13. Isla A, *et al.* Meropenem and continuous renal replacement therapy: in vitro permeability of 2 continuous renal replacement therapy membranes and influence of patient renal function on the pharmacokinetics in critically ill patients. *J Clin Pharmacol* 2005; **45:** 1294–1304.
14. Novelli A, *et al.* Pharmacokinetic evaluation of meropenem and imipenem in critically ill patients with sepsis. *Clin Pharmacokinet* 2005; **44:** 539–49.
15. Du X, *et al.* Population pharmacokinetics and pharmacodynamics of meropenem in pediatric patients. *J Clin Pharmacol* 2006; **46:** 69–75.

Uses and Administration

Meropenem is a carbapenem beta-lactam antibacterial with actions and uses similar to those of imipenem (p.287). It is more stable to renal dehydropeptidase I than imipenem and need not be given with an enzyme inhibitor such as cilastatin. It is used in the treatment of susceptible infections including intra-abdominal infections, gynaecological infections, meningitis, respiratory-tract infections (including in cystic fibrosis patients), septicaemia, skin and skin structure infections, urinary-tract infections, and infections in immunocompromised patients. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Meropenem is given intravenously as the trihydrate, but doses are expressed in terms of the amount of anhydrous meropenem; 1.14 g of meropenem trihydrate is equivalent to about 1 g of anhydrous meropenem. It is given by slow injection over 3 to 5 minutes or by infusion over 15 to 30 minutes in a usual adult dose of 0.5 to 1 g every 8 hours. A dose of 2 g every 8 hours is given for meningitis; doses of up to 2 g every 8 hours have also been used in cystic fibrosis. For details of reduced doses in renal impairment, see below.

For details of doses in infants and children, see below.

◊ Reviews.

1. Wiseman LR, *et al.* Meropenem: a review of its antibacterial activity, pharmacokinetic properties and clinical efficacy. *Drugs* 1995; **50:** 73–101.
2. Finch RG, *et al.* eds. Meropenem: focus on clinical performance. *J Antimicrob Chemother* 1995; **36** (suppl A): 1–223.
3. Hellinger WC, Brewer NS. Carbapenems and monobactams: imipenem, meropenem, and aztreonam. *Mayo Clin Proc* 1999; **74:** 420–34.
4. Hurst M, Lamb HM. Meropenem: a review of its use in patients in intensive care. *Drugs* 2000; **59:** 653–80.
5. Lowe MN, Lamb HM. Meropenem: an updated review of its use in the management of intra-abdominal infections. *Drugs* 2000; **60:** 619–46.
6. Edwards SJ, *et al.* Systematic review comparing meropenem with imipenem plus cilastatin in the treatment of severe infections. *Curr Med Res Opin* 2005; **21:** 785–94.
7. Linden P. Safety profile of meropenem: an updated review of over 6000 patients treated with meropenem. *Drug Safety* 2007; **30:** 657–68.
8. Baldwin CM, *et al.* Meropenem: a review of its use in the treatment of serious bacterial infections. *Drugs* 2008; **68:** 803–38.

Administration in children. Use of meropenem is licensed in both the UK and the USA for infants and children over 3 months of age and weighing less than 50 kg. The usual dose is 10 to 20 mg/kg every 8 hours. A dose of 40 mg/kg is given every 8 hours for meningitis; doses of 25 to 40 mg/kg every 8 hours have been used in children aged 4 to 18 years with cystic fibrosis.

