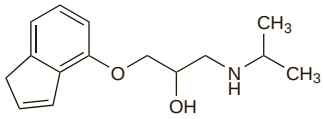
### Indenolol Hydrochloride *(BANM, rINNM)* ⊗

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†.

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### Indobufen *(rINN)*

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

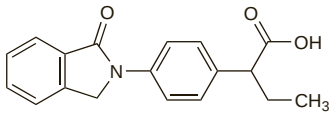
Индобуфен

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

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## 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.

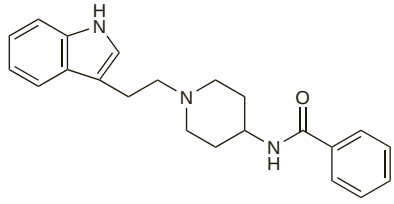
Индорамина Гидрохлорид

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

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### Inositol Nicotinate *(BAN, rINN)*

Inositol Niacinate *(USAN)*; Inositol, Nicotinate d'; Inositoli Nicotinas; Inositolinikotinaatti; Inositolnikotinat; Nicotinato de inositol; NSC-49506; Win-9154. *meso*-Inositol hexanicotinate; *myo*-Inositol hexanicotinate.

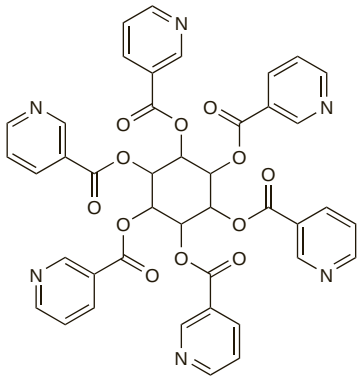
Инозитола Никотинат

$C_{42}H_{30}N_6O_{12}$ = 810.7.

*CAS — 6556-11-2.*

*ATC — C04AC03.*

*ATC Vet — QC04AC03.*



**Pharmacopoeias.** In *Br.*

**BP 2008** (Inositol Nicotinate). A white or almost white, odourless or almost odourless powder. Practically insoluble in water, in alcohol, in acetone, and in ether; sparingly soluble in chloroform. It dissolves in dilute mineral acids.

#### Profile

Inositol nicotinate is a vasodilator and is believed to be slowly hydrolysed to nicotinic acid (p.1957). It is given orally in the management of peripheral vascular disease (p.1178). The usual dose is 3 g daily given in divided doses. The dose may be increased to 4 g daily if necessary.

Inositol nicotinate has been used in hyperlipidaemias.

#### Preparations

***BP 2008:*** Inositol Nicotinate Tablets.

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Evicyl†; ***Ger.:*** Hamovannad†; Nicolip; ***Irl.:*** Hexogen†; Hexopal; ***Neth.:*** Palohex; ***UK:*** Hexopal.

**Multi-ingredient:** ***Ger.:*** Zellaforte N Plus†; ***S.Afr.:*** Geratar.

## Irbesartan *(BAN, USAN, rINN)*

BMS-186295; Irbesartaani; Irbésartan; Irbesartán; Irbesartanum; SR-47436. 2-Butyl-3-[*p*-(*o*-1*H*-tetrazol-5-ylphenyl)benzyl]-1,3-diazaspiro[4.4]non-1-en-4-one.

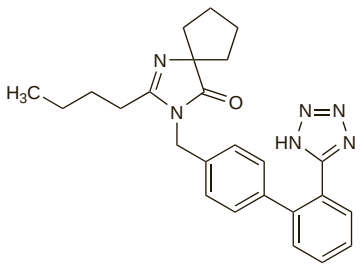
Ирбесартан

$C_{25}H_{28}N_6O$ = 428.5.

*CAS — 138402-11-6.*

*ATC — C09CA04.*

*ATC Vet — QC09CA04.*



**Pharmacopoeias.** In *US.*

**USP 31** (Irbesartan). A white to off-white, crystalline powder. Practically insoluble in water; slightly soluble in alcohol and in dichloromethane. Store in airtight containers at a temperature below 30°.

