and for biliary-tract infections (cholangitis). Other indications have included uncomplicated gonorrhoea due to penicillin-sensitive gonococci, and urinary-tract infections. It has also been used for surgical infection prophylaxis. For details of these infections and their treatment, see under Choice of Antibacterial, p.162. For the treatment of serious infections piperacillin is commonly used with an aminoglycoside, but they should be given separately because of possible incompatibility.

Administration and dosage. Piperacillin is given by injection as the sodium salt. Doses are expressed in terms of the equivalent amount of piperacillin; 1.04 g of piperacillin sodium is equivalent to about 1 g of piperacillin. Doses should generally be reduced in moderate to severe renal impairment.

Piperacillin may be given by slow intravenous injection over 3 to 5 minutes, by intravenous infusion over 20 to 30 minutes, or by deep intramuscular injection. Single doses of more than 2 g for adults or 500 mg for children should not be given by the intramuscular route.

For the treatment of serious or complicated infections, adults may be given piperacillin 200 to 300 mg/kg daily in divided doses intravenously; the usual dose is 3 to 4 g every 4 or 6 hours. In life-threatening infections, particularly those caused by *Pseudomonas* or *Klebsiella* spp., it should be given in a dose of not less than 16 g daily. The usual maximum daily dose is 24 g, although this has been exceeded.

For mild or uncomplicated infections, 100 to 125 mg/kg daily may be given to adults; usual doses are 2 g every 6 or 8 hours, or 4 g every 12 hours, intravenously, or 2 g every 8 or 12 hours intramuscularly.

Uncomplicated gonorrhoea may be treated by a single intramuscular dose of 2 g. Probenecid 1 g may be given orally 30 minutes before the injection.

For the prophylaxis of infection during surgery, 2 g just before the procedure, or when the umbilical cord is clamped in caesarean section, followed by at least 2 doses of 2 g at intervals of 4 or 6 hours within 24 hours of the procedure, may be given.

The intravenous route is preferred for infants and children. Those aged 1 month to 12 years may be given 100 to 300 mg/kg daily in 3 or 4 divided doses. Neonates less than 7 days old or weighing less than 2 kg may be given 150 mg/kg daily in 3 divided doses. Those more than 7 days old and weighing more than 2 kg may be given 300 mg/kg daily in 3 or 4 divided doses.

Piperacillin with tazobactam. Piperacillin has also been used with tazobactam (p.344), a beta-lactamase inhibitor, to widen its antibacterial spectrum to organisms usually resistant because of the production of beta-lactamases. The combination is given intravenously in a ratio of piperacillin (as the sodium salt) 8 parts to 1 part of tazobactam (as the sodium salt). Doses, calculated on piperacillin content, are similar to those of piperacillin alone.

◊ References.
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3. Perry CM, Markham A. Piperacillin/tazobactam: an updated review of its use in the treatment of bacterial infections. *Drugs* 1999; **57:** 805–43.
4. Kotapati S, *et al.* The clinical and economic benefits of administering piperacillin-tazobactam by continuous infusion. *Intensive Crit Care Nurs* 2005; **21:** 87–93.
5. Gin A, *et al.* Piperacillin-tazobactam: a beta-lactam/beta-lactamase inhibitor combination. *Expert Rev Anti Infect Ther* 2007; **5:** 365–83.

Preparations

BP 2008: Piperacillin Intravenous Infusion;
USP 31: Piperacillin for Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Algiseptico†; Piperac†; ***Austral.:*** Pipril†; ***Austria:*** Pipril; ***Belg.:*** Pipcil†; ***Canad.:*** Pipracil†; ***Cz.:*** Pipraks†; Pipril†; ***Denm.:*** Ivacin†; ***Ger.:*** Pipera†; Pipril†; ***Gr.:*** Pipril; Zobactam; Zoracilin; ***Hong Kong:*** Pipracil†; ***Hung.:*** Pipril†; ***India:*** Pipracil; ***Irl.:*** Pipril†; ***Israel:*** Picillin†; Pipracin; Pipril†; ***Ital.:*** Avocin†; Biopiper†; Cilpier; Dipenil; Ecosette; Eril†; Farecillin; Peracil; Perasint; Picillin; Piperital; Pipersal; Pipertex; Reparcillin; Semipenil; Sintoplus; Viracillina†; ***Jpn:*** Pentcillin; ***Malaysia:*** Pipracil†; ***NZ:*** Pipril†; ***Switz.:*** Pipril†; ***Thai.:*** Peracin; Pipracil†; ***Turk.:*** Pipraks; ***USA:*** Pipracil†.

