infant would be very low. No adverse effects were noted in the infants in this study, and the American Academy of Pediatrics considers[2] that captopril is therefore usually compatible with breast feeding.

1. Devlin RG, Fleiss PM. Captopril in human blood and breast milk. *J Clin Pharmacol* 1981; **21:** 110–113.
2. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 05/07/04)

Porphyria. Captopril is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems.

Interactions

As for ACE inhibitors, p.1196.

Pharmacokinetics

About 60 to 75% of a dose of captopril is absorbed from the gastrointestinal tract and peak plasma concentrations are achieved within about an hour. Absorption has been reported to be reduced in the presence of food, but this may not be clinically relevant (see below). Captopril is about 30% bound to plasma proteins. It crosses the placenta and is found in breast milk at about 1% of maternal blood concentrations. It is largely excreted in the urine, 40 to 50% as unchanged drug, the rest as disulfide and other metabolites. The elimination half-life has been reported to be 2 to 3 hours but this is increased in renal impairment. Captopril is removed by haemodialysis.

◊ Reviews.

1. Duchin KL, *et al.* Pharmacokinetics of captopril in healthy subjects and in patients with cardiovascular diseases. *Clin Pharmacokinet* 1988; **14:** 241–59.

Absorption. The bioavailability and peak plasma concentrations of captopril have been shown to be reduced by 25 to 55% when given with food in single dose studies[1-4] and with chronic dosing.[5] However, this may not be clinically significant since several studies[3,4,6] indicated that food intake had no effect on the antihypertensive activity of captopril.

1. Williams GM, Sugerman AA. The effect of a meal, at various times relative to drug administration, on the bioavailability of captopril. *J Clin Pharmacol* 1982; **22:** 18A.
2. Singhvi SM, *et al.* Effect of food on the bioavailability of captopril in healthy subjects. *J Clin Pharmacol* 1982; **22:** 135–40.
3. Mäntylä R, *et al.* Impairment of captopril bioavailability by concomitant food and antacid intake. *Int J Clin Pharmacol Ther Toxicol* 1984; **22:** 626–9.
4. Müller HM, *et al.* The influence of food intake on pharmacodynamics and plasma concentration of captopril. *J Hypertens* 1985; **3** (suppl 2): S135–S136.
5. Öhman KP, *et al.* Pharmacokinetics of captopril and its effects on blood pressure during acute and chronic administration and in relation to food intake. *J Cardiovasc Pharmacol* 1985; **7** (suppl 1): S20–S24.
6. Izumi Y, *et al.* Influence of food on the clinical effect of angiotensin I converting enzyme inhibitor (SQ 14225). *Tohoku J Exp Med* 1983; **139:** 279–86.

Renal impairment. A study of 9 patients with chronic renal failure undergoing dialysis found that peak plasma concentrations of captopril were 2.5 times higher and peak concentrations of the disulfide metabolites were 4 times higher than in patients with normal renal function following a single dose of captopril.[1] Peak concentrations occurred later in uraemic patients and the apparent half-life of total captopril was 46 hours in uraemic patients compared with 2.95 hours in patients with normal renal function.

1. Drummer OH, *et al*. The pharmacokinetics of captopril and captopril disulfide conjugates in uraemic patients on maintenance dialysis: comparison with patients with normal renal function. *Eur J Clin Pharmacol* 1987; **32:** 267–71.

Uses and Administration

Captopril is a sulfhydryl-containing ACE inhibitor (p.1193). It is used in the management of hypertension (p.1171), in heart failure (p.1165), after myocardial infarction (p.1175), and in diabetic nephropathy (see Kidney Disorders, p.1199).

After oral doses captopril produces a maximum effect within 1 to 2 hours, although the full effect may not develop for several weeks during chronic dosing. The duration of action is dose-dependent and may persist for 6 to 12 hours.

