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.

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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

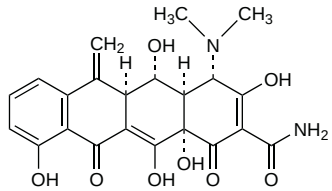
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Arg.:*** Gentocelina†.

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.

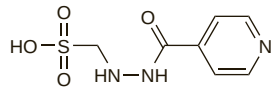
Proprietary Preparations (details are given in Part 3)
Fr.: Lysocline; Physiomycine; ***Ital.:*** Esarondil; Rotilen; Stafilon.

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

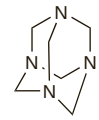
Proprietary Preparations (details are given in Part 3)
Austria: Neo-Tizide; ***India:*** Erbazide†.
Multi-ingredient: ***India:*** Strepto-Erbazide†.

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-