

**Profile**

Cloridarol is a vasodilator that has been used in ischaemic heart disease.

**Colesevelam Hydrochloride**

(USAN, rINNM)

Colésévélam, Chlorhydrate de; Colesevelami Hydrochloridum; GT31-104HB; Hidrocloruro de colesevelam. Allylamine polymer with epichlorohydrin (1-chloro-2,3-epoxypropane), [6-(allylamino)hexyl]trimethylammonium chloride and N-allyldecylamine, hydrochloride.

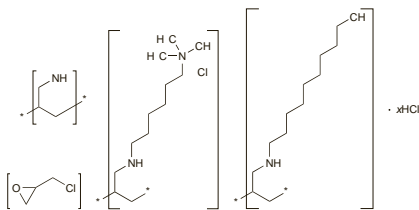
Колезевелама Гидрохлорида

$(C_3H_7N)_m(C_3H_5ClO)_n(C_{12}H_{27}ClN_2)_o(C_{13}H_{27}N)_p \cdot xHCl$ .

CAS — 182815-44-7.

ATC — C10AC04.

ATC Vet — QC10AC04.

**Adverse Effects and Precautions**

As for Colestyramine, p.1252.

**Interactions**

Colesevelam, like colestyramine (see p.1253), has the potential to interfere with the absorption of other drugs; those with a narrow therapeutic range should be given at least 1 hour before or 4 hours after colestyramine unless there is known to be no interaction.

## ◇ References.

- Donovan JM, *et al.* Drug interactions with colestyramine hydrochloride, a novel, potent lipid-lowering agent. *Cardiovasc Drugs Ther* 2000; **14**: 681–90.

**Uses and Administration**

Colesevelam hydrochloride is a nonabsorbable hydrogel. It binds bile acids in the intestine and has actions similar to those of colestyramine (p.1253). It is used for the treatment of hypercholesterolaemia (p.1169), particularly type IIa hyperlipoproteinaemia, either alone or with a statin. It may also be used as an adjunct to improve glycaemic control in type 2 diabetes mellitus (p.431). The usual oral dose is 3.75 g daily, as a single dose or in two divided doses, with meals. When used as monotherapy for hypercholesterolaemia, the dose may be increased to 4.375 g daily if required. When used with a statin, the dose is 2.5 to 3.75 g daily.

## ◇ References.

- Davidson MH, *et al.* Colesevelam hydrochloride (Cholestagel): a new, potent bile acid sequestrant associated with a low incidence of gastrointestinal side effects. *Arch Intern Med* 1999; **159**: 1893–1900.
- Aldridge MA, Ito MK. Colesevelam hydrochloride: a novel bile acid-binding resin. *Ann Pharmacother* 2001; **35**: 898–907.
- Steinmetz KL. Colesevelam hydrochloride. *Am J Health-Syst Pharm* 2002; **59**: 932–9.
- Zieve FJ, *et al.* Results of the glucose-lowering effect of Wel-Chol study (GLOWS): a randomized, double-blind, placebo-controlled pilot study evaluating the effect of colestyramine hydrochloride on glycaemic control in subjects with type 2 diabetes. *Clin Ther* 2007; **29**: 74–83.
- Bays H, Jones PH. Colesevelam hydrochloride: reducing atherosclerotic coronary heart disease risk factors. *Vasc Health Risk Manag* 2007; **3**: 733–42.
- Florentin M, *et al.* Colesevelam hydrochloride in clinical practice: a new approach in the treatment of hypercholesterolaemia. *Curr Med Res Opin* 2008; **24**: 995–1009.
- Goldberg RB, *et al.* Efficacy and safety of colestyramine in patients with type 2 diabetes mellitus and inadequate glycaemic control receiving insulin-based therapy. *Arch Intern Med* 2008; **168**: 1531–40.
- Fonseca VA, *et al.* Colesevelam HCl improves glycaemic control and reduces LDL cholesterol in patients with inadequately controlled type 2 diabetes on sulfonylurea-based therapy. *Diabetes Care* 2008; **31**: 1479–84.

