release Capsules; Propranolol Hydrochloride and Hydrochlorothiazide Tablets; Propranolol Hydrochloride Extended-release Capsules; Propranolol Hydrochloride Injection; Propranolol Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Inderal; Pirimetan; Propalong†; Propaneitor; Propayerst†; ***Austral.:*** Deralin; Inderal; ***Austria:*** Inderal; Proprahexal; ***Belg.:*** Inderal; ***Braz.:*** Antitensin; Cardiopranol†; Cardix; Hipernolol; Inderal; Neo Propranol†; Polol; Pradinolol; Pranolal; Propacor; Propalol†; Propanox†; Proparil†; Propramed; Propranol†; Propranolil†; Propranolum†; Rebaten; Sanpronol; Uni Propralol; ***Canad.:*** Inderal; Novo-Pranol; ***Chile:*** Coriodal; ***Denm.:*** Inderal†; Propal; ***Fin.:*** Inderal†; Propral; Ranoprin; ***Fr.:*** Adrexan†; Avlocardyl; Hemipralon†; ***Ger.:*** Beta-Tablinen; Dociton; Efektolol†; Elbrol; Obsidan; Propabloc†; Prophylux; propra; Propra-ratiopharm; Propranur; ***Gr.:*** Inderal; ***Hong Kong:*** Becardin†; Hopranolol†; Inderal; Inpanol; Palon†; Prolol†; Propa†; ***Hung.:*** Huma-Pronol; ***India:*** Betabloc; Betaspan; Ciplar; Corbeta; Inderal; Propal; ***Indon.:*** Farmadral; Inderal; ***Irl.:*** Half Inderal; Inderal; Tiperal†; ***Israel:*** Deralin; Inderal; Prolol; Slow Deralin; ***Ital.:*** Inderal; ***Malaysia:*** Inderal; Indon†; Propanol†; ***Mex.:*** Acifol†; Inderalici; Pranoral†; Prochor†; Propalem; Propalgin†; Sintaser; ***Norw.:*** Inderal; Pranolol; ***NZ:*** Angilol; Cardinol; Inderal; ***Philipp.:*** Duranol; Inderal; Phanerol; ***Port.:*** Corpendol†; Inderal; ***Rus.:*** Анаприлин (Anaprilin); Obsidan (Обзидан); ***S.Afr.:*** Cardiblok; Inderal; Prodorol; Pur-Bloka; ***Singapore:*** Inderal; Inpanol; ***Spain:*** Sumial; ***Swed.:*** Inderal; ***Switz.:*** Inderal; ***Thai.:*** Alperol; Atensin†; Betalol; Betapress; Cardenol; Emforal; Inderal; Normpress; Palon; Perlol; Pralol; Prolol; Syntonol; ***Turk.:*** Dideral; ***UAE:*** Cardilol; ***UK:*** Angilol; Bedranol; Beta-Prograne; Half Beta-Prograne; Half Inderal; Inderal; Slo-Pro; Syprol; ***USA:*** Inderal; InnoPran; ***Venez.:*** Algoren; Docitral; Galenol†; Indal†; Inderal; Parinex†.

Multi-ingredient: ***Arg.:*** Propayerst Plus†; ***Austria:*** Inderetic†; ***Belg.:*** Inderetic†; ***Braz.:*** Polol-H; Tenadren; ***Ger.:*** Beta-Turfa; Diutensat comp†; Docidrazin†; Dociretic; Dociteren; Nitro-Obsidan†; Obsilazin N†; Pertenso N; Propra comp; Triamteren tri-comp; ***India:*** Beptazine; Beptazine-H; Ciplar-H; Corbetazine; Zopax Plus; ***Neth.:*** Inderetic; ***S.Afr.:*** Inderetic†; ***Spain:*** Betadipresan Diu†; Betadipresan†; ***Switz.:*** Inderetic†; ***UK:*** Inderetic†; Inderex†; ***USA:*** Inderide†.

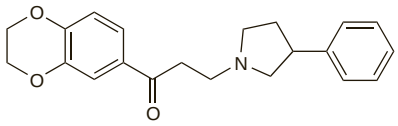
Proroxan *(pINN)*

Proroxano; Proroxanum. 1-(2,3-Dihydro-1,4-benzodioxin-6-yl)-3-(3-phenyl-1-pyrrolidinyl)-1-propanone.

Пророксан

$C_{21}H_{23}NO_3$ = 337.4.

CAS — 33743-96-3 (proroxan).



Proroxan Hydrochloride *(USAN, pINNM)*

AY-24269; Hidrocloruro de proroxano; Proroxan, Chlorhydrate de; Proroxani Hydrochloridum.

