Pharmacokinetics
Mecamylamine hydrochloride is almost completely absorbed from the gastrointestinal tract. It crosses the placenta and the blood-brain barrier. About 50% of the dose is excreted unchanged in the urine over 24 hours, but the rate is diminished in alkaline urine.

Uses and Administration
Mecamylamine hydrochloride is a ganglion blocker with actions similar to those of trimetaphan (p.1419). It is given orally in the management of hypertension (p.1171), although other antihypertensives with fewer adverse effects are preferred.

The usual initial dosage is 2.5 mg twice daily, gradually increased or decreased, usually in steps of 2.5 mg at intervals of not less than 2 days, until a satisfactory response is obtained. The average maintenance dose is 25 mg daily in three divided doses. Tolerance may develop.

◊ Reviews.

1. Young JM, *et al.* Mecamylamine: new therapeutic uses and toxicity/risk profile. *Clin Ther* 2001; **23:** 532–65.

Smoking cessation. Mecamylamine acts centrally as a nicotinic antagonist and might be of some benefit in assisting withdrawal from smoking. Two studies[1,2] have shown that addition of low-dose oral mecamylamine (2.5 to 5 mg twice daily) appeared to enhance the effectiveness of nicotine skin patches. However, a later controlled study[3] found that a patch containing both mecamylamine and nicotine was not significantly better than transdermal nicotine alone. Smoking cessation is discussed under Nicotine, p.2354.

1. Rose JE, *et al.* Mecamylamine combined with nicotine skin patch facilitates smoking cessation beyond nicotine patch treatment alone. *Clin Pharmacol Ther* 1994; **56:** 86–99.
2. Rose JE, *et al.* Nicotine-mecamylamine treatment for smoking cessation: the role of pre-cessation therapy. *Exp Clin Psychopharmacol* 1998; **6:** 331–43.
3. Glover ED, *et al.* A randomized, controlled trial to assess the efficacy and safety of a transdermal delivery system of nicotine/mecamylamine in cigarette smokers. *Addiction* 2007; **102:** 795–802.

Tourette's syndrome. Mecamylamine has been tried[1-3] in the management of Tourette's syndrome (see under Tics, p.954) although results have been mixed.

1. Sanberg PR, *et al.* Treatment of Tourette's syndrome with mecamylamine. *Lancet* 1998; **352:** 705–6.
2. Silver AA, *et al.* Mecamylamine in Tourette's syndrome: a two-year retrospective case study. *J Child Adolesc Psychopharmacol* 2000; **10:** 59–68.
3. Silver AA, *et al.* Multicenter, double-blind, placebo-controlled study of mecamylamine monotherapy for Tourette's disorder. *J Am Acad Child Adolesc Psychiatry* 2001; **40:** 1103–10.

Preparations
USP 31: Mecamylamine Hydrochloride Tablets.

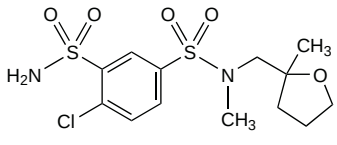
Proprietary Preparations (details are given in Part 3)
USA: Inversine.

Mefruside *(BAN, USAN, rINN)* ⊗

Bay-1500; FBA-1500; Mefrusid; Mefrusida; Méfruside; Mefrusidi; Mefrusidum. 4-Chloro-*N*^{1}-methyl-*N*^{1}-(tetrahydro-2-methylfurfuryl)benzene-1,3-disulphonamide.

Мефрузид

$C_{13}H_{19}ClN_2O_5S_2$ = 382.9.
CAS — 7195-27-9.
ATC — C03BA05.
ATC Vet — QC03BA05.



Pharmacopoeias. In *Jpn.*

Profile
Mefruside is a diuretic with properties similar to those of the thiazide diuretics (see Hydrochlorothiazide, p.1307) even though it does not contain a thiazide ring system. It is given orally for oedema, including that associated with heart failure (p.1165), and for hypertension (p.1171).

