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.

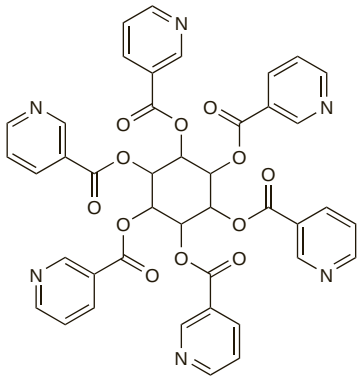
Инозитола Никотинат

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

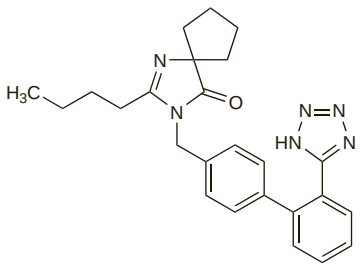
Ирбесартан

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

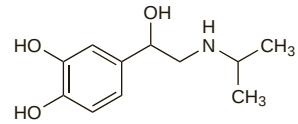
Изопреналин

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