In addition, the *BNFC* suggests the following doses for those under 3 months of age:

- neonates under 7 days of age: 20 mg/kg every 12 hours (or 40 mg/kg every 12 hours in severe infections and in meningitis)
- neonates 7 to 28 days of age: 20 mg/kg every 8 hours (or 40 mg/kg every 8 hours in severe infections and in meningitis)
- infants 1 to 3 months of age: 10 mg/kg every 8 hours (or 20 mg/kg every 8 hours in severe infections; 40 mg/kg every 8 hours in meningitis)

Administration in renal impairment. Doses of meropenem should be reduced in patients with renal impairment. The following doses may be given to adults based on creatinine clearance (CC):

- CC 26 to 50 mL/minute: the usual dose given every 12 hours
- CC 10 to 25 mL/minute: one-half the usual dose every 12 hours
- CC less than 10 mL/minute: one-half the usual dose every 24 hours
- haemodialysis patients: the usual dose after the dialysis session

Preparations

USP 31: Meropenem for Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Meroefectil; Merotenk; Merozen; Merpem; Zeropenem†; ***Austral.:*** Merrem; ***Austria:*** Optinem; ***Belg.:*** Meronem; ***Braz.:*** Meronem; Meroxil†; ***Canad.:*** Merrem; ***Chile:*** Meronem; ***Cz.:*** Meronem; ***Denm.:*** Meronem; ***Fin.:*** Meronem; ***Ger.:*** Meronem; ***Gr.:*** Meronem; ***Hong Kong:*** Meronem; ***Hung.:*** Meronem; ***India:*** Meronem; ***Indon.:*** Merofen; Meronem; Ronem; Tripenem; ***Irl.:*** Meronem; ***Israel:*** Meronem; ***Ital.:*** Merrem; ***Jpn:*** Meropen; ***Malaysia:*** Meronem; ***Mex.:*** Merrem; ***Neth.:*** Meronem; ***Norw.:*** Meronem; ***NZ:*** Merrem; ***Philipp.:*** Meronem; ***Pol.:*** Meronem; ***Port.:*** Meronem; ***Rus.:*** Meronem (Меронем); ***S.Afr.:*** Meronem; ***Singapore:*** Meronem; ***Spain:*** Meronem; ***Swed.:*** Meronem; ***Switz.:*** Meronem; ***Thai.:*** Meronem; ***Turk.:*** Meronem; ***UK:*** Meronem; ***USA:*** Merrem; ***Venez.:*** Meronem.

Metampicillin Sodium *(rINNM)*

Metampicilina sódica; Métampicilline Sodique; Natrii Metampicillinum. Sodium (6*R*)-6-(D-2-methyleneamino-2-phenylacetamido)penicillanate.

Натрий Метампициллин

$C_{17}H_{18}N_3NaO_4S$ = 383.4.
CAS — 6489-97-0 (metampicillin); 6489-61-8 (metampicillin sodium).
ATC — J01CA14.
ATC Vet — QJ01CA14.

Profile

Metampicillin has actions and uses similar to those of ampicillin (p.204).

After oral doses it is almost completely hydrolysed to ampicillin. When given parenterally, however, a proportion of the dose exists in the circulation as unchanged metampicillin which has some antibacterial activity of its own.

Preparations

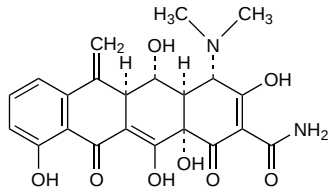
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Arg.:*** Gentocelina†.

Methacycline *(BAN, USAN)*

Metacycline *(pINN)*; GS-2876; Metaciclina; Métacycline; Metacyclinum; Metacyklin; Metasykliini. (4*S*,4a*R*,5*S*,5a*R*,6*S*,12a*S*)-4-Dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methylene-1,11-dioxonaphthacene-2-carboxamide; 6-Demethyl-6-deoxy-5β-hydroxy-6-methylenetetracycline.

Метациклин

$C_{22}H_{22}N_2O_8$ = 442.4.
CAS — 914-00-1.
ATC — J01AA05.
ATC Vet — QJ01AA05.



Methacycline Hydrochloride *(BANM)*

Metacycline Hydrochloride *(pINNM)*; Hidrocloruro de metaciclina; Métacycline, Chlorhydrate de; Metacyclini Chloridum; Metacyclini Hydrochloridum; Metacykliny chlorowodorek; Méthylènecycline Chlorhydrate; 6-Methyleneoxytetracycline Hydrochloride.