#### Adverse Effects and Precautions

As for Losartan Potassium, p.1326.

#### Interactions

As for Losartan Potassium, p.1327.

#### Pharmacokinetics

Irbesartan is rapidly absorbed from the gastrointestinal tract with an oral bioavailability of 60 to 80%. Peak plasma concentrations of irbesartan occur 1.5 to 2 hours after an oral dose. Irbesartan is about 96% bound to plasma proteins. It undergoes some metabolism in the liver, primarily by the cytochrome P450 isoenzyme CYP2C9, to inactive metabolites. It is excreted as unchanged drug and metabolites in the bile and in urine; about 20% of an oral or intravenous dose is excreted in the urine, with less than 2% as unchanged drug. The terminal elimination half-life is about 11 to 15 hours.

◊ References.


1. Sica DA, *et al.* The pharmacokinetics of irbesartan in renal failure and maintenance hemodialysis. *Clin Pharmacol Ther* 1997; **62:** 610–18.
2. Marino MR, *et al.* Pharmacokinetics and pharmacodynamics of irbesartan in healthy subjects. *J Clin Pharmacol* 1998; **38:** 246–55.
3. Marino MR, *et al.* Pharmacokinetics and pharmacodynamics of irbesartan in patients with hepatic cirrhosis. *J Clin Pharmacol* 1998; **38:** 347–56.
4. Vachharajani NN, *et al.* Oral bioavailability and disposition characteristics of irbesartan, an angiotensin antagonist, in healthy volunteers. *J Clin Pharmacol* 1998; **38:** 702–7.
5. Vachharajani NN, *et al.* The effects of age and gender on the pharmacokinetics of irbesartan. *Br J Clin Pharmacol* 1998; **46:** 611–13.
6. Sakarcan A, *et al.* The pharmacokinetics of irbesartan in hypertensive children and adolescents. *J Clin Pharmacol* 2001; **41:** 742–9.


#### Uses and Administration

Irbesartan is an angiotensin II receptor antagonist with actions similar to those of losartan (p.1327). It is used in the management of hypertension (p.1171) including the treatment of renal disease in hypertensive diabetic patients (see Kidney Disorders, under Uses of Losartan, p.1328). Irbesartan is also under investigation in heart failure.

Irbesartan is given orally. After a dose the hypotensive effect peaks within 3 to 6 hours and persists for at least 24 hours. The maximum hypotensive effect is achieved within 4 to 6 weeks after starting therapy.

In **hypertension**, irbesartan is given in a dose of 150 mg once daily increased, if necessary, to 300 mg once daily. A lower initial dose of 75 mg once daily may be considered in elderly patients over 75 years, for patients with intravascular volume depletion, and for those receiving haemodialysis.

For the treatment of **renal disease** in hypertensive type 2 diabetics, irbesartan should be given in an initial dose of 150 mg once daily, increased to 300 mg once daily for maintenance.

◊ Reviews.


1. Gillis JC, Markham A. Irbesartan: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic use in the management of hypertension. *Drugs* 1997; **54:** 885–902.
2. Brown MJ. Irbesartan treatment in hypertension. *Hosp Med* 1998; **59:** 808–11.
3. Markham A, *et al.* Irbesartan: an updated review of its use in cardiovascular disorders. *Drugs* 2000; **59:** 1187–1206.
4. Croom KF, *et al.* Irbesartan: a review of its use in hypertension and in the management of diabetic nephropathy. *Drugs* 2004; **64:** 999–1028.
5. Ravera M, *et al.* Prevention and treatment of diabetic nephropathy: the program for irbesartan mortality and morbidity evaluation. *J Am Soc Nephrol* 2005; **16** (suppl 1): S48–S52.
6. Palmer AJ, *et al.* Irbesartan treatment of patients with type 2 diabetes, hypertension and renal disease: a UK health economics analysis. *Int J Clin Pract* 2007; **61:** 1626–33.
7. Flack JM. Maximising antihypertensive effects of angiotensin II receptor blockers with thiazide diuretic combination therapy: focus on irbesartan/hydrochlorothiazide. *Int J Clin Pract* 2007; **61:** 2093–1102.


