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

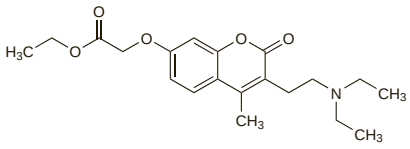
Preparations

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

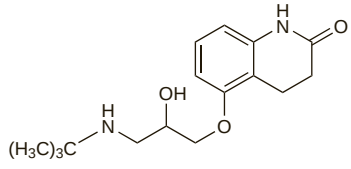
Proprietary Preparations (details are given in Part 3)
Jpn: Hanp.

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.

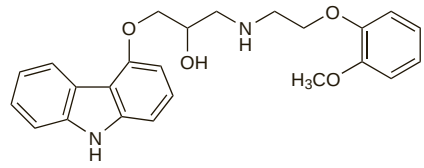
Proprietary Preparations (details are given in Part 3)
Arg.: Elebloc; Glacout; Glauteolol; Poenglaucol; Singlauc; Tenoftal†; ***Austria:*** Arteoptic; Endak; ***Belg.:*** Arteoptic; Carteol; ***Cz.:*** Arteoptic; Carteol; ***Denm.:*** Arteoptic†; ***Fin.:*** Arteoptic†; ***Fr.:*** Carteabak; Carteol; 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