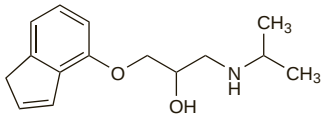
Indenolol Hydrochloride *(BANM, rINNM)* ⊗

Hidrocloruro de indenolol; Indénolol, Chlorhydrate d'; Indenololi Hydrochloridum; Sch-28316Z (indenolol); YB-2.

Инденолола Гидрохлорид

$C_{15}H_{21}NO_2.HCl$ = 283.8.

CAS — 60607-68-3 (indenolol); 68906-88-7 (indenolol hydrochloride).



(indenolol)

Description. Indenolol hydrochloride is a 2:1 tautomeric mixture of 1-(inden-7-yloxy)-3-isopropylaminopropan-2-ol hydrochloride and 1-(inden-4-yloxy)-3-isopropylaminopropan-2-ol hydrochloride.

Pharmacopoeias. In *Jpn.*

Profile

Indenolol is a non-cardioselective beta blocker (p.1225). It is reported to possess potent membrane-stabilising properties and intrinsic sympathomimetic activity.

Indenolol has been used orally as the hydrochloride in the management of various cardiovascular disorders.

Preparations

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

Indobufen *(rINN)*

Indobufén; Indobufène; Indobufenum; K-3920. (±)-2-[4-(1-Oxoisoindolin-2-yl)phenyl]butyric acid.

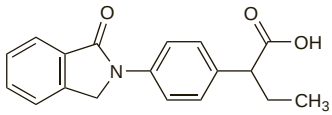
Индобуфен

$C_{18}H_{17}NO_3$ = 295.3.

CAS — 63610-08-2.

ATC — B01AC10.

ATC Vet — QB01AC10.



Profile

Indobufen is an inhibitor of platelet aggregation used in various thromboembolic disorders (p.1187) in oral doses of 200 to 400 mg daily given in 2 divided doses. For patients over the age of 65, the dose should be reduced to 100 to 200 mg daily. Doses should also be reduced in renal impairment (see below). Indobufen has also been given parenterally as the sodium salt.

◊ References.

1. Wiseman LR, *et al.* Indobufen: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy in cerebral, peripheral and coronary vascular disease. *Drugs* 1992; **44:** 445–64.
2. Bhana N, McClellan KJ. Indobufen: an updated review of its use in the management of atherothrombosis. *Drugs Aging* 2001; **18:** 369–88.

Administration in renal impairment. In patients with renal impairment the dose of indobufen should be reduced to 100 mg twice daily; it should not be used if the creatinine clearance is under 30 mL/minute.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Ibustrin; ***Cz.:*** Ibustrin; ***Ital.:*** Ibustrin; ***Mex.:*** Ibustrin; ***Pol.:*** Ibustrin; ***Port.:*** Ibustrin; ***Venez.:*** Ibustrin.

Indoramin Hydrochloride

(BANM, USAN, rINNM)

Hidrocloruro de indoramina; Indoramine, Chlorhydrate d'; Indoramini Hydrochloridum; Wy-21901 (indoramin). *N*-[1-(2-Indol-3-ylethyl)-4-piperidyl]benzamide hydrochloride.

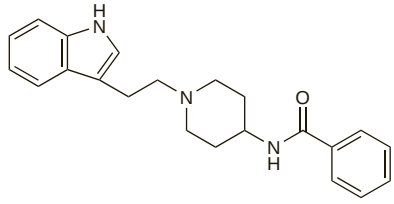
Индорамина Гидрохлорид

$C_{22}H_{25}N_3O.HCl$ = 383.9.

CAS — 26844-12-2 (indoramin); 33124-53-7 (indoramin hydrochloride); 38821-52-2 (indoramin hydrochloride).

ATC — C02CA02.

ATC Vet — QC02CA02.



(indoramin)

Pharmacopoeias. In *Br.*

BP 2008 (Indoramin Hydrochloride). A white or almost white powder. It exhibits polymorphism. Slightly soluble in water; sparingly soluble in alcohol; very slightly soluble in ether; soluble in methyl alcohol. A 2% suspension in water has a pH of 4.0 to 5.5. Protect from light.

Adverse Effects, Treatment, and Precautions

The most common adverse effects in patients receiving indoramin are sedation and dizziness; dry mouth, nasal congestion, headache, fatigue, depression, weight gain (almost certainly due to fluid retention), and failure of ejaculation may also occur. Tachycardia does not seem to be a problem with therapeutic doses but orthostatic hypotension may occur and may produce syncope. Extrapyramidal disturbances have been reported.

After overdosage, coma, convulsions, and hypotension may occur; hypothermia has been reported in *animals*. In acute poisoning appropriate symptomatic and supportive care should be given; if the patient presents within 1 hour, activated charcoal may be considered.

Indoramin should be avoided in patients with heart failure; it has been recommended that incipient heart failure should be controlled before giving indoramin. Caution should be observed in patients with hepatic or renal impairment, a history of depression, epilepsy, or Parkinson's disease. Elderly patients may respond to lower doses.

Because indoramin can cause drowsiness care should be taken in patients who drive or operate machinery.

