

agement of colostomies or ileostomies to reduce the volume of discharge.

In **acute diarrhoea** the usual initial dose for adults is loperamide hydrochloride 4 mg followed by 2 mg after each loose stool to a maximum of 16 mg daily; the usual daily dose is 6 to 8 mg. In the UK, it is not licensed for children under 4 years of age. Suggested doses for older children are: 4 to 8 years, 1 mg three or four times daily for up to 3 days; 9 to 12 years, 2 mg four times daily for up to 5 days. In the USA, loperamide is not recommended for children under the age of 2 years and an initial dose of 1 mg three times daily is suggested for children aged 2 to 5 years. (For restrictions on the use of loperamide in children and the view that antidiarrhoeal drugs should not be used at all in children, see Diarrhoea, below.)

In **chronic diarrhoea** the usual initial dose for adults is 4 to 8 mg daily in divided doses subsequently adjusted as necessary; doses of 16 mg daily should not be exceeded. If no improvement has been seen after treatment with 16 mg daily for at least 10 days, further use is unlikely to be of benefit. Although not licensed for use in children for chronic diarrhoea, in the UK the *BNFC* allows for the following oral doses of loperamide hydrochloride:

- 1 month to 1 year: 100 to 200 micrograms/kg twice daily, given 30 minutes before feeds; up to a maximum of 2 mg/kg daily in divided doses may be required
- 1 to 12 years: 100 to 200 micrograms/kg (maximum dose 2 mg) three to four times daily; up to 1.25 mg/kg daily in divided doses may be required, to a maximum of 16 mg daily
- 12 to 18 years: 2 to 4 mg two to four times daily, to a maximum of 16 mg daily

Loperamide is also given as the prodrug, **loperamide oxide**, which is converted to loperamide in the gastrointestinal tract. It has been given for acute diarrhoea in doses of 2 to 4 mg initially followed by 1 mg after each loose stool, to a maximum of 8 mg daily.

Diarrhoea. The mainstay of treatment for acute diarrhoea (p.1694) is rehydration therapy. Antidiarrhoeals may have a role for symptomatic relief in adults with acute diarrhoea, and loperamide is often chosen in such circumstances,¹ but WHO does not recommend the use of any antidiarrhoeal drug in children with diarrhoea. Similarly, in the UK the *BNFC* considers that antimotility drugs are not to be recommended for acute diarrhoea in children under 12 years of age. There have been problems regarding the use of antidiarrhoeals such as loperamide in young children in developing countries. Manufacturers have considered that a lower age limit is acceptable in those countries than is recommended in the UK or USA; even that lower limit is not always observed in practice and there have been reports of serious toxicity in very young children.² In response to such reports the manufacturers withdrew concentrated drops of loperamide worldwide and the syrup from countries where the WHO had a programme for control of diarrhoeal diseases,³ but tablets and capsules remain available. In some countries the use of antidiarrhoeals is now restricted by law.

In the UK, NICE states that loperamide is the antidiarrhoeal of first choice in adults with faecal incontinence;⁴ it can be used long-term in doses from 500 micrograms to 16 mg daily as needed. Loperamide should be started at a very low dose which can be increased as needed, and then adjusted in response to stool consistency. It should not be given to those with hard or infrequent stools, those with acute diarrhoea of unknown cause, or with acute ulcerative colitis. Patients who are unable to tolerate loperamide may be offered codeine phosphate (p.37) or co-pemotrope (see Diphenoxylate Hydrochloride, p.1724).

For mention of the use of loperamide in the management of diarrhoea caused by chemotherapy, see p.640.

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3. Gussin RZ. Withdrawal of loperamide drops. *Lancet* 1990; **335**: 1603–4.
4. NICE. Faecal incontinence: the management of faecal incontinence in adults (issued June 2007). Available at: <http://www.nice.org.uk/nicemedia/pdf/CG49NICEGuidance.pdf> (accessed 31/03/08)

PRODRUG THERAPY. References to the use of *loperamide oxide* in diarrhoea.

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2. Hughes IW, *et al.* First-line treatment in acute non-dysenteric diarrhoea: clinical comparison of loperamide oxide, loperamide and placebo. *Br J Clin Pract* 1995; **49**: 181–5.
3. van Outryve M, Toussaint J. Loperamide oxide for the treatment of chronic diarrhoea in Crohn's disease. *J Int Med Res* 1995; **23**: 335–41.
4. Sun WM, *et al.* Effects of loperamide oxide on gastrointestinal transit time and anorectal function in patients with chronic diarrhoea and faecal incontinence. *Scand J Gastroenterol* 1997; **32**: 34–8.

