Administration in children. In the UK, children may be given the following oral doses of lactulose 3.35 g per 5 mL solution for constipation; doses may be adjusted according to response:

- 1 month to 1 year: 2.5 mL twice daily
- 1 to 5 years: 5 mL twice daily
- 5 to 10 years: 10 mL twice daily
- 10 to 18 years: 15 mL twice daily

Diagnosis and testing. ***THE SUGAR ABSORPTION TEST.*** In healthy individuals lactulose is largely unabsorbed from the gastrointestinal tract, but in, for example, coeliac disease there is increased permeability to disaccharides such as lactulose and a paradoxical decrease in the absorption of monosaccharides. This led to the development of the differential sugar absorption test in which 2 sugars are given simultaneously by mouth and the urinary recovery of each is determined; mannitol is commonly used as the monosaccharide component and lactulose as the disaccharide. Alternatives include mannitol plus cellobiose and rhamnose plus lactulose. This absorption test is useful in the investigation of intestinal disease.[1]

The lack of a standardised test solution has hampered comparison of test results. Although hyperosmolar solutions are better at determining intestinal damage,[2] some have preferred to use low osmolar solutions because of the risk of inducing osmotic diarrhoea, especially in children.

A study found the sugar absorption test to be strongly predictive of an organic cause of chronic diarrhoea; it may be useful in improving the selection of patients who need further evaluation.[3]

THE LACTOSE BREATH TEST (hydrogen breath test). Lactulose is converted by bacteria in the large bowel to short chain fatty acids with the production of small quantities of hydrogen gas. The hydrogen is rapidly absorbed and is exhaled in the breath and measurement of its production is used to measure orocaecal transit time and carbohydrate malabsorption. However, even small doses of lactulose shortens transit time, which may limit the value of this test.[4]

The test is also diagnostic for bacterial overgrowth in the small intestine, which is increased in irritable bowel syndrome. Although hydrogen is produced in most subjects, methane is also produced in up to 50% of healthy subjects, and data suggest there may be clinical implications to different gas profiles. A study found that the presence of methane was associated with constipation, and with constipation-predominant irritable bowel syndrome. Methane production was infrequent in diarrhoea-predominant irritable bowel syndrome and virtually absent in inflammatory bowel disease. Diarrhoea and inflammatory bowel disease were associated with hydrogen production. Whether the type of bacterial flora causally determines symptoms is as yet unknown.[5]

1. Uil JJ, *et al.* Clinical implications of the sugar absorption test: intestinal permeability test to assess mucosal barrier function. *Scand J Gastroenterol* 1997; **223** (suppl): 70–8.
2. Uil JJ, *et al.* Sensitivity of a hyperosmolar or "low"-osmolar test solution for sugar absorption in recognizing small intestinal mucosal damage in coeliac disease. *Dig Liver Dis* 2000; **32:** 195–200.
3. Di Leo V, *et al.* Lactulose/mannitol test has high efficacy for excluding organic causes of chronic diarrhea. *Am J Gastroenterol* 2003; **98:** 2245–52.
4. Miller MA, *et al.* Comparison of scintigraphy and lactulose breath hydrogen test for assessment of orocecal transit: lactulose accelerates small bowel transit. *Dig Dis Sci* 1997; **42:** 10–18.
5. Pimentel M, *et al.* Methane production during lactulose breath test is associated with gastrointestinal disease presentation. *Dig Dis Sci* 2003; **48:** 86–92.

Preparations

BP 2008: Lactulose Oral Powder;
Ph. Eur.: Liquid Lactulose;
USP 31: Lactulose Solution.

