soluble in dilute mineral acids with the evolution of carbon dioxide. A 4% suspension in water has a pH of 9.9 to 10.2. Store in airtight containers.

Profile
Dihydroxyaluminum sodium carbonate is an antacid with general properties similar to aluminium hydroxide (p.1706) that is given in doses of about 300 to 600 mg by mouth.

Preparations
USP 31: Dihydroxyaluminum Sodium Carbonate Tablets.

Proprietary Preparations (details are given in Part 3)
Austria: Antacidum; ***Denm.:*** Noacid; ***Ger.:*** Kompensan; ***Pol.:*** Alugastrin; Gastrinal; ***Port.:*** Kompensan; ***Switz.:*** Kompensan; ***Turk.:*** Dank; Kompensan.

Multi-ingredient: ***Ger.:*** Kompensan-S†; ***Port.:*** Kompensan-S.

Diisopromine Hydrochloride *(rINNM)*

Diisopromine, Chlorhydrate de; Di-isopromine Hydrochloride; Diisopromini Hydrochloridum; Hidrocloruro de diisopromina. *NN*-Di-isopropyl-3,3-diphenylpropylamine hydrochloride.

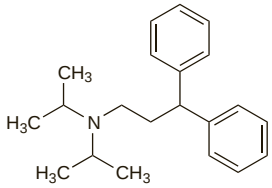
Диизопромина Гидрохлорид

$C_{21}H_{29}N,HCl$ = 331.9.

CAS — 5966-41-6 (diisopromine); 24358-65-4 (diisopromine hydrochloride).

ATC — A03AX02.

ATC Vet — QA03AX02.



(diisopromine)

Profile
Diisopromine hydrochloride is an antispasmodic used with sorbitol in various gastrointestinal disorders.

Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Braz.:*** Biliflux†; ***S.Afr.:*** Agofell.

Diphenoxylate Hydrochloride

(BANM, rINNM)

Difenoksilaattihydrokloridi; Difenoksilat Hidroklorür; Difenoksilato hidrochloridas; Difenoxilát-hidroklorid; Difenoxilathydroklorid; Difenoxylát-hydrochlorid; Diphénoxylate, chlorhydrate de; Diphenoxylati hydrochloridum; Hidrocloruro de difenoxilato; R-1132. Ethyl 1-(3-cyano-3,3-diphenylpropyl)-4-phenylpiperidine-4-carboxylate hydrochloride.

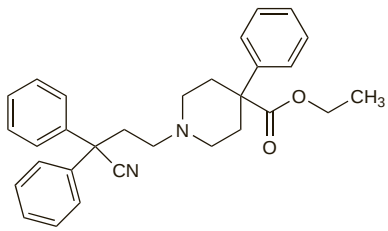
Дифеноксилата Гидрохлорид

$C_{30}H_{32}N_2O_2,HCl$ = 489.0.

CAS — 915-30-0 (diphenoxylate); 3810-80-8 (diphenoxylate hydrochloride).

ATC — A07DA01.

ATC Vet — QA07DA01.



(diphenoxylate)

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

- Co-phenotrope (*BAN*)—diphenoxylate hydrochloride 100 parts and atropine sulfate 1 part (w/w).

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, and *US*.
Ph. Eur. 6.2 (Diphenoxylate Hydrochloride). A white or almost white, crystalline powder. Very slightly soluble in water; sparingly soluble in alcohol; freely soluble in dichloromethane. Protect from light.
USP 31 (Diphenoxylate Hydrochloride). A white odourless crystalline powder. Slightly soluble in water and in isopropyl alcohol; sparingly soluble in alcohol and in acetone; freely soluble in chloroform; practically insoluble in ether and in petroleum spirit; soluble in methyl alcohol. A saturated solution in water has a pH of about 3.3.

Dependence and Withdrawal
Preparations of diphenoxylate usually contain subclinical amounts of atropine sulfate in an attempt to discourage abuse. Short-term use of diphenoxylate with atropine in the recommended dosage carries a negligible risk of dependence, although prolonged use or use of high doses may produce dependence of the morphine type (see p.101).

Adverse Effects and Treatment
Diphenoxylate is related to the opioid analgesics (p.102), and its adverse effects and their treatment are similar, particularly in overdosage. Reported adverse effects include: gastrointestinal effects such as anorexia, nausea and vomiting, abdominal distension or discomfort, paralytic ileus, toxic megacolon, and pancreatitis; nervous system effects such as headache, drowsiness, dizziness, restlessness, euphoria, depression, numbness of the extremities; and hypersensitivity reactions including angioedema, urticaria, pruritus, and swelling of the gums. Signs of overdosage may be delayed and patients should be observed for at least 48 hours. Young children are particularly susceptible to the effects of overdosage.

The presence of subclinical doses of atropine sulfate in preparations containing diphenoxylate may give rise to the adverse effects of atropine in susceptible individuals or in overdosage—see Atropine Sulfate, p.1219.

Precautions
Diphenoxylate hydrochloride should be avoided in patients with jaundice, intestinal obstruction, antibiotic-associated colitis, or diarrhoea associated with enterotoxin-producing bacteria, and should be used with caution in patients with hepatic impairment. It should also be used with caution in young children, in whom response is more variable, and is not generally recommended for use in infants. Patients with inflammatory bowel disease receiving diphenoxylate should be carefully observed for signs of toxic megacolon and diphenoxylate stopped promptly should abdominal distension occur.

