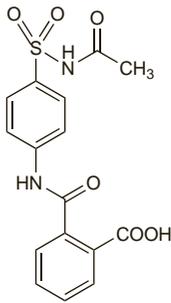


Phthalylsulfacetamide (BAN)

Phthalylsulphacetamide; Sulfanilacetamidum Phthalylum. 4'-(Acetylsulphamoyl)phthalanilic acid.
 $C_{16}H_{14}N_2O_6S = 362.4$.
 CAS — 131-69-1.

**Profile**

Phthalylsulfacetamide is a sulfonamide antibacterial. It is poorly absorbed when given orally and has been used for gastrointestinal infections.

Preparations

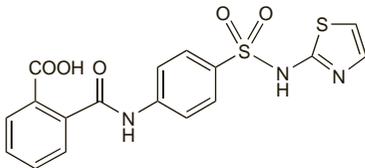
Proprietary Preparations (details are given in Part 3)

Multi-ingredient: **Braz:** Dimicin†; **Chile:** Enterol; Enterol Con Nifuroxácida; Kordinol Compuesto†; **Mex:** Facetin-D.

Phthalylsulfathiazole (BAN, rINN)

Ftalilsulfatiázol; Ftalilsulfatiázolas; Ftállisulfatiázol; Ftalysulfathiazol; Ftalysulfatiázol; Ftalylisulfatiázoli; Phtalysulfathiazol; Phthalazolium; Phthalylsulfathiazolum; Phthalylsulphathiazole; Sulfaphtalylthiazol. 4'-(1,3-Thiazol-2-ylsulphamoyl)phthalanilic acid.

Фталисульфатиазол
 $C_{17}H_{13}N_3O_5S_2 = 403.4$.
 CAS — 85-73-4.
 ATC — A07AB02.
 ATC Vet — QA07AB02.



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

Ph. Eur. 6.2 (Phthalylsulfathiazole). A white or yellowish-white crystalline powder. Practically insoluble in water; slightly soluble in alcohol and in acetone; freely soluble in dimethylformamide. Protect from light.

Profile

Phthalylsulfathiazole is a sulfonamide with properties similar to those of sulfamethoxazole (p.340). It is poorly absorbed, about 95% remaining in the intestine and only about 5% being slowly hydrolysed to sulfathiazole and absorbed.

It is given, with other antibacterials, for its antibacterial action in the gastrointestinal tract in the treatment of infections and for bowel decontamination before surgery.

Preparations

Proprietary Preparations (details are given in Part 3)

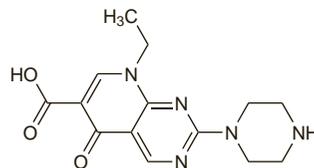
Multi-ingredient: **Arg:** Antidiar†; Carbon Tabs; Colistop; Colistoral†; Diarocalmol; Estreptocarbocetiazol; Gemipasmol†; Lefa Enteril†; Opocarbon; Opocler†; **Braz:** Parenterin; Sanadiar†; **Chile:** Imecol; Liracol; Testisan; **Mex:** Bontal; Ditayod; Sultroquin†; **Port:** Cloranpectinat†; **Spain:** Estreptoenterol†; **Thai:** Chlorotracin; Cocclia†; Disento; Endothaly; Medicoinf†.

Pipemidic Acid (BAN, rINN)

Acide Pipémidique; Ácido pipemídico; Acidum Pipemidicum; Acidum pipemidicum trihydricum; Kyselina pipemidová trihydrát; Pipemidihappo; Pipemidiinappotrihydraatti; Pipemidinsav-trihidrát; Pipemidinsyrtrihydrát; Pipémidique (acide) trihydraté; Pipemido rūgštis trihidratas; Pipemidsyra; Piperamic Acid; 1489-RB. 8-Ethyl-5,8-dihydro-5-oxo-2-(piperazin-1-yl)pyrido[2,3-d]pyrimidine-6-carboxylic acid.

Пипемидовая Кислота
 $C_{14}H_{17}N_5O_3 = 303.3$.
 CAS — 51940-44-4 (anhydrous pipemidic acid); 72571-82-5 (pipemidic acid trihydrate).
 ATC — J01MB04.
 ATC Vet — QJ01MB04.

The symbol † denotes a preparation no longer actively marketed



(anhydrous pipemidic acid)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn* (all as the trihydrate).

