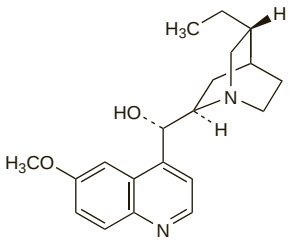
Hydroquinidine Hydrochloride

Dihydrochinidin Hydrochloride; Dihydroquinidine Hydrochloride; Hidrocloruro de dihidroquinidina; Hidroquinidina, hidrocloruro de; Hydroconchinine Hydrochloride. (8*R*,9*S*)-10,11-Dihydro-6′-methoxycinchonan-9-ol hydrochloride.

Гидрохинидина Гидрохлорид

$C_{20}H_{26}N_2O_2$,HCl = 362.9.

CAS — 1435-55-8 (hydroquinidine); 1476-98-8 (hydroquinidine hydrochloride).



(hydroquinidine)

Pharmacopoeias. In *Fr.*

Profile

Hydroquinidine is a class Ia antiarrhythmic with actions and uses similar to those of quinidine (p.1383). It is given orally as the hydrochloride in a usual maintenance dose of 600 mg daily in divided doses.

Hydroquinidine alginate and quinalbital (the hydroquinidine salt of amobarbital) have also been used in the treatment of cardiac arrhythmias.

◊ References.

1. Hermida J-S, *et al.* Hydroquinidine therapy in Brugada syndrome. *J Am Coll Cardiol* 2004; **43:** 1853–60.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Serecor; ***Spain:*** Lentoquine.

Ibopamine *(BAN, USAN, rINN)* ⊗

Ibopamina; Ibopaminum; SB-7505; SKF-100168. 4-(2-Methylaminoethyl)-*o*-phenylene di-isobutyrate.

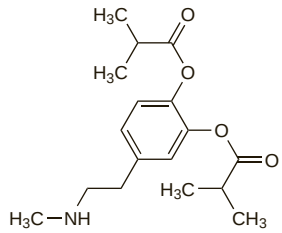
Ибопамин

$C_{17}H_{25}NO_4$ = 307.4.

CAS — 66195-31-1.

ATC — C01CA16; S01FB03.

ATC Vet — QC01CA16; QS01FB03.



Ibopamine Hydrochloride *(BANM, rINNM)* ⊗

Hidrocloruro de ibopamina; Ibopamiinihydrokloridi; Ibopamine, Chlorhydrate d'; Ibopaminhydroklorid; Ibopamini Hydrochloridum.

Ибопамина Гидрохлорид

$C_{17}H_{25}NO_4$,HCl = 343.8.

ATC — C01CA16; S01FB03.

ATC Vet — QC01CA16; QS01FB03.

Adverse Effects and Precautions

As for Sympathomimetics, p.1407. Ibopamine should not be used in patients with severe heart failure in whom, similarly to xamoterol (p.1433), it has been reported to increase the risk of death.

Effects on the cardiovascular system. A multicentre study (PRIME II) of the use of ibopamine in patients with severe (NYHA class III or IV) heart failure was stopped early when it was found that the drug was associated with an increased risk of death.[1] Subgroup analysis found that use of an antiarrhythmic drug was independently predictive of an adverse effect in ibopamine-treated patients. Excess mortality in heart failure has also been reported with dobutamine and xamoterol, and with flosequinan and the phosphodiesterase inhibitors amrinone, enoximone, milrinone, and vesnarinone, all of which produce positive inotropic effects through catecholamine-receptor stimulation or post-receptor pathway stimulation.[2] The association with antiarrhythmic therapy in the ibopamine study might reflect an interaction with amiodarone, the most commonly used antiarrhythmic in this study, or might simply be a marker for patients at risk of ibopamine-induced tachyarrhythmias.

1. Hampton JR, *et al.* Randomised study of effect of ibopamine on survival in patients with advanced severe heart failure. *Lancet* 1997; **349:** 971–7.
2. Niebauer J, Coats AJS. Treating chronic heart failure: time to take stock. *Lancet* 1997; **349:** 966–7.

Interactions

As for Sympathomimetics, p.1407. It has been recommended that ibopamine should not be given to patients taking amiodarone in the light of the increased mortality seen in the PRIME II study in patients given both drugs (see above), although it is not clear that this represents a genuine interaction.

Uses and Administration

Ibopamine is a prodrug and is rapidly converted to its active metabolite, epinine, which is a peripheral dopamine agonist and sympathomimetic (p.1408). At low doses its dopaminergic effects predominate, leading to vasodilatation and a weak positive inotropic effect; at high concentrations it has a stimulant action on alpha and beta adrenoceptors.

Ibopamine is used in the management of mild heart failure (p.1165). It is given as the hydrochloride but doses are often expressed in terms of the base; 111.9 mg of hydrochloride is equivalent to about 100 mg of base. Doses of 100 to 200 mg orally two or three times daily have been used.

Ibopamine is also used topically as a mydriatic (p.1874) in the form of eye drops containing ibopamine hydrochloride 2%.

Preparations

Proprietary Preparations (details are given in Part 3)
Belg.: Scandine; ***Braz.:*** Escandine†; ***Ital.:*** Scandine; Trazyl; ***Neth.:*** Inopamil; ***Spain:*** Escandine†.

Ibutilide Fumarate *(BANM, USAN, rINNM)*

Fumarato de ibutilida; Ibutilide, Fumarate d'; Ibutilidi Fumaras; U-70226E. (±)-4′-[4-(Ethylheptylamino)-1-hydroxybutyl]methanesulfonanilide fumarate (2:1).

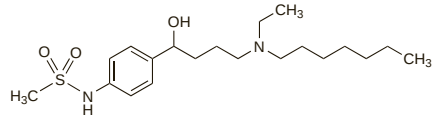
Ибутилида Фумарат

$(C_{20}H_{36}N_2O_3S)_2,C_4H_4O_4$ = 885.2.