Метациклина Гидрохлорид

$C_{22}H_{22}N_2O_8$,HCl = 478.9.
CAS — 3963-95-9.
ATC — J01AA05.
ATC Vet — QJ01AA05.

Pharmacopoeias. In *Chin.*, *Pol.*, and *US.*

USP 31 (Methacycline Hydrochloride). A yellow to dark yellow crystalline powder. Soluble 1 in 100 of water, 1 in 300 of alcohol, and 1 in 25 of 0.1N sodium hydroxide; very slightly soluble in chloroform and in ether. pH of a solution in water containing the equivalent of methacycline 1% is between 2.0 and 3.0. Store in airtight containers. Protect from light.

Profile

Methacycline is a tetracycline derivative with uses similar to those of tetracycline (p.347). Like demeclocycline, it is excreted more slowly than tetracycline and effective blood concentrations are maintained for longer periods; the plasma elimination half-life is about 14 hours.

Methacycline hydrochloride is given orally in a usual adult dose of 600 mg daily in 2 divided doses, preferably 1 hour before or 2 hours after meals.

Preparations

USP 31: Methacycline Hydrochloride Capsules; Methacycline Hydrochloride Oral Suspension.

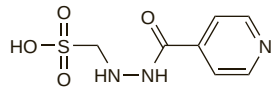
Proprietary Preparations (details are given in Part 3)
Fr.: Lysocline; Physiomycine; ***Ital.:*** Esarondil; Rotilen; Stafilon.

Methaniazide *(rINN)*

Isoniazid Mesylate; Isoniazid Methanesulfonate; Metaniazida; Méthaniazide; Methaniazidum. 2-Isonicotinoylhydrazinomethanesulphonic acid.

Метаниазид

$C_7H_9N_3O_4S$ = 231.2.
CAS — 13447-95-5 (methaniazide); 6059-26-3 (methaniazide calcium); 3804-89-5 (methaniazide sodium).



Profile

Methaniazide is a derivative of isoniazid (p.288). It has been used orally and by injection as the calcium and sodium salts respectively in the treatment of tuberculosis.

Preparations

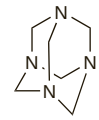
Proprietary Preparations (details are given in Part 3)
Austria: Neo-Tizide; ***India:*** Erbazide†.
Multi-ingredient: ***India:*** Strepto-Erbazide†.

Methenamine *(rINN)*

Aminoform; E239; Esametilentetrammina; Esammina; Formine; Heksamin; Hexamethylenamine; Hexamine; Metenamiini; Meténamin; Metenamin; Metenamina; Metenaminas; Metenammina; Methenamin; Méthénamine; Methenaminum; Urotropine. Hexamethylenetetramine; 1,3,5,7-Tetraazatricyclo[3.3.1.1^{3,7}]decane.

Метенамин

$C_6H_{12}N_4$ = 140.2.
CAS — 100-97-0.
ATC — J01XX05.
ATC Vet — QJ01XX05.



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

Ph. Eur. 6.2 (Methenamine). A white, or almost white, crystalline powder or colourless crystals. Freely soluble in water; soluble in alcohol and in dichloromethane. Protect from light.

USP 31 (Methenamine). Colourless, practically odourless, lustrous crystals or white crystalline powder. Soluble 1 in 1.5 of water, 1 in 12.5 of alcohol, 1 in 10 of chloroform, and 1 in 320 of ether. Its solutions are alkaline to litmus.

Methenamine Hippurate *(BAN, USAN, rINNM)*

Heksamin Hippurat; Hexamine Hippurate; Hipurato de metenamina; Metenamin Hippurat; Méthénamine, Hippurate de; Methenamini Hippuras. Hexamethylenetetramine hippurate.

Метенамина Гиппурат

$C_6H_{12}N_4$,$C_9H_9NO_3$ = 319.4.
CAS — 5714-73-8.
ATC — J01XX05.
ATC Vet — QJ01XX05.

Pharmacopoeias. In *US.*

Methenamine Mandelate *(rINNM)*

Heksamin Mandelat; Hexamine Amygdalate; Hexamine Mandelate; Mandelato de metenamina; Metenamin Mandelat; Méthénamine, Mandelate de; Methenamini Mandelas. Hexamethylenetetramine mandelate.

