Ispaghula

Egyiptomi útifűmag (ispaghula seed); Egyiptomi útifűmaghéj (ispaghula husk); Ispaghul, graine d' (ispaghula seed); Ispaghul (graine d'), tégument de la (ispaghula husk); Ispagula; Ispagula Kabuğu; Ispagulafrö (ispaghula seed); Ispagulafröskal (ispaghula husk); Ispagulansiemen (ispaghula seed); Ispagulansiemenkuori (ispaghula husk); Kepek; Kiaušininių gysločių sėklos (ispaghula seed); Kiaušininių gysločių sėklų luobelės (ispaghula husk); Łupina nasienna babki jajowatej (ispaghula husk); Nasienie babki jajowatej (ispaghula seed); Osemení jitrocele vejčitého (ispaghula husk); Plantaginis ovatae semen (ispaghula seed); Plantaginis ovatae seminis tegumentum (ispaghula husk); Psilio; Semeno jitrocele vejčitého (ispaghula seed); Zaragatona.

Шелуха Исфагулы (ispaghula husk)

Pharmacopoeias. Monographs for the husk and seed are included in *Eur.* (see p.vii) and *US*.

Ph. Eur. 6.2 (Ispaghula Husk; Plantaginis Ovatae Seminis Tegumentum). The episperm and collapsed adjacent layers removed from the seeds of *Plantago ovata* (*P. ispaghula*). The powdered drug loses not more than 12.0% of its weight on drying. Protect from light.

Ph. Eur. 6.2 (Ispaghula Seed; Plantaginis Ovatae Semen). The dried ripe seeds of *Plantago ovata* (*P. ispaghula*). The powdered drug loses not more than 10.0% of its weight on drying. Protect from light.

USP 31 (Psyllium Husk). The cleaned, dried seed coat (epidermis), in whole or in powdered form, separated by winnowing and threshing from the seeds of *Plantago ovata* (known in commerce as Blond Psyllium, Indian Psyllium, or Ispaghula), or from *Plantago arenaria* (*Plantago psyllium*), known in commerce as Spanish or French Psyllium.

USP 31 (Plantago Seed). The cleaned, dried, ripe seed of *Plantago ovata*, or of *Plantago psyllium*, or of *Plantago indica* (*P. arenaria*).

Psyllium Hemicellulose *(USAN)*

CAS — 9034-32-6.

Pharmacopoeias. In *US*.

USP 31 (Psyllium Hemicellulose). The alkali soluble fraction of the husk from *Plantago ovata* consisting of highly substituted arabinoxylan polysaccharides. These polysaccharides are linear chains of xylose units to which are attached single units of arabinose and additional xylose. Rhamnose, galactose, glucose, and rhamnosyluronic acid residues are also present as minor constituents. It contains not less than 75.0% of dietary soluble fibre, calculated on the dried basis. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°.

Psyllium Seed

Blešníkové semeno; Bolhafűmag; Flea Seed; Loppfrö; Nasienie płesznika; Psilio, semilla de; Psyllii semen; Psyllium, graine de; Psyliuminsiemen; Smiltyninių gysločių sėklos.

ATC — A06AC01.

ATC Vet — QA06AC01.

Pharmacopoeias. In *Eur.* (see p.vii). Also in *US* under the title of Plantago Seed.

Ph. Eur. 6.2 (Psyllium Seed). The ripe, whole, dry seeds of *Plantago afra* (*P. psyllium*) or *Plantago indica* (*P. arenaria*). It loses not more than 14.0% of its weight on drying. Protect from light and moisture.

USP 31 (Plantago Seed). The cleaned, dried, ripe seed of *Plantago ovata*, or of *Plantago psyllium*, or of *Plantago indica* (*P. arenaria*) (see also Ispaghula, above).

Adverse Effects and Precautions

Large quantities of ispaghula and other bulk laxatives may temporarily increase flatulence and abdominal distension; hypersensitivity reactions have been reported. There is a risk of intestinal or oesophageal obstruction and faecal impaction, especially if such compounds are taken with insufficient fluid. Therefore, they should always be taken with at least 150 mL of water or other liquid. Ispaghula and bulk laxatives should not be taken immediately before going to bed because reduced gastric motility may impair intestinal passage and cause obstruction. They should be avoided by patients who have difficulty swallowing.

Bulk laxatives should not be given to patients with pre-existing faecal impaction, intestinal obstruction, or colonic atony.