In the treatment of **hypertension** the initial oral dose is 12.5 mg twice daily, increased gradually at intervals of 2 to 4 weeks according to the response. 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 6.25 mg twice daily is recommended if captopril is given in addition to a *diuretic* or to elderly patients; if possible the diuretic should be stopped 2 or 3 days before introducing captopril. The usual maintenance dose is 25 to 50 mg twice daily and should not normally exceed 50 mg three times daily. If hypertension is not satisfactorily controlled at this dosage, addition of a second drug or substitution of an alternative drug should be considered. In the USA higher doses of up to 150 mg three times daily have been suggested for patients with hypertension uncontrolled by lower doses of captopril in conjunction with diuretic therapy.

In the treatment 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 an initial oral dose of 6.25 to 12.5 mg of captopril is given under close medical supervision; the usual maintenance dose is 25 mg two or three times daily, and doses should not normally exceed 50 mg three times daily. Again, in the USA higher doses of up to 150 mg three times daily have been suggested.

After **myocardial infarction**, captopril is used prophylactically in clinically stable patients with symptomatic or asymptomatic left ventricular dysfunction to improve survival, delay the onset of symptomatic heart failure, and reduce recurrent infarction. It may be started 3 days after myocardial infarction in an initial oral dose of 6.25 mg, increased over several weeks to 150 mg daily in divided doses if tolerated.

In **diabetic nephropathy** (microalbuminuria greater than 30 mg/day) in type 1 diabetics, 75 to 100 mg of captopril may be given daily, in divided oral doses. Other antihypertensives may be used with captopril if a further reduction in blood pressure is required.

Doses may need to be reduced in patients with renal impairment (see below).

Administration. Captopril is generally given orally. Sublingual[1] and intravenous[2,3] dosage has also been tried, but these routes are not established.

1. Angeli P, *et al.* Comparison of sublingual captopril and nifedipine in immediate treatment of hypertensive emergencies: a randomized, single-blind clinical trial. *Arch Intern Med* 1991; **151:** 678–82.
2. Savi L, *et al.* A new therapy for hypertensive emergencies: intravenous captopril. *Curr Ther Res* 1990; **47:** 1073–81.
3. Langes K, *et al.* Efficacy and safety of intravenous captopril in congestive heart failure. *Curr Ther Res* 1993; **53:** 167–76.

Administration in children. Experience with captopril in children is limited. UK licensed product information suggests an initial dose of 300 micrograms/kg in children and adolescents; half this dose should be given initially to neonates and infants (including premature infants), and children with renal impairment. The dose is adjusted according to response and is usually given three times daily.

Captopril, given in an initial dose of 250 micrograms/kg daily, increased to up to 2.5 or 3.5 mg/kg daily in 3 divided doses has also been reported to produce benefit in infants with severe heart failure secondary to congenital defects (mainly manifesting as left-to-right shunt).[1,2]

The following doses of captopril are suggested by the *BNFC* for hypertension, heart failure, proteinuria in nephritis, or diabetic nephropathy:

- neonate: test dose, 10 to 50 micrograms/kg (10 micrograms/kg if the neonate is less than 37 weeks postmenstrual age); if tolerated, give 10 to 50 micrograms/kg 2 or 3 times daily, increased as necessary to a maximum of 2 mg/kg daily in divided doses (maximum of 300 micrograms/kg daily in divided doses if the neonate is less than 37 weeks postmenstrual age)
- child 1 month to 12 years: test dose, 100 micrograms/kg (maximum 6.25 mg); if tolerated, give 100 to 300 micrograms/kg 2 or 3 times daily, increased as necessary to a maximum of 6 mg/kg daily in divided doses (maximum of 4 mg/kg daily in divided doses in child 1 month to 1 year)
- child 12 years to 18 years: test dose, 100 micrograms/kg or 6.25 mg; if tolerated, give 12.5 to 25 mg 2 or 3 times daily, increased as necessary to a maximum of 150 mg daily in divided doses

1. Scammell AM, *et al.* Captopril in treatment of infant heart failure: a preliminary report. *Int J Cardiol* 1987; **16:** 295–301.
2. Shaw NJ, *et al.* Captopril in heart failure secondary to a left to right shunt. *Arch Dis Child* 1988; **63:** 360–3.