**Preparations**

**Proprietary Preparations** (details are given in Part 3)

**Cz.:** Cholestagel; **Neth.:** Cholestagel; **Port.:** Cholestagel; **UK:** Cholestagel; **USA:** Welchol.

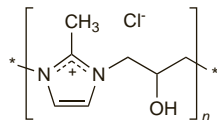
**Colestilan (rINN)**

Colestilan Chloride (USAN); Colestilanum; Colestimide; MCI-196. 2-Methylimidazole polymer with 1-chloro-2,3-epoxypropane.

Колестилян

$(C_4H_6N_2 \cdot C_3H_5ClO)_n$ .

CAS — 95522-45-5.

**Profile**

Colestilan, a bile-acid binding resin, is a lipid regulating drug with similar properties to colestyramine (p.1252). It is used to reduce cholesterol in the management of hyperlipidaemias (p.1169) and is given orally in a usual dose of 1.5 g twice daily. It is also under investigation in diabetes mellitus and as a phosphate binder in haemodialysis patients.

## ◇ References.

- Kurihara S, *et al.* Effect of MCI-196 (colestilan) as a phosphate binder on hyperphosphataemia in haemodialysis patients: a double-blind, placebo-controlled, short-term trial. *Nephrol Dial Transplant* 2005; **20**: 424–30.
- Yamakawa T, *et al.* Effect of colestimide therapy for glycaemic control in type 2 diabetes mellitus with hypercholesterolemia. *Endocr J* 2007; **54**: 53–8.

**Preparations**

**Proprietary Preparations** (details are given in Part 3)

**Jpn:** Cholebine.

**Colestipol Hydrochloride**

(BANM, USAN, rINNM)

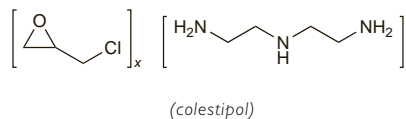
Colestipol, chlorhydrate de; Colestipoli hydrochloridum; Hidrocloruro de colestipol; Kolestipol Hidroklorür; U-26597A.

Колестилола Гидрохлорида

CAS — 26658-42-4 (colestipol); 50925-79-6 (colestipol); 37296-80-3 (colestipol hydrochloride).

ATC — C10AC02.

ATC Vet — QC10AC02.

**Pharmacopoeias.** In Br. and US.

**BP 2008** (Colestipol Hydrochloride). A copolymer of diethylenetriamine and epichlorohydrin (1-chloro-2,3-epoxypropane). Each g binds not less than 1.1 mEq and not more than 1.7 mEq of sodium cholate, calculated as the cholate binding capacity and with reference to the dried substance. Yellow to orange hygroscopic beads. Swells but does not dissolve in water and in dilute solutions of acids or alkalis. Practically insoluble in alcohol and in dichloromethane. The supernatant of a 10% w/w suspension in water has a pH of 6.0 to 7.5. Store in airtight containers.

**USP 31** (Colestipol Hydrochloride). A basic anion-exchange resin. It is the hydrochloride of a copolymer of diethylenetriamine and epichlorohydrin (1-chloro-2,3-epoxypropane). Each g binds not less than 1.1 mEq and not more than 1.6 mEq of sodium cholate, calculated as cholate binding capacity. Yellow to orange beads. Swells but does not dissolve in water or dilute aqueous solutions of acids or alkalis. Insoluble in common organic solvents. The supernatant of a 10% w/w suspension in water has a pH of 6.0 to 7.5. Store in airtight containers.

**Adverse Effects and Precautions**

As for Colestyramine, p.1252.