Proprietary Preparations (details are given in Part 3)
Arg.: Genocolan; Lactulon; Lafelax; Medixin; Tenualax; ***Austral.:*** Actilax; Duphalac; Genlac; Lac-Dol; Lactocur; ***Austria:*** Bifiteral; Duphalac; Laevolac; ***Belg.:*** Bifiteral; Certalac†; Duphalac; ***Braz.:*** Colonac; Farlac; Lactulona; Pentalac†; ***Canad.:*** Acilac†; Gen-Lac; Laxilose†; ***Chile:*** Axant; Dismam; Duphalac; Rencef†; ***Cz.:*** Duphalac; Lactecon; Laevolac†; ***Denm.:*** Danilax†; Medilax; ***Fin.:*** Duphalac; Levolac; Loraga†; ***Fr.:*** Duphalac; Laxaron; ***Ger.:*** Bifinorma; Bifiteral; Eugalac; Hepa-Merz Lact†; Hepaticum-Lac-Medice†; Kattwilact†; Lactocur; Lactuflor; Lactuverlan; Laevilac S; Medilet†; Tulotract; ***Gr.:*** Duphalac; Purgolac†; ***Hong Kong:*** Danilax; Duphalac; Laevolac; Martulose; ***Hung.:*** Duphalac; Laevolac; ***India:*** Duphalac; Livoluk; ***Indon.:*** Constipen; Dulcolactol; Duphalac; Lactulax; Lantulos; Laxadilac; Opilax; Pralax; Solac; ***Irl.:*** Dulax; Duphalac; Gerelax; Laxose; ***Israel:*** Avilac; Gerelax; Lactulax; Laevolac; ***Ital.:*** Biolac†; Dia-Colon; Duphalac; Epalat EPS; Epalfen; Lactoger†; Laevolac; Lassifar†; Lattubio†; Lattulac; Lis†; Normase; Osmolac†; Sintolatt; Verelait; ***Jpn:*** Monilac; ***Malaysia:*** Dhactulose; Duphalac; Lactul; Lactumed†; ***Mex.:*** Lactulax; Regulact; ***Neth.:*** Duphalac; Epalfen; Laxeersiroop; Legendal; ***Norw.:*** Duphalac; Levolac; ***NZ:*** Laevolac; ***Philipp.:*** Duphalac; Lilac; ***Pol.:*** Duphalac; Lactulol; Normalac; Normase; ***Port.:*** Colsanac; Duphalac; Lactecon†; Laevolac; Obstipar; ***Rus.:*** Duphalac (Дюфалак); Normase (Нормазе); Portalac (Порталак); ***S.Afr.:*** Adco-Liquilax; Duphalac; Lacson; Laxette; ***Singapore:*** Dhactulose; Duphalac; Lactus; ***Spain:*** Belmalax; Duphalac; ***Swed.:*** Duphalac; Laktipex; Loraga; ***Switz.:*** Duphalac; Gatinar; Legendal; Rudolac; ***Thai.:*** Duphalac; Hepalac; Laevolac†; ***Turk.:*** Duphalac; Lactulac; Laevolac; Laktol; Osmolak; ***UAE:*** Soflax; ***UK:*** Duphalac; Lactugal; Lemlax; Regulose; ***USA:*** Cephulac; Cholac†; Chronulac; Constilac; Constulose; Duphalac; Enulose; Kristalose; ***Venez.:*** Lactulona; Moderan.

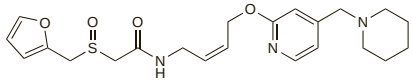
Multi-ingredient: ***Arg.:*** Bifidosa; ***Fr.:*** Melaxose; Transulose; ***Ger.:*** Eugalan Topfer; ***Indon.:*** Laktobion; ***Ital.:*** Combilax; Lactolas; Lactomannan; Levoplus; Naturalass; ***Neth.:*** Transulose; ***Port.:*** Melaxose.

Lafutidine *(rINN)*

FRG-8813; Lafutidina; Lafutidinum. (±)-2-(Furfurylsulfinyl)-*N*-[(*Z*)-4-{[4-(piperidinomethyl)-2-pyridyl]oxy}-2-butenyl]acetamide.

Лафутидин

$C_{22}H_{29}N_3O_4S$ = 431.5.
CAS — 118288-08-7.
ATC — A02BA08.
ATC Vet — QA02BA08.



Profile

Lafutidine, like cimetidine (p.1716), is a histamine H_2-antagonist. It is used in the management of peptic ulcer disease.

