Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Braz.:*** Jalapa Composta†; ***Canad.:*** Herbal Laxative; ***S.Afr.:*** SB 3 Triple Action Pills.

Kaolin

Bolus Alba; Caolín; E559; Kaoliini; Kaolinas; Kaolinum; Weisser Ton.

Каолин

CAS — 1332-58-7.
ATC — A07BC02.
ATC Vet — QA07BC02.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.* Some pharmacopoeias do not differentiate between the heavy and light varieties.

Ph. Eur. 6.2 (Kaolin, Heavy). A purified, natural, hydrated aluminium silicate of variable composition. It is a fine, white or greyish-white, unctuous powder. Practically insoluble in water and in organic solvents.

BP 2008 (Light Kaolin). A native hydrated aluminium silicate, freed from most of its impurities by elutriation, and dried. It contains a suitable dispersing agent. It is a light, white, odourless or almost odourless, unctuous powder free from gritty particles. Practically insoluble in water and in mineral acids.

The BP 2008 directs that when Kaolin or Light Kaolin is prescribed or demanded, Light Kaolin shall be dispensed or supplied, unless it is ascertained that Light Kaolin (Natural) is required.

BP 2008 (Light Kaolin (Natural)). It is Light Kaolin which does not contain a dispersing agent. It is a light, white, odourless or almost odourless, unctuous powder free from gritty particles. Practically insoluble in water and in mineral acids.

The BP 2008 directs that when Kaolin or Light Kaolin is prescribed or demanded, Light Kaolin shall be dispensed or supplied, unless it is ascertained that Light Kaolin (Natural) is required.

USP 31 (Kaolin). A native hydrated aluminium silicate, powdered and freed from gritty particles by elutriation. It is a soft, white or yellowish-white powder or lumps with an earthy or clay-like taste and when moistened with water assumes a darker colour and develops a marked clay-like odour. Insoluble in water, in cold dilute acids, and in solutions of alkali hydroxides.

Profile

Light kaolin and light kaolin (natural) are adsorbent antidiarrhoeal agents that have been used as adjuncts to rehydration therapy in the management of diarrhoea (p.1694). Up to about 24 g daily may be taken orally in divided doses. Kaolin is often combined with other antidiarrhoeals, especially pectin.

Kaolin can form insoluble complexes with some drugs in the gastrointestinal tract and reduce their absorption; oral doses should not be taken at the same time.

Externally, light kaolin is used as a dusting powder. Kaolin is liable to be heavily contaminated with bacteria, and when used in dusting powders, it should be sterilised.

Heavy kaolin is used in the preparation of kaolin poultice, which is applied topically with the intention of reducing inflammation and alleviating pain (see Rubefacients and Topical Analgesia, p.5).

Light kaolin is also used as a food additive.

Preparations

BP 2008: Kaolin and Morphine Mixture; Kaolin Mixture; Kaolin Poultice.

Proprietary Preparations (details are given in Part 3)

Braz.: Kaogel†; ***UK:*** Childrens Diarrhoea Mixture; Entrocalm.

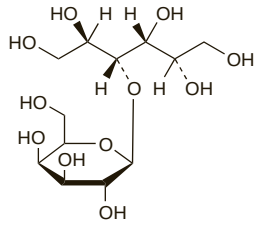
Multi-ingredient: ***Arg.:*** Anusol-A; Argeal; Endomicina†; Gastranil†; Opocarbon; Opocler†; ***Austral.:*** Bis-Pectin†; Chemists Own Diarrhoea Mixture†; Diarcalm; Donnagel; Kaomagma with Pectin†; Kaomagma†; ***Belg.:*** Alopate; Neutroses; ***Braz.:*** Atalin†; Digastril†; Eviprostat†; Gastrobene; Kaomagma; Kaopectin†; ***Chile:*** Furazolidona; ***Fr.:*** Anti-H†; Antiphlogistine†; Argeal; Gastropax; Kaobrol†; Kaologeais; Kaomuth; Karayal; Keracnyl; Neutroses; ***Ger.:*** Kaoprompt-H; rohasal†; ***Gr.:*** Fissan-Pate†; Kaopectate†; ***Hong Kong:*** Calamine-D†; Uni-Kaotin; ***Hung.:*** Bolus Adstringens; Bolus Laxans; ***Indon.:*** Kaopectate; Neo Diaform; Neo Kaocitin; Neo Kaolana; Neo Kaominal; ***Irl.:*** Kaopectate†; ***Israel:*** Digestif-Ara†; Kaopectin; Kapectin Forte†; Zincod; ***Ital.:*** Katoxyn; Neutrose S Pellegrino; Streptomagma; ***Malaysia:*** Beakopectin†; Kaopectate†; ***Mex.:*** Ameban; Caopecfar; Colfur; Contefur†; Coralzul; Depofin; Dia-Par Compuesto; Dibapec Compuesto; Estibal; Exofur; Facetin-D; Farpectol; Furoxona CP; Fuzotyl†; Hidromagma†; Isocar; K-Omistron; Kaomycin; Kaopectate; Kapecfuran; Kediar; Lactopectin; Neokap; Neoxil; Olam; Optazol; Quimefuran; Suyodil; Tapzol con Neomicina†; Treda; Trilor†; Yodozona; ***S.Afr.:*** Betapect; Bipectinol; Biskapect; Bolus Eucalypti Comp; Chloropect; Collodene; Enterolyte; Gastropect; Kao†; Kaopectin†; Kaostatex; Pectin-K; Pectrolyte; SB Diarrhoea Mixture; ***Singapore:*** Beakopectin; Kaomix; Kaopectate†; ***Switz.:*** Argent†; Cicafissan; Fissan†; Gyrosan†; Neo-Decongestine; Neutroses; Padma-Lax; Padmed Laxan; Phlogantin; ***Thai.:*** Alkamine; Alumag; Alupep; Antacil†; Cenopec; Coccila†; Conmag; Di-Su-Frone†; Difuran; Disento; Disento PF; Droximag†; Furasian; Furopectin†; Kaopectal; Med-Kafuzone†; ***UAE:*** Kaptin; ***UK:*** Collis Browne's; De Witt's Antacid; Junior Kao-C; Kaodene†; KLN; Moorland; Opazimes; ***USA:*** K-C; Kao-Paverin; Kao-Spen; Kaodene Non-Narcotic; Mexsana; ***Venez.:*** Kaopecon†; Kaopectate†; Klincosal; Niosilin; Parepectolin†; Pec-Kao†; Sendafur†.