Метенамина Манделат

$C_6H_{12}N_4$,$C_8H_8O_3$ = 292.3.
CAS — 587-23-5.
ATC — J01XX05.
ATC Vet — QJ01XX05.

Pharmacopoeias. In *US.*

USP 31 (Methenamine Mandelate). A white, practically odourless crystalline powder. Very soluble in water; soluble 1 in 10 of alcohol, 1 in 20 of chloroform, and 1 in 350 of ether. Its solutions have a pH of about 4.

Adverse Effects and Precautions

Methenamine and its salts are generally well tolerated but may cause gastrointestinal disturbances such as nausea, vomiting, and diarrhoea. Skin rashes, pruritus, and occasionally other hypersensitivity reactions, may occur.

Comparatively large amounts of formaldehyde may be formed during prolonged use or when large doses are given. This may produce irritation and inflammation of the urinary tract, especially the bladder, as well as painful and frequent micturition, hae-

maturia, and proteinuria. The effect of the formaldehyde may be reduced by alkalinising drugs, such as sodium bicarbonate, or large quantities of water, but it is then less effective.

Methenamine and its salts are contra-indicated in patients with hepatic impairment because of the liberation of ammonia in the gastrointestinal tract. Although methenamine itself is not contra-indicated in renal impairment, its salts should be avoided in severe impairment because of the risk of mandelate or hippurate crystalluria. They should also be avoided in patients with severe dehydration, metabolic acidosis, or gout.

Interference with laboratory estimations for catecholamines, 17-hydroxycorticosteroids, and oestrogens in the urine has been reported.

Interactions

The use of drugs that alkalinise the urine, including some antacids, potassium citrate, and diuretics such as acetazolamide or the thiazides, should be avoided because the activation of methenamine to formaldehyde may be inhibited (but see above).

Use of methenamine with sulfonamides may increase the risk of crystalluria since methenamine requires low urinary pH for its effect, at which sulfonamides and their metabolites are poorly soluble; methenamine may also form poorly soluble compounds with some sulfonamides.

Antimicrobial Action

Methenamine owes its antibacterial properties to formaldehyde, a non-specific bactericide, which is slowly liberated by hydrolysis at acid pH. Most Gram-positive and Gram-negative organisms and fungi are susceptible. Hippuric and mandelic acids have some antibacterial activity *in vitro*, but their contribution to the antibacterial action of the salts *in vivo*, beyond assisting the maintenance of low urinary pH, is uncertain. Urea-splitting organisms such as *Proteus* and some *Pseudomonas* spp. tend to increase urinary pH and inhibit the release of formaldehyde, thereby decreasing the effectiveness of methenamine. Use with acetohydroxamic acid, a potent inhibitor of bacterial urease, has been suggested for urinary infections due to these organisms. True resistance to formaldehyde does not appear to be a problem in clinical use.

Pharmacokinetics

Methenamine is readily absorbed from the gastrointestinal tract and widely distributed in the body. Under acid conditions methenamine is slowly hydrolysed to formaldehyde and ammonia: about 10 to 30% of an oral dose may be converted in the stomach unless it is given as an enteric-coated preparation. Almost no hydrolysis of methenamine takes place at physiological pH, and it is therefore virtually inactive in the body. The half-life is reported to be about 4 hours. Methenamine is rapidly and almost completely eliminated in the urine, and provided this is acidic (preferably below pH 5.5) bactericidal concentrations of formaldehyde are achieved. Because of the time taken for hydrolysis, however, these are not achieved until the urine reaches the bladder, with peak concentrations occurring up to 2 hours after an oral dose. Absorption, and hence excretion, may be somewhat delayed in patients given enteric-coated formulations.

Methenamine crosses the placenta and small amounts may be distributed into breast milk.

The mandelate and hippurate moieties are also rapidly absorbed and are excreted in urine by tubular secretion as well as glomerular filtration.