◊ References.
1. Uesugi T, *et al.* The efficacy of lafutidine in improving preoperative gastric fluid property: a comparison with ranitidine and rabeprazole. *Anesth Analg* 2002; **95:** 144–7.
2. Mikawa K, *et al.* Lafutidine vs cimetidine to decrease gastric fluid acidity and volume in children. *Can J Anaesth* 2003; **50:** 425–6.
3. Isomoto H, *et al.* Lafutidine, a novel histamine H2-receptor antagonist, vs lansoprazole in combination with amoxicillin and clarithromycin for eradication of Helicobacter pylori. *Helicobacter* 2003; **8:** 111–19.
4. Inamori M, *et al.* Early effects of lafutidine or rabeprazole on intragastric acidity: which drug is more suitable for on-demand use? *J Gastroenterol* 2005; **40:** 453–8.
5. Higuchi K, *et al.* Lafutidine can improve the quality of gastric ulcer healing in humans: a randomized, controlled, multicenter trial. *Inflammopharmacology* 2006; **14:** 226–30.
6. Yamagishi H, *et al.* Stronger inhibition of gastric acid secretion by lafutidine, a novel H(2) receptor antagonist, than by the proton pump inhibitor lansoprazole. *World J Gastroenterol* 2008; **14:** 2406–10.

Preparations

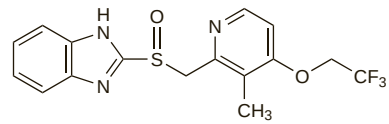
Proprietary Preparations (details are given in Part 3)
Jpn: Protecadin; Stogar.

Lansoprazole *(BAN, USAN, rINN)*

A-65006; AG-1749; Lansopratsoli; Lansoprazol; Lansoprazolum. 2-({3-Methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl)methyl} sulphinylbenzimidazole.

Лансопразол

$C_{16}H_{14}F_3N_3O_2S$ = 369.4.
CAS — 103577-45-3.
ATC — A02BC03.
ATC Vet — QA02BC03.



Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
Ph. Eur. 6.2 (Lansoprazole). A white or brownish powder. Practically insoluble in water; soluble in anhydrous alcohol; very slightly soluble in acetonitrile. It exhibits polymorphism. Store in airtight containers. Protect from light.
USP 31 (Lansoprazole). A white to brownish-white powder. Practically insoluble in water; freely soluble in dimethylformamide. Store in airtight containers at a temperature not exceeding 40°. Protect from light.

Adverse Effects and Precautions

As for Omeprazole, p.1753.

◊ Reviews.
1. Freston JW, *et al.* Safety profile of lansoprazole: the US clinical trial experience. *Drug Safety* 1999; **20:** 195–205.

Effects on the blood. For a report of thrombocytopenia with lansoprazole, see under Omeprazole, p.1753.

Effects on the endocrine system. For cases of gynaecomastia associated with lansoprazole, see p.1753.

Effects on the gastrointestinal tract. Glossitis (associated in some cases with black tongue or stomatitis) has been reported in a few patients taking lansoprazole as part of a triple therapy regimen for *Helicobacter pylori* elimination in peptic ulcer disease.[1] Discoloured tongue has been reported in a patient taking lansoprazole alone.[2]

An increase in gastritis occurred in patients infected with *Helicobacter pylori* when given long-term lansoprazole therapy.[3] For further discussion of the link between *H. pylori*, gastritis, and proton pump inhibitor use, see Gastrointestinal Tumours, p.1754.

For a suggestion that the incidence of diarrhoea may be greater with lansoprazole than omeprazole see Incidence of Adverse Effects, p.1753. Cases of microscopic colitis have been reported with use of lansoprazole.[4] UK licensed product information states that stopping therapy should be considered in the case of severe and/or persistent diarrhoea.

1. Greco S, *et al.* Glossitis, stomatitis, and black tongue with lansoprazole plus clarithromycin and other antibiotics. *Ann Pharmacother* 1997; **31:** 1548.
2. Scully C. Discoloured tongue: a new cause? *Br J Dermatol* 2001; **144:** 1293–4.
3. Berstad AE, *et al.* Helicobacter pylori gastritis and epithelial cell proliferation in patients with reflux oesophagitis after treatment with lansoprazole. *Gut* 1997; **41:** 740–7.
4. Hilmer SN, *et al.* Microscopic colitis associated with exposure to lansoprazole. *Med J Aust* 2006; **184:** 185–6.