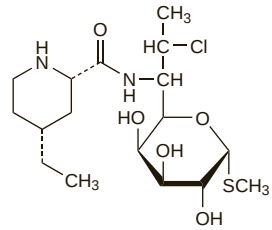
Multi-ingredient: ***Arg.:*** Pipetexina; Tazonam; ***Austral.:*** Tazocin; ***Austria:*** Tazonam; ***Belg.:*** Tazocin; ***Braz.:*** Tazocin; Tazoxil†; Tazpen†; ***Canad.:*** Tazocin; ***Chile:*** Tazonam; ***Cz.:*** Tazocin; ***Denm.:*** Tazocin; ***Fin.:*** Tazocin; ***Fr.:*** Tazocilline; ***Ger.:*** Tazobac; ***Gr.:*** Bactalin; Gramenox; Oliten; Tazepen; Tazidron; Tazobion; Tazocin; Tazorex; ***Hong Kong:*** Tazocin; ***Hung.:*** Tazocin; ***India:*** Tazact; Tazofast; Tazopen; Zosyn; ***Indon.:*** Tazocin; ***Irl.:*** Tazocin; ***Israel:*** Tazocin; ***Ital.:*** Tazobac; Tazocin; ***Malaysia:*** Tazocin; ***Mex.:*** Tasovak; Tazocin; ***Neth.:*** Tazocin; ***Norw.:*** Tazocin; ***NZ:*** Tazocin; ***Philipp.:*** Tazocin; ***Pol.:*** Tazocin; ***Port.:*** Tazobac; ***S.Afr.:*** Tazobax; Tazocin; ***Singapore:*** Tazocin; ***Spain:*** Tazocel; ***Swed.:*** Tazocin; ***Switz.:*** Tazobac; ***Thai.:*** Tazocin; ***Turk.:*** Tazocin; ***UK:*** Tazocin; ***USA:*** Zosyn; ***Venez.:*** Tazopril; Tazpen.

Pirlimycin Hydrochloride *(USAN, rINNM)*

Hidrocloruro de pirlimicina; Pirlimycine, Chlorhydrate de; Pirlimycinhydroklorid; Pirlimycini Hydrochloridum; Pirlimysiinihydrokloridi; U-57930E. Methyl 7-chloro-6,7,8-trideoxy-6-(*cis*-4-ethyl-L-pipecolamido)-1-thio-L-*threo*-α-D-*galacto*-octopyranoside monohydrochloride monohydrate.

Пирлимицина Гидрохлорид

$C_{17}H_{31}ClN_2O_5S,HCl,H_2O$ = 465.4.
CAS — 79548-73-5 (pirlimycin); 77495-92-2 (pirlimycin hydrochloride).



(pirlimycin)

Profile

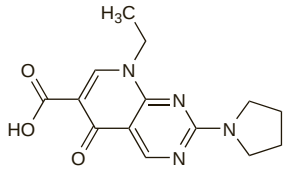
Pirlimycin is a lincosamide antibacterial used in veterinary medicine.

Piromidic Acid *(rINN)*

Acide Piromidique; Ácido piromídico; Acidum Piromidicum; PD-93; Piromidihappo; Piromidsyra. 8-Ethyl-5,8-dihydro-5-oxo-2-(pyrrolidin-1-yl)pyrido[2,3-*d*]pyrimidine-6-carboxylic acid.

Пиромидовая Кислота

$C_{14}H_{16}N_4O_3$ = 288.3.
CAS — 19562-30-2.
ATC — J01MB03.
ATC Vet — QJ01MB03.



Profile

Piromidic acid is a 4-quinolone antibacterial with properties similar to those of nalidixic acid (p.303). It has been used in the treatment of susceptible infections. There have been a number of reports of acute renal failure associated with piromidic acid.

Preparations

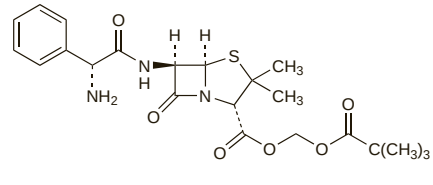
Proprietary Preparations (details are given in Part 3)
Ital.: Enteromix†.

Pivampicillin *(BAN, rINN)*

MK-191; Pivampicilin; Pivampicilina; Pivampicilinas; Pivampicilline; Pivampicillinum; Pivampisilliini. Pivaloyloxymethyl (6*R*)-6-(α-D-phenylglycylamino)penicillanate.

Пивампициллин

$C_{22}H_{29}N_3O_6S$ = 463.5.
CAS — 33817-20-8.
ATC — J01CA02.
ATC Vet — QJ01CA02.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Pivampicillin). A white or almost white crystalline powder. Practically insoluble in water; soluble in dehydrated alcohol; freely soluble in methyl alcohol. It dissolves in dilute acids. Store in airtight containers.