Trimetaphan Camsilate *(BAN, rINN)*

Cansilato de trimetafán; Méthioplégium; Trimetaphan Camphorsulfonate; Trimétaphan, Camsilate de; Trimetaphan Camsylate; Trimetaphani Camsilas; Trimetaphani Camsylas; Trimethaphan Camsylate. (+)-1,3-Dibenzylperhydro-2-oxothieno-[1′,2′:1,2]thieno[3,4-*d*]-imidazol-5-ium 2-oxobornane-10-sulfonate; 4,6-Dibenzyl-4,6-diaza-1-thioniatricyclo[6.3.0.0^{3,7}]undecan-5-one 2-oxobornane-10-sulfonate.

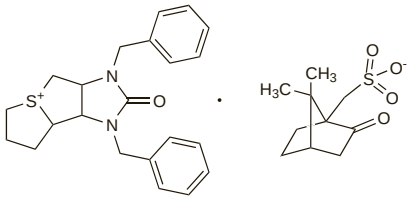
Триметафана Камзилат

$C_{22}H_{25}N_2OS,C_{10}H_{15}O_4S$ = 596.8.

CAS — 7187-66-8 (trimetaphan); 68-91-7 (trimetaphan camsilate).

ATC — C02BA01.

ATC Vet — QC02BA01.



Incompatibility. Trimetaphan is incompatible with thiopental sodium, gallamine triethiodide, iodides, bromides, and strongly alkaline solutions.

Adverse Effects and Treatment

The adverse effects of trimetaphan are mainly due to ganglionic blockade. A reduction in gastrointestinal motility may cause constipation and, on prolonged use, paralytic ileus. Urinary retention, cycloplegia, mydriasis, tachycardia, precipitation of angina, and gastrointestinal disturbances such as anorexia, nausea, or vomiting, may occur. Orthostatic hypotension may be severe. Rapid intravenous infusion can result in respiratory arrest. Other adverse effects include raised intra-ocular pressure, dry mouth, hypoglycaemia, hypokalaemia, fluid retention, weakness, urticaria, and itching. Trimetaphan crosses the placenta and can cause paralytic or meconium ileus in the neonate.

If severe hypotension occurs, trimetaphan should be stopped and the patient positioned with the head lower than the feet. A vasopressor may be given cautiously if necessary.

Effects on the eyes. Although trimetaphan may increase intraocular pressure, a sudden and dramatic reduction of intra-ocular pressure to very low levels was noted in 5 patients undergoing surgery when the systolic blood pressure was reduced to 60 mmHg with trimetaphan infusion.[1]

1. Dias PLR, *et al*. Effect on the intraocular pressure of hypotensive anaesthesia with intravenous trimetaphan. *Br J Ophthalmol* 1982; **66:** 721–4.

Precautions

Trimetaphan should be avoided in patients with asphyxia or respiratory insufficiency, uncorrected anaemia, shock or hypovolaemia, severe arteriosclerosis, severe ischaemic heart disease, or pyloric stenosis and should only be used with extreme caution in those with hepatic or renal impairment, degenerative disease of the CNS, Addison's disease, prostatic hyperplasia, glaucoma, cerebral or coronary vascular insufficiency, and diabetes. It should be used with care in elderly or debilitated patients and should be avoided in pregnancy. Owing to a histamine-liberating effect it should be used with caution in allergic subjects.

Interactions

Trimetaphan should be used with caution in patients being treated with other antihypertensives, drugs that depress cardiac function, or muscle relaxants, and in those taking NSAIDs or corticosteroids. The hypotensive effect is enhanced by general and spinal anaesthetics. Adrenaline should not be infiltrated locally at the site of incision when trimetaphan is being given since this may antagonise the effect of trimetaphan.

Neuromuscular blockers. For a reference to possible potentiation of neuromuscular blockade by trimetaphan, see Ganglion Blockers, under Interactions of Atracurium, p.1904.

Uses and Administration

Trimetaphan is a ganglion blocker that inhibits the transmission of nerve impulses in both sympathetic and parasympathetic ganglia. The sympathetic blockade produces peripheral vasodilatation. Trimetaphan also has a direct vasodilator effect on peripheral blood vessels. It has been used for inducing controlled hypotension during surgical procedures; it acts rapidly to produce a hypotensive response which persists for about 10 to 15 minutes. Trimetaphan has also been used for the emergency treatment of hypertensive crises (p.1171), especially in the presence of pulmonary oedema or acute dissecting aortic aneurysms. However, sodium nitroprusside is now preferred.