Effects on the musculoskeletal system. For reference to a case of eosinophilia and myalgia related to lansoprazole therapy, see p.1753.

Effects on the skin. For mention of skin reactions to lansoprazole, see p.1754.

Interactions

As for Omeprazole, p.1755. Antacids and sucralfate may reduce the bioavailability of lansoprazole, and should not be taken within 1 hour of a dose of lansoprazole.

◊ For reference to a lack of effect of lansoprazole on diazepam, see Gastrointestinal Drugs, p.991, and for a clinically insignificant effect on theophylline clearance, see p.1145. For reference to glossitis occurring when lansoprazole was used with some antibacterials, see Effects on the Gastrointestinal Tract, above.

Pharmacokinetics

Lansoprazole is rapidly absorbed after oral doses, with peak plasma concentrations achieved after about 1.5 to 2 hours. Bioavailability is reported to be 80% or more even with the first dose, although the drug must be given in an enteric-coated form since lansoprazole is unstable at acid pH. Food slows the absorption of lansoprazole and reduces the bioavailability by about 50%. It is extensively metabolised in the liver, primarily by cytochrome P450 isoenzyme CYP2C19 to form 5-hydroxyl-lansoprazole and by CYP3A4 to form lansoprazole sulfone. Metabolites are excreted mainly in faeces via the bile; only about 15 to 30% of a dose is excreted in urine. The plasma elimination half-life is around 1 to 2 hours but the duration of action is much longer. Lansoprazole is about 97% bound to plasma protein. Clearance is decreased in elderly patients, and in hepatic impairment.

◊ References.
1. Hussein Z, *et al.* Age-related differences in the pharmacokinetics and pharmacodynamics of lansoprazole. *Br J Clin Pharmacol* 1993; **36:** 391–8.
2. Flouvat B, *et al.* Single and multiple dose pharmacokinetics of lansoprazole in elderly subjects. *Br J Clin Pharmacol* 1993; **36:** 467–9.
3. Delhotal-Landes B, *et al.* Pharmacokinetics of lansoprazole in patients with renal or liver disease of varying severity. *Eur J Clin Pharmacol* 1993; **45:** 367–71.
4. Delhotal Landes B, *et al.* Clinical pharmacokinetics of lansoprazole. *Clin Pharmacokinet* 1995; **28:** 458–70.
5. Karol MD, *et al.* Lansoprazole pharmacokinetics in subjects with various degrees of kidney function. *Clin Pharmacol Ther* 1997; **61:** 450–8.
6. Tran A, *et al.* Pharmacokinetic-pharmacodynamic study of oral lansoprazole in children. *Clin Pharmacol Ther* 2002; **71:** 359–67.

Metabolism. As for omeprazole (p.1755), the cytochrome P450 isoenzyme CYP2C19 (*S*-mephenytoin hydroxylase) is involved in the hydroxylation of lansoprazole, and individuals who are deficient in this enzyme are poor metabolisers of lansoprazole.[1,2] There is some suggestion that the effect of this genetic polymorphism on lansoprazole may be less than the effect on omeprazole.[3]

1. Pearce RE, *et al.* Identification of the human P450 enzymes involved in lansoprazole metabolism. *J Pharmacol Exp Ther* 1996; **277:** 805–16.
2. Sohn DR, *et al.* Metabolic disposition of lansoprazole in relation to the S-mephenytoin 4′-hydroxylation phenotype status. *Clin Pharmacol Ther* 1997; **61:** 574–82.
3. Kim K-A, *et al.* Enantioselective disposition of lansoprazole in extensive and poor metabolizers of CYP2C19. *Clin Pharmacol Ther* 2002; **72:** 90–9.

