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.

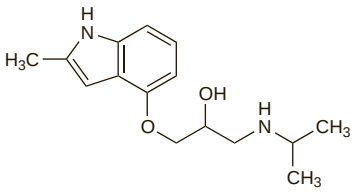
Мепиндолола Сульфат

$(C_{15}H_{22}N_2O_2)_2,H_2SO_4$ = 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 ⊗

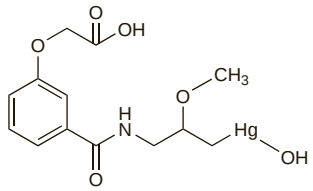
Acidum Mersalylicum; Mersal. Acid; Mersálico, ácido; Mersalylum Acidum. A mixture of {3-[2-(carboxymethoxy)benzamido]-2-methoxypropyl}hydroxymercury and its anhydrides.

$C_{13}H_{17}HgNO_6$ = 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diuretics were widely used before the introduction of thiazide and other diuretics but have now been almost completely superseded by these orally active drugs, which are both potent and less toxic.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.

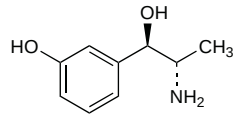
Метараминола Тартрат

$C_9H_{13}NO_2,C_4H_6O_6$ = 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.

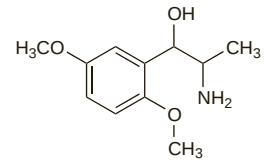
Метоксамина Гидрохлорид

$C_{11}H_{17}NO_3$,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