Hypersensitivity. Hypersensitivity reactions associated with the ingestion or inhalation of ispaghula or psyllium have been reported.[1-9] Symptoms have included rash, rhinitis, urticaria, bronchospasm, and anaphylactic shock; in one case, anaphylaxis was fatal.[9] In most patients, sensitisation was thought to have occurred during occupational exposure.

1. Busse WW, Schoenwetter WF. Asthma from psyllium in laxative manufacture. *Ann Intern Med* 1975; **83:** 361–2.
2. Gross R. Acute bronchospasm associated with inhalation of psyllium hydrophilic mucilloid. *JAMA* 1979; **241:** 1573–4.
3. Suhonen R, *et al.* Anaphylactic shock due to ingestion of psyllium laxative. *Allergy* 1983; **38:** 363–5.
4. Zaloga GP, *et al.* Anaphylaxis following psyllium ingestion. *J Allergy Clin Immunol* 1984; **74:** 79–80.
5. Kaplan MJ. Anaphylactic reaction to "Heartwise". *N Engl J Med* 1990; **323:** 1072–3.
6. Lantner RR, *et al.* Anaphylaxis following ingestion of a psyllium-containing cereal. *JAMA* 1990; **264:** 2534–6.
7. Freeman GL. Psyllium hypersensitivity. *Ann Allergy* 1994; **73:** 490–2.
8. Vaswani SK, *et al.* Psyllium laxative-induced anaphylaxis, asthma, and rhinitis. *Allergy* 1996; **51:** 266–8.
9. Khalili B, *et al.* Psyllium-associated anaphylaxis and death: a case report and review of the literature. *Ann Allergy Asthma Immunol* 2003; **91:** 579–84.

Interactions

Ispaghula and other bulk-forming laxatives may delay or reduce the gastrointestinal absorption of other drugs such as cardiac glycosides, coumarin derivatives, lithium, or vitamins (such as vitamin B_{12}) and minerals (such as calcium, iron, or zinc). Intervals of 30 minutes to 1 hour are recommended between ispaghula and other drugs or food, although some recommend as much as 3 hours between bulk-forming laxatives and other drugs. The dose of insulin may need to be reduced in diabetic patients taking ispaghula.

Lithium. For reference to ispaghula possibly reducing the absorption of lithium, see Gastrointestinal Drugs, p.405.

Uses and Administration

Ispaghula seed, ispaghula husk, and psyllium seed are bulk laxatives (p.1693). They absorb water in the gastrointestinal tract to form a mucilaginous mass which increases the volume of faeces and hence promotes peristalsis. They are used in the treatment of constipation (p.1693), especially in diverticular disease (p.1695) and irritable bowel syndrome (p.1699), and when excessive straining at stool must be avoided, for example after anorectal surgery or in the management of haemorrhoids. The ability to absorb water and increase faecal mass means that they may also be used in the management of diarrhoea (p.1694) and for adjusting faecal consistency in patients with colostomies.

The usual oral dose is about 3.5 g one to three times daily, although higher doses have been given. It should be taken immediately after mixing in at least 150 mL water or fruit juice. The full effect may not be achieved for up to 3 days.

Ispaghula is also given for mild to moderate hypercholesterolaemia as an adjunct to a lipid-lowering diet. The recommended dose is about 7 g daily.

Hyperlipidaemias. Preparations of ispaghula have been reported[1-4] to lower serum-cholesterol concentrations in patients with mild to moderate hypercholesterolaemia. They have also been given with reduced doses of a bile-acid binding resin in the treatment of hyperlipidaemia,[5] which is reported to be effective and better tolerated than full doses of the resin alone. Similarly, psyllium supplementation with 10 mg of simvastatin was found to be as effective in lowering cholesterol as 20 mg of simvastatin alone.[6] However, ispaghula or psyllium should be regarded as adjuncts to dietary modification rather than substitutes for it. For a discussion of the hyperlipidaemias and their management, see p.1169.

1. Anderson JW, *et al.* Cholesterol-lowering effect of psyllium hydrophilic mucilloid for hypercholesterolemic men. *Arch Intern Med* 1988; **148:** 292–6.
2. Bell LP, *et al.* Cholesterol-lowering effects of psyllium hydrophilic mucilloid: adjunct therapy to a prudent diet for patients with mild to moderate hypercholesterolemia. *JAMA* 1989; **261:** 3419–23.
3. Anderson JW, *et al.* Cholesterol-lowering effects of psyllium intake adjunctive to diet therapy in men and women with hypercholesterolemia: meta-analysis of 8 controlled trials. *Am J Clin Nutr* 2000; **71:** 472–9.
4. Anderson JW, *et al.* Long-term cholesterol-lowering effects of psyllium as an adjunct to diet therapy in the treatment of hypercholesterolemia. *Am J Clin Nutr* 2000; **71:** 1433–8.
5. Spence JD, *et al.* Combination therapy with colestipol and psyllium mucilloid in patients with hyperlipidemia. *Ann Intern Med* 1995; **123:** 493–9.
6. Moreyra AE, *et al.* Effect of combining psyllium fiber with simvastatin in lowering cholesterol. *Arch Intern Med* 2005; **165:** 1161–6.