Uses and Administration

Lansoprazole is a proton pump inhibitor with actions and uses similar to those of omeprazole (p.1755). It is used in the treatment of peptic ulcer disease and in oth-

er conditions where inhibition of gastric acid secretion may be beneficial.

Lansoprazole is usually given orally as capsules, dispersible tablets, or suspension containing enteric-coated granules. Once daily regimens are taken before food in the morning. An intravenous formulation is also available.

For the relief of acid-related **dyspepsia** (p.1695) intermittent courses of lansoprazole may be given in doses of 15 or 30 mg once daily, for 2 to 4 weeks.

In the treatment of **gastro-oesophageal reflux disease** (p.1696) the dose is 15 to 30 mg once daily for 4 to 8 weeks; thereafter maintenance therapy can be continued with 15 or 30 mg once daily according to response. In patients unable to take oral therapy, lansoprazole may be given by intravenous infusion for the treatment of erosive oesophagitis for up to 7 days; a dose of 30 mg over 30 minutes daily is recommended.

Lansoprazole is given for the treatment of **peptic ulcer disease** (p.1702) in the UK in doses of 30 mg once daily. Treatment is continued for 2 to 4 weeks for duodenal and 4 to 8 weeks for gastric ulcer. In the USA, a dose of 15 mg daily for 4 weeks is recommended for duodenal ulcer, and 30 mg once daily is given for up to 8 weeks for gastric ulceration. When appropriate, 15 mg daily may be used as maintenance therapy for the prevention of relapse of duodenal ulcer. Lansoprazole may be combined with antibacterials in one-week **triple therapy** regimens for the eradication of *Helicobacter pylori*. Effective regimens include lansoprazole 30 mg twice daily combined with clarithromycin 500 mg twice daily and amoxicillin 1 g twice daily, or combined with clarithromycin 250 mg twice daily and metronidazole 400 mg twice daily; lansoprazole with amoxicillin and metronidazole has also been used. In patients with **NSAID-associated ulceration** a dose of 30 mg daily for 4 to 8 weeks is recommended; 15 to 30 mg daily may be used as prophylaxis for patients who require continued NSAID treatment.

In the treatment of pathological hypersecretory states such as the **Zollinger-Ellison syndrome** (p.1704) the initial dose is 60 mg once daily, adjusted as required. Doses of up to 90 mg twice daily have been used. Daily doses greater than 120 mg should be given in divided doses.

In the USA, **children** aged from 1 to 11 years may be given lansoprazole for the short-term treatment of erosive oesophagitis and symptomatic gastro-oesophageal reflux disease. Children weighing 30 kg or less should be given 15 mg once daily, and those weighing more than 30 kg are given 30 mg once daily, for up to 12 weeks. Doses of up to 30 mg twice daily have been used. In children aged from 12 to 17 years, lansoprazole 30 mg once daily for up to 8 weeks may be used for erosive oesophagitis, and 15 mg once daily for up to 8 weeks may be used for symptomatic gastro-oesophageal reflux disease. Although not licensed for children in the UK, the *BNFC* recommends comparable oral daily doses of 0.5 to 1 mg/kg in children up to 30 kg in weight, and 15 or 30 mg once daily in those over 30 kg.

Doses of lansoprazole may need to be reduced in patients with hepatic impairment (see below).

◊ General references. For general reviews of proton pump inhibitors, see Omeprazole, p.1756.

1. Langtry HD, Wilde MI. Lansoprazole: an update of its pharmacological properties and clinical efficacy in the management of acid-related disorders. *Drugs* 1997; **54:** 473–500.
2. Matheson AJ, Jarvis B. Lansoprazole: an update of its place in the management of acid-related disorders. *Drugs* 2001; **61:** 1801–33.
3. Freston JW, *et al.* Lansoprazole for maintenance of remission of erosive oesophagitis. *Drugs* 2002; **62:** 1173–84.
4. Dando TM, Plosker GL. Intravenous lansoprazole: in erosive oesophagitis. *Drugs* 2004; **64:** 2085–9.
5. Croom KF, Scott LJ. Lansoprazole: in the treatment of gastro-oesophageal reflux disease in children and adolescents. *Drugs* 2005; **65:** 2129–35.

