Pivampicillin Hydrochloride *(BANM, USAN, rINNM)*

Hidrocloruro de pivampicilina; Pivampicilline, Chlorhydrate de; Pivampicillini Hydrochloridum.

Пивампициллина Гидрохлорид

$C_{22}H_{29}N_3O_6S,HCl$ = 500.0.

CAS — 26309-95-5.

ATC — J01CA02.

ATC Vet — QJ01CA02.

Adverse Effects and Precautions

As for Ampicillin, p.204. Pivampicillin is reported to cause a lower incidence of diarrhoea than ampicillin. Upper gastrointestinal discomfort may be more frequent when pivampicillin is taken on an empty stomach.

Pivaloyloxymethyl esters such as pivampicillin have been associated with the induction of carnitine deficiency (see below).

Carnitine deficiency. Carnitine deficiency (see p.1933) has been reported after the use of pivampicillin and pivmecillinam.[1] It is thought that the pivalic acid liberated on hydrolysis of these pivaloyloxymethyl esters *in vivo* is excreted as pivaloyl-carnitine with a consequent depletion in plasma and muscle concentrations of carnitine.[2] Low plasma-carnitine concentrations persisted in a patient after stopping pivampicillin, despite 6 weeks of replacement therapy with oral carnitine 1g daily. She had originally presented with skeletal myopathy when given pivampicillin for 3 months. A more intensive carnitine replacement regimen might be necessary in such patients.[3]

1. Holme E, *et al.* Carnitine deficiency induced by pivampicillin and pivmecillinam therapy. *Lancet* 1989; **ii:** 469–73.
2. Anonymous. Carnitine deficiency. *Lancet* 1990; **335:** 631–3.
3. Rose SJ, *et al.* Carnitine deficiency associated with long-term pivampicillin treatment: the effect of a replacement therapy regime. *Postgrad Med J* 1992; **68:** 932–4.

Porphyria. Pivampicillin has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Interactions

As for Benzylpenicillin, p.214.

There is a theoretical possibility that carnitine deficiency may be increased in patients receiving pivampicillin and valproate.

Antimicrobial Action

Pivampicillin has the antimicrobial activity of ampicillin to which it is hydrolysed *in vivo* (p.204).

Pharmacokinetics

Pivampicillin is acid-stable and is readily absorbed from the gastrointestinal tract. On absorption it is rapidly and almost completely hydrolysed to ampicillin, pivalic acid, and formaldehyde. Plasma-ampicillin concentrations 1 hour after a dose are 2 to 3 times those attained after an equivalent dose of ampicillin. The absorption of pivampicillin is generally not significantly affected by food. About 70% of a dose is excreted in the urine as ampicillin within 6 hours.

Uses and Administration

Pivampicillin is the pivaloyloxymethyl ester of ampicillin (p.205) and has similar uses; 1.3 g of pivampicillin and 1.43 g of pivampicillin hydrochloride are each equivalent to about 1 g of ampicillin.

Pivampicillin is given orally to adults and children over 10 years of age in doses of 500 mg twice daily with food, which may be doubled in severe infections. In children aged 3 months to 1 year a dose of 20 to 30 mg/kg twice daily may be used. Children older than 1 year may be given 12.5 to 17.5 mg/kg twice daily, up to 500 mg twice daily.

In areas where gonococci remain sensitive a single dose of 1.5 g is given for gonorrhoea, with probenecid 1 g.

Pivampicillin hydrochloride has been used in some countries.

Pivampicillin has also been given with pivmecillinam (below).

Preparations

Proprietary Preparations (details are given in Part 3)

Canad.: Pondocillin; ***Denm.:*** Pondocillin; ***Fr.:*** Proampi; ***Norw.:*** Pondocillin; ***Swed.:*** Pondocillin.

Pivmecillinam *(BAN, rINN)*

Amdinocillin Pivoxil *(USAN)*; FL-1039; Pivamdinocillin; Pivmecilinam; Pivmécillinam; Pivmecillinamum; Pivmesillinaami; Ro-10-9071. Pivaloyloxymethyl (6*R*)-6-(perhydroazepin-1-ylmethyleneamino)penicillanate.