Administration in renal impairment. The dose of captopril should be reduced or the dosage interval increased in adults with renal impairment, depending on their creatinine clearance (CC). The following doses have been suggested:

- CC 21 to 40 mL/minute per 1.73 m^2: initial daily dose 25 mg and maximum daily dose 100 mg
- CC 10 to 20 mL/minute per 1.73 m^2: initial daily dose 12.5 mg and maximum daily dose 75 mg
- CC below 10 mL/minute per 1.73 m^2: initial daily dose 6.25 mg and maximum daily dose 37.5 mg

If a diuretic also needs to be given, a loop diuretic should be chosen rather than a thiazide.

Nitrate tolerance. For reference to the use of captopril as a sulfhydryl donor in the management of nitrate tolerance, see under Precautions for Glyceryl Trinitrate, p.1297.

Preparations

BP 2008: Captopril Tablets;
USP 31: Captopril and Hydrochlorothiazide Tablets; Captopril Oral Solution; Captopril Oral Suspension; Captopril Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Antasten; ***Austral.:*** Acenorm; Capoten; Captohexal; Enzace†; Topace; ***Austria:*** Capace; Capostad; Captomed; Captor; Captotyrol†; Debax; Lopirin; ***Belg.:*** Capoten; Capriltop; Captoprimed; Doccaptopri; ***Braz.:*** Cabioten†; Capobal; Capoten; Capotrat; Capotril†; Capox; Capril; Captil†; Captobel†; Captocord†; Captolab; Captolin†; Captomed; Capton†; Captopiril; Captopron; Captosen†; Captosif†; Captotec†; Captozen†; Captrizin; Cardilom†; Carditril†; Catoprol; Ductopril; Hipoten; Normapril; Pressomax; Prilpressin; Tompril†; Venopril†; ***Canad.:*** Apo-Capto; Capoten; Novo-Captoril; Nu-Capto; ***Chile:*** Capoten; Propenil; ***Cz.:*** Alkadil†; Apo-Capto†; Capoten; Katopil†; Tensiomin; ***Denm.:*** Capoten; Captodan; Captol; Catonet†; ***Fin.:*** Capoten; Captomin; Captostad†; Lopril; ***Fr.:*** Captolane; Lopril; ***Ger.:*** ACE-Hemmer; Acenorm†; Adocor; Capto; Capto-dura M†; Captobeta; Captodoc; Captoflux; Captogamma; Captohexal; Captomerck†; Captopress; Cardiagen; cor tensobon; Coronorm; Epicordin†; Jucapt; Lopirin; Mundil†; Phamopril†; Sigacap Cor†; Tensiomin; Tensiomin-Cor; Tensobon; Tensostad; ***Gr.:*** Capoten; Ftonavil†; Hypotensor; Neo-Ipertas; Normolose; Odupril†; Pertacilon; Sancap†; ***Hong Kong:*** Apo-Capto; Capocard†; Capoten; Capril; Dexacap†; Epsitron†; Kimafan; Novo-Captoril; Rilcapton†; Ropril; Tensiomin; ***Hung.:*** Aceomel; Capin†; Captogamma; Huma-Captoril†; Tensiomin; ***India:*** Aceten; Capace; ***Indon.:*** Acepress; Capoten; Captensin; Casipril; Dexacap; Farmoten; Forten; Locap; Lotensin; Metopril; Otoryl; Praten; Scantensin; Tenofax; Tensicap; Tensobon; ***Irl.:*** Aceomel; Actopril†; Capoten; Caprill; Captor; Geroten; Tensopril†; ***Israel:*** Acenil; Captil†; Inhibace†; ***Ital.:*** Acepress; Aceprilex; Capoten; Maxipril; Merapril†; Tenpril; ***Malaysia:*** Apo-Capto†; Apuzin; Capoten†; ***Mex.:*** Altiver; Atrisol; Biodezil; Bioxil; Brucap; Bugazon; Capotena; Captoser; Captral; Cardipril; Catona; Cryopril; Eca Presan; Ecapril; Ecaten; Enlace; Hipertex; Kenapril†; Kenolan; Keyerpril†; Lenpryl; Midrat; Miocap; Novapres; Precaptil; Prinarten; Proldin; Reductel; Reduprec; Romir; Tensil; Toprilem; Tropisol†; Tropix-HC; Varaxil; ***Neth.:*** Capoten; ***Norw.:*** Capoten; ***NZ:*** Capoten; Captohexal; ***Philipp.:*** Capomed; Capoten; Hartylox; Normil; Prelat; Primace; Retensin; Tensoril; Unihype; Vasostad; ***Port.:*** Calpix†; Capoten; Capritin; Carencil†; Convertal†; Hipertil; Hipotensil; Mereprine†; Pressil; Prilovase; Tensopril†; Vidapril; Xenam; ***Rus.:*** Aceten (Ацетен); Angiopril (Ангиоприл); Apo-Capto (Апо-капто); Capoten (Капотен); Rilcapton (Римкаптон); ***S.Afr.:*** Aceten; Capace; Capoten; Captohexal; Captomax; Cardiace; Zapto; ***Singapore:*** Apo-Capto; Capoten†; Catoplin; Ketanine†; Pertacilon†; Rilcapton; Tensoprel†; ***Spain:*** Alopresin†; Capoten; Captosina; Cesplon; Dardex†; Dilabar; Garanil; Tensoprel; ***Swed.:*** Capoten; ***Switz.:*** capto-basan†; Captosol; Lopirin; ***Thai.:*** Capoten; Epsitron; Gemzil; Tensiomin†; ***Turk.:*** Kapril; Kaptoril; ***UAE:*** Captophar; ***UK:*** Acepril; Capoten; Ecopace; Kaplon; Tensopril; ***USA:*** Capoten; ***Venez.:*** Capoten; Ceplon†; Tabulan.