Administration. Lansoprazole *capsules* should be swallowed whole and not crushed or chewed. Lansoprazole *dispersible tablets* should be placed on the tongue and allowed to disintegrate and the resultant granules swallowed; alternatively, the tablets may be swallowed whole with a glass of water. The tablets should not be crushed or chewed. The tablets may also be dispersed in a small amount of water and given via an oral syringe, or via a nasogastric tube. Lansoprazole *granules for oral suspension* should be reconstituted in a little water and swallowed immediately. Where the suspension formulation is not available, the contents of the capsules (enteric-coated granules) can be sprinkled on a small amount of soft food (such as yogurt or apple sauce) or mixed with a little fruit juice and swallowed. For administration via a nasogastric tube, the contents of a capsule may be mixed with 40 mL of apple juice; additional apple juice may be used to flush the tube.

Administration in hepatic impairment. Exposure to lansoprazole is increased in patients with hepatic impairment. Licensed product information recommends that patients with moderate to severe liver disease should be kept under supervision, and that the daily dose should be reduced by 50%.

Preparations

USP 31: Lansoprazole Delayed-Release Capsules.

Proprietary Preparations (details are given in Part 3)
Arg.: Ilsatec†; Lanzopral; Mesactol; Ogasto†; ***Austral.:*** Zoton; ***Austria:*** Agopton; Lansobene; ***Belg.:*** Dakar; ***Braz.:*** Anzoprol†; Lanogastro; Lanz; Lanzol; Lanzopept; Neozol; Ogastro; Prazol; ***Canad.:*** Prevacid; ***Chile:*** Fudermex; Gastride; Lanzopral; Ogasto†; Unival; ***Cz.:*** Lansone†; Lansoprol; Lanzul; ***Denm.:*** Lanzo; ***Fin.:*** Lanzo; Zolt; ***Fr.:*** Lanzor; Ogast; Ogastoro; ***Ger.:*** Agopton; Lanzor; ***Gr.:*** Elcodil; Lanciprol; Lanso; Laprazol; ***Hong Kong:*** Takepron; ***Hung.:*** Lansacid; Lansogen; Lansone; Lansoptol; Levant; Protonexa; Refluxon; ***India:*** Chexid; Lancus; Lanzol; ***Indon.:*** Compraz; Digest; Gastrolan; Inhipraz; Lancid; Lapraz; Laproton; Lasgan; Laz; Loprezol; Nufaprazol; Prazotec; Prolanz; Prosogan; Protica; Pysolan; Solans; Sopralan; Ulceran; ***Irl.:*** Lanziop; Lanzol; Razolager; Zomel; Zoton; Zotrole; ***Israel:*** Lanton; Zoton; ***Ital.:*** Lansox; Limpidex; Zoton; ***Jpn:*** Prevacid; Takepron; ***Malaysia:*** Prevacid; ***Mex.:*** Bonzol; Ilsatec; Imidex; Keval; Lafin; Lanodizol; Mavilan; Mediprim; Ogastro; Olan; Palatrin; Pranix; Safemar; Uldapril; Ulpax; ***Neth.:*** Prezal; ***Norw.:*** Lanzo; ***NZ:*** Solox; Zoton†; ***Philipp.:*** Lanzohex; Prevacid; Pylison; ***Pol.:*** LansoLek; Lanzostad; Lanzul; ***Port.:*** Alexin; Dispepci; Gastrex; Gastrolanzo; Gastroliber; Lansox; Lanzogastro; Lapol; Lizul†; Monolitum†; Ogasto; Pampe; Pepzol†; Ulcertec; ***Rus.:*** Acrilans (Акриланз); Epicur (Эпикур); Helicol (Геликол); Lanzap (Ланзап); ***S.Afr.:*** Adco-Roznal; Lancap; Lansoloc; Lanzor; ***Singapore:*** Prevacid; ***Spain:*** Bamalite; Estomil; Eudiges; Lanzol; Monolitum; Opiren; Pro Ulco; Protoner; ***Swed.:*** Lanzo; ***Switz.:*** Agopton; ***Thai.:*** Prevacid; ***Turk.:*** Aprazol; Degastrol; Helicol; Lansazol; Lansoprol; Lansor; Lanzedin; Ogastro; Opagis; Vogast; Zoprol; ***UAE:*** Lanfast; ***UK:*** Zoton; ***USA:*** Prevacid; ***Venez.:*** Biolanz; Gastrazol; Ilsatec†; Lansovax; Lanzap†; Lanzol; Lanzopral; Ogastro.