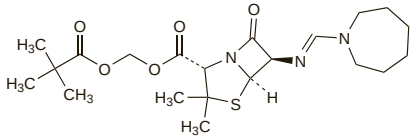
Пивмециллинам

$C_{21}H_{33}N_3O_5S$ = 439.6.

CAS — 32886-97-8.

ATC — J01CA08.

ATC Vet — QJ01CA08.



Pivmecillinam Hydrochloride *(BANM, rINNM)*

Hidrocloruro de pivmecilinam; Pivmecilinam-hydrochlorid; Pivmecilinamo hidrochloridas; Pivmécillinam, Chlorhydrate de; Pivmecillinám-hidroklorid; Pivmecillinamhydroklorid; Pivmecillinami hydrochloridum; Pivmesillinaamihydrokloridi.

Пивмециллинама Гидрохлорид

$C_{21}H_{33}N_3O_5S,HCl$ = 476.0.

CAS — 32887-03-9.

ATC — J01CA08.

ATC Vet — QJ01CA08.

Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn*.

Ph. Eur. 6.2 (Pivmecillinam Hydrochloride). A white or almost white crystalline powder. Freely soluble in water, in dehydrated alcohol, and in methyl alcohol; slightly soluble in acetone. A 10% solution in water has a pH of 2.8 to 3.8. Store at a temperature of 2° to 8°. Protect from light.

Adverse Effects and Precautions

As for Benzylpenicillin, p.213.

Pivaloyloxymethyl esters such as pivmecillinam have been associated with the induction of carnitine deficiency (see Pivampicillin, above).

Administration. Oesophageal injury has been associated rarely with pivmecillinam tablets.[1,2] Patients are advised to take them during a meal, while sitting or standing, and with at least half a glass of water.[3]

1. Committee on Safety of Medicines. Pivmecillinam and oesophageal injury. *Current Problems 19* 1987. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024426&RevisionSelectionMethod=LatestReleased (accessed 22/07/08)
2. Mortimer Ö, Wiholm B-E. Oesophageal injury associated with pivmecillinam tablets. *Eur J Clin Pharmacol* 1989; **37:** 605–7.
3. Anonymous. CSM warning on pivmecillinam. *Pharm J* 1987; **238:** 443.

Porphyria. Pivmecillinam has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Interactions

As for Benzylpenicillin, p.214.

Antimicrobial Action

Pivmecillinam has the antimicrobial activity of mecillinam (p.297) to which it is hydrolysed *in vivo*.

Pharmacokinetics

Pivmecillinam is well absorbed from the gastrointestinal tract and is rapidly hydrolysed to the active drug mecillinam (p.297), pivalic acid, and formaldehyde. The presence of food in the stomach does not appear to have a significant effect on absorption. Peak plasma concentrations of mecillinam of 5 micrograms/mL have been achieved 1 to 2 hours after a 400-mg dose of pivmecillinam.

About 45% of a dose may be excreted in the urine as mecillinam, mainly within the first 6 hours.

◊ References.

1. Heikkilä A, *et al.* The pharmacokinetics of mecillinam and pivmecillinam in pregnant and non-pregnant women. *Br J Clin Pharmacol* 1992; **33**; 629–33.

Uses and Administration

Pivmecillinam is the pivaloyloxymethyl ester of mecillinam (p.297), to which it is hydrolysed after oral dosage. It is used in the treatment of urinary-tract infections (p.199).

Doses of pivmecillinam have often been expressed in a confusing manner since no differentiation has been made between the hydrochloride, used in tablets, and the base, used in suspensions for oral use. Pivmecillinam 1.35 g and pivmecillinam hydrochloride 1.46 g are each equivalent to about 1 g of mecillinam.

Pivmecillinam should preferably be taken with food (see also Administration, under Adverse Effects and Precautions, above).

