drug costs. However, thioacetazone is now used as a second-line drug for multidrug-resistant tuberculosis and is not generally recommended for use in HIV-positive patients because of the risk of severe adverse reactions (but see Effects on the Skin, above).

Thioacetazone has been used in the treatment of leprosy (p.176), but WHO now considers that such use is no longer justified.

In the treatment of tuberculosis, thioacetazone has been given orally in doses of 150 mg daily or 2.5 mg/kg daily. Daily use is recommended as the drug is less effective when given intermittently.

Preparations

Proprietary Preparations (details are given in Part 3)
Turk.: Citazon.

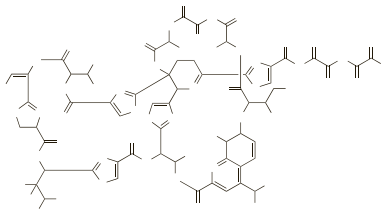
Multi-ingredient: ***India:*** Isokin-T Forte.

Thiostrepton

Thiostreptonum; Tiostreptón; Tiostrepton; Tiostreptoni.

Тиострептон

$C_{72}H_{85}N_{19}O_{18}S_5$ = 1664.9.
CAS — 1393-48-2.



Pharmacopoeias. In *US* for veterinary use only.
USP 31 (Thiostrepton). An antibacterial substance produced by the growth of strains of *Streptomyces azureus*. It has a potency of not less than 900 units/mg, calculated on the dried basis. A white to off-white crystalline solid. Practically insoluble in water, in the lower alcohols, in nonpolar organic solvents, and in dilute aqueous acids or alkalis; soluble in glacial acetic acid, in chloroform, in dimethylformamide, in dimethyl sulfoxide, in dioxan, and in pyridine. Store in airtight containers.

Profile

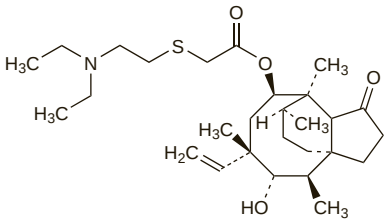
Thiostrepton is an antibacterial produced by strains of *Streptomyces azureus*. It is included in topical antibacterial preparations for veterinary use.

Tiamulin Fumarate *(BANM, USAN, rINNM)*

Fumarato de tiamulina; 81723-hfu; SQ-14055 (tiamulin); SQ-22947 (tiamulin fumarate); Tiamuliinivetyfumaraatti; Tiamuline, Fumarate de; Tiamuline, hydrogénofumarate de; Tiamulin-fumarát; Tiamulini Fumaras; Tiamulini hydrogenofumaras; Tiamulinvätefumarat. 11-Hydroxy-6,7,10,12-tetramethyl-1-oxo-10-vinylperhydro-3a,7-pentanoinden-8-yl (2-diethylaminoethylthio)acetate hydrogen fumarate.

Тиамулина Фумарат

$C_{28}H_{47}NO_4S,C_4H_4O_4$ = 609.8.
CAS — 55297-95-5 (tiamulin); 555297-96-6 (tiamulin fumarate).



(tiamulin)

Pharmacopoeias. In *Eur.* (see p.vii) and *US* for veterinary use only. *Eur.* and *US* also include tiamulin for veterinary use only.
Ph. Eur. 6.2 (Tiamulin Hydrogen Fumarate for Veterinary Use; Tiamulin Hydrogen Fumarate BP(Vet) 2008). A white or light yellow, crystalline powder. Soluble in water and in methyl alcohol; freely soluble in dehydrated alcohol. A 1% solution in water has a pH of 3.1 to 4.1. Protect from light.
USP 31 (Tiamulin Fumarate). A 1.0% solution in water has a pH of 3.1 to 4.1. Store in airtight containers. Protect from light.

Profile

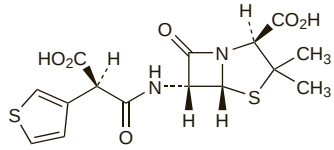
Tiamulin fumarate is an antibacterial used in veterinary medicine.