Trimetazidine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de trimetazidina; Trimetatsidiinidihydrokloridi; Trimetazidin Hidroklorür; Trimetazidindihidroklorid; Trimetazidindihydrochlorid; Trimetazidindihydroklorid; Trimétazidine, Chlorhydrate de; Trimétazidine, dichlorhydrate de; Trimetazidine Dihydrochloride; Trimetazidini dihydrochloridum; Trimetazidini Hydrochloridum; Trimetazidino hidrochloridas; Trimetazine Hydrochloride. 1-(2,3,4-Trimethoxybenzyl)piperazine dihydrochloride.

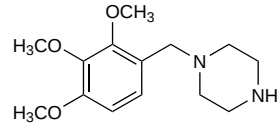
Триметазидина Гидрохлорид

$C_{14}H_{22}N_2O_3$,2HCl = 339.3.

CAS — 5011-34-7 (trimetazidine); 13171-25-0 (trimetazidine hydrochloride).

ATC — C01EB15.

ATC Vet — QC01EB15.



(trimetazidine)

Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn.*

Ph. Eur. 6.2 (Trimetazidine Dihydrochloride; Trimetazidine Hydrochloride BP 2008). A slightly hygroscopic, white or almost white crystalline powder. Freely soluble in water; sparingly soluble in alcohol. Store in airtight containers.

Profile

Trimetazidine hydrochloride is used in angina pectoris (p.1157) and in ischaemia of neurosensorial tissues as in Ménière's disease (p.564); 40 to 60 mg is given daily by mouth in divided doses.

◊ References.

1. McClellan KJ, Plosker GL. Trimetazidine: a review of its use in stable angina pectoris and other coronary conditions. *Drugs* 1999; **58:** 143–57.
2. Ciapponi A, *et al*. Trimetazidine for stable angina. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2005 (accessed 24/01/06).
3. Danchin N. Clinical benefits of a metabolic approach with trimetazidine in revascularized patients with angina. *Am J Cardiol* 2006; **98** (suppl): 8J–13J.

Effects on the nervous system. Eight elderly patients aged between 72 and 94 years were reported[1] to have developed signs of parkinsonism while taking trimetazidine; the parkinsonism regressed completely when the drug was stopped. A retrospective study[2] found that adverse effects on motor function, including parkinsonism, gait disorders, and tremor, occurred in 56 of 130 patients taking trimetazidine and were more common in older patients.

1. Marti Massó JF. Parkinsonismo por trimetazidina. *Neurologia* 2004; **19:** 392–5.
2. Martí Massó J-F, *et al*. Trimetazidine induces parkinsonism, gait disorders and tremor. *Therapie* 2005; **60:** 419–22.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Vastarel; ***Austria:*** Vastarel; ***Braz.:*** Vastarel; ***Chile:*** Vastarel; ***Cz.:*** Adexor; Preductal; ***Denm.:*** Vastarel; ***Fr.:*** Centrophene†; Vastarel; ***Gr.:*** Atanol; Imovexil; Intervein; Latrimet†; Liomagen; Novazidine; Trimedin; Trimedor; Trimevert; Vastarel; Zidin; ***Hong Kong:*** Vastarel; ***Hung.:*** Adexor; Preductal; ***India:*** Flavedon; Mayozest; Metacard; Metagard; Trivedon; ***Indon.:*** Trizedon; ***Irl.:*** Vastarel; ***Ital.:*** Vastarel; ***Malaysia:*** Metagard; Vastarel; ***Philipp.:*** Angirel; Vastarel; ***Pol.:*** Metazydyna; Preductal; Trimetaratio; ***Port.:*** Tacirel; Vastarel; ***Rus.:*** Deprenorm (Депренорм); Medarum (Медарум); Preductal (Предуктал); Rimecor (Римекор); Trimetazide (Триметазид); ***Singapore:*** Metagard; Vastarel; ***Spain:*** Idaptan; Vaso Rimal†; ***Thai.:*** Matenol; Trizidine; Vastarel; Vastinol; ***Turk.:*** Vastarel; ***Venez.:*** Vastarel.

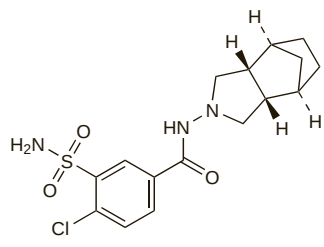
Tripamide *(USAN, rINN)* ⊗

ADR-033; E-614; Tripamida; Tripamidum. 4-Chloro-*N*-(*endo*-hexahydro-4,7-methanoisoindolin-2-yl)-3-sulphamoylbenzamide.

