



**FRESENIUS
KABI**

caring for life

Lactulose

A gentle helper in medicine and nutrition

Lactulose

NATURAL

>> a carbohydrate derived from nature

Though lactulose does not occur in nature, it is an isomer of lactose, the natural milk sugar, and is produced directly from lactose. Lactulose is a disaccharide of the simple sugars galactose and fructose. Enzymes in the gut can split lactose, but not lactulose.

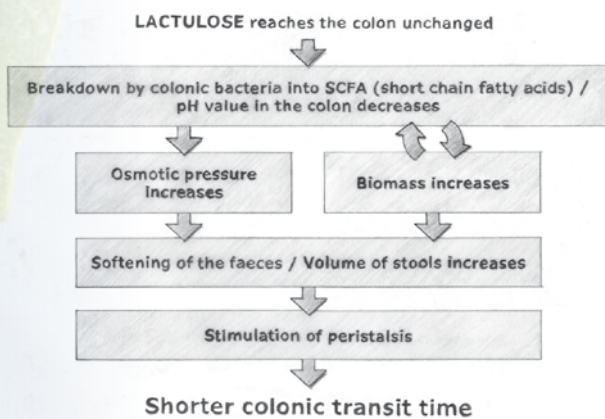




INDICATIONS

Constipation

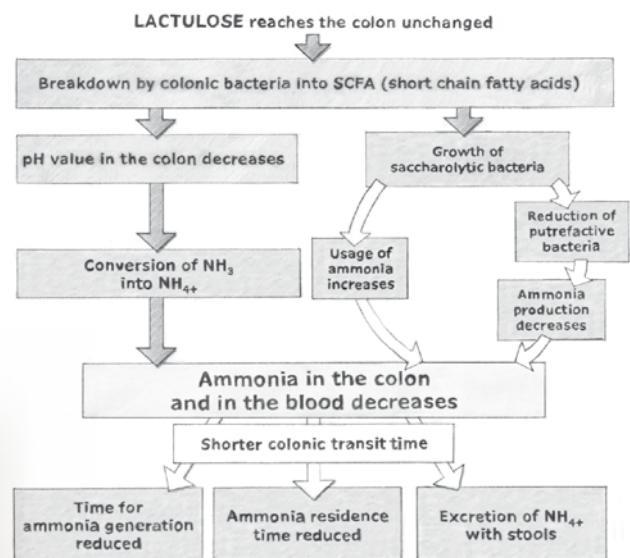
» a gentle and effective laxative
 Lactulose is a laxative that is widely used to treat chronic constipation. It has a particularly gentle and natural mode of action that involves prebiotic, osmotic and peristalsis-activating effects. It has been in regular use since the 1960s and has an excellent safety profile in patients of all ages. Lactulose is well tolerated in long-term use, even in patient groups regarded as sensitive, such as pregnant women, babies and people with diabetes.

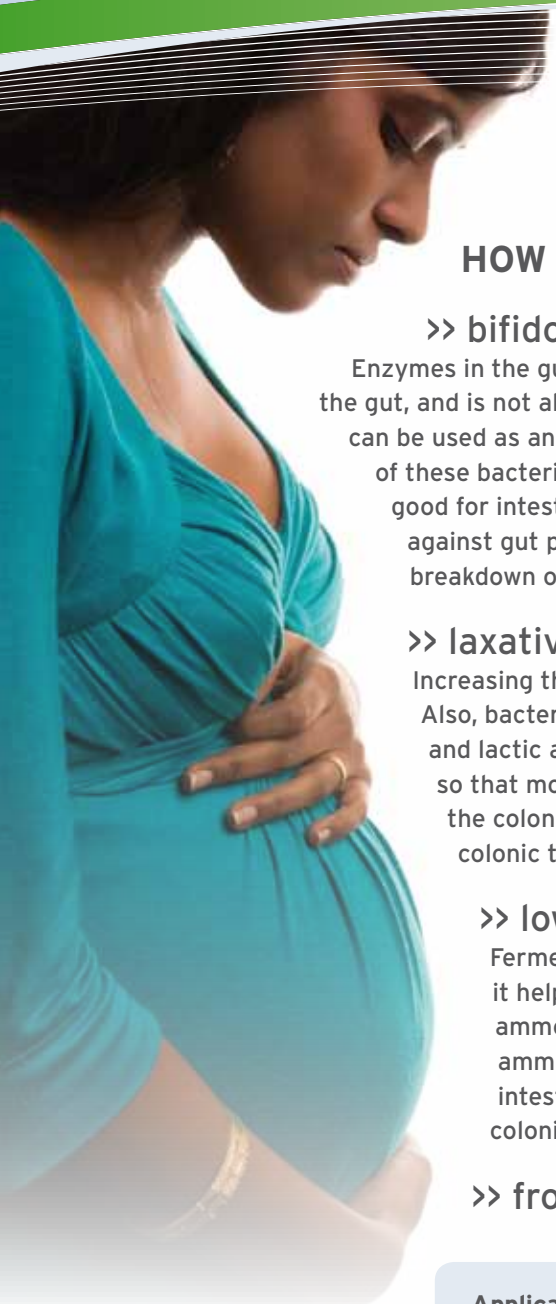


Portal systemic encephalopathy

» the gold standard for blood ammonia reduction

The other indication for lactulose is portal systemic encephalopathy (PSE), also known as hepatic encephalopathy. This is a disease state that results from liver damage, for example in advanced cirrhosis. The impaired liver function allows toxic substances, including ammonia, to accumulate in the bloodstream. Elevated blood ammonia interferes with brain functions, causing cognitive dysfunction and psychiatric disorders. Lactulose is an effective agent for reducing ammonia levels in this condition, and helps restore normal neurological function.