Multi-ingredient: ***Arg.:*** Heliklar†; ***Braz.:*** Anzopac†; H-Bacter; Helicopac; Heliklar; Lansodom; Lansoprid; Pylorikit; Pyloripac; Pyloritrat; ***Canad.:*** Hp-Pac; ***Fin.:*** Helipak A; Helipak K; Helipak T; ***India:*** Okalan D; Pylokit; ***Mex.:*** Pylopac; ***Turk.:*** Helipak; ***UK:*** Helicleat†; HeliMet†; ***USA:*** Prevpac.

Used as an adjunct in: ***USA:*** Prevacid NapraPAC.

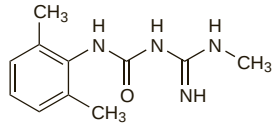
Lidamidine Hydrochloride *(USAN, rINNM)*

Hidrocloruro de lidamidina; Lidamidine, Chlorhydrate de; Lidamidini Hydrochloridum; WHR-1142A. *N*-(2,6-Dimethylphenyl)-*N'*-[imino(methylamino)methyl]urea hydrochloride.

Лидамидина Гидрохлорид

$C_{11}H_{16}N_4O,HCl$ = 256.7.

CAS — 66871-56-5 (lidamidine); 65009-35-0 (lidamidine hydrochloride).



(lidamidine)

Profile
Lidamidine is an alpha$_2$-adrenergic receptor stimulant used as the hydrochloride for the management of diarrhoea and other gastrointestinal disorders.

Preparations
Proprietary Preparations (details are given in Part 3)
Mex.: Idealid†; Supra.

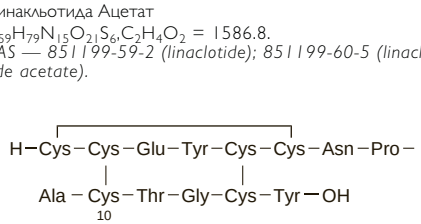
Linaclotide Acetate *(USAN, rINNM)*

Acetato de linaclotida; Linaclotide, Acétate de; Linaclotidi Acetas; MD-1100; MM-416775. [9-L-Tyrosine]heat-stable enterotoxin (Escherichia coli)-(6-19)-peptide monoacetate salt.

Линакльотида Ацетат

$C_{59}H_{79}N_{15}O_{21}S_6,C_2H_4O_2$ = 1586.8.

CAS — 851199-59-2 (linaclotide); 851199-60-5 (linaclotide acetate).



Profile
Linaclotide is a guanylate cyclase-C agonist being studied in the treatment of constipation-predominant irritable bowel syndrome and chronic constipation.

◊ References.

1. Harris LA, Crowell MD. Linaclotide, a new direction in the treatment of irritable bowel syndrome and chronic constipation. *Curr Opin Mol Ther* 2007; **9:** 403–10.
2. Andresen V, *et al.* Effect of 5 days linaclotide on transit and bowel function in females with constipation-predominant irritable bowel syndrome. *Gastroenterology* 2007; **133:** 761–8.

Liquorice

Alcaçuz; Édesgyökér; Gancao; Glycyrrhiza; Korzeń lukrecji; Lakritsijuuri; Lakritsrot; Lékořicový kořen; Licorice; Liquiritiae radix; Liquorice Root; Orozuz; Raiz de Regaliz; Regaliz; Réglisse, racine de; Saldymedžių šaknys; Süssholzwurzel.