Diuresis begins about 2 to 4 hours after an oral dose and reaches a maximum between 6 and 12 hours.

In the treatment of oedema the usual dose is 25 to 50 mg daily, increasing if necessary to 75 to 100 mg. For long-term therapy a dose of 25 to 50 mg every second or third day is preferable.

In the treatment of hypertension the usual dose is 25 mg daily, either alone, or with other antihypertensives; initial doses of 25 to 50 mg daily have been recommended; alternate-day maintenance dosage may be used.

Preparations
Proprietary Preparations (details are given in Part 3)
Neth.: Baycaron†.

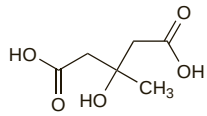
Multi-ingredient: ***Ger.:*** Bendigon N†; duranifin Sali†; Sali-Adalat; Sali-Prent.

Meglutol *(USAN, rINN)*

CB-337; Méglutol; Meglutolum. 3-Hydroxy-3-methylglutaric acid.

Мелутол

$C_6H_{10}O_5$ = 162.1.
CAS — 503-49-1.
ATC — C10AX05.
ATC Vet — QC10AX05.



Profile
Meglutol is a lipid regulating drug that has been used in the treatment of hyperlipidaemias.

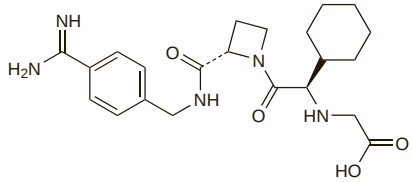
Preparations
Proprietary Preparations (details are given in Part 3)
Ital.: Mevalon†.

Melagatran *(rINN)*

H-319/68; Mélagatran; Melagatrán; Melagatranum. *N*-[(*R*)-({(2*S*)-2-[(*p*-Amidinobenzyl)carbamoyl]-1-azetidinyl}carbonyl)cyclohexylmethyl]glycine.

Мелагатран

$C_{22}H_{31}N_5O_4$ = 429.5.
CAS — 159776-70-2.
ATC — B01AE04.
ATC Vet — QB01AE04.



Ximelagatran *(USAN, rINN)*

H-376/95; Ximélagatran; Ximelagatrán; Ximelagatranum. Ethyl *N*-{(*R*)-cyclohexyl[((2*S*)-2-{[4-(hydroxycarbamimidoyl)benzyl]carbamoyl}-1-azetidinyl)carbonyl]methyl}glycinate.

Ксимелагатран

$C_{24}H_{35}N_5O_5$ = 473.6.
CAS — 192939-46-1.
ATC — B01AE05.
ATC Vet — QB01AE05.

Profile
Melagatran is a direct thrombin inhibitor with actions similar to lepirudin, p.1323, that was used as an anticoagulant in the prevention of postoperative venous thromboembolism in patients undergoing hip or knee replacement surgery. It is the active metabolite of ximelagatran and was given subcutaneously; ximelagatran was given orally. It was withdrawn worldwide because of reported liver toxicity.

◊ References.

1. Wallentin L, *et al.* Oral ximelagatran for secondary prophylaxis after myocardial infarction: the ESTEEM randomised controlled trial. *Lancet* 2003; **362:** 789–97.
2. Executive Steering Committee on behalf of the SPORTIF III Investigators. Stroke prevention with the oral direct thrombin inhibitor ximelagatran compared with warfarin in patients with non-valvular atrial fibrillation (SPORTIF III): randomised controlled trial. *Lancet* 2003; **362:** 1691–8.
3. Evans HC, *et al.* Ximelagatran/Melagatran: a review of its use in the prevention of venous thromboembolism in orthopaedic surgery. *Drugs* 2004; **64:** 649–78.
4. SPORTIF Executive Steering Committee for the SPORTIF V Investigators. Ximelagatran vs warfarin for stroke prevention in patients with nonvalvular atrial fibrillation: a randomized trial. *JAMA* 2005; **293:** 690–8.