HOW IT WORKS

>> bifidogenic

Enzymes in the gut can split lactose, but not lactulose. Since lactulose is not split in the gut, and is not absorbed, it passes on to the lower part of the intestine unchanged. It can be used as an energy source by Bifidobacteria and Lactobacilli, and promotes growth of these bacteria – the bifidogenic effect. High counts of Bifidobacteria are considered good for intestinal health. Beneficial effects of balanced gut flora include protection against gut pathogens, improved digestion, “training” of the immune system, breakdown of carcinogenic substances and biosynthesis of vitamins.

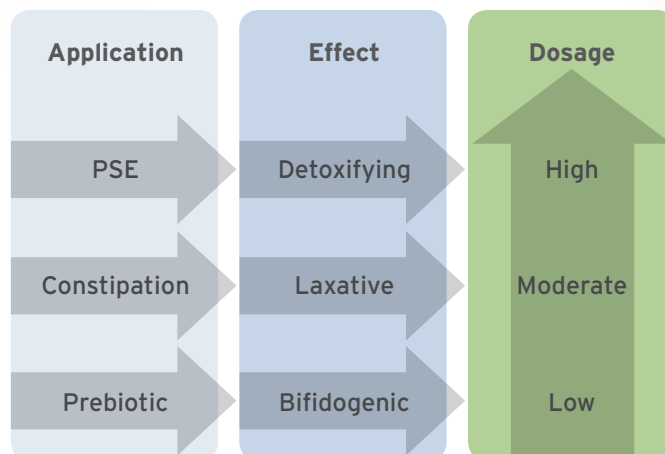
>> laxative

Increasing the amount of live bacteria in the colon helps make the stool softer. Also, bacteria using lactulose as their energy source produce short chain fatty acids and lactic acid – and the resulting increase in acidity raises the osmotic pressure, so that more water is retained in the colon. The acidity and the increase in bulk of the colon contents both stimulate peristalsis. The results: both a real reduction in colonic transit time and subjective ease of passing stool.

>> lowering ammonia

Fermentation of lactulose by Bifidobacteria has another beneficial effect: it helps lower blood ammonia levels. Bifidobacteria growth helps suppress ammonia-producing bacteria. Increased acidity ionizes ammonia (NH_3) to ammonium ions (NH_4^+). Since ammonium ions are not absorbed from the intestine, this draws more ammonia from the bloodstream. The reduced colonic transit time also means that ammonia is excreted more effectively.

>> from bifidogenic to ammonia binding





ADVANTAGES

>> unique

Other laxatives may act by increasing bulk, directly stimulating colonic movement or by simple osmotic effects. By promoting growth of Bifidobacteria, lactulose triggers natural responses of the intestine, with a combination of all three mechanisms.

>> at a glance

- No restriction for age or patient groups
- Suitable for long-term use
- Gentle and well tolerated
- Improvement of natural intestinal flora
- Not habit forming
- Minimal energy value (0.1 - 1.0 kcal/g)
- Convenient presentation forms



Lactulose





IN FOOD

>> healthy gut - healthy body

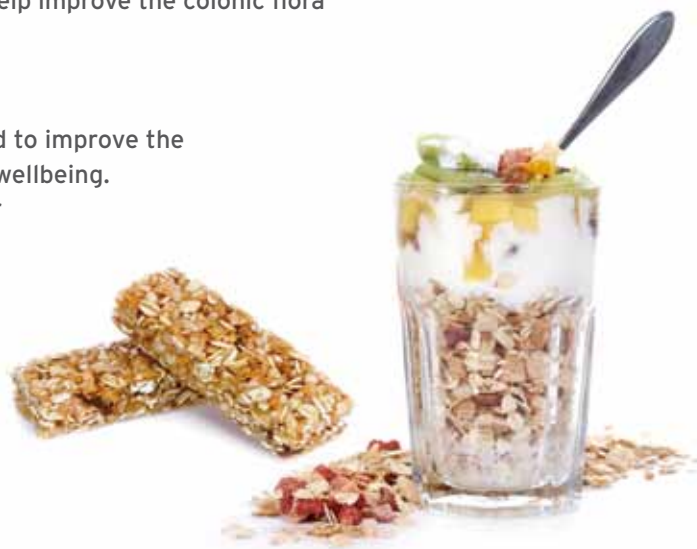
In today's fast-moving world, living and eating habits often have a negative impact on metabolism and digestion. Improving the interaction of food, metabolism, and the immune system, lactulose can help restore some balance.

