A Summary of Product Characteristic (SmPC)

1. Name of the medicinal product

LACASAT

2. Qualitative and quantitative composition

Each 5 ml contains lactulose 3.3 g

3. Pharmaceutical form

Oral solution

Clear yellow syrupy liquid

4. Clinical particulars

4.1 Therapeutic indications

Symptomatic treatment of constipation

Treatment of portal systemic encephalopathy

4.2 Posology and method of administration

Posology

The posology should be adjusted according to the individual needs of the patient. The starting dose can be adjusted after adequate treatment effect individually (maintenance dose). Several days (2-3 days) of treatment may be needed in some patients before adequate treatment effect occurs. In case of single daily dose, this should be taken at the same time of the day, e.g. during breakfast. During the therapy with laxatives it is recommended to drink sufficient amounts of fluids (1.5- 2 l/day, equal to 6-8 glasses).

Constipation:

Adults

Starting dose 15-45 ml corresponding to 10-30 g lactulose

Maintenance dose 15-30 ml corresponding to 10-20 g lactulose

Paediatric population

Adolescents over 14 years

Starting dose 15-45 ml corresponding to 10-30 g lactulose

Maintenance dose 15-30 ml corresponding to 10-20 g lactulose

Children (7-14 years)

Starting dose 15 ml corresponding to 10 g lactulose

Maintenance dose 10-15 ml corresponding to 7-10 g lactulose

Children (1-6 years)

Starting dose 5-10 ml corresponding to 3-7 g lactulose

Babies

Starting dose up to 5 ml corresponding to up to 3 g lactulose

If diarrhoea occurs, the dosing regimen should be reduced.

Treatment of portal systemic encephalopathy - for adults only:

Beginning with 30 - 50 ml 3 times daily (corresponding to 60 - 100 g Lactulose). The dosage has to be adopted to get 2-3 soft stools daily, pH of the stools should be between 5.0 to 5.5.

In elderly patients and patients with renal or hepatic insufficiency no special dosage recommendations exist.

Paediatric population

The safety and efficacy in children aged 0 - 18 years has not been established. No data are available.

Method of administration

The lactulose solution may be administered diluted or undiluted. The dose should be titrated according to the clinical response. Lactulose may be given as a single daily dose or up to three divided daily doses, using the measuring cup.

A single dose of lactulose should be swallowed in one and should not be kept in the mouth for an extended period of time.

The duration of treatment has to be adopted according to the symptoms

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Use in patients with galactosaemia.

Acute inflammatory bowel disease (ulcerative colitis, Crohn's disease), gastrointestinal obstruction or subocclusive syndromes, digestive perforation or risk of digestive perforation, painful abdominal syndromes of undetermined cause

4.4 Special warnings and precautions for use

In case of insufficient therapeutic effect after several days consultation of a physician is advised.

From the route of synthesis Lactulose may contain traces of sugars (not more than 67 mg/ml lactose, 100 mg/mlgalactose, 67 mg/ml epilactose, 27 mg/ml tagatose and 7 mg/ml fructose). Lactulose should be administered with care to patients who are intolerant to lactose.

The dose normally used in constipation should not pose a problem for diabetics. However, higher doses used for treatment of portal systemic encephalopythy may need to be taken into considerations for diabetics. 15 ml of Lactulose contain 42,7 KJ (10,2 kcals) = 0,21 bu.

The defecation reflex may be altered during the treatment with lactulose.

Patients with rare hereditary problems of galactose or fructose intolerance, lactase deficiency or glucose-galactose malabsorption should not take this medicine.

For patients with gastro-cardiac syndrome (Roemheld syndrome) lactulose should only be taken after consultation of a physician. If symptoms like meteorism or bloating occur in such patients after lactulose intake, the dose should be reduced or the treatment should be discontinued.

Chronic use of unadjusted doses and misuse can lead to diarrhoea and disturbance of the electrolyte balance.

For elderly patients or patients that are in bad general condition and who take lactulose for more than a 6 months period,periodic control of electrolytes is indicated.