Cataract surgery. For a warning about intraoperative floppy iris syndrome during cataract surgery in patients taking alpha blockers, see Surgical Procedures, under Precautions for Tamsulosin Hydrochloride, p.2197.

Effects on mental function. Sleep disturbances and vivid dreams were reported during a study in hypertensive patients when indoramin was added to therapy with a thiazide diuretic and a beta blocker.[1]

1. Marshall AJ, *et al.* Evaluation of indoramin added to oxprenolol and bendrofluazide as a third agent in severe hypertension. *Br J Clin Pharmacol* 1980; **10:** 217–21.

Overdosage. A 43-year-old woman with a long history of heavy alcohol intake died after taking 100 tablets of indoramin 25 mg.[1] The main clinical features were deep sedation, respiratory depression, hypotension, and convulsions. Although the hypotension was satisfactorily controlled the CNS effects were resistant to treatment and proved fatal. Other clinical features included areflexia, metabolic acidosis, tachycardia, and later bradyarrhythmias.

1. Hunter R. Death due to overdose of indoramin. *BMJ* 1982; **285:** 1011.

Interactions

The hypotensive effects of indoramin may be enhanced by diuretics and other antihypertensives. It has been reported that the ingestion of alcohol can increase the rate and extent of absorption and the sedative effects of indoramin (see below) and that indoramin should not be given to patients already receiving MAOIs.

Alcohol. In a study[1] in 9 healthy subjects alcohol 500 mg/kg significantly enhanced plasma-indoramin concentrations after an oral dose of 50 mg. The effect was most marked in the early period, corresponding to the absorptive phase. The mean maximum plasma-indoramin concentration was increased from 15.0 to 23.7 nanograms/mL by alcohol; the area under the concentration/time curve was increased by 25%. Alcohol did not affect the pharmacokinetics of intravenous indoramin. The results suggest that alcohol increases indoramin bioavailability either by enhancing absorption or reducing first-pass metabolism. The combination was more sedative than either drug alone.

1. Abrams SML, *et al.* Pharmacokinetic interaction between indoramin and ethanol. *Hum Toxicol* 1989; **8:** 237–41.

Pharmacokinetics

Indoramin is readily absorbed from the gastrointestinal tract and undergoes extensive first-pass metabolism. It is reported to be about 90% bound to plasma proteins. It has a half-life of about 5 hours which is reported to be prolonged in elderly patients. It is extensively metabolised and is excreted mainly as metabolites in the urine and faeces. There is evidence to suggest that some metabolites may have some alpha-adrenoceptor blocking activity.

The elderly. The plasma half-life of indoramin in 5 healthy elderly subjects following a single oral dose ranged from 6.6 to 32.8 hours with a mean of 14.7 hours.[1] The increased half-life may have been caused by reduced clearance in elderly patients.

1. Norbury HM, *et al.* Pharmacokinetics of oral indoramin in elderly and middle-aged female volunteers. *Eur J Clin Pharmacol* 1984; **27:** 247–9.

Uses and Administration

Indoramin is a selective and competitive alpha$_1$-adrenoceptor blocker (p.1153) with actions similar to those of prazosin (p.1376); it is also reported to have membrane-stabilising properties and to be a competitive antagonist at histamine H_1 and 5-hydroxytryptamine receptors. Indoramin is used in the management of hypertension (p.1171), and in benign prostatic hyperplasia (p.2178) to relieve symptoms of urinary obstruction. It has also been used in the prophylactic treatment of migraine.

Indoramin is given orally as the hydrochloride, but doses are usually expressed in terms of the base. Indoramin hydrochloride 11.0 mg is equivalent to about 10 mg of indoramin.

In **hypertension**, the initial dose is 25 mg twice daily, increased in steps of 25 or 50 mg at intervals of 2 weeks to a maximum of 200 mg daily in 2 or 3 divided doses.

In **benign prostatic hyperplasia**, the initial dose is 20 mg twice daily, increased if necessary by 20 mg at 2-week intervals, to a maximum of 100 mg daily in divided doses.

Lower doses may be required in the elderly.

◊ Reviews.

1. Holmes B, Sorkin EM. Indoramin: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy in hypertension and related vascular, cardiovascular and airway diseases. *Drugs* 1986; **31:** 467–99.

Migraine. Propranolol is probably the most well-established drug for prophylaxis of migraine (p.616). Many other drugs have been used including indoramin. In a double-blind study,[1] indoramin in a dose of 25 mg twice daily was reported to be as effective as dihydroergotamine mesilate in reducing the frequency of migraine attacks.

1. Pradalier A, *et al.* Etude comparative indoramine versus dihydroergotamine dans le traitement préventif de la migraine. *Therapie* 1988; **43:** 293–7.

Preparations

BP 2008: Indoramin Tablets.

Proprietary Preparations (details are given in Part 3)
Austria: Wypresin†; ***Fr.:*** Vidora; ***Ger.:*** Wydora; ***Irl.:*** Baratol†; Doralese; ***S.Afr.:*** Baratol; ***UK:*** Baratol; Doralese.