Ticarcillin Monosodium *(BANM, rINNM)*

Ticarcilina monosódica; Ticarcilline Monosodique; Ticarcillinum Mononatricum. Monosodium (6*R*)-6-[2-carboxy-2-(3-thienyl)acetamido]penicillanate monohydrate.

Мононатрий Тикарциллин

$C_{15}H_{15}N_2NaO_6S_2,H_2O$ = 424.4.
CAS — 34787-01-4 (ticarcillin); 3973-04-4 (ticarcillin); 74682-62-5 (ticarcillin monosodium).



(ticarcillin)

Pharmacopoeias. In *US*.
USP 31 (Ticarcillin Monosodium). Store in airtight containers.

Ticarcillin Sodium *(BANM, rINNM)*

BRL-2288; Natrii Ticarcillinum; Ticarcilina sódica; Ticarcillin Disodium *(USAN)*; Ticarcilline sodique; Ticarcillinum Dinatricum; Ticarcillinum natricum; Tikarcilin disodná sůl; Tikarcilin sodná sůl; Tikarcilino natrio druska; Tikarcillinnatrium; Tikarcillin-nátrium; Tikarsilliininatrium; Tykarcylina sodowa. Disodium (6*R*)-6-[2-carboxy-2-(3-thienyl)acetamido]penicillanate.

Натрий Тикарциллин

$C_{15}H_{14}N_2Na_2O_6S_2$ = 428.4.
CAS — 4697-14-7; 29457-07-6.
ATC — J01CA13.
ATC Vet — QJ01CA13.

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
Ph. Eur. 6.2 (Ticarcillin Sodium). A white or slightly yellow, hygroscopic powder. Freely soluble in water; soluble in methyl alcohol. A 5% solution in water has a pH of 5.5 to 7.5. Store in airtight containers at a temperature of 2° to 8°.
USP 31 (Ticarcillin Disodium). A white to pale yellow powder or solid. 1 mg of monograph substance has a potency equivalent to not less than 800 micrograms of ticarcillin, calculated on the anhydrous basis. Freely soluble in water. A 1% solution in water has a pH of 6.0 to 8.0. Store in airtight containers.

Incompatibility. Ticarcillin sodium has been reported to be incompatible with aminoglycosides.

References.

1. Swenson E, *et al.* Compatibility of ticarcillin disodium clavulanate potassium with commonly used intravenous solutions. *Curr Ther Res* 1990; **48**: 385–94.

Stability. References.

1. 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.

Cholestatic jaundice and hepatitis have been reported when ticarcillin was used with clavulanic acid; the clavulanic acid component has been implicated.

Ticarcillin should be given with caution to patients with renal impairment.

Breast feeding. Although ticarcillin is distributed into breast milk in small amounts,[1] no adverse effects have been seen in breast-fed infants and the American Academy of Pediatrics considers that it is usually compatible with breast feeding.[2]

1. von Kobyletzki D, *et al.* Ticarcillin serum and tissue concentrations in gynecology and obstetrics. *Infection* 1983; **11:** 144–9.
2. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 28/05/04)

Effects on the bladder. The Australian Adverse Drug Reactions Advisory Committee had received 15 reports of haemorrhagic cystitis associated with ticarcillin or ticarcillin-clavulanic acid between 1980 and June 2002, mainly in paediatric cystic fibrosis patients.[1] Almost all patients recovered quickly after the withdrawal of ticarcillin.

1. Adverse Drug Reactions Advisory Committee (ADRAC). Haemorrhagic cystitis with ticarcillin in cystic fibrosis patients. *Aust Adverse Drug React Bull* 2002; **21:** 6–7. Also available at: http://www.tga.gov.au/adr/aadrb/aadr0206.pdf (accessed 29/07/08)

Effects on the liver. Cholestatic jaundice and hepatitis have been associated with combined preparations of a penicillin and clavulanic acid (see Amoxicillin, p.202) and 2 cases had been reported to the UK CSM with ticarcillin and clavulanic acid.[1] It appeared that the clavulanic acid was probably responsible.