Пророксана Гидрохлорид

$C_{21}H_{23}NO_3HCl$ = 373.9.

CAS — 33025-33-1.

Profile

Proroxan has been used as an antihypertensive and in the treatment of Ménière's disease, motion sickness, and allergic dermatitis.

Proscillaridin *(BAN, USAN, rINN)*

2936; A-32686; Proscilaridina; Proscillaridiini; Proscillaridin A; Proscillaridine; Proscillaridinum; PSC-801. 14-Hydroxy-3β-(α-L-rhamnopyranosyloxy)-14β-bufa-4,20,22-trienolide.

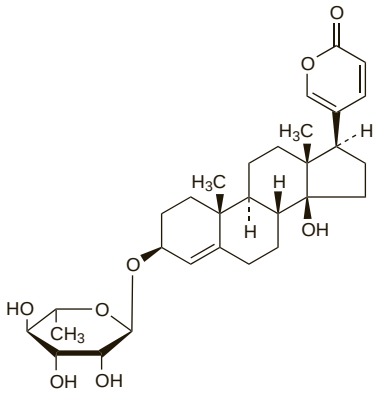
Просцилларидин

$C_{30}H_{42}O_8$ = 530.6.

CAS — 466-06-8.

ATC — C01AB01.

ATC Vet — QC01AB01.



Profile

Proscillaridin is a cardiac glycoside obtained from *Drimia maritima* (Liliaceae). It is a positive inotrope with general properties similar to those of digoxin (p.1259). It is reported to have a rapid onset and a short duration of action.

Proscillaridin is used in the treatment of heart failure (p.1165). It is given orally in usual initial and maintenance doses of 1 to 1.5 mg daily; maintenance doses may range from 0.75 to 2 mg daily as required.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Talusin; ***Pol.:*** Talusin.

Quinapril Hydrochloride

(BANM, USAN, rINNM)

CI-906 (quinapril); Hidrocloruro de quinapril; Kinapril Hidroklorür; Quinapril, chlorhydrate de; Quinaprili hydrochloridum. (3*S*)-2-{*N*-[(*S*)-1-Ethoxycarbonyl-3-phenylpropyl]-L-alanyl}-1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid hydrochloride.

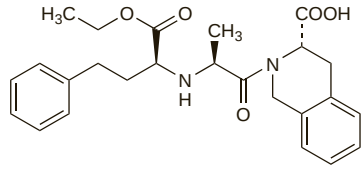
Хинаприла Гидрохлорид

$C_{25}H_{30}N_2O_5$,HCl = 475.0.

CAS — 85441-61-8 (quinapril); 82586-55-8 (quinapril hydrochloride).

ATC — C09AA06.

ATC Vet — QC09AA06.



(quinapril)

Pharmacopoeias. In *US*.

USP 31 (Quinapril Hydrochloride). A white to off-white powder, with a pink cast at times. Freely soluble in aqueous solvents.

Suspension. Extemporaneous formulations of quinapril 1 mg/mL made by adding crushed Accupril tablets (*Pfizer, US*) to the following vehicles were found to be stable for 6 weeks when stored at 5°:

- *Kphos* 15% (*Beach, US*), *Bicitra* 15% (*Draxis Pharma, US*), *OraSweet* 70% (*Paddock, US*)
- *Kphos* 15%, *Bicitra* 15%, *OraSweet SF* 70%
- *Kphos* 15%, *Bicitra* 15%, simple syrup 70%

The suspension containing *OraSweet SF* was considered to be the formulation of choice.[1]

1. Freed AL, *et al.* The development and stability assessment of extemporaneous pediatric formulations of Accupril. *Int J Pharm* 2005;**304:** 135–44.

Adverse Effects, Treatment, and Precautions

As for ACE inhibitors, p.1193.

Breast feeding. After of a single dose of quinapril 20 mg in 6 women, quinapril was detected in the breast milk in a milk to plasma ratio of 0.12; no quinaprilat was detected.[1] It was estimated that the dose received by the infant would only be about 1.6% of the maternal dose.

1. Begg EJ, *et al.* Quinapril and its metabolite quinaprilat in human milk. *Br J Clin Pharmacol* 2001; **51:** 478–81.

Interactions

As for ACE inhibitors, p.1196.

Antibacterials. Quinapril has been reported to reduce the absorption of *tetracyclines* due to the presence of magnesium carbonate in the tablet formulation.