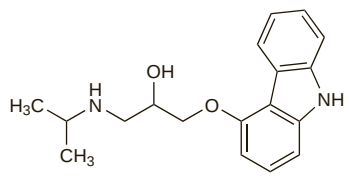
Multi-ingredient: ***Austria:*** Capozide; Captocomp; Captohexal Comp; Captopril Compositum; Captopril-HCT; Co-Captopril; Co-Captotyrol†; Veracapt; ***Braz.:*** Capox H; Captotec + HCT†; Hidropril; Lopril; ***Cz.:*** Captohexal Comp†; ***Denm.:*** Capozid; ***Fr.:*** Captea; Ecazide; ***Ger.:*** ACE-Hemmer comp; Acenorm HCT†; Adocomp; Capozide; Capto Comp; Capto Plus; Captobeta Comp; Captodoc Comp; Captogamma HCT; Captohexal Comp; Captopril Comp; Captopril HCT; Captopril Plus; Cardiagen HCT; Jutacor comp; Tensobon comp; ***Gr.:*** Anastol; Captopress; Captospes+H; Dosturel; Ekzevit†; Empirol; Fetylan; Kifarol; Normolose-H; Pentatec; Piesital; Return; Sancazid; Sedapressin; Superace; Uresan; Zidepril; ***Indon.:*** Capozide; ***Irl.:*** Capozide; Captor-HCT; Half Capozide; ***Ital.:*** Acediur; Aceplus; ***Mex.:*** Capozide; Captral ASA; Co-Captral; ***Neth.:*** Capozide†; ***NZ:*** Capozide; ***Port.:*** Lopiretic; Normotil†; ***Rus.:*** Capozide (Капозид); ***S.Afr.:*** Capozide; Captoretic; Zapto Co; ***Spain:*** Alopresin Diu†; Cesplon Plus; Decresco†; Dilabar Diu; Ecadiu; Ecazide; ***Switz.:*** Capozide; Captosol comp; Tensobon comp; ***UK:*** Acezide; Capozide; Capto-Co; ***USA:*** Capozide; ***Venez.:*** Capozide; Cartazid†.