1. Committee on Safety of Medicines/Medicines Control Agency. Cholestatic jaundice with co-amoxiclav. *Current Problems* 1993; **19:** 2. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024454&RevisionSelectionMethod=LatestReleased (accessed 22/07/08)

Sodium content. Each g of ticarcillin sodium contains about 4.7 mmol of sodium.

Interactions

As for Benzylpenicillin, p.214.

Antimicrobial Action

Ticarcillin is bactericidal and has a mode of action and range of activity similar to that of carbenicillin (p.216), but is reported to be 2 to 4 times more active against *Pseudomonas aeruginosa*.

Combinations of ticarcillin and aminoglycosides have been shown to be synergistic *in vitro* against *Ps. aeruginosa* and Enterobacteriaceae.

The activity of ticarcillin against organisms usually resistant because of the production of certain beta-lactamases is enhanced by clavulanic acid, a beta-lactamase inhibitor. Such organisms have included staphylococci, many Enterobacteriaceae, *Haemophilus influenzae*, and *Bacteroides* spp.; the activity of ticarcillin against *Ps. aeruginosa* is not enhanced by clavulanic acid. Resistance to ticarcillin with clavulanic acid has been reported.

There is cross-resistance between carbenicillin and ticarcillin.

◊ References.

1. Pulverer G, *et al.* In-vitro activity of ticarcillin with and without clavulanic acid against clinical isolates of Gram-positive and Gram-negative bacteria. *J Antimicrob Chemother* 1986; **17** (suppl C): 1–5.
2. Masterton RG, *et al.* Timentin resistance. *Lancet* 1987; **ii:** 975–6.
3. Fass RJ, Prior RB. Comparative in vitro activities of piperacillin-tazobactam and ticarcillin-clavulanate. *Antimicrob Agents Chemother* 1989; **33:** 1268–74.
4. Kempers J, MacLaren DM. Piperacillin/tazobactam and ticarcillin/clavulanic acid against resistant Enterobacteriaceae. *J Antimicrob Chemother* 1990; **26:** 598–9.
5. Klepser ME, *et al.* Comparison of the bactericidal activities of piperacillin-tazobactam, ticarcillin-clavulanate, and ampicillin-sulbactam against clinical isolates of Bacteroides fragilis, Enterococcus faecalis, Escherichia coli, and Pseudomonas aeruginosa. *Antimicrob Agents Chemother* 1997; **41:** 435–9.

Pharmacokinetics

Ticarcillin is not absorbed from the gastrointestinal tract. After intramuscular injection of 1 g peak plasma concentrations in the range of 22 to 35 micrograms/mL are achieved after 0.5 to 1 hour. About 50% of ticarcillin in the circulation is bound to plasma proteins. A plasma half-life of 70 minutes has been reported. A shorter half-life in patients with cystic fibrosis (about 50 minutes in one study) has been attributed to increased renal and non-renal elimination. The half-life is prolonged in neonates and also in patients with renal impairment, especially if hepatic function is also impaired. A half-life of about 15 hours has been reported in severe renal impairment.

Distribution of ticarcillin in the body is similar to that of carbenicillin. Relatively high concentrations have been reported in bile, but ticarcillin is excreted principally by glomerular filtration and tubular secretion. Concentrations of 2 to 4 mg/mL are achieved in the urine after the intramuscular injection of 1 or 2 g. Ticarcillin is metabolised to a limited extent. Up to 90% of a dose is excreted unchanged in the urine, mostly within 6 hours after a dose. Plasma concentrations are enhanced by probenecid.

Ticarcillin is removed by haemodialysis and, to some extent, by peritoneal dialysis.

Ticarcillin crosses the placenta and small amounts are distributed into breast milk.