Interactions
Because of the structural relationship of diphenoxylate to pethidine (p.113) there is a theoretical risk of hypertensive crisis if diphenoxylate is used with MAOIs. Diphenoxylate may potentiate the effects of other CNS depressants such as alcohol, barbiturates, and some anxiolytics.

Pharmacokinetics
Diphenoxylate hydrochloride is well absorbed from the gastrointestinal tract. It is rapidly and extensively metabolised in the liver, mainly to diphenoxylic acid (difenoxin, p.1723), which has antidiarrhoeal activity; other metabolites include hydroxydiphenoxylic acid. It is excreted mainly as metabolites and their conjugates in the faeces; lesser amounts are excreted in urine. It may be distributed into breast milk.

Uses and Administration
Diphenoxylate hydrochloride is a synthetic derivative of pethidine (p.113) with little or no analgesic activity; it reduces intestinal motility and is used in the symptomatic treatment of acute and chronic diarrhoea (p.1694). It may also be used to reduce the frequency and fluidity of the stools in patients with colostomies or ileostomies.

Preparations of diphenoxylate usually contain subclinical amounts of atropine sulfate in an attempt to discourage abuse; UK preparations are all in the form of co-phenotrope (see above).

In **acute diarrhoea** the usual initial dose for adults is 10 mg orally, followed by 5 mg every six hours, later reduced as the diarrhoea is controlled. In the UK, diphenoxylate hydrochloride is not licensed for children under 4 years of age. Suggested initial doses for children are: 4 to 8 years, 2.5 mg three times daily; 9 to 12 years, 2.5 mg four times daily; over 12 years, 5 mg three times daily. While emphasising that antimotility drugs are not recommended for acute diarrhoea in children under 12 years of age, the *BNFC* allows for a dose of 1.25 mg three times daily for children aged 2 to 4 years. In the USA, diphenoxylate is not recommended for children under the age of 2 years and an initial dose of 0.3 to 0.4 mg/kg (up to an effective maximum of 10 mg) daily in 4 divided doses is suggested for children aged 2 to 12 years. (For the view that antidiarrhoeal drugs should not be used at all in children, see p.1694.)

Similar initial doses are used for **chronic diarrhoea**, and subsequently reduced as necessary. If clinical improvement is not seen after 10 days of treatment with the maximum daily dose of 20 mg (in adults) further use is unlikely to result in any benefit.

Diarrhoea. Co-phenotrope (see above) may be considered as an alternative to loperamide in the management of faecal incontinence in adults, see Diarrhoea, under Loperamide, p.1742.

Substance dependence. Diphenoxylate may be useful[1] in the symptomatic management of diarrhoea associated with opioid withdrawal syndromes (p.101).

1. DOH. *Drug misuse and dependence: guidelines on clinical management*. London: HMSO, 1999. Also available at: http://www.dh.gov.uk/assetRoot/04/07/81/98/04078198.pdf (accessed 18/01/06)

Preparations
USP 31: Diphenoxylate Hydrochloride and Atropine Sulfate Oral Solution; Diphenoxylate Hydrochloride and Atropine Sulfate Tablets.

Proprietary Preparations (details are given in Part 3)
Austral.: Lofenoxal; Lomotil; ***Braz.:*** Lomotil; ***Canad.:*** Lomotil; ***Cz.:*** Reasec; ***Fr.:*** Diarsed; ***Hong Kong:*** Dhamotil; Dimotil; Lomotil; ***Hung.:*** Reasec; ***India:*** Lomotil; ***Irl.:*** Lomotil; ***Malaysia:*** Atrotil†; Beamotil; Dhamotil; Lomotil†; Setmotil†; ***NZ:*** Diastop; Lomotil†; ***Pol.:*** Reasec; ***Port.:*** Lomotil†; ***S.Afr.:*** Lomotil; ***Singapore:*** Beamotil; Dhamotil; Lomotil; Remodil†; ***Thai.:*** Dilomil†; Lomotil; ***Turk.:*** Lomotil; ***UAE:*** Intard; ***UK:*** Dymotil; Lomotil; ***USA:*** Logen; Lomotil; Lonox; ***Venez.:*** Lomotil†.

Multi-ingredient: ***Braz.:*** Colestase; ***India:*** Lomofen.

Docusates

Docusatos.

Docusate Calcium *(USAN)*

Dioctyl Calcium Sulfosuccinate; Dioctyl Calcium Sulphosuccinate; Docusato cálcico. Calcium 1,4-bis(2-ethylhexyl) sulphosuccinate.

Докузат Кальция

$C_{40}H_{74}CaO_{14}S_2$ = 883.2.

CAS — 128-49-4.

Pharmacopoeias. In *US*.
USP 31 (Docusate Calcium). A white amorphous solid with the characteristic odour of octil alcohol. Soluble 1 in 3300 of water; very soluble in alcohol, in macrogol 400, and in maize oil.

Docusate Potassium *(USAN)*

Dioctyl Potassium Sulfosuccinate; Dioctyl Potassium Sulphosuccinate; Docusato potásico. Potassium 1,4-bis(2-ethylhexyl) sulphosuccinate.

Докузат Калия

$C_{20}H_{37}KO_7S$ = 460.7.

CAS — 7491-09-0.

Pharmacopoeias. In *US*.
USP 31 (Docusate Potassium). A white amorphous solid with a characteristic odour suggestive of octil alcohol. Sparingly soluble in water; soluble in alcohol and in glycerol; very soluble in petroleum spirit.