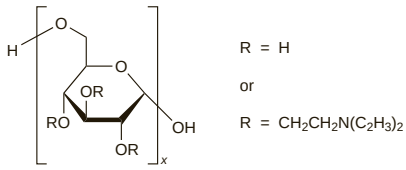
Colextran Hydrochloride *(rINNM)*

Colextran, Chlorhydrate de; Colextrani Hydrochloridum; DEAE-dextran Hydrochloride; Detaxtran Hydrochloride; Diethylaminoethyl-dextran Hydrochloride; Hidrocloruro de colextrán. Dextran 2-(diethylamino)ethyl ether hydrochloride.

Колекстрана Гидрохлорид

CAS — 9015-73-0 (colextran); 9064-91-9 (colextran hydrochloride).
ATC — C10AC03.
ATC Vet — QC10AC03.



Profile
Colextran hydrochloride, an anion-exchange resin that binds bile acids in the intestine, is a lipid regulating drug used in the treatment of hyperlipidaemias (p.1169). It is given in a usual dose of 2 to 3 g daily orally in divided doses.

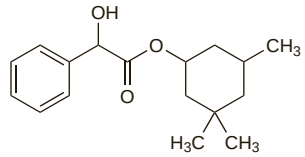
Preparations
Proprietary Preparations (details are given in Part 3)
Ital.: Pulsar; Rationale; ***Spain:*** Dexide.

Cyclandelate *(BAN, rINN)*

BS-572; Ciclandelato; Cyclandélate; Cyclandelatum; Cyklandelat; Syklandelaatti. 3,3,5-Trimethylcyclohexyl mandelate.

Циклanделат

$C_{17}H_{24}O_3$ = 276.4.
CAS — 456-59-7.
ATC — C04AX01.
ATC Vet — QC04AX01.



Pharmacopoeias. In *Chin.* and *US.*
USP 31 (Cyclandelate). A white crystalline powder. M.p. about 58°. Practically insoluble in water; very soluble in alcohol, in acetonitrile, and in ether. Store in airtight containers below 40°, preferably between 15° and 30°. Protect from light.

Profile
Cyclandelate is a vasodilator used in the management of cerebrovascular (p.1165) and peripheral vascular disorders (p.1178). It is given orally in an initial dosage of up to 2 g daily in divided doses; a usual maintenance dose is 0.8 to 1.2 g daily.

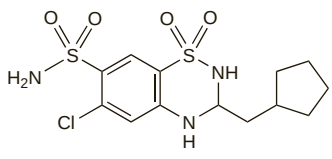
Preparations
Proprietary Preparations (details are given in Part 3)
Belg.: Cyclospasmol†; ***Fin.:*** Cyclospasmol†; ***Fr.:*** Cyclergine†; Vascunormyl†; ***Ger.:*** Natil; Spasmocyclon†; ***India:*** Martispasmol†; ***Ital.:*** Ciclospasmol†; ***Neth.:*** Cyclospasmol; ***Port.:*** Cyclospasmol†; ***Swed.:*** Cyclomandol†.

Cyclopenthiazide *(BAN, USAN, rINN)* ⊗

Ciclopentiazida; Cyclopenthiaz.; Cyclopenthiazidum; Cyklopentiazid; NSC-107679; Su-8341; Syklopentiatsidi. 6-Chloro-3-cyclopentylmethyl-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulphonamide 1,1-dioxide.

Циклопентиазид

$C_{13}H_{18}ClN_3O_4S_2$ = 379.9.
CAS — 742-20-1.
ATC — C03AA07.
ATC Vet — QC03AA07.



NOTE. Compounded preparations of cyclopenthiazide may be represented by the following names:

- Co-prenozide (*BAN*)—cyclopenthiazide 1 part and oxprenolol hydrochloride 640 parts (w/w).

Pharmacopoeias. In *Br.*
BP 2008 (Cyclopenthiazide). A white, odourless or almost odourless powder. Practically insoluble in water; soluble in alcohol and in acetone; practically insoluble in chloroform; very slightly soluble in ether.