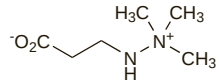
Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Exanta†; ***Austria:*** Exanta†; ***Denm.:*** Exanta†; ***Fin.:*** Exanta†; ***Fr.:*** Exanta†; ***Ger.:*** Exanta†; ***Neth.:*** Exanta†; ***Norw.:*** Exanta†; ***Swed.:*** Exarta†.

Meldonium *(rINN)*

Meldonio; MET-88; 3-(2,2,2-Trimethylhydrazinium)propionate. 3-(2,2,2-Trimethyldiazaniumyl)propanoate.

Мельдоний

$C_6H_{14}N_2O_2$ = 146.2.
CAS — 76144-81-5 (meldonium); 86426-17-7 (meldonium dihydrate).



Profile
Meldonium is an inhibitor of carnitine synthesis and is reported to have cardioprotective and anti-ischaemic effects. It has been used in a variety of disorders. In the management of ischaemic heart disease and ischaemic cerebrovascular disturbances oral doses have ranged from 500 mg to 1 g daily. A course of 500 mg given four times daily for 7 to 10 days has been used in alcohol abstinence syndrome. Meldonium has also been given intravenously in doses similar to those used orally.

◊ References.

1. Dambrova M, *et al.* Mildronate: cardioprotective action through carnitine-lowering effect. *Trends Cardiovasc Med* 2002; **12:** 275–9.
2. Sjakste N, *et al.* Mildronate: an antiischemic drug for neurological indications. *CNS Drug Rev* 2005; **11:** 151–68.

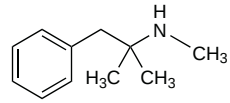
Preparations
Proprietary Preparations (details are given in Part 3)
Rus.: Mildronate (Милдронат); Mildroxyn (Милдроксин).

Mephentermine Sulfate *(rINNM)* ⊗

Méphentermine, Sulfate de; Mephentermine Sulphate *(BANM)*; Mephentermini Sulfas; Mephetedrine Sulphate; Sulfato de mefentermina. *N*,α,α-Trimethylphenethylamine sulphate dihydrate.

Мефентермина Сульфат

$(C_{11}H_{17}N)_2.H_2SO_4.2H_2O$ = 460.6.
CAS — 100-92-5 (mephentermine); 1212-72-2 (anhydrous mephentermine sulfate); 6190-60-9 (mephentermine sulfate dihydrate).
ATC — C01CA11.
ATC Vet — QC01CA11.



(mephentermine)

Adverse Effects, Treatment, and Precautions
As for Sympathomimetics, p.1407; adverse effects may be related to alpha- or beta-adrenergic stimulation. Mephentermine may produce CNS stimulation, especially in overdosage; anxiety, drowsiness, incoherence, hallucinations, and convulsions have been reported.

Interactions
As for Sympathomimetics, p.1407.

Pharmacokinetics
Mephentermine acts in about 5 to 15 minutes after intramuscular injection and has a duration of action of up to about 4 hours; it acts almost immediately after intravenous injection with a duration of action of up to about 30 minutes. It is rapidly metabolised in the body by demethylation; hydroxylation may follow. It is excreted as unchanged drug and metabolites in the urine; excretion is more rapid in acidic urine.

Uses and Administration
Mephentermine is a sympathomimetic (p.1408) with mainly indirect effects on adrenergic receptors. It has alpha- and beta-adrenergic activity, and a slight stimulating effect on the CNS. It has an inotropic effect on the heart.

Mephentermine has been used to maintain blood pressure in hypotensive states, for example after spinal anaesthesia. It is given as the sulfate but doses are expressed in terms of the base; 21 mg of sulfate is equivalent to about 15 mg of base. Typical doses are up to 45 mg by slow intravenous injection, or 15 to 30 mg intramuscularly.