CAS — 122647-31-8 (ibutilide); 122647-32-9 (ibutilide fumarate).

ATC — C01BD05.

ATC Vet — QC01BD05.



(ibutilide)

Adverse Effects

Adverse cardiovascular effects associated with ibutilide include heart block, hypotension, hypertension, and bradycardia. It prolongs the QT interval and, like other antiarrhythmics, can cause arrhythmias, including torsade de pointes. Other adverse effects include nausea and vomiting.

Effects on the heart. Ibutilide prolongs the QT interval and has been associated with torsade de pointes, particularly in women.[1] A small study[2] suggested that this effect could be prevented by magnesium sulfate (p.1679), which might therefore be suitable for use as prophylaxis. Although magnesium could theoretically reduce the antiarrhythmic effect of ibutilide as well as the proarrhythmic effect, a retrospective study[3] found that the rate of cardioversion was higher in patients given both ibutilide and magnesium than in those given ibutilide alone, an effect confirmed in a later study.[4]

1. Gowda RM, *et al.* Female preponderance in ibutilide-induced torsade de pointes. *Int J Cardiol* 2004; **95:** 219–22.
2. Caron MF, *et al.* Effects of intravenous magnesium sulfate on the QT interval in patients receiving ibutilide. *Pharmacotherapy* 2003; **23:** 296–300.
3. Kalus JS, *et al.* Impact of prophylactic i.v. magnesium on the efficacy of ibutilide for conversion of atrial fibrillation or flutter. *Am J Health-Syst Pharm* 2003; **60:** 2308–12.
4. Tercius AJ, *et al.* Intravenous magnesium sulfate enhances the ability of intravenous ibutilide to successfully convert atrial fibrillation or flutter. *Pacing Clin Electrophysiol* 2007; **30:** 1331–5.

Effects on the kidneys. Acute renal failure with biopsy evidence of acute tubular necrosis developed in a 52-year-old man shortly after he received 2 doses of ibutilide for an episode of atrial flutter.[1] Renal function returned to normal after 4 sessions of haemodialysis.

1. Franz M, *et al.* Acute renal failure after ibutilide. *Lancet* 1999; **353:** 467.

Precautions

ECG monitoring should be carried out during, and for at least 4 hours after, ibutilide infusion, and the infusion should be stopped if the QT interval becomes markedly prolonged. Electrolyte abnormalities should be corrected before treatment is started.

Interactions

Use of ibutilide with other antiarrhythmics or drugs that prolong the QT interval should be avoided.

Magnesium. For the synergistic effect of magnesium and ibutilide in producing cardioversion, see Effects on the Heart, above.

Pharmacokinetics

Ibutilide is widely distributed in the body after intravenous infusion. It has low plasma protein binding (about 40%) and undergoes extensive metabolism in the liver to form several metabolites. Ibutilide is excreted mainly in the urine, as metabolites and a small amount of unchanged drug (about 7%), with about 19% being excreted in the faeces. The elimination half-life is reported to range from 2 to 12 hours.

Uses and Administration

Ibutilide is a class III antiarrhythmic (p.1153) used for the acute treatment of atrial fibrillation or flutter (p.1160).

Ibutilide is given intravenously as the fumarate. For the termination of atrial fibrillation or flutter, ibutilide fumarate is given as a single dose of 1 mg in patients weighing 60 kg and over, or 10 micrograms/kg in patients weighing less than 60 kg, infused over 10 minutes; the infusion should be stopped as soon as the arrhythmia is terminated. If the arrhythmia persists 10 minutes after completion of the infusion, a second infusion of the same dose may be given.

◊ References.

1. Foster RH, *et al.* Ibutilide: a review of its pharmacological properties and clinical potential in the acute management of atrial flutter and fibrillation. *Drugs* 1997; **54:** 312–30.
2. Granberry MC. Ibutilide: a new class III antiarrhythmic agent. *Am J Health-Syst Pharm* 1998; **55:** 255–60.
3. Howard PA. Ibutilide: an antiarrhythmic agent for the treatment of atrial fibrillation or flutter. *Ann Pharmacother* 1999; **33:** 38–47.
4. Doggrell SA, Hancox JC. Ibutilide—recent molecular insights and accumulating evidence for use in atrial flutter and fibrillation. *Expert Opin Invest Drugs* 2005; **14:** 655–69.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Corvert; ***Cz.:*** Corvert†; ***Fin.:*** Corvert; ***Fr.:*** Corvert†; ***Gr.:*** Corvert; ***Ital.:*** Corvert; ***Neth.:*** Corvert; ***Norw.:*** Corvert; ***Swed.:*** Corvert; ***Switz.:*** Corvert; ***USA:*** Corvert.

Idraparinux Sodium *(USAN, rINN)*

Idraparinux sódico; Idraparinux Sodique; Idraparinuxum Natricum; Org-34006; SANORG-34006; SR-34006. Methyl *O*-2,3,4-tri-*O*-methyl-6-*O*-sulfo-α-D-glucopyranosyl-(1→4)-*O*-2,3-di-*O*-methyl-β-D-glucopyranuronosyl-(1→4)-*O*-2,3,6-tri-*O*-sulfo-α-D-glucopyranosyl-(1→4)-*O*-2,3-di-*O*-methyl-α-L-idopyranuronosyl-(1→4)-2,3,6-tri-*O*-sulfo-α-D-glucopyranoside nonasodium.

Идрапаринукс Натрия

$C_{38}H_{55}Na_9O_{49}S_7$ = 1727.2.

CAS — 162610-17-5 (idraparinux); 149920-56-9 (idraparinux sodium).