Uses and Administration

Methenamine is used, usually as the hippurate or mandelate, in the prophylaxis and treatment of chronic or recurrent, uncomplicated, lower urinary-tract infections and asymptomatic bacteriuria. It has been considered suitable for long-term use because acquired resistance does not appear to develop.

Methenamine and its salts should not be used in upper urinary-tract infections because it is eliminated too rapidly to exert an effect, nor in acute urinary infections. It is only active in acidic urine, when formaldehyde is released, and although hippuric or mandelic acid helps to acidify the urine, ammonium chloride or ascorbic acid may be tried. If urea-splitting bacteria such as *Proteus* or some *Pseudomonas* spp. are present they may produce so much ammonia that the urine cannot be acidified (see also Antimicrobial Action, above).

The usual oral adult dose of methenamine or methenamine mandelate is 1 g given four times daily. Methenamine hippurate is given orally in a usual dose of 1 g twice daily; the dose may be increased to three times daily in catheterised patients.

For details of doses in children, see below.

Methenamine has been used topically in deodorant preparations, since in the presence of acid sweat it liberates formaldehyde. Methenamine calcium thiocyanate has been used in combination preparations for upper respiratory-tract disorders.

◊ Reviews.

1. Schiøtz HA, Guttu K. Value of urinary prophylaxis with methenamine in gynecologic surgery. *Acta Obstet Gynecol Scand* 2002; **81:** 743–6.
2. Lee BB, *et al.* Methenamine hippurate for preventing urinary tract infections. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2007 (accessed 11/01/08).

Administration in children. In the USA, the usual recommended oral dose of methenamine mandelate in children up to 6 years old is about 18 mg/kg given four times daily; those aged 6 to 12 years may be given methenamine or methenamine mandelate 500 mg four times daily.

In the UK, methenamine hippurate may be given in a usual oral dose of 500 mg twice daily in children aged 6 to 12 years. Doses of up to 1 g twice daily have been given in the USA.

Preparations

USP 31: Methenamine Elixir; Methenamine Hippurate Tablets; Methenamine Mandelate Delayed-release Tablets; Methenamine Mandelate for Oral Solution; Methenamine Mandelate Oral Suspension; Methenamine Mandelate Tablets; Methenamine Tablets.

Proprietary Preparations (details are given in Part 3)
Austral.: Hiprex; ***Austria:*** Hiprex; ***Belg.:*** Hiprex†; ***Canad.:*** Dehydral; Hiprex; Mandelamine; Urasal†; ***Denm.:*** Geasalol†; Haiprex; ***Fin.:*** Hipeksal; Hiprex; ***Ger.:*** Antihydral; Urotractan; ***Irl.:*** Hiprex†; ***Israel:*** Hiprex; ***Mex.:*** Bioran; ***Neth.:*** Reflux; ***Norw.:*** Hiprex; ***NZ:*** Hiprex; ***Philipp.:*** Hiprex; ***Pol.:*** Stoppot; ***S.Afr.:*** Hippramine†; Mandelamine†; ***Swed.:*** Hiprex; ***Switz.:*** Antihydral; ***Turk.:*** Helpa; Hippurin; Manuprin; Neturone; Purinol; Uron; ***UK:*** Hiprex; ***USA:*** Hiprex; Mandelamine; Urex; ***Venez.:*** Mandelamine.

Multi-ingredient: ***Arg.:*** Calculina†; ***Belg.:*** Carbobel; Mictasol-P; Mictasol†; ***Braz.:*** Abacateirol†; Acridin; Cystex; Sepurin; Urodonal†; ***Chile:*** Uroknop; ***Fr.:*** Mictasol; Pedi-Relax Anti-Transpirant; ***Ger.:*** Antihydral M†; ***Hong Kong:*** Antihydral M†; ***Hung.:*** Bilagit†; ***Mex.:*** Furanton†; ***Pol.:*** Dezorol; Pedipur; Urosal; ***Turk.:*** Helmobleu; ***USA:*** Atrosept; Cystex; Dolsed†; MHP-A; MSP-Blu; Prosed/DS; Trac Tabs 2X†; UAA; Urelle; Uretron; Uridon Modified†; Urimar-T; Urimax; Urised; Uriseptic; UriSym†; Uritact; Uro Blue; Urogesic Blue; Utira; ***Venez.:*** Azo-Mandelamine.