Lactitol *(BAN, rINN)*

E966; β-Galactosido-sorbitol; Lactit; Lactitolum; Lactobiosit; Lactositol; Laktitol; Laktitoli; Laktitolis. 4-*O*-(β-D-Galactopyranosyl)-D-glucitol.

Лактитол

$C_{12}H_{24}O_{11}$ = 344.3.
CAS — 585-86-4.
ATC — A06AD12.
ATC Vet — QA06AD12.



Pharmacopoeias. In *USNF*. *Eur.* (see p.vii) includes the monohydrate.

Ph. Eur. 6.2 (Lactitol Monohydrate). A white or almost white crystalline powder. Very soluble in water; slightly soluble in alcohol; practically insoluble in dichloromethane.

USNF 26 (Lactitol). It may be the anhydrous form, the monohydrate, or the dihydrate. White or light brown, odourless, crystals. It has a mild, sweet taste, and no aftertaste.

Profile

Lactitol is a disaccharide analogue of lactulose (below) and has similar actions and uses.

Lactitol monohydrate is used as an oral powder or solution in the management of hepatic encephalopathy (p.1697) and in constipation (p.1693). Lactitol monohydrate 1.05 g is equivalent to about 1 g of anhydrous lactitol.

In the treatment of hepatic encephalopathy, lactitol monohydrate is given in usual oral doses of 500 to 700 mg/kg daily in 3 divided doses at meal times. The dose is subsequently adjusted to produce 2 soft stools daily.

In the treatment of constipation, lactitol monohydrate is given in an initial dose of 20 g daily as a single dose with the morning or evening meal, subsequently adjusted to produce one stool daily. A dose of 10 g daily may be sufficient for many patients.

Doses should be mixed with food or liquid, and 1 to 2 glasses of liquid should be drunk with the meal.

Lactitol is a permitted sweetener in foods.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Importal; Neda-Lactitol; Portolac†; ***Belg.:*** Importal; Normolaxil; Portolac; ***Braz.:*** Sigmalac; ***Cz.:*** Importal†; ***Denm.:*** Importal; ***Fin.:*** Lalax; ***Fr.:*** Importal; ***Ger.:*** Importal; ***Gr.:*** Importal; ***Israel:*** Importal†; Novolax; ***Ital.:*** Portolac; ***Jpn:*** Portolac; ***Neth.:*** Importal; ***Norw.:*** Importal†; ***NZ:*** Importal; ***Port.:*** Importal; ***Spain:*** Emportal; Oponaf; ***Swed.:*** Importal; ***Switz.:*** Importal; ***Thai.:*** Importal; ***Turk.:*** Importal.

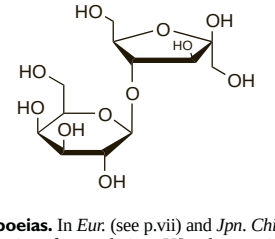
Multi-ingredient: ***Ital.:*** Levoplus.

Lactulose *(BAN, USAN, rINN)*

Lactulosa; Lactulosum; Laktuliozė; Laktuloosi; Laktulos; Laktulosa; Laktüloz; Laktulóz. 4-*O*-β-D-Galactopyranosyl-D-fructose.

Лактулоза

$C_{12}H_{22}O_{11}$ = 342.3.
CAS — 4618-18-2.
ATC — A06AD11.
ATC Vet — QA06AD11.



Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn*. *Chin.* only contains specifications for a solution. *US* only contains specifications for a solution and a concentrated liquid.

Ph. Eur. 6.2 (Lactulose). A white or almost white, crystalline powder. Freely soluble in water; sparingly soluble in methyl alcohol; practically insoluble in toluene.

Ph. Eur. 6.2 (Lactulose, Liquid; Lactulose Solution BP 2008). An aqueous solution of lactulose. It contains not less than 62.0% w/v of lactulose; it may contain lesser amounts of other sugars including lactose, epilactose, galactose, tagatose, and fructose. It may contain a suitable antimicrobial preservative. It is a clear, colourless or pale brownish-yellow, viscous liquid. Miscible with water. It may be a supersaturated solution or may contain crystals that disappear on heating.

USP 31 (Lactulose Concentrate). A colourless to amber syrupy liquid that may exhibit some precipitation and darkening on standing. Miscible with water. Store in airtight containers preferably at a temperature between 2° and 30°.

Adverse Effects

Lactulose may cause abdominal discomfort associated with flatulence or cramps. Nausea and vomiting have occasionally been reported after high doses. Some consider the taste to be unpleasant; this can be minimised by dilution in water, fruit juice, or milk, or by mixing the dose with food. Prolonged use or excessive dosage may result in diarrhoea with excessive loss of water and electrolytes, particularly potassium. Hypernatraemia has been reported.

Lactic acidosis. Severe lactic acidosis developed in a patient with adynamic ileus who was being given lactulose for hepatic encephalopathy.[1]

1. Mann NS, *et al*. Lactulose and severe lactic acidosis. *Ann Intern Med* 1985; **103:** 637.

Precautions

Lactulose should not be given to patients with galactosaemia or intestinal obstruction. It should not be used in patients on a low galactose diet and care should be taken in patients with lactose intolerance or in diabetic patients because of the presence of some free galactose and lactose.

Pharmacokinetics

Taken orally, lactulose passes essentially unchanged into the large intestine where it is metabolised by saccharolytic bacteria with the formation of simple organic acids, mainly lactic acid and small amounts of acetic and formic acids. The small amount of absorbed lactulose is subsequently excreted unchanged in the urine.

Uses and Administration

Lactulose is a synthetic disaccharide osmotic laxative (p.1693) used in the treatment of constipation (p.1693) and in hepatic encephalopathy (p.1697). Lactulose is broken down by colonic bacteria mainly into lactic acid. This exerts a local osmotic effect in the colon resulting in increased faecal bulk and stimulation of peristalsis. It may take up to 48 hours before an effect is obtained. When larger doses are given for hepatic encephalopathy the pH in the colon is reduced significantly and the absorption of ammonium ions and other toxic nitrogenous compounds is decreased, leading to a fall in blood-ammonia concentration and an improvement in mental function.

Lactulose is usually given orally as a solution containing about 3.35 g of lactulose per 5 mL, with other sugars such as galactose and lactose; an oral powder formulation is also available in some countries. In the treatment of **constipation**, the usual initial dose is 10 to 20 g (15 to 30 mL) given daily in a single dose or in 2 divided doses; doses up to 45 mL daily of the solution (or up to 40 g of the reconstituted oral powder formulation) have been given. The dose is gradually adjusted according to the patient's needs. For doses in children, see below.

In **hepatic encephalopathy**, an oral dose of 60 to 100 g (90 to 150 mL) is given daily in 3 divided doses. The dose is subsequently adjusted to produce 2 or 3 soft stools each day. Lactulose solution 200 g (300 mL) mixed with 700 mL of water or sodium chloride 0.9% has been used as a retention enema; the enema is retained for 30 to 60 minutes, repeated every 4 to 6 hours until the patient is able to take oral medication.

◊ References.

1. Clausen MR, Mortensen PB. Lactulose, disaccharides and colonic flora: clinical consequences. *Drugs* 1997; **53:** 930–42.
2. Schumann C. Medical, nutritional and technological properties of lactulose: an update. *Eur J Nutr* 2002; **41** (suppl): I17–I25.

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.

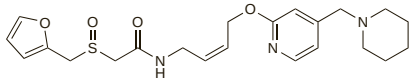
Multi-ingredient: ***Arg.:*** Bifidosa; ***Fr.:*** Melaxose; Transulose; ***Ger.:*** Eugalan Topfer; ***Indon.:*** Laktobion; ***Ital.:*** Combilax; Lactolas; Lactomannan; Levoplus; Naturalass; ***Neth.:*** Transulose; ***Port.:*** Melaxose.

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

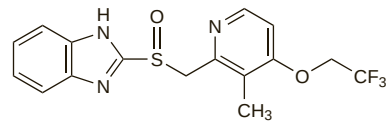
Proprietary Preparations (details are given in Part 3)
Jpn: Protecadin; Stogar.

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.
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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]

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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-