Carazolol *(BAN, rINN)* ⊗

BM-51052; Carazololum. 1-(Carbazol-4-yloxy)-3-isopropylaminopropan-2-ol.

Каразолол

$C_{18}H_{22}N_2O_2$ = 298.4.
CAS — 57775-29-8.
ATC Vet — QC07AA90.



Profile
Carazolol is a beta blocker (p.1225) that has been given orally in the management of various cardiovascular disorders.

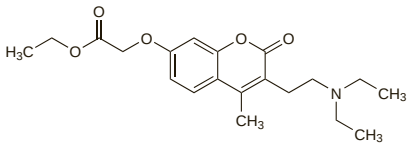
Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Conducton†; ***Ger.:*** Conducton†.

Carbocromen Hydrochloride *(rINNM)*

A-27053; AG-3; Carbocromène, Chlorhydrate de; Carbocromeni Hydrochloridum; Cassella-4489; Chromonar Hydrochloride *(USAN)*; Hidrocloruro de carbocromeno; NSC-110430. Ethyl 3-(2-diethylaminoethyl)-4-methylcoumarin-7-yloxyacetate hydrochloride.

Карбокромена Гидрохлорид
$C_{20}H_{27}NO_5$,HCl = 397.9.
CAS — 804-10-4 (carbocromen); 655-35-6 (carbocromen hydrochloride).
ATC — C01DX05.
ATC Vet — QC01DX05.



(carbocromen)

Profile
Carbocromen hydrochloride is a vasodilator that has been used in ischaemic heart disease.

Carperitide *(USAN, rINN)* ⊗

Carperitida; Carpéritide; Carperitidum; SUN-4936.

Карперитид
CAS — 89213-87-6.

Profile
Carperitide is a recombinant atrial natriuretic peptide (see p.1347) used in the management of acute heart failure.

◊ References.

1. Suwa M, *et al.* Multicenter prospective investigation on efficacy and safety of carperitide for acute heart failure in the 'real world' of therapy. *Circ J* 2005; **69:** 283–90.

Preparations

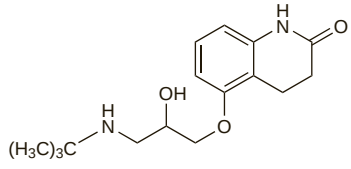
Proprietary Preparations (details are given in Part 3)
Jpn: Hanp.

Carteolol Hydrochloride

(BANM, USAN, rINNM) ⊗

Abbott-43326; Cartéolol, chlorhydrate de; Carteololi hydrochloridum; Hidrocloruro de carteolol; Karteolol Hidroklorür; Karteolol-hidroklorid; Karteolol-hydrochlorid; Karteololhydroklorid; Karteololihydrokloridi; Karteololio hidrochloridas; OPC-1085. 5-(3-*tert*-Butylamino-2-hydroxypropoxy)-3,4-dihydroquinolin-2(1*H*)-one hydrochloride.

Картеолола Гидрохлорид
$C_{16}H_{24}N_2O_3$,HCl = 328.8.
CAS — 51781-06-7 (carteolol); 51781-21-6 (carteolol hydrochloride).
ATC — C07AA15; S01ED05.
ATC Vet — QC07AA15; QS01ED05.