Meticillin Sodium *(rINNM)*

BRL-1241; Dimethoxyphenecillin Sodium; Dimethoxyphenyl Penicillin Sodium; Methicillin Sodium *(BANM, USAN)*; Meticilina sódica; Méticilline Sodique; Meticillinum Natricum; Natrii Meticillinum; SQ-16123; X-1497. Sodium (6*R*)-6-(2,6-dimethoxybenzamido)penicillanate monohydrate.

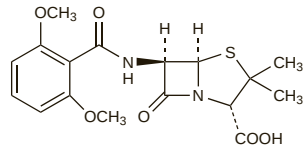
Натрий Метициллин

$C_{17}H_{19}N_2NaO_6S,H_2O$ = 420.4.

CAS — 61-32-5 (meticillin); 132-92-3 (anhydrous meticillin sodium); 7246-14-2 (meticillin sodium monohydrate).

ATC — J01CF03.

ATC Vet — QJ01CF03.



(meticillin)

Incompatibility. Meticillin sodium has been reported to be incompatible with aminoglycosides and a number of other antimicrobials. It has also been reported to be incompatible with acidic and alkaline drugs.

Adverse Effects and Precautions

As for Benzylpenicillin, p.213.

Meticillin is the penicillin most commonly associated with acute interstitial nephritis.

Effects on the kidneys. References.

1. Sanjad SA, *et al.* Nephropathy, an underestimated complication of methicillin therapy. *J Pediatr* 1974; **84:** 873–7.
2. Galpin JE, *et al.* Acute interstitial nephritis due to methicillin. *Am J Med* 1978; **65:** 756–65.

Sodium content. Each g of meticillin sodium contains about 2.4 mmol of sodium.

Interactions

As for Benzylpenicillin, p.214.

Antimicrobial Action

Meticillin has a mode of action similar to that of benzylpenicillin (p.214) but it is resistant to staphylococcal penicillinase. There is evidence that meticillin is more stable to staphylococcal penicillinase than the other penicillinase-resistant penicillins.

Meticillin is active against both penicillinase-producing and non-penicillinase-producing staphylococci, and also against *Streptococcus pyogenes* (group A beta-haemolytic streptococci), *Str. pneumoniae*, and some viridans streptococci. Its activity against penicillin-sensitive staphylococci and streptococci is less than that of benzylpenicillin. It is virtually ineffective against *Enterococcus faecalis*.

Resistance of staphylococci to meticillin is due to the expression of an altered penicillin-binding protein and is not dependent on penicillinase production. There is cross-resistance with other penicillins, including the penicillinase-resistant penicillins cloxacillin, dicloxacillin, flucloxacillin, nafcillin, and oxacillin, and with the cephalosporins. Meticillin-resistant staphylococci are also frequently resistant to other antibacterials, including aminoglycosides, chloramphenicol, ciprofloxacin, clindamycin, erythromycin, and tetracycline. The incidence of such resistance has varied considerably. However, both endemic (restricted to one hospital) and epidemic (affecting more than one hospital) strains of meticillin-resistant *Staphylococcus aureus* (MRSA) are now recognised and infections are a problem in many hospitals.

There have been fewer studies on coagulase-negative staphylococci, but patterns of meticillin resistance in *Staph. epidermidis* are similar to those for MRSA and the frequency of resistance may be higher.

For further details on meticillin-resistant staphylococci and the management of infections, see under Staphylococcal Infections, p.195.

Resistance. References to meticillin-resistant staphylococci.

