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.

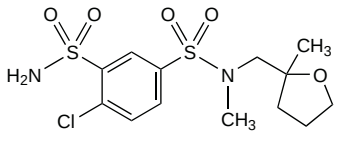
Proprietary Preparations (details are given in Part 3)
USA: Inversine.

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†.

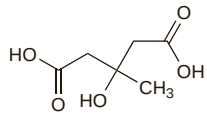
Multi-ingredient: ***Ger.:*** Bendigon N†; duranifin Sali†; Sali-Adalat; Sali-Prent.

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.

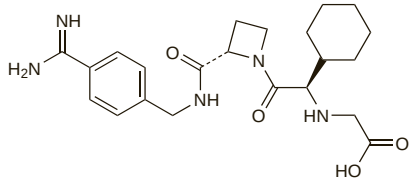
Preparations
Proprietary Preparations (details are given in Part 3)
Ital.: Mevalon†.

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.

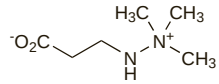
Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Exanta†; ***Austria:*** Exanta†; ***Denm.:*** Exanta†; ***Fin.:*** Exanta†; ***Fr.:*** Exanta†; ***Ger.:*** Exanta†; ***Neth.:*** Exanta†; ***Norw.:*** Exanta†; ***Swed.:*** Exarta†.

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.

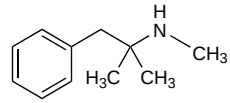
Preparations
Proprietary Preparations (details are given in Part 3)
Rus.: Mildronate (Милдронат); Mildroxyn (Милдроксин).

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.