(carteolol)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Carteolol Hydrochloride). White or almost white crystals or crystalline powder. Soluble in water; slightly soluble in alcohol; practically insoluble in dichloromethane; sparingly soluble in methyl alcohol. A 1% solution in water has a pH of 5.0 to 6.0. Store in airtight containers.
USP 31 (Carteolol Hydrochloride). pH of a 1% solution in water is between 5.0 and 6.0.

Adverse Effects, Treatment, and Precautions

As for Beta Blockers, p.1226.

Interactions

The interactions associated with beta blockers are discussed on p.1228.

Pharmacokinetics

Carteolol is well absorbed from the gastrointestinal tract with a peak plasma concentration being reached within 1 to 4 hours of oral doses. The bioavailability is about 84%. It has low lipid solubility. About 20 to 30% is protein bound. The plasma half-life is reported to be 3 to 6 hours. The major route of elimination is renal with 50 to 70% of a dose being excreted unchanged in the urine; carteolol therefore accumulates in patients with renal disease. Major metabolites are 8-hydroxycarteolol and glucuronic acid conjugates of carteolol and 8-hydroxycarteolol. The 8-hydroxycarteolol metabolite is active; its half-life is reported to be 8 to 12 hours.

Uses and Administration

Carteolol is a non-cardioselective beta blocker (see p.1225). It is reported to possess intrinsic sympathomimetic activity but lacks significant membrane-stabilising activity.

Carteolol is used as the hydrochloride in the management of glaucoma (p.1873), hypertension (p.1171), and some cardiac disorders such as angina pectoris (p.1157) and cardiac arrhythmias (p.1160).

Eye drops containing carteolol hydrochloride 1% or 2% are instilled twice daily to reduce raised intra-ocular pressure in open-angle **glaucoma** and ocular hypertension.

In **hypertension** carteolol hydrochloride is given orally in a usual dose range of 2.5 to 20 mg daily, adjusted according to response, although up to 40 mg daily has been given. In cardiac disorders such as **angina pectoris** and **arrhythmias** carteolol hydrochloride has been used in doses of up to 30 mg daily.

The oral dose of carteolol hydrochloride should be reduced in patients with renal impairment (see below).

◊ Reviews.

1. Chrisp P, Sorkin EM. Ocular carteolol: a review of its pharmacological properties, and therapeutic use in glaucoma and ocular hypertension. *Drugs Aging* 1992; **2:** 58–77. Correction. *ibid.* 1994; **4:** 62.

Administration in renal impairment. The oral dose of carteolol hydrochloride should be reduced in patients with renal impairment. A suggested regimen based on creatine clearance (CC) for patients with hypertension is as follows:

- CC 30 to 80 mL/minute: 10 mg daily
- CC less than 30 mL/minute: use not recommended

Preparations

BP 2008: Carteolol Eye Drops;
USP 31: Carteolol Hydrochloride Ophthalmic Solution; Carteolol Hydrochloride Tablets.

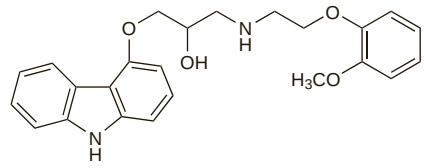
Proprietary Preparations (details are given in Part 3)
Arg.: Elebloc; Glacout; Glauteolol; Poenglaucol; Singlauc; Tenoftal†; ***Austria:*** Arteoptic; Endak; ***Belg.:*** Arteoptic; Carteol; ***Cz.:*** Arteoptic; Carteol; ***Denm.:*** Arteoptic†; ***Fin.:*** Arteoptic†; ***Fr.:*** Carteabak; Carteol; Mikelan; ***Ger.:*** Arteoptic; Endak; ***Gr.:*** Carteodose†; Fortinol; Napolit†; Vinitus; Zymoptic†; ***Hong Kong:*** Arteoptic; ***Hung.:*** Arteoptic†; ***Irl.:*** Teoptic; ***Ital.:*** Carteol; ***Jpn:*** Mikelan; ***Neth.:*** Arteoptic; Carteabak; Teoptic; ***Philipp.:*** Mikelan; ***Pol.:*** Arteoptic; ***Port.:*** Arteoptic; Carteabak; Physioglau; ***S.Afr.:*** Mikelan†; Teoptic; ***Spain:*** Arteolol; Elebloc; Mikelan; ***Swed.:*** Arteoptic†; ***Switz.:*** Arteoptic; ***Thai.:*** Arteoptic; ***Turk.:*** Carteol; ***UK:*** Teoptic; ***USA:*** Cartrol; Ocupress†.