Трипамид

$C_{16}H_{20}ClN_3O_3S$ = 369.9.

CAS — 73803-48-2.



Profile

Tripamide is a diuretic structurally related to indapamide. It is used in the treatment of hypertension.

Preparations

Proprietary Preparations (details are given in Part 3)
Thai.: Normonal.

Urapidil *(BAN, rINN)*

B-66256M; Urapidili; Urapidilum. 6-[3-(4-o-Methoxyphenylpiperazin-1-yl)propylamino]-1,3-dimethyluracil.

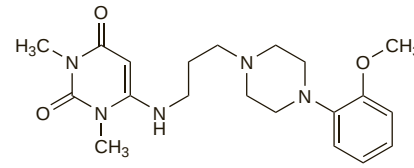
Урапидил

$C_{20}H_{29}N_5O_3$ = 387.5.

CAS — 34661-75-1.

ATC — C02CA06.

ATC Vet — QC02CA06.



Pharmacopoeias. In *Jpn.*

Urapidil Hydrochloride *(BANM, rINNM)*

Hidrocloruro de urapidil; Urapidil, Chlorhydrate d'; Urapidili Hydrochloridum.

Урапидила Гидрохлорид

$C_{20}H_{29}N_5O_3$,HCl = 423.9.

CAS — 64887-14-5.

ATC — C02CA06.

ATC Vet — QC02CA06.

Adverse Effects and Precautions

Urapidil is reported to be well-tolerated, with adverse effects generally transient and most frequent at the beginning of therapy. Dizziness, nausea, headache, fatigue, orthostatic hypotension, palpitations, nervousness, pruritus, and allergic skin reactions have been reported.

It should be used with care in elderly patients and those with severe hepatic impairment. Intravenous urapidil should not be used in patients with aortic stenosis.

Urinary incontinence. Enuresis was reported[1] to be associated with the use of urapidil in 2 elderly patients.

1. Jonville A-P, *et al*. Urapidil and enuresis. *Lancet* 1992; **339:** 688.

Pharmacokinetics

After oral doses urapidil is rapidly absorbed with a reported bioavailability of 70 to 80%. It is reported to be about 80% bound to plasma proteins. Urapidil is extensively metabolised in the liver, mainly by hydroxylation, and excreted mostly in urine, as metabolites and 10 to 20% of unchanged drug. The elimination half-life is reported to be about 4.7 hours when given orally as capsules and about 2.7 hours after intravenous dosage.

◊ Reviews.

1. Kirsten R, *et al*. Clinical pharmacokinetics of urapidil. *Clin Pharmacokinet* 1988; **14:** 129–40.

Uses and Administration

Urapidil is an antihypertensive drug that is reported to block peripheral alpha$_1$ adrenoceptors (see Alpha Blockers, p.1153) and to have central actions. It produces a reduction in peripheral resistance and a fall in systolic and diastolic blood pressure, usually without reflex tachycardia.

Urapidil is used in the management of hypertension (p.1171), including hypertensive crises.

Urapidil is given orally as the base and intravenously as the hydrochloride, but doses are usually expressed in terms of the base. Urapidil hydrochloride 10.94 mg is equivalent to about 10 mg of urapidil. Urapidil fumarate has also been given orally.

In hypertension doses of 30 to 90 mg are given twice daily by mouth. In hypertensive crises a suggested regimen is to give an initial dose of 25 mg by slow intravenous injection over 20 seconds, repeated if necessary after 5 minutes. This may be followed by a dose of 50 mg after a further 5 minutes if the response is still inadequate. Treatment should continue with a maintenance infusion of 9 to 30 mg/hour once the blood pressure is sufficiently reduced.

◊ Reviews.

1. Dooley M, Goa KL. Urapidil: a reappraisal of its use in the management of hypertension. *Drugs* 1998; **56:** 929–55.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Ebrantil; ***Belg.:*** Ebrantil; ***Cz.:*** Ebrantil; ***Fr.:*** Eupressyl; Mediatensyl; ***Ger.:*** Ebrantil; ***Hung.:*** Ebrantil; ***Ital.:*** Ebrantil; ***Neth.:*** Ebrantil; ***Pol.:*** Ebrantil; ***Port.:*** Ebrantil; ***Spain:*** Elgadil; ***Switz.:*** Ebrantil.