Profile
Cyclopenthiazide is a thiazide diuretic with properties similar to those of hydrochlorothiazide (p.1307). It is given orally for hypertension (p.1171), and for oedema, including that associated with heart failure (p.1165).

Diuresis is induced in 1 to 3 hours after an oral dose, reaches a maximum in 4 to 8 hours, and lasts up to about 12 hours.

In the treatment of hypertension the usual dose is 250 to 500 micrograms daily either alone, or with other antihypertensives. In the treatment of oedema the usual initial dose is 250 to 500 micrograms daily; up to 1 mg daily may be given in heart failure but higher doses rarely achieve any further benefit. The dose should be reduced to the lowest effective dose for maintenance.

Porphyria. Cyclopenthiazide is considered to be unsafe in patients with porphyria although there is conflicting experimental evidence of porphyrinogenicity.

Preparations
BP 2008: Cyclopenthiazide Tablets.

Proprietary Preparations (details are given in Part 3)
NZ: Navidrex†; ***UK:*** Navidrex.

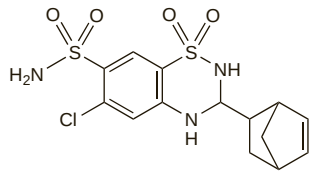
Multi-ingredient: ***Hong Kong:*** Navispare; ***S.Afr.:*** Lenurex-K; ***UK:*** Navispare; Trasidrex.

Cyclothiazide *(BAN, USAN, rINN)* ⊗

Ciclotiazida; Compound 35483; Cyclothiazidum; Cyklotiazid; MDi-193; Syklotiatsidi. 6-Chloro-3,4-dihydro-3-(norborn-5-en-2-yl)-2*H*-1,2,4-benzothiadiazine-7-sulphonamide 1,1-dioxide.

Циклотиазид

$C_{14}H_{16}ClN_3O_4S_2$ = 389.9.
CAS — 2259-96-3.
ATC — C03AA09.
ATC Vet — QC03AA09.



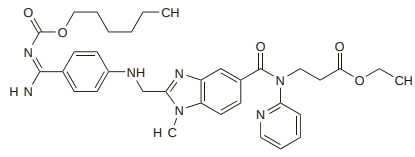
Profile
Cyclothiazide is a thiazide diuretic (see Hydrochlorothiazide, p.1307) that has been used, usually in combination preparations, in the management of hypertension and oedema.

Dabigatran Etexilate *(rINN)*

BIBR-1048; BIBR-953 (dabigatran); Dabigatran Étexilate; Dabigatrán etexilato; Dabigatranum Etexilatum. Ethyl 3-({[2-({[4-({[(hexyloxy)carbonyl]amino}iminomethyl)phenyl]amino}methyl)-1-methyl-1*H*-benzimidazol-5-yl]carbonyl}(pyridin-2-yl)amino)propanoate.

Дабигатран Этексилат

$C_{34}H_{41}N_7O_5$ = 627.7.
CAS — 211914-51-1 (dabigatran); 211915-06-9 (dabigatran etexilate).
ATC — B01AE07.
ATC Vet — QB01AE07.



Adverse Effects and Treatment
The most common adverse effect with dabigatran is bleeding. Raised liver enzyme values have been reported but are uncommon. There is no antidote to dabigatran. If haemorrhagic complications occur treatment should be stopped; surgical haemostasis or transfusion of fresh frozen plasma may be considered.

Precautions
Dabigatran should not be used in patients with clinically significant bleeding or who are at high risk for bleeding. It should be used with caution in patients with hepatic or renal impairment and is contra-indicated if creatinine clearance is less than 30 mL/minute.

Interactions
Dabigatran should not be given with other drugs that affect coagulation, such as anticoagulants, thrombolytics, or antiplatelet drugs. It should be used with caution with NSAIDs since the risk of bleeding may be increased. Dabigatran is a substrate for the efflux transporter P-glycoprotein and interactions may occur with drugs that affect P-glycoprotein function; use of dabigatran with quinidine is contra-indicated, and the dose of dabigatran should be reduced in patients receiving amiodarone (see Uses and Administration, below).