Preparations

BP 2008: Ispaghula Husk Effervescent Granules; Ispaghula Husk Granules; Ispaghula Husk Oral Powder;
USP 31: Psyllium Hydrophilic Mucilloid for Oral Suspension.

Proprietary Preparations (details are given in Part 3)
Arg.: Agarol Fibras Naturales†; Agiofibras; Herbaccion Laxante†; Konsyl; Lostamucil; Metamucil; Motional; Mucofalk; Plantaben; ***Austral.:*** Agiofibe; Ford Fibre; Fybogel; Metamucil; Mucilax†; Natural Fibre†; ***Austria:*** Agiocur; Laxans; Metamucil; ***Belg.:*** Colofiber; Fybogel†; Spagulax; ***Braz.:*** Agiofibra; Fibracare; Loraga†; Metamucil; Plantaben; ***Canad.:*** Laxucil; Metamucil; Mucillium; Natural Source Laxative†; Novo-Mucilax; Prodiem Plain†; ***Chile:*** Euromucil; Fibrasol; Metamucil†; Plantaben; ***Denm.:*** Vi-Siblin; ***Fin.:*** Agiocur; Laxamucil; Vi-Siblin; ***Fr.:*** Mucivital; Spagulax; Spagulax Mucilage; Transilane; ***Ger.:*** Agiocur; Flosa; Flosine; Laxiplant Soft†; Metamucil; Mucofalk; Pascomucil; ***Hong Kong:*** Agiocur; Fibermate; Fybogel†; Metamucil; Mucofalk; Naturlax; Transilane; ***India:*** Isogel; ***Indon.:*** Mucofalk; Mulax; ***Irl.:*** Fybogel; Regulan; ***Israel:*** Agiocur; Konsyl; Mucivital†; Planten†; ***Ital.:*** Agiofibre; Fibrolax; Planten; Psyllogel; ***Malaysia:*** Fybogel; Mucofalk; ***Mex.:*** Agiofibra; Fibromucil; Finalax; Fybogel; Hormolax; Konsyl†; Metamucil; Mucilag; Mugasin; Novagon; Plantaben; Siludane†; ***Neth.:*** Metamucil; Mucofalk; Regucol; Volcolon; ***Norw.:*** Lunelax; Vi-Siblin; ***NZ:*** Isogel; Metamucil; Mucilax; ***Philipp.:*** Fibermate; Mucofalk; ***Pol.:*** Mucofalk; ***Port.:*** Agiocur; Laxat; Mucofalk; Prontolax; Vetilax; ***S.Afr.:*** Agiobulk; Agiogel†; Fybogel; Metamucil†; ***Singapore:*** Fybogel; Mucilin; Mucofalk; ***Spain:*** Biolid; Cenat; Duphafibra; Laxabene; Laxisoft†; Metamucil; Plantaben; ***Swed.:*** Lunelax; Vi-Siblin; ***Switz.:*** Agiolax mite; Colosoft†; Laxiplant Soft; Metamucil; Mucilar; Valverde regulateur du transit intestinal granules†; ***Thai.:*** Agiocur†; Fybogel; Metamucil; Mucilin; Mucofalk†; ***Turk.:*** Otaci Musillium; ***UK:*** Fibrelief; Fybogel; Isogel; Ispagel; Konsyl†; Regulan; ***USA:*** Fiberall; Hydrocil Instant; Konsyl; Konsyl-D; Metamucil; Mylanta Natural Fiber†; Reguloid; Serutan; Syllact; ***Venez.:*** Agiofibe; Siliumbran.