Ph. Eur. 6.2 (Pipemidic Acid Trihydrate). A pale yellow or yellow crystalline powder. Very slightly soluble in water. It dissolves in dilute solutions of acids and of alkali hydroxides. Protect from light.

Profile

Pipemidic acid is a 4-quinolone antibacterial with properties similar to those of nalidixic acid (p.303), but is more active *in vitro* against some bacteria, including *Pseudomonas aeruginosa*. It is used (as the trihydrate) in the treatment of urinary-tract infections in oral doses equivalent to 400 mg of the anhydrous substance twice daily.

Interactions. For the effect of pipemidic acid on the clearance of xanthines, see under Caffeine, p.1117, and Theophylline, p.1143.

Porphyria. Pipemidic acid is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg: Finuret; Memento; Priper; **Austria:** Deblaston; **Braz:** Balurot; Elofuran; Pipram; Pipuro; Uroxina; **Chile:** Nupraj†; Purid; Uropimide; **Fr:** Pipram; **Ger:** Deblaston; **Hong Kong:** Urotractin; **Indon:** Impresial; Urin-er; Urixin; Urotractin; Utrex; **Ital:** Acipem†; Biosoviran; Cistomid; Diperep; Faremid; Filtrax†; Pipeacid†; Pipecad; Pipefort; Pipemid; Pipram; Pipurin; Urodene; Uropimid; Urosan; Urosetici; Urotractin; **Jpn:** Dolcol; **Malaysia:** Urinix†; Urotractin†; **Mex:** Urinac†; Urinect†; Unipser; Uronovag; Uropimide; **Neth:** Pipram; **Philipp:** Urixin; **Pol:** Palin; Urolin; **Rus:** Palin (Палин); Pimidel (Пимидель); **S.Afr:** Deblaston; Septidron†; **Singapore:** Urotractin; **Spain:** Galusan; Nuri; Unisan; Uropipedil; **Thai:** Pipecid†; Urotractin.

Multi-ingredient: **Arg:** Priper Plus.

Piperacillin (BAN, rINN)

Piperacillin monohydrát; Piperacilina; Piperacilinas; Pipéracilline; Piperacillinum; Piperacillinum Monohydricum; Piperasillini. (6R)-6-[R-2-(4-Ethyl-2,3-dioxopiperazine-1-carboxamido)-2-phenylacetamido]penicillanic acid monohydrate; 3-Dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid monohydrate.

Пиперациллин
 $C_{23}H_{27}N_5O_7S_2 \cdot H_2O = 535.6$.
 CAS — 61477-96-1 (anhydrous piperacillin); 66258-76-2 (piperacillin monohydrate).
 ATC — J01CA12.
 ATC Vet — QJ01CA12.

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

Ph. Eur. 6.2 (Piperacillin). A white or almost white powder. Slightly soluble in water and in ethyl acetate; freely soluble in methyl alcohol.

USP 31 (Piperacillin). A white to off-white crystalline powder. Very slightly soluble in water; slightly soluble in ethyl acetate; sparingly soluble in isopropyl alcohol; very soluble in methyl alcohol.

Piperacillin Sodium (BANM, USAN, rINNM)

CL-227193; Natrii Piperacillinum; Piperacillin sodná sůl; Piperacilina sódica; Piperacilino natrio druska; Pipéracilline sodique; Piperacillin-nátrium; Piperacillinatrium natriicum; Piperacillinum; Piperacillinum natriicum; Piperacylina sodowa; Piperasillin Sodyum; Piperasillininatrium; T-1220.

Натрий Пиперациллин
 $C_{23}H_{26}N_5NaO_7S = 539.5$.
 CAS — 59703-84-3.
 ATC — J01CA12.
 ATC Vet — QJ01CA12.

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

Ph. Eur. 6.2 (Piperacillin Sodium). A white or almost white, hygroscopic powder. Freely soluble in water and in methyl alcohol; practically insoluble in ethyl acetate. A 10% solution in water has a pH of 5.0 to 7.0. Store in airtight containers.

USP 31 (Piperacillin Sodium). A white to off-white solid. Freely soluble in water and in alcohol. pH of a 40% solution in water is between 5.5 and 7.5. Store in airtight containers.

Incompatibility. Piperacillin sodium has been reported to be incompatible with aminoglycosides and sodium bicarbonate.

Stability. References.