In acute uncomplicated cystitis, the initial adult dose is 400 mg orally followed by 200 mg three times daily for 8 doses. In chronic or recurrent bacteriuria, 400 mg may be given 3 or 4 times daily. The dose for children (weighing less than 40 kg) with urinary-tract infections is 20 to 40 mg/kg daily in 3 or 4 divided doses.

Pivmecillinam has been given with other beta lactams, particularly pivampicillin (p.316), to extend the spectrum of antimicrobial activity to Gram-positive organisms and because of reported synergism against Gram-negative bacteria *in vitro*.

For parenteral use, mecillinam is given.

◊ References.

1. Nicolle LE. Pivmecillinam in the treatment of urinary tract infections. *J Antimicrob Chemother* 2000; **46** (suppl S1): 35–9.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Selexid; ***Belg.:*** Selexid†; ***Canad.:*** Selexid†; ***Denm.:*** Selexid; ***Fin.:*** Selexid; ***Fr.:*** Selexid; ***Norw.:*** Selexid; ***NZ:*** Selexid; ***Port.:*** Selecid†; ***Swed.:*** Selexid; ***UK:*** Selexid.

Polymyxin B Sulfate *(rINNM)*

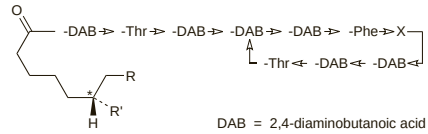
Polimiksin B Sülfat; Polimiksino B sulfatas; Polimixin-B-szulfát; Polimyksyny B siarczan; Polimyxini b sulfas; Polymyksiini-B-sulfaatti; Polymyxin B sulfat; Polymyxin B Sulphate *(BANM)*; Polymyxin-B-sulfát; Polymyxine B, sulfate de; Polymyxini B sulfas; Polymyxinum B Sulfas; Sulfato de polimixina B.

Полимиксина В Сульфат

CAS — 1404-26-8 (polymyxin B); 1405-20-5 (polymyxin B sulfate); 4135-11-9 (polymyxin B1); 34503-87-2 (polymyxin B2); 71140-58-4 (polymyxin B3).

ATC — A07AA05; J01XB02; S01AA18; S02AA11; S03AA03.

ATC Vet — QA07AA05; QJ01XB02; QS01AA18; QS02AA11; QS03AA03.



Polymyxin	R	R'	X	Mol. Formula
B1	CH	CH	-Leu	C H N O
B2	H	CH	-Leu	C H N O
B3	CH	H	-Leu	C H N O
B1-I	CH	CH	-Ile	C H N O

(polymyxin B)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.

Ph. Eur. 6.2 (Polymyxin B Sulphate). A mixture of the sulfates of polypeptides produced by the growth of certain strains of *Bacillus polymyxa* or obtained by any other means. A white or almost white, hygroscopic powder. Soluble in water; slightly soluble in alcohol. A 2% solution in water has a pH of 5.0 to 7.0. Store in airtight containers. Protect from light.

USP 31 (Polymyxin B Sulfate). The sulfate salt of a kind of polymyxin, a substance produced by the growth of *Bacillus polymyxa* (Bacillaceae), or a mixture of two or more such salts. A white to buff-coloured, powder, odourless or has a faint odour. It has a potency of not less than 6000 Polymyxin B units/mg, calculated on the dried substance. Freely soluble in water; slightly soluble in alcohol. pH of a 0.5% solution in water is between 5.0 and 7.5. Store in airtight containers. Protect from light.

Incompatibility. Incompatibility has been reported with many other drugs including antibacterials. Polymyxin B sulfate is rapidly inactivated by strong acids and alkalis.

Units

The second International Standard Preparation (1969) of polymyxin B sulfate contains 8403 units/mg.

NOTE. The available forms of polymyxin B sulfate are generally less pure than the International Standard Preparation. Doses have sometimes been stated in terms of pure polymyxin base; 100 mg of pure polymyxin B is considered to be equivalent to 1 million units (1 mega unit).