**Administration in children.** Although irbesartan appears to be well-tolerated in children with hypertension and has been shown to reduce blood pressure in small studies,[1] US licensed product information notes that doses of up to 4.5 mg/kg once daily were ineffective in children aged 6 to 16 years and no longer recommends use in such patients.

In children with chronic kidney diseases, irbesartan has been reported to reduce blood pressure and proteinuria.[2,3] The initial dose was 37.5 mg once daily for children weighing 10 to 20 kg, 75 mg once daily for those weighing 21 to 40 kg, and 150 mg once daily for those weighing more than 40 kg; doses could be doubled if the blood pressure response was inadequate.


1. Sakarcan A, *et al.* The pharmacokinetics of irbesartan in hypertensive children and adolescents. *J Clin Pharmacol* 2001; **41:** 742–9.
2. Franscini LMD, *et al.* Effectiveness and safety of the angiotensin II antagonist irbesartan in children with chronic kidney diseases. *Am J Hypertens* 2002; **15:** 1057–63.
3. Gartenmann AC, *et al.* Better renoprotective effect of angiotensin II antagonist compared to dihydropyridine calcium channel blocker in childhood. *Kidney Int* 2003; **64:** 1450–4.


#### Preparations

***USP 31:*** Irbesartan and Hydrochlorothiazide Tablets; Irbesartan Tablets.

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Adana; Aprovel; Avapro; ***Austral.:*** Avapro; Karvea; ***Belg.:*** Aprovel; ***Braz.:*** Aprovel; Avapro; ***Canad.:*** Avapro; ***Chile:*** Aprovel; ***Cz.:*** Aprovel; Karvea; ***Denm.:*** Aprovel; ***Fin.:*** Aprovel; ***Fr.:*** Aprovel; ***Ger.:*** Aprovel; Karvea; ***Gr.:*** Aprovel; Karvea; ***Hong Kong:*** Aprovel; ***Hung.:*** Aprovel; ***India:*** Iroveł; Xarb; ***Indon.:*** Aprovel; Fristens; Iretensa; Irvell; ***Irl.:*** Aprovel; ***Israel:*** Irban†; ***Ital.:*** Aprovel; Karvea; ***Malaysia:*** Aprovel; ***Mex.:*** Aprovel; Avapro; ***Neth.:*** Aprovel; Karvea; ***Norw.:*** Aprovel; ***NZ:*** Karvea; ***Philipp.:*** Aprovel; ***Pol.:*** Aprovel; ***Port.:*** Aprovel; Karvea; ***Rus.:*** Aprovel (Апровель); ***S.Afr.:*** Aprovel; ***Singapore:*** Aprovel; ***Spain:*** Aprovel; Karvea; ***Swed.:*** Aprovel; ***Switz.:*** Aprovel; ***Thai.:*** Aprovel; ***Turk.:*** Karvea; ***UK:*** Aprovel; ***USA:*** Avapro; ***Venez.:*** Aprovel.

**Multi-ingredient:** ***Arg.:*** Adana Plus; Avapro HCT; CoAprovel; ***Austral.:*** Avapro HCT; Karvezide; ***Belg.:*** CoAprovel; ***Braz.:*** Aprozide; ***Canad.:*** Avalide; ***Chile:*** CoAprovel; ***Cz.:*** CoAprovel; Karvezide; ***Denm.:*** CoAprovel; ***Fr.:*** CoAprovel; ***Ger.:*** CoAprovel; Karvezide; ***Gr.:*** CoAprovel; Karvezide; ***Hong Kong:*** Aprovel HCT†; CoAprovel; ***Hung.:*** CoAprovel; ***India:*** Xarb-H; ***Indon.:*** CoAprovel; Irtan Plus; ***Irl.:*** CoAprovel; ***Israel:*** Irban Plus†; ***Ital.:*** CoAprovel; Karvezide; ***Malaysia:*** CoAprovel; ***Mex.:*** Avalide; CoAprovel; ***Neth.:*** CoAprovel; Karvezide; ***Norw.:*** CoAprovel; ***NZ:*** Karvezide; ***Philipp.:*** CoAprovel; ***Port.:*** CoAprovel; Karvezide; ***S.Afr.:*** CoAprovel; ***Singapore:*** CoAprovel; ***Spain:*** CoAprovel; Karvezide; ***Swed.:*** CoAprovel; ***Switz.:*** CoAprovel; ***Thai.:*** Aprovel HCT†; CoAprovel; ***Turk.:*** Karvezide; ***UK:*** CoAprovel; ***USA:*** Avalide; ***Venez.:*** CoAprovel.