- Zhang Y, Trissel LA. Stability of piperacillin and ticarcillin in AutoDose Infusion System bags. *Ann Pharmacother* 2001; **35**: 1360-3.

Adverse Effects and Precautions

As for Carbenicillin Sodium, p.216.

Prolongation of bleeding time has been less frequent and less severe with piperacillin than with carbenicillin.

Effects on the blood. References.

- Scheetz MH, *et al.* Systematic review of piperacillin-induced neutropenia. *Drug Safety* 2007; **30**: 295-306.

Hypersensitivity. In the mid 1980s there were reports of a relatively high incidence of adverse reactions to piperacillin, especially fever, in patients with cystic fibrosis.¹⁻³ However, the manufacturers⁴ considered such patients to be particularly prone to allergy and cited reactions with other semisynthetic penicillins including carbenicillin and azlocillin.

Similar apparent hypersensitivity reactions have been reported in patients taking high doses of piperacillin and other ureidopenicillins, over long periods for other indications,⁵ and with other penicillins in patients with cystic fibrosis,⁶ although piperacillin does appear to be most frequently implicated.⁶

- Stead RJ, *et al.* Adverse reactions to piperacillin in cystic fibrosis. *Lancet* 1984; **i**: 857-8.
- Strandvik B. Adverse reactions to piperacillin in patients with cystic fibrosis. *Lancet* 1984; **i**: 1362.
- Stead RJ, *et al.* Adverse reactions to piperacillin in adults with cystic fibrosis. *Thorax* 1985; **40**: 184-6.
- Brock PG, Roach M. Adverse reactions to piperacillin in cystic fibrosis. *Lancet* 1984; **i**: 1070-1.
- Lang R, *et al.* Adverse reactions to prolonged treatment with high doses of carbenicillin and ureidopenicillins. *Rev Infect Dis* 1991; **13**: 68-72.
- Pleasant RA, *et al.* Allergic reactions to parenteral beta-lactam antibiotics in patients with cystic fibrosis. *Chest* 1994; **106**: 1124-8.

Sodium content. Each g of piperacillin sodium contains about 1.85 mmol of sodium. As piperacillin sodium has a lower sodium content than carbenicillin sodium, hypernatraemia and hypokalaemia are less likely to occur.

Interactions

As for Benzylpenicillin, p.214.

Neuromuscular blockers. Piperacillin and other ureidopenicillins are reported to prolong the action of competitive muscle relaxants such as *vecuronium* (see Atracurium, p.1903).

Antimicrobial Action

Piperacillin has a similar antimicrobial action to carbenicillin (p.216) and ticarcillin (p.352), but is active against a wider range of Gram-negative organisms, including *Klebsiella pneumoniae*. It is also generally more active *in vitro*, especially against *Pseudomonas aeruginosa* and the Enterobacteriaceae, against Gram-positive *Enterococcus faecalis*, and possibly against *Bacteroides fragilis*. There is, however, an inoculum effect, i.e. minimum inhibitory concentrations of piperacillin increase with the size of the inoculum.

Combinations of piperacillin and aminoglycosides have been shown to be synergistic *in vitro* against *Ps. aeruginosa* and Enterobacteriaceae. The effect of using piperacillin with other beta lactams has been less predictable. The activity of piperacillin against some organisms, resistant because of the production of beta-lactamases, may be restored by tazobactam, a beta-lactamase inhibitor. Such organisms include beta-lactamase-producing strains of staphylococci, *Escherichia coli*, *Haemophilus influenzae*, and *Bacteroides* spp.; the activity of piperacillin against *Ps. aeruginosa* is not enhanced by tazobactam.

Resistance has developed in *Ps. aeruginosa* during treatment with piperacillin, especially when used alone. There may be some cross-resistance with other antipseudomonal penicillins.

◇ References.

- Higashitani F, *et al.* Inhibition of β-lactamases by tazobactam and in-vitro antibacterial activity of tazobactam combined with piperacillin. *J Antimicrob Chemother* 1990; **25**: 567-74.
- Mehtar S, *et al.* The in-vitro activity of piperacillin/tazobactam, ciprofloxacin, ceftazidime and imipenem against multiple resistant Gram-negative bacteria. *J Antimicrob Chemother* 1990; **25**: 915-19.
- Kempers J, MacLaren DM. Piperacillin/tazobactam and ticarcillin/clavulanic acid against resistant Enterobacteriaceae. *J Antimicrob Chemother* 1990; **26**: 598-9.