Лакрица

Description. Liquorice is the dried rhizome and roots of *Glycyrrhiza glabra*. Those of *G. glabra* var. *typica* are known in commerce as Spanish Liquorice, those of *G. glabra* var. *glandulifera* as Russian Liquorice, and those of *G. glabra* var. *β-violacea* as Persian Liquorice.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*. *Eur.* (see p.vii) also includes Liquorice Dry Extract for Flavouring Purposes. *US* also includes Powdered Liquorice and Powdered Licorice Extract. *Br.* also includes Liquorice Root for use in Traditional Herbal Medicine and Processed Liquorice Root for use in Traditional Herbal Medicinal Product.

Ph. Eur. 6.2 (Liquorice Root; Liquorice BP 2008). The dried unpeeled or peeled, whole or cut root and stolons of *Glycyrrhiza glabra* and/or *G. inflata* and/or *G. uralensis*. It contains not less than 4% of glycyrrhizic acid. Protect from light.

USP 31 (Licorice). The roots, rhizomes, and stolons of *Glycyrrhiza glabra* or *G. uralensis*. It contains not less than 2.5% of glycyrrhizic acid, calculated on the dried basis. Store in a cool, dry place.

BP 2008 (Liquorice Root for use in THM). It is the dried unpeeled root and rhizome of *Glycyrrhiza uralensis*, *G. inflata*, or *G. glabra*. For use in traditional Chinese medicines. It contains not less than 2.0% of glycyrrhizic acid calculated with reference to the dried material. Protect from moisture.

BP 2008 (Processed Liquorice Root for use in THMP). Liquorice Root for use in THM which has been cleaned, softened, sliced transversely or longitudinally to form uniform pieces, and dried. It contains not less than 2.0% of glycyrrhizic acid calculated with reference to the dried material. Protect from moisture.

Adverse Effects and Precautions
Liquorice has mineralocorticoid-like actions manifesting as sodium and water retention and hypokalaemia (see below).

Deglycyrrhizinised liquorice is not usually associated with such adverse effects.

Mineralocorticoid effects. Mineralocorticoid effects have been reported after excessive or prolonged ingestion of liquorice. The liquorice may be ingested in confectionery (including liquorice-flavoured chewing gum), tea, soft drinks, herbal medicines, cough mixtures, or by chewing tobacco. The enzyme 11-β-hydroxysteroid dehydrogenase (cortisol oxidase) converts cortisol to cortisone, preventing cortisol gaining access to non-specific mineralocorticoid receptors. This enzyme is inhibited by glycyrrhetinic acid (produced by the hydrolysis of glycyrrhizic acid, a natural constituent of liquorice), resulting in increased concentrations of cortisol in the body, enhancing its physiological effects.[1-3]

Clinical manifestations include consequences of sodium retention such as hypertension,[4-10] and hypokalaemia, which can result in neuromuscular disturbances ranging from muscle weakness,[11] myoclonus,[12] and myopathy[10] to paralysis[13-15] and rhabdomyolysis.[15-17] Arrhythmias[16,18] and fatal cardiac arrest[19] have also been reported.

Increased amounts of cortisol in vascular smooth muscle may cause vasoconstriction. Vasospasm of vessels supplying the optic nerve may have caused transient visual disturbances reported after liquorice ingestion.[2]

Other reported effects of liquorice include growth retardation in a boy with Addison's disease;[20] liquorice was thought to have potentiated the effect of hydrocortisone.

Endocrine effects of liquorice have been reviewed.[21] Conflicting effects on testosterone and prolactin have been reported. Components of liquorice root (which has been tried for menopausal symptoms) have both oestrogenic and anti-oestrogenic activity, and it has reportedly caused gynaecomastia.

Individuals vary markedly in their susceptibility to liquorice-induced adverse effects.[1] Those consuming 400 mg glycyrrhetinic acid daily generally experience adverse effects, but a regular daily intake of no more than 100 mg of glycyrrhetinic acid (about 50 g of liquorice sweets) has produced adverse effects in some who appear more sensitive to its effects. Some consider a daily intake of 10 mg glycyrrhetinic acid to be a safe daily dose for adults; the amount of salt consumed needs to be considered as