Multi-ingredient: ***Arg.:*** Agiolax; Cholesterol Reducing Plan†; Gelax; Isalax Fibras; Kronolax†; Medilaxan; Mermelax; Prompt†; Rapilax Fibras; Salutaris; ***Austral.:*** Agiolax; Bioglan Psylli-Mucil Plus; Herbal Cleanse†; Nucolox; PC Regulax†; ***Austria:*** Agiolax; ***Belg.:*** Agiolax; Spagulax K; Spagulax Sorbitol; ***Braz.:*** Agiolax; Parapsyl; Plantax†; ***Canad.:*** Prodiem Plus†; ***Chile:*** Bilaxil; ***Cz.:*** Agiolax; ***Fin.:*** Agiolax; ***Fr.:*** Agiolax; Carres Parapsyllium; Filigel; Imegul†; Parapsyllium; Spagulax au Citrate de Potassium; Spagulax au Sorbitol; ***Ger.:*** Agiolax; ***Hong Kong:*** Agiolax; Fybogel Mebeverine†; ***Irl.:*** Fybogel Mebeverine; ***Israel:*** Agiolax; ***Ital.:*** Agiolax; Agioslim; Duolaxan†; Fibrolax Complex; Psyllogel Fermenti; ***Mex.:*** Agiolax; Psilumax; ***Neth.:*** Agiolax; ***Norw.:*** Agiolax; ***NZ:*** Nucolox†; ***Pol.:*** Agiolax; Laxamix; Otrebuski; ***Port.:*** Agiolax; Excess†; ***S.Afr.:*** Agiolax; ***Spain:*** Agiolax; ***Swed.:*** Agiolax; Vi-Siblin S; ***Switz.:*** Agiolax; Mucilar Avena; ***Thai.:*** Agiolax; ***Turk.:*** Otaci Diyet Life Psyllium Plus; ***UK:*** Cleansing Herbs; Fibre Dophilus; Fibre Plus; Fybogel Mebeverine; Lion Cleansing Herbs; Manevac; ***USA:*** Perdiem; Senna Prompt; ***Venez.:*** Agiolax; Avensyl; Fiberfull; Fibralax†; Senokot con Fibra†.

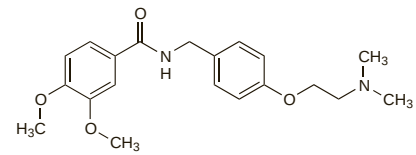
Itopride Hydrochloride *(rINNM)*

HC-803; Hidrocloruro de itoprida; HSR-803; Itopride, Chlorhydrate d'; Itopridi Hydrochloridum. *N*-{*p*-[2-(Dimethylamino)ethoxy]benzyl}veratramide hydrochloride.

Итоприда Гидрохлорид

$C_{20}H_{26}N_2O_4.HCl$ = 394.9.

CAS — 122898-67-3 (itopride).



(itopride)

Profile

Itopride hydrochloride is a substituted benzamide with general properties similar to those of metoclopramide (p.1747) that has been used for its prokinetic and antiemetic actions in oral doses of 50 mg three times daily before meals.

◊ References.

1. Holtmann G, *et al.* A placebo-controlled trial of itopride in functional dyspepsia. *N Engl J Med* 2006; **354:** 832–40.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Ganaton; ***India:*** Itoprid; ***Jpn:*** Ganaton; ***Malaysia:*** Ganaton.

Jalap

Jalap Root; Jalap Tuber; Jalapa; Jalapenwurzel; Vera Cruz Jalap.

Ялапа

Jalap Resin

Jalapa, resina de; Jalapenharz.

CAS — 9000-35-5.

Profile

Jalap is the dried tubercles of *Ipomoea purga* (=*Exogonium purga*) (Convolvulaceae). Jalap resin is a mixture of glycosidal resins obtained by extraction of jalap with alcohol and it has a drastic purgative and irritant action. It has been superseded by less toxic laxatives.

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.

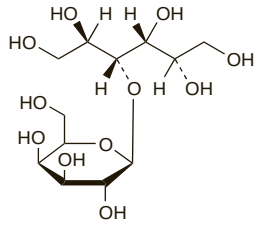
Multi-ingredient: ***Arg.:*** Anusol-A; Argeal; Endomicina†; Gastranil†; Opocarbon; Opocler†; ***Austral.:*** Bis-Pectin†; Chemists Own Diarrhoea Mixture†; Diarcalm; Donnagel; Kaomagma with Pectin†; Kaomagma†; ***Belg.:*** Alopate; Neutroses; ***Braz.:*** Atalin†; Digastril†; Eviprostat†; Gastrobene; 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.

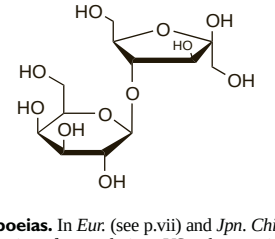
Multi-ingredient: ***Ital.:*** Levoplus.

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.