**Effects on thyroid function.** Reductions in total serum-thyroxine and thyroxine-binding globulin concentrations were found during routine monitoring of thyroid function in patients receiving colestipol and nicotinic acid, but were considered to be benign.<sup>1</sup> This effect has been used therapeutically in patients with hyperthyroidism (see under Uses of Colestyramine, p.1253).

- Cashin-Hemphill L, *et al.* Alterations in serum thyroid hormonal indices with colestipol-niacin therapy. *Ann Intern Med* 1987; **107**: 324–9.

**Interactions**

As for Colestyramine, p.1253.

**Uses and Administration**

Colestipol hydrochloride is a bile-acid binding resin and lipid regulating drug with actions similar to those of colestyramine (p.1253). It is used to reduce cholesterol in the treatment of hyperlipidaemias (p.1169), particularly type IIa hyperlipoproteinaemia.

Colestipol hydrochloride is available as granules and is given orally as a suspension in water or a flavoured vehicle. The initial dose is 5 g daily or twice daily, increasing gradually at intervals of 1 to 2 months to up to 30 g daily in a single dose or two divided doses as necessary.

Colestipol hydrochloride is also available as tablets; doses range from 2 to 16 g daily.

**Preparations**

**BP 2008:** Colestipol Granules;

**USP 31:** Colestipol Hydrochloride for Oral Suspension; Colestipol Hydrochloride Tablets.

**Proprietary Preparations** (details are given in Part 3)

**Austral.:** Colestid; **Belg.:** Colestid; **Canad.:** Colestid; **Cz.:** Colestid; **Denm.:** Lestid; **Fin.:** Lestid; **Ger.:** Cholestabyl; Colestid; **Gr.:** Lestid; **Irl.:** Colestid; **Israel:** Colestid; **Mex.:** Colestid; **Neth.:** Colestid; **Norw.:** Lestid; **NZ:** Colestid; **Port.:** Colestid; **Spain:** Colestid; **Swed.:** Lestid; **Switz.:** Colestid; **UK:** Colestid; **USA:** Colestid.

**Colestyramine (BAN, rINN)**

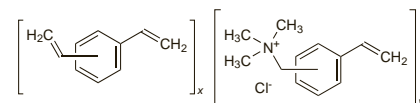
Colestyramine; Colestyramine Resin; Colestiramina; Colestyraminum; Divistryramine; Kolestiramin; Kolestiraminas; Kolestyramini; Kolestyramin; Kolestyramina; MK-135.

Колестирамин

CAS — 11041-12-6.

ATC — C10AC01.

ATC Vet — QC10AC01.

**Pharmacopoeias.** In Eur. (see p.vii) and US.

**Ph. Eur. 6.2** (Colestyramine). A strongly basic anion-exchange resin in the chloride form, consisting of styrene-divinylbenzene copolymer with quaternary ammonium groups. Each g exchanges not less than 1.8 g and not more than 2.2 g of sodium glycocholate, calculated with reference to the dried material. A white or almost white, fine, hygroscopic powder. Insoluble in water, in alcohol, and in dichloromethane. A 1% suspension in water has a pH of 4.0 to 6.0 after standing for 10 minutes. Store in airtight containers.

**USP 31** (Colestyramine Resin). A strongly basic anion-exchange resin containing quaternary ammonium functional groups which are attached to a styrene-divinylbenzene copolymer. Each g exchanges not less than 1.8 g and not more than 2.2 g of sodium glycocholate, calculated on the dried basis. It is used in the chloride form. A white to buff-coloured, hygroscopic, fine powder, odourless or has not more than a slight amine-like odour. It loses not more than 12% of its weight on drying. Insoluble in water, in alcohol, in chloroform, and in ether. A 1% slurry in water has a pH of 4.0 to 6.0. Store in airtight containers.

**Adverse Effects**

The most common adverse effect of colestyramine is constipation; faecal impaction may develop and haemorrhoids may be aggravated. Other gastrointestinal adverse effects include abdominal discomfort or pain, heartburn, flatulence, nausea, vomiting, and diarrhoea.