## Isoprenaline *(BAN, rINN)* ⊗

Isoprenaliini; Isoprenalin; Isoprenalina; Isoprénaline; Isoprenalinum; Isopropylarterenol; Isopropylnoradrenaline; Isoproterenol. 1-(3,4-Dihydroxyphenyl)-2-isopropylaminoethanol.

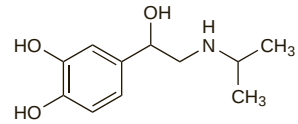
Изопреналин

$C_{11}H_{17}NO_3$ = 211.3.

*CAS — 7683-59-2.*

*ATC — C01CA02; R03AB02; R03CB01.*

*ATC Vet — QC01CA02; QR03AB02; QR03CB01.*



### Isoprenaline Hydrochloride *(BANM, rINNM)* ⊗

Hidrocloruro de isoprenalina; Isoprenaliinihydrokloridi; Isoprénaline, chlorhydrate d'; Isoprenalin-hydrochlorid; Isoprenalinhydroklorid; Isoprenalini hydrochloridum; Isopropylarterenol Hydrochloride; Isopropylnoradrenaline Hydrochloride; Isoproterenol Hydrochloride; Izoprenalin Hidroklorür; Izoprenalin-hidroklorid; Izoprenalino hidrochloridas.

Изопреналина Гидрохлорид

$C_{11}H_{17}NO_3$,HCl = 247.7.

*CAS — 51-30-9.*

*ATC — C01CA02; R03AB02; R03CB01.*

*ATC Vet — QC01CA02; QR03AB02; QR03CB01.*

**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*

**Ph. Eur. 6.2** (Isoprenaline Hydrochloride). A white or almost white crystalline powder. Freely soluble in water; sparingly soluble in alcohol; practically insoluble in dichloromethane. A 5% solution in water has a pH of 4.3 to 5.5. Store in airtight containers. Protect from light.

**USP 31** (Isoproterenol Hydrochloride). A white to practically white, odourless, crystalline powder. It gradually darkens on exposure to air and light. Soluble 1 in 3 of water and 1 in 50 of alcohol; less soluble in dehydrated alcohol; insoluble in chloroform and in ether. A 1% solution in water has a pH of about 5. Solutions become pink to brownish-pink on standing exposed to air and almost immediately so when made alkaline. Store in airtight containers. Protect from light.

### Isoprenaline Sulfate *(rINNM)* ⊗

Isoprenaliinisulfaatti; Isoprenalin sulfát dihydrát; Isoprénaline, sulfate d'; Isoprenaline Sulphate *(BANM)*; Isoprenalini sulfas; Isoprenalini Sulfas Dihydricus; Isoprenalinsulfat; Isopropylarterenol Sulphate; Isopropylnoradrenaline Sulphate; Isoproterenol Sulfate; Izoprenalino sulfatas; Izoprenalin-szulfát; Izoprenaliny siarczan; Sulfato de isoprenalina.

Изопреналина Сульфат

$(C_{11}H_{17}NO_3)_2,H_2SO_4,2H_2O$ = 556.6.

*CAS — 299-95-6 (anhydrous isoprenaline sulfate); 6700-39-6 (isoprenaline sulfate dihydrate).*

*ATC — C01CA02; R03AB02; R03CB01.*

*ATC Vet — QC01CA02; QR03AB02; QR03CB01.*