Pharmacokinetics
When given orally, dabigatran etexilate is rapidly and completely hydrolysed to its active metabolite, dabigatran, by an esterase-catalysed reaction. The absolute oral bioavailability of dabigatran when given as dabigatran etexilate is about 6.5%. Peak plasma concentrations of dabigatran occur within 0.5 to 2 hours after an oral dose. Food delays the time to peak concentrations but the bioavailability is not affected. Dabigatran has low plasma-protein binding. It is metabolised to a limited extent to active acylglucuronide conjugates; about 85% of a dose is excreted in the urine, mainly as unchanged dabigatran. The terminal plasma half-life is about 12 to 17 hours. Dabigatran is removed by dialysis.

◊ Reviews.

1. Stangier J. Clinical pharmacokinetics and pharmacodynamics of the oral direct thrombin inhibitor dabigatran etexilate. *Clin Pharmacokinet* 2008; **47:** 285–95.

Uses and Administration
Dabigatran is a direct thrombin inhibitor that is used for the prophylaxis of venous thromboembolism (p.1189) in patients undergoing elective orthopaedic surgery; it has also been investigated in other thromboembolic disorders.

Dabigatran is given orally as the mesilate of the prodrug dabigatran etexilate. The usual initial dose is the equivalent of 110 mg of dabigatran etexilate given within 1 to 4 hours of the completion of surgery, followed by 220 mg once daily; the dose should be reduced in the elderly and in patients with renal impairment (see below). Treatment should be continued for a total of 10 days after knee replacement and 28 to 35 days after hip replacement.

◊ References.

1. Stangier J, *et al.* The pharmacokinetics, pharmacodynamics and tolerability of dabigatran etexilate, a new oral direct thrombin inhibitor, in healthy male subjects. *Br J Clin Pharmacol* 2007; **64:** 292–303.
2. Eriksson BI, *et al.* Oral dabigatran etexilate vs. subcutaneous enoxaparin for the prevention of venous thromboembolism after total knee replacement: the RE-MODEL randomized trial. *J Thromb Haemost* 2007; **5:** 2178–85.
3. Eriksson BI, *et al.* RE-NOVATE Study Group. Dabigatran etexilate versus enoxaparin for prevention of venous thromboembolism after total hip replacement: a randomised, double-blind, non-inferiority trial. *Lancet* 2007; **370:** 949–56.
4. Ezekowitz MD, *et al.* Dabigatran with or without concomitant aspirin compared with warfarin alone in patients with nonvalvular atrial fibrillation (PETRO Study). *Am J Cardiol* 2007; **100:** 1419–26.
5. Sanford M, Plosker GL. Dabigatran etexilate. *Drugs* 2008; **68:** 1699–1709.

Administration in the elderly. There is limited clinical experience with dabigatran in patients over the age of 75 years but plasma concentrations appear to be higher in older subjects[1] and dose reduction is recommended. UK licensed product information recommends an initial dose of 75 mg of dabigatran etexilate (as the mesilate) given within 1 to 4 hours of the completion of surgery, followed by 150 mg once daily for a total of 10 days after knee replacement and 28 to 35 days after hip replacement.

1. Stangier J, *et al.* Pharmacokinetics and pharmacodynamics of the direct oral thrombin inhibitor dabigatran in healthy elderly subjects. *Clin Pharmacokinet* 2008; **47:** 47–59.

Administration in renal impairment. Dabigatran is excreted mainly by the kidneys but there is limited clinical experience with its use in renal impairment. It is contra-indicated in patients with creatinine clearance (CC) below 30 mL/minute. In patients with CC between 30 and 50 mL/minute the initial dose should be the equivalent of 75 mg of dabigatran etexilate given within 1 to 4 hours of the completion of surgery, followed by 150 mg once daily for a total of 10 days after knee replacement and 28 to 35 days after hip replacement.

Preparations
Proprietary Preparations (details are given in Part 3)
Cz.: Pradaxa; ***UK:*** Pradaxa.