Preparations
Proprietary Preparations (details are given in Part 3)
India: Mephentine; ***USA:*** Wyamine†.

Multi-ingredient: ***USA:*** Emergent-Ez.

Mepindolol Sulfate *(rINNM)* ⊗

LF-17895 (mepindolol); Mépindolol, Sulfate de; Mepindolol Sulphate *(BANM)*; Mepindololi Sulfas; SHE-222; Sulfato de mepindolol. 1-Isopropylamino-3-(2-methylindol-4-yloxy)propan-2-ol sulfate.

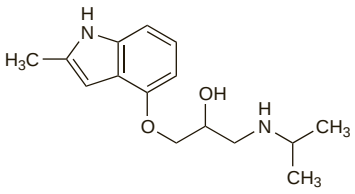
Мепиндолола Сульфат

$(C_{15}H_{22}N_2O_2)_2,H_2SO_4$ = 622.8.

CAS — 23694-81-7 (mepindolol); 56396-94-2 (mepindolol sulfate).

ATC — C07AA14.

ATC Vet — QC07AA14.



(mepindolol)

Profile

Mepindolol, the methyl analogue of pindolol, is a non-cardioselective beta blocker (p.1225). It is reported to possess intrinsic sympathomimetic activity. It has been given orally as the sulfate in the management of various cardiovascular disorders.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Corindolan.

Multi-ingredient: ***Ger.:*** Corindocomb†.

Mersalyl Acid ⊗

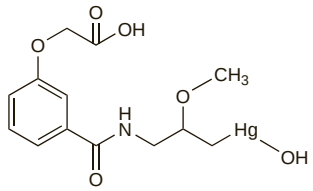
Acidum Mersalylicum; Mersal. Acid; Mersálico, ácido; Mersalylum Acidum. A mixture of {3-[2-(carboxymethoxy)benzamido]-2-methoxypropyl}hydroxymercury and its anhydrides.

$C_{13}H_{17}HgNO_6$ = 483.9.

CAS — 486-67-9.

ATC — C03BC01.

ATC Vet — QC03BC01.



Mersalyl Sodium ⊗

Mersalyl *(pINN)*; Mersalilo; Mersalylum; Mersalyyli. The sodium salt of mersalyl acid.

Мерсалил

$C_{13}H_{16}HgNNaO_6$ = 505.8.

CAS — 492-18-2.

ATC — C03BC01.

ATC Vet — QC03BC01.

Profile

Mersalyl acid, in the form of its salts, is a powerful diuretic that acts on the renal tubules, increasing the excretion of sodium and chloride, in about equal amounts, and of water. Organic mercurial diuretics were widely used before the introduction of thiazide and other diuretics but have now been almost completely superseded by these orally active drugs, which are both potent and less toxic. The most frequent adverse effects of mersalyl are stomatitis, gastric disturbance, vertigo, febrile reactions, and skin eruptions and irritation. Thrombocytopenia, neutropenia, and agranulocytosis have followed the use of mercurial diuretics. Intravenous injection may cause severe hypotension and cardiac arrhythmias and has been followed by sudden death.

Mersalyl acid was usually given by injection as the sodium salt with theophylline as this lessened the local irritant reaction and increased absorption. It was given by deep intramuscular injection after a test dose for hypersensitivity. Other organic mercurial diuretics include chlormerodrin, meralluride, mercaptomerin sodium, mercurophylline sodium, and merethoxylline procaine. They were mainly given by intramuscular injection or, for those which were less irritant, subcutaneous injection.

Metaraminol Tartrate *(BANM, rINNM)* ⊗

Hydroxynorephedrine Bitartrate; Metaradrine Bitartrate; Metaraminol Acid Tartrate; Metaraminol Bitartrate; Métaraminol, Tartrate de; Metaraminoli Tartras; Tartrato de metaraminol. (–)-2-Amino-1-(3-hydroxyphenyl)propan-1-ol hydrogen tartrate.