>> a growth factor for health-promoting bacteria

Prebiotics are food ingredients that improve health and wellbeing by selectively stimulating the growth and activity of beneficial intestinal bacteria. It has been demonstrated that lactulose is used as an energy source by Bifidobacteria and Lactobacilli, stimulating their growth and activity. This means lactulose can help improve the colonic flora and stabilize a healthy mix of organisms.

>> food ingredient

The prebiotic effects of lactulose mean it can be used to improve the contribution of diverse convenience foods to overall wellbeing. Also, food products tailored for special age groups or persons with special nutrition requirements can be designed with lactulose as an ingredient.



ANIMAL FEED

>> new directions in animal nutrition

Reducing the use of antibiotics is a major issue in livestock breeding. Consumer acceptance of contaminated products is in fast decline. There is a strong need for health-promoting and health-maintaining feed ingredients. The positive effects of lactulose on animal gastrointestinal health make it an attractive ingredient for the development of balanced pet food or animal feed.



PRODUCT INFORMATION

>> from API to finished products

Fresenius Kabi Austria is one of the world's major lactulose suppliers, with more than 40 years of experience in its production and distribution. We manufacture and distribute lactulose in liquid and crystalline form, as an active pharmaceutical ingredient (API) or as finished, packaged pharmaceutical products.

>> wide range of API formulations

Lactulose Liquid

Standard (67% w/v)

Special (up to 70% w/v)

Purified Lactulose Solution (50 - 55% w/w)

Lactulose Crystals (97% w/w)

>> flexibility of final dosage forms

We have our production and filling lines side by side, so we can make lactulose finished product seamlessly after the bulk process. The range of dosage and presentation forms covers PET or HDPE bottles of various sizes (100ml to 1000ml) and convenient single dose sachets for liquid (10g/15ml) or crystalline lactulose (10g) in boxes of up to 100 single doses.

>> continual development

To meet the demands and need of our customers, Fresenius Kabi Austria is constantly expanding its product portfolio. For example, although unflavored lactulose is very popular, we also offer flavored versions.

>> specifications

The production of lactulose API is in line with current Good Manufacturing Practice (GMP/cGMP) guidelines, ISO 9001:2008, and ISO 14001:2009. It meets the specifications of European, Japanese and US pharmacopeias.





MANUFACTURING

>> excellent logistics

Our lactulose API production process runs around the clock, seven days a week. An order-related and just-in-time production system ensures the delivery of API to our customers all over the world with a maximum shelf life.

>> top quality

Strict quality control with pharmacopeial and/or precisely validated methods for all analyses is done at all stages from the incoming raw materials to the final products. The manufacturing process is embedded in a comprehensive quality assurance program.

>> always under review

Our quality assurance unit continually reviews all processes and documentations to safeguard compliance with current certifications. Fulfillment of all applicable regulations is audited by local as well as international regulatory authorities, and also by customers.

PRODUCTION SITES

>> two plants - one mission

Fresenius Kabi Austria distributes API lactulose in liquid and crystalline form manufactured at two production sites in Linz, Austria, and in Vicchio, Italy, to customers all over the world.

>> linz, austria

The lactulose production process was developed in the laboratories in Linz and patented in 1969. A high level of automation, the electronic batch handling system, and the environment-friendly process developed in-house support constantly high quality and excellent flexibility of the production process. A pharmaceutical production unit on site enables us to process lactulose without delay into finished products.

>> vicchio, italy

The Italian plant has long experience in the manufacture of the API lactulose liquid and crystals. The facility in Vicchio is an up-to-date production site of the highest quality standards. With the unique and patented process it is the only plant in Europe that manufactures lactulose crystals to the EP specification.



Lactulose

BUSINESS DEVELOPMENT

>> from approval to market

An experienced and highly qualified regulatory affairs team will provide you with European or US drug master files (USDMF, ASMF, and CEP). We also prepare common technical document (e-CTD) dossiers for registration of pure or flavored lactulose in multi- and single-dose formats. Precise adherence to the requirements of our customers is guaranteed.



>> adding value to your product

We offer professional assistance with packaging design in order to give our lactulose product the look of your choice. With in-house expertise, we support local marketing and medical teams in developing appropriate materials in accordance with applicable legal requirements. Fresenius Kabi Austria's own successful lactulose brand is registered in numerous countries all over the world.

WORLDWIDE DISTRIBUTION

>> service is our concern

Our highly motivated and competent service team coordinates the worldwide distribution of lactulose, helping you to deliver value across the whole supply chain. With the aim of achieving 100% customer satisfaction, we develop best-case solutions for our customers throughout the world.





ABOUT US

>> fresenius kabi

The international Fresenius Kabi group runs two production sites for lactulose. In Vicchio del Mugello, Italy, Società Chimica Mugello S.r.l. produces the APIs lactulose liquid and lactulose crystals (FDA approved). The facility in Linz manufactures the API lactulose liquid (FDA approved), but also the APIs Hydroxyethyl Starch (HES; FDA approved), and Sinistrin.

>> contact us

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