Pharmacokinetics

Quinapril acts as a prodrug of the diacid quinaprilat, its active metabolite. About 60% of an oral dose of quinapril is absorbed. Quinapril is metabolised mainly in the liver to quinaprilat and inactive metabolites. Peak plasma concentrations of quinaprilat are achieved within 2 hours of an oral dose of quinapril. Quinaprilat is about 97% bound to plasma proteins. After an oral dose, quinapril is excreted in the urine and faeces, as quinaprilat, other metabolites, and unchanged drug, with the urinary route predominating; up to 96% of an intravenous dose of quinaprilat is excreted in the urine.

The effective half-life for accumulation of quinaprilat is about 3 hours after multiple doses of quinapril; a long terminal phase half-life of 25 hours may represent strong binding of quinaprilat to angiotensin-converting enzyme.

The pharmacokinetics of both quinapril and quinaprilat are affected by renal and hepatic impairment. Dialysis has little effect on the excretion of quinapril or quinaprilat.

Small amounts of quinapril are distributed into breast milk.

◊ References.

1. Begg EJ, *et al.* The pharmacokinetics and pharmacodynamics of quinapril and quinaprilat in renal impairment. *Br J Clin Pharmacol* 1990; **30:** 213–20.
2. Halstenson CE, *et al.* The pharmacokinetics of quinapril and its active metabolite, quinaprilat, in patients with various degrees of renal function. *J Clin Pharmacol* 1992; **32:** 344–50.
3. Wolter K, Fritschka E. Pharmacokinetics and pharmacodynamics of quinaprilat after low dose quinapril in patients with terminal renal failure. *Eur J Clin Pharmacol* 1993; **44** (suppl 1): S53–6.
4. Begg EJ, *et al.* The pharmacokinetics of quinapril and quinaprilat in patients with congestive heart failure. *Br J Clin Pharmacol* 1994; **37:** 302–4.
5. Squire IB, *et al.* Haemodynamic response and pharmacokinetics after the first dose of quinapril in patients with congestive heart failure. *Br J Clin Pharmacol* 1994; **38:** 117–23.
6. Breslin E, *et al.* A pharmacodynamic and pharmacokinetic comparison of intravenous quinaprilat and oral quinapril. *J Clin Pharmacol* 1996; **36:** 414–21.

Uses and Administration

Quinapril is an ACE inhibitor (p.1193). It is used in the treatment of hypertension (p.1171) and heart failure (p.1165).

Quinapril is converted in the body to its active metabolite quinaprilat. The haemodynamic effects are seen within 1 hour of a single oral dose and the maximum effect occurs after about 2 to 4 hours, although the full effect may not develop for 1 to 2 weeks during chronic use. The haemodynamic action persists for about 24 hours, allowing once-daily dosing. Quinapril is given orally as the hydrochloride, but doses are expressed in terms of the base. Quinapril hydrochloride 10.8 mg is equivalent to about 10.0 mg of quinapril.

In the treatment of **hypertension** the initial dose is 10 mg of quinapril once daily. Since there may be a precipitous fall in blood pressure in some patients when starting therapy with an ACE inhibitor, the first dose should preferably be given at bedtime. An initial dose of 2.5 mg daily is recommended in the elderly, in patients with renal impairment, or in those taking a *diuretic*; if possible, the diuretic should be withdrawn 2 or 3 days before quinapril is started and resumed later if necessary.

The usual maintenance dose is 20 to 40 mg daily, as a single dose or divided into 2 doses, although up to 80 mg daily has been given.

In the management of **heart failure**, severe first-dose hypotension on introduction of an ACE inhibitor is common in patients on loop diuretics, but their temporary withdrawal may cause rebound pulmonary oedema. Thus treatment should begin with a low dose under close medical supervision. Quinapril is given in an initial dose of 2.5 mg daily. Usual maintenance doses range from 10 to 20 mg daily, as a single dose or divided into 2 doses; up to 40 mg daily has been given.

Quinaprilat may be given intravenously in patients unable to take quinapril orally; doses range from 1.25 to 10 mg twice daily.

◊ Reviews.

1. Wadworth AN, Brogden RN. Quinapril: a review of its pharmacological properties, and therapeutic efficacy in cardiovascular disorders. *Drugs* 1991; **41:** 378–99.
2. Plosker GL, Sorkin EM. Quinapril: a reappraisal of its pharmacology and therapeutic efficacy in cardiovascular disorders. *Drugs* 1994; **48:** 227–52.
3. Culy CR, Jarvis B. Quinapril: a further update of its pharmacology and therapeutic use in cardiovascular disorders. *Drugs* 2002; **62:** 339–85.

Preparations

USP 31: Quinapril Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Accupril; ***Austral.:*** Accupril; Acquin; Asig; Filpril; ***Austria:*** Accupro; ***Belg.:*** Accupril; ***Braz.:*** Accupril; ***Canad.:*** Accupril; ***Chile:*** Accupril; ***Cz.:***