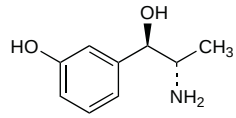
Метараминола Тартрат

$C_9H_{13}NO_2,C_4H_6O_6$ = 317.3.

CAS — 54-49-9 (metaraminol); 33402-03-8 (metaraminol tartrate).

ATC — C01CA09.

ATC Vet — QC01CA09.



(metaraminol)

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

BP 2008 (Metaraminol Tartrate). An odourless or almost odourless, white, crystalline powder. Freely soluble in water; sparingly soluble in alcohol; practically insoluble in chloroform and in ether. A 5% solution in water has a pH of 3.2 to 3.5.

USP 31 (Metaraminol Bitartrate). A 5% solution in water has a pH of between 3.2 and 3.5. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Adverse Effects, Treatment, and Precautions

As for Sympathomimetics, p.1407. The adverse effects of metaraminol primarily relate to its alpha-agonist action. Metaraminol has a longer duration of action than adrenaline or noradrenaline and therefore an excessive vasopressor response may cause a prolonged rise in blood pressure. Tissue necrosis can occur as a result of accidental extravasation during intravenous injection.

Interactions

As for Sympathomimetics, p.1407. The interactions of metaraminol relate to both its direct and indirect actions.

Pharmacokinetics

Metaraminol acts about 10 minutes after intramuscular injection with a duration of action of up to about 1 hour. Effects are seen 1 to 2 minutes after intravenous injection with a duration of action of about 20 minutes.

Uses and Administration

Metaraminol is a sympathomimetic (p.1408) with direct and indirect effects on adrenergic receptors. It has alpha- and beta-adrenergic activity, the former being predominant. Metaraminol has an inotropic effect and acts as a peripheral vasoconstrictor, thus increasing cardiac output, peripheral resistance, and blood pressure. Coronary blood flow is increased and the heart rate slowed.

Metaraminol tartrate is used for its pressor action in **hypotensive states** such as those that may occur after spinal anaesthesia. Doses are expressed in terms of the base; metaraminol tartrate 9.5 mg is equivalent to about 5 mg of metaraminol. An intravenous infusion of 15 to 100 mg of metaraminol in 500 mL of glucose 5% or sodium chloride 0.9% may be used for maintaining the blood pressure, the rate of infusion being adjusted according to blood pressure response. Higher concentrations have been given. As the maximum effects are not immediately apparent, at least 10 minutes should elapse before increasing the dose and the possibility of a cumulative effect should be borne in mind. In an emergency an initial dose of 0.5 to 5 mg may be given by direct intravenous injection followed by an intravenous infusion as above.

Metaraminol tartrate has also been given by intramuscular or subcutaneous injection for the prevention of hypotension in doses equivalent to 2 to 10 mg of metaraminol. Subcutaneous injection increases the risk of local tissue necrosis and sloughing.

Priapism. Priapism[1,2] or prolonged penile erection may occur due to either decreased venous outflow (low-flow priapism) or increased arterial inflow (high-flow priapism). Low-flow priapism is a medical emergency since inflow is also impaired, leading to the development of ischaemia. It may be related to the use of drugs that cause smooth muscle relaxation, such as alpha blockers; intraluminal obstruction, such as in sickle-cell disease, may also be a cause. It is usually treated with corporal aspiration, followed if necessary by irrigation with a low dosage of a dilute solution of an alpha agonist such as metaraminol.

Intracavernosal metaraminol has been used successfully to treat drug-induced priapism,[3] as well as priapism associated with chronic myeloid leukaemia,[4] haemodialysis,[5] spinal block,[6] or fentanyl-induced general anaesthesia.[6] It may also be used to reverse the effects of alprostadil or papaverine given intracavernosally for the management of some types of erectile dysfunction, although this has been associated with fatal hypertensive crisis (see also Alprostadil, p.2184).