1. Hackbarth CJ, Chambers HF. Methicillin-resistant staphylococci: genetics and mechanisms of resistance. *Antimicrob Agents Chemother* 1989; **33:** 991–4.
2. Maple PAC, *et al.* World-wide antibiotic resistance in methicillin-resistant Staphylococcus aureus. *Lancet* 1989; **i:** 537–40.
3. Mouton RP, *et al.* Correlations between consumption of antibiotics and methicillin resistance in coagulase negative staphylococci. *J Antimicrob Chemother* 1990; **26:** 573–83.
4. Marples RR, Reith S. Methicillin-resistant Staphylococcus aureus in England and Wales. *Commun Dis Rep* 1992; **2:** R25–R29.
5. de Lencastre H, *et al.* Molecular aspects of methicillin resistance in Staphylococcus aureus. *J Antimicrob Chemother* 1994; **33:** 7–24.
6. Fluckiger U, Widmer AF. Epidemiology of methicillin-resistant Staphylococcus aureus. *Chemotherapy* 1999; **45:** 121–34.
7. Livermore DM. Antibiotic resistance in staphylococci. *Int J Antimicrob Agents* 2000; **16** (suppl 1): S3–S10.
8. Turnidge JD, Bell JM. Methicillin-resistant Staphylococcal aureus evolution in Australia over 35 years. *Microb Drug Resist* 2000; **6:** 223–9.

Pharmacokinetics

Meticillin is inactivated by gastric acid and must be given by injection. Peak plasma concentrations are attained within 0.5 to 1 hour of an intramuscular injection; concentrations of up to 18 micrograms/mL have been achieved after a dose of 1 g. A half-life of 0.5 to 1 hour has been reported, although this may be increased to 3 to 6 hours in renal impairment. About 40% of the meticillin in the circulation is bound to plasma proteins. It is widely distributed in body fluids and in tissues, but there is little diffusion into the CSF unless the meninges are inflamed. Meticillin also crosses the placenta and appears in breast milk. Relatively high concentrations are achieved in bile compared with plasma, although only small amounts are excreted in bile. The majority is rapidly excreted by tubular secretion and glomerular filtration; up to 80% of an injected dose has been detected unchanged in the urine.

Plasma concentrations are enhanced by probenecid. They may be reduced in patients with cystic fibrosis.

Uses and Administration

Meticillin is a penicillinase-resistant penicillin and has been used similarly to flucloxacillin (p.277) in the treatment of staphylococcal infections resistant to benzylpenicillin. It is not active orally and has been given by injection as the sodium salt.

Mezlocillin *(BAN, USAN, rINN)*

Metslosilliini; Mezlocilina; Mezlocilline; Mezlocillinum. 6-[*N*-(3-Methylsulfonyl-2-oxoimidazolidin-1-ylcarbonyl)-D-phenylglycylamino]penicillanic acid.

Мезлоциллин

$C_{21}H_{25}N_5O_8S_2$ = 539.6.

CAS — 51481-65-3.

ATC — J01CA10.

ATC Vet — QJ01CA10.

Mezlocillin Sodium *(BANM, rINNM)*

Bay-f-1353; Mezlocilina sódica; Mezlocilline Sodique; Natrii Mezlocillinum. Sodium (6*R*)-6-[D-2-(3-mesyl-2-oxoimidazolidine-1-carboxamido)-2-phenylacetamido]penicillanate monohydrate.

Натрий Мезлоциллин

$C_{21}H_{24}N_5NaO_8S_2,H_2O$ = 579.6.

CAS — 42057-22-7 (anhydrous mezlocillin sodium); 80495-46-1 (mezlocillin sodium monohydrate).

ATC — J01CA10.

ATC Vet — QJ01CA10.

Pharmacopoeias. In *US*.

USP 31 (Mezlocillin Sodium). A white to pale yellow crystalline powder. Freely soluble in water. pH of a 10% solution in water is between 4.5 and 8.0. Store in airtight containers.

Incompatibility. Mezlocillin sodium has been reported to be incompatible with aminoglycosides, ciprofloxacin, metronidazole, and tetracyclines.

Adverse Effects and Precautions

As for Carbenicillin Sodium, p.216.

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