Preparations

BP 2008: Loperamide Capsules;

USP 31: Loperamide Hydrochloride Capsules; Loperamide Hydrochloride Oral Solution; Loperamide Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Arg: Colifim; Contem; Custey; Dotalsec; Elcoman; Ionet; Lansek A; Lefa Enteril L; Mimicam; Plexol; Florinoc; Regulane; Salvaxil; Suprasec; Viltar; **Austral:** Chemists Own; Diarrhoea Relief; Gastro-Stop; Harmonise; Imodium; Neogastro; **Austria:** Enterobene; Imodium; Lopedium; Normakut; **Belg:** Imodium; **Braz:** Diafuran; Diaresec; Diasec; Imosec; Loperin; **Canada:** Anti-Diarrheal; Diahalt; Dian-Eze; Diarrhoea Relief; **Chile:** Capent; Coliper; Lopediar; **Cz:** Dissenten; Imodium; Loperacap; **Denm:** Dialope; Imodium; Propiden; Travello; **Fin:** Imocur; Imodium; LopeX; **Fr:** Altoceft; Arestal; Diaretyl; Dyspagon; Ercestop; Imodium; Imodiumlingual; Imosel; Indiaral; Nabutil; **Ger:** Azuperamid; Boxolip; duralopt; Endialop; Endiaron; Imodium; Lop-Dia; Lopalind; Lopedium; Lopedipharm; Lopera akut; Loperhoer; **Gr:** Imodium; Neo-Enteroseptol; **Hong Kong:** Colodium; Diatabs Reformulated; Imodium; Imodon; Loper; Loperamil; Loperax; Loperium; Loperamide; Mar-Loper; Reximide; Synodium; Vacontil; **Hung:** Enterobene; Imodium; Lopedium; Loperacap; **India:** Diarlop; Lopamide; Roko; **Indon:** Alphamid; Amerol; Antidia; Colidium; Diadium; Diasec; Imodium; Imomed; Imore; Imosa; Inamid; Lexadium; Lodia; Loremid; Motilex; Normotil; Normudal; Opor; Oramide; Primodium; Renamid; Xepare; Zerofarm; **Irl:** Arret; Diarrest RF; Imodium; **Israel:** Imodium; Loperid; Loperium; Rekamide; Shilshul X; Stopit; **Ital:** Diarstop; Diarzero; Dissenten; Imodium; Lopedim; Ramidox; **Japan:** Loperax; Loperamide; Loramide; Miraton; Imodium; Imotab; **Malaysia:** Beamodium; Diatrol; Imocap; Imodium; **Mex:** Acanol; Acqta; Apo-Pera; Biolid; Cryoperacid; Deroser; Dialacid; Diaperol; Dilostop; Exclatin; F9; Hurplex; Imodium; Lomotil; Lop; Nodiamec; Permial; Pramidal; Raxamid; Redian; Top-Dal; Valfam; **Neth:** Arestal; Diacure; Diarem; Imodium; Kruidvat Diarreeremmer; Trekpleister Diarreeremmer; **Norw:** Imodium; Travello; **NZ:** Diamide; Dicap; Imodium; Nodia; **Philipp:** Diamide; Diaperyl; Diatabs (Reformulated); Imodium; Lormide; Tymed; **Pol:** Imodium; Laremid; Stoperan; **Port:** Dyspagon; Fulcalac; Imodium; Loprex; Loride; **Rus:** Imodium (ИМОДИУМ); Lopedium (Лопедийум); **S.Afr:** Betaperamide; Gastron; Imodium; Lenide-T; Lopedium; Loperastat; Norimode; Prodiem; **Singapore:** Colodium; IMD; Imodium; Loperamil; Loperamide; Loran; Vacontil; **Spain:** Elissan; Fortasec; Imodium; Imosec; Loperan; Loperkey; Protector; Salvacolina; Taguino; **Swed:** Dimor; Imodium; Primodium; Travello; **Switz:** Binaldan; Imodium; Lopimed; Zorotop; **Thai:** Diarent; Diarodil; Entermed; Imodium; Impelium; Lomide; Lomy; Lopamine; Lopela; Lopercin; Loperid; Lopera; Lopermid; Operium; **Persian:** SBOB; **Turk:** Diadef; Lopermid; **UK:** Arret; Diah-Limit; Diaquitte; Diareze; Diocalm Ultra; Diocaps; Entrocalm; Imodium; Norimode; Norimode; **USA:** Imodium; K-Pek II; Kao-Paverin; Kapectate II; Neo-Diaral; Pepto Diarrhea Control; **Venez:** Glucitol; Imodium; Loperam; Mentaden; Oldan; Polonit.

Multi-ingredient: **Arg:** Neo Kef Neomas L; Regulane AF; **Austral:** Imodium Advanced; **Austria:** Imodium Plus; **Belg:** Imodium Plus; **Braz:** Imodium Plus; **Canada:** Imodium Advanced; **Cz:** Imodium Plus; **Denm:** Imodium med Simethicon; **Fr:** Imodium duo; **Ger:** Imodium Plus; **Hong Kong:** Imodium Plus; **Hung:** Imodium Komplett; **Mex:** Imodium Plus; **NZ:** Imodium Advanced; **Pol:** Imodium Plus; **Port:** Imodium Plus; **S.Afr:** Imodium Plus; **Spain:** Imodium Plus; **Switz:** Imodium Plus; **Thai:** Imodium Plus; **UK:** Imodium Plus; **USA:** Imodium Advanced.