Alternative alpha agonists that have been used include intracavernosal phenylephrine,[7] and intracavernosal adrenaline, again in a low dosage and dilute solution. Phenylpropanolamine,[7] or pseudoephedrine,[8] given orally, have also been used. In patients with priapism due to sickle-cell disease, intracavernosal irrigation with a dilute adrenaline solution or intracavernosal injection of etilefrine have been used (see p.1205); oral etilefrine has been given for prophylaxis. Many other drugs have been tried or suggested, including baclofen, gabapentin, terbutaline, and, paradoxically, low doses of phosphodiesterase type-5 inhibitors such as sildenafil or tadalafil.[2] Surgery is usually favoured in low-flow priapism unresponsive to drug therapy.

In high-flow priapism, which is less of an emergency, embolisation of the source of abnormal inflow is the usual treatment.

1. Maan Z, *et al.* Priapism—a review of the medical management. *Expert Opin Pharmacother* 2003; **4:** 2271–7.
2. Yuan J, *et al.* Insights of priapism mechanism and rationale treatment for recurrent priapism. *Asian J Androl* 2008; **10:** 88–101.
3. Brindley GS. New treatment for priapism. *Lancet* 1984; **ii:** 220–1.
4. Stanners A, Colin-Jones D. Metaraminol for priapism. *Lancet* 1984; **ii:** 978.
5. Branger B, *et al.* Metaraminol for haemodialysis-associated priapism. *Lancet* 1985; **i:** 641.
6. Tsai SK, Hong CY. Intracavernosal metaraminol for treatment of intraoperative penile erection. *Postgrad Med J* 1990; **66:** 831–3.
7. Harmon WJ, Nehra A. Priapism: diagnosis and management. *Mayo Clin Proc* 1997; **72:** 350–5.
8. Millard RJ, *et al.* Risks of self-injection therapy for impotence. *Med J Aust* 1996; **165:** 117–18.

Preparations

BP 2008: Metaraminol Injection;
USP 31: Metaraminol Bitartrate Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Fadamine; ***Austral.:*** Aramine; ***Braz.:*** Aramin; ***Gr.:*** Aramine†; Levicor†; ***Norw.:*** Aramine†; ***NZ:*** Aramine; ***Thai.:*** Aramine†; ***USA:*** Aramine.

Methoxamine Hydrochloride *(BANM, rINNM)* ⊗

Hidrocloruro de metoxamina; Methoxamedrine Hydrochloride; Méthoxamine, Chlorhydrate de; Methoxamini Hydrochloridum. 2-Amino-1-(2,5-dimethoxyphenyl)propan-1-ol hydrochloride.

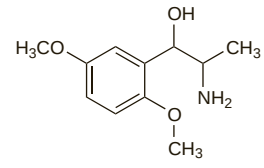
Метоксамина Гидрохлорид

$C_{11}H_{17}NO_3$,HCl = 247.7.

CAS — 390-28-3 (methoxamine); 61-16-5 (methoxamine hydrochloride).

ATC — C01CA10.

ATC Vet — QC01CA10.



(methoxamine)

Pharmacopoeias. In *Br.* and *Chin.*

BP 2008 (Methoxamine Hydrochloride). Colourless crystals or white plate-like crystals or white crystalline powder; odourless or almost odourless. Freely soluble in water; soluble in alcohol; very slightly soluble in chloroform and in ether. A 2% solution in water has a pH of 4.0 to 6.0.

Profile

Methoxamine is a sympathomimetic (p.1407) with mainly direct effects on adrenergic receptors. It has alpha-adrenergic activity entirely; beta-adrenergic activity is not demonstrable and beta-adrenoceptor blockade may occur at high doses. Methoxamine hydrochloride has been used parenterally for its pressor action in the management of hypotensive states, particularly in anaesthesia, and also in the management of paroxysmal supraventricular