Multi-ingredient: ***Belg.:*** Carteopil; ***Fr.:*** Carpilo; ***Switz.:*** Arteopilo.

Carvedilol *(BAN, USAN, rINN)* ⊗

BM-14190; Carvédilol; Carvedilolum; Karvedilol; Karvediloli; Karvedilolis. 1-Carbazol-4-yloxy-3-[2-(2-methoxyphenoxy)ethylamino]propan-2-ol.

Карведилол
$C_{24}H_{26}N_2O_4$ = 406.5.
CAS — 72956-09-3.
ATC — C07AG02.
ATC Vet — QC07AG02.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Carvedilol). A white or almost white crystalline powder. It exhibits polymorphism. Practically insoluble in water; slightly soluble in alcohol; practically insoluble in dilute acids.

Adverse Effects, Treatment, and Precautions

As for Beta Blockers, p.1226.

Liver function abnormalities, reversible on stopping treatment with carvedilol, have been reported rarely. Carvedilol is extensively metabolised in the liver and is not recommended in patients with hepatic impairment. Acute renal failure and renal abnormalities have been reported in patients with heart failure who also suffered from diffuse vascular disease and/or renal impairment.

The risk of hypotension may be reduced by taking carvedilol with food to decrease the rate of absorption.

Effects on the liver. Pruritus and elevated serum transaminase concentrations occurred[1] in a man who had been taking carvedilol for 6 months. Liver function tests returned to normal within 3 weeks of stopping carvedilol. However, pruritus recurred when the patient was started on metoprolol about 1 year later.

1. Hagmeyer KO, Stein J. Hepatotoxicity associated with carvedilol. *Ann Pharmacother* 2001; **35:** 1364–6.

Interactions

The interactions associated with beta blockers are discussed on p.1228.

Pharmacokinetics

Carvedilol is well absorbed from the gastrointestinal tract but is subject to considerable first-pass metabolism in the liver; the absolute bioavailability is about 25%. Peak plasma concentrations occur 1 to 2 hours after an oral dose. It has high lipid solubility. Carvedilol is more than 98% bound to plasma proteins. It is extensively metabolised in the liver, primarily by the cytochrome P450 isoenzymes CYP2D6 and CYP2C9, and the metabolites are excreted mainly in the bile. The elimination half-life is about 6 to 10 hours. Carvedilol has been shown to accumulate in breast milk in *animals*.

◊ References.

1. McTavish D, *et al.* Carvedilol: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy. *Drugs* 1993; **45:** 232–58.
2. Morgan T. Clinical pharmacokinetics and pharmacodynamics of carvedilol. *Clin Pharmacokinet* 1994; **26:** 335–46.
3. Tenero D, *et al.* Steady-state pharmacokinetics of carvedilol and its enantiomers in patients with congestive heart failure. *J Clin Pharmacol* 2000; **40:** 844–53.

Uses and Administration

Carvedilol is a non-cardioselective beta blocker (p.1225). It has vasodilating properties, which are attributed mainly to its blocking activity at alpha$_1$ receptors; at higher doses calcium-channel blocking activity may contribute. It also has antioxidant properties. Carvedilol is reported to have no intrinsic sympathomimetic activity and only weak membrane-stabilising activity.

Carvedilol is used in the management of hypertension (p.1171) and angina pectoris (p.1157), and as an adjunct to standard therapy in symptomatic heart failure