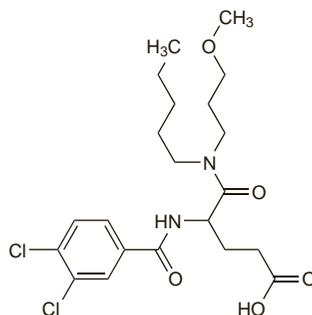
Loxiglumide (rINN)

CR-1505; CR-2017 (dexloxiglumide); Loxiglumida; Loxiglumidum. (±)-4-(3,4-Dichlorobenzamido)-N-(3-methoxypropyl)-N-pentylglutaramic acid.

Локсиглуида

$C_{21}H_{30}Cl_2N_2O_5 = 461.4$.

CAS — 107097-80-3 (loxiglumide); 119817-90-2 (dexloxiglumide).



Profile

Loxiglumide is a specific cholecystokinin antagonist related to proglumide (see p.1764), and has been investigated in biliary and gastrointestinal dyskinesias, constipation and irritable bowel syndrome, and pancreatitis.

The *R*-isomer of loxiglumide, dexloxiglumide is also under investigation for constipation-predominant irritable bowel syndrome.

References

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3. Persiani S, *et al.* Pharmacokinetic profile of dexloxiglumide. *Clin Pharmacokinet* 2006; **45**: 1177–88.

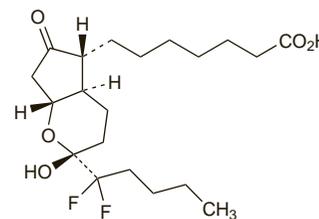
Lubiprostone (USAN, rINN)

Lubiprostona; Lubiprostonum; RU-0211; SPI-0211. (–)-7-[[[2*R*,4*R*,5*R*,7*R*]-2-(1,1-Difluoropentyl)-2-hydroxy-6-oxooctahydrocyclopenta[*b*]pyran-5-yl]heptanoic acid.

Лубипростон

$C_{30}H_{32}F_2O_5 = 390.5$.

CAS — 136790-76-6; 333963-40-9.



Adverse Effects and Precautions

The most common adverse effect of lubiprostone is nausea, which is dose-dependent and may be severe in some patients. Symptoms can be reduced by taking lubiprostone with food. Diarrhoea also occurs commonly, and other gastrointestinal effects include abdominal distension and pain, flatulence, and vomiting. Other reported adverse effects include headache, dizziness, fatigue, dyspnoea, and peripheral oedema. Chest discomfort, back pain, and arthralgia can occur.

Lubiprostone is contra-indicated in patients with a history of mechanical gastrointestinal obstruction.

Pharmacokinetics

A negligible amount of lubiprostone is absorbed systemically after an oral dose. It is rapidly and extensively metabolised by carbonyl reductase, probably in the stomach and jejunum.

Uses and Administration

Lubiprostone is a chloride-channel activator that acts locally in the gut to increase intestinal fluid secretion, which increases motility. It is used in the treatment of chronic idiopathic constipation (p.1693) in a dose of 24 micrograms twice daily, taken orally with food. It is also under investigation in the treatment of constipation-predominant irritable bowel syndrome.

References

1. McKeage K, *et al.* Lubiprostone. *Drugs* 2006; **66**: 873–9.
2. Anonymous. Lubiprostone (Amitiza) for chronic constipation. *Med Lett Drugs Ther* 2006; **48**: 47–8.
3. Ambizas EM, Ginzburg R. Lubiprostone: a chloride channel activator for treatment of chronic constipation. *Ann Pharmacother* 2007; **41**: 957–64.

Preparations

Proprietary Preparations (details are given in Part 3)

USA: Amitiza.

Magaldrate (BAN, USAN, rINN)

Aluminium Magnesium Hydroxide Sulfate; AY-5710; Magaldratti; Magaldrát; Magaldrat; Magaldrato; Magaldratum.

Магальдрат

$Al_3Mg_{10}(OH)_{31}(SO_4)_2 \cdot xH_2O = 1097.3$ (anhydrous).

CAS — 74978-16-8.

ATC — A02AD02.

ATC Vet — QA02AD02.

NOTE. Magaldrate was formerly described as Aluminium Magnesium Hydroxide (AlMg₂(OH)₇ monohydrate, CAS—1317-26-6).

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

Ph. Eur. 6.2 (Magaldrate). A combination of aluminium and magnesium hydroxides (see p.1706 and p.1743 respectively) and sulfates. It contains the equivalent of 90 to 105% of Al₃Mg₁₀(OH)₃₁(SO₄)₂, calculated with reference to the dried substance. A white or almost white crystalline powder. Practically insoluble in water and in alcohol; soluble in dilute mineral acids. It loses between 10 and 20% of its weight on drying at 200° for 4 hours.

USP 31 (Magaldrate). A combination of aluminium and magnesium hydroxides and sulfates. It contains the equivalent of 90 to