In patients with portal systemic encephalopathy, concomitant administration of other laxatives should be avoided,because it hinders the individualization of drug dose. Furthermore, for the patients referred above, it should be taken into account the chance of causing electrolyte imbalance and, mainly, hypokalaemia that could aggravate encephalopathy. During the therapy with laxatives it is recommended to drink sufficient amounts of fluids (1.5-2 l/day, equal to 6-8 glasses).

Paediatric population

Use of laxatives in children should be exceptional and under medical supervision. Lactulose should be administrated with caution in infants and small children with autosomal recessive hereditary fructose intolerance.

4.5 Interaction with other medicinal products and other forms of interaction

Lactulose may increase the loss of potassium induced by other drugs (e.g. thiazides, steroids and amphothericin B). Concomitant use of cardiac glycosides can increase the effect of the glycosides through potassium deficiency.

With increasing dosage a decrease of pH-value in the colon is found. Therefore drugs which are released in the colon pH-dependently (e.g. 5-ASA) can be inactivated.

4.6 Fertility, pregnancy and lactation

Pregnancy: Limited data on pregnant patients indicate neither malformative nor foeto/neonatal toxicity. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3).
The use of Lacasat may be considered during pregnancy if necessary.

Breast-feeding: Lacasat can be used during breastfeeding.

Fertility: For Lacasat no clinical data on the effects on fertility are available.

4.7 Effects on ability to drive and use machines

Lacasat has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Flatulence may occur during the first few days of treatment. As a rule it disappears after a couple of days. When dosages higher than instructed are used, abdominal pain and diarrhoea may occur. In such a case the dosage should be decreased.

Gastrointestinal disorders

Very common (≥ 1/10): flatulence, abdominal pain.

Common (≥ 1/100 < 1/10): nausea and vomiting; if dosed too high, diarrhoea

Investigations

Electrolyte imbalance due to diarrhoea.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme.

4.9 Overdose

If the dose is too high, the following may occur:

Symptom: diarrhoea and abdominal pain.

Treatment: cessation of treatment or dose reduction. Extensive fluid loss by diarrhoea or vomiting may require correction of electrolyte disturbances.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Osmotically acting laxatives.

ATC code: A06A D11

Lactulose is a synthetic disaccharide formed from D-galactose and fructose. In the colon lactulose is metabolised by bacterial enzymes to short chained fatty acids mainly lactic and acetic acid as well as methane and hydrogen. This effect leads to a decrease of the pH-value and an increase of the osmotic pressure in the colon. This causes stimulation of peristalsis and an increase of the water content of the faeces.

In higher dosage lactulose causes a reduction of the pH-value, which results in an increased H+-concentration and a shift from NH3 (absorbable) to NH4+ (non- absorbable). The nitrogen excretion in the stool is accelerated. This effect may be used in the treatment of hyperammonaemia. In the treatment of hepatic encephalopathy lactulose reduces the concentration of NH3 in the blood by about 25-50 %.

Lower pH in the colon leads to suppression of proteolytic bacteria, which are involved in the formation of ammonia. Decrease in pH is caused by increasing the content of acidophilic bacteria (eg Lactobacillus). Reduced pH and the osmotic effect cleanse the colon; this stimulates the bacteria to use ammonia for bacterial protein synthesis

5.2 Pharmacokinetic properties

Lactulose is practically not absorbed, because in man there is no corresponding disaccharidase available in the upper intestinal tract. Not being absorbed as such, it reaches the colon unchanged. There it is metabolised by the colonic bacterial flora. Metabolism is complete at doses up to 25-50 g or 40-75 ml; at higher dosages, a proportion may be excreted unchanged.

5.3 Preclinical safety data

Preclinical data based on studies of single and repeated dose toxicity reveal no special hazards for humans. A long-term animal study does not give reference to tumorigenic potential. Lactulose was not teratogenic in mice, rats and rabbits. After oral administration systemic toxicity is not to be expected due to the pharmacological and pharmacokinetic properties of lactulose.

6. Pharmaceutical particulars

6.1 List of excipients

None

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Storage Condition: Store below 30 °C. Store in original packaging and protected from direct sunlight. Do not use this medicine after expiry date. Keep this medicine out of the reach and sight of children.

6.5 Nature and contents of container

Bottle containing 100 ml made of High-Density Polyethylene

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing authorisation holder

Manufacturer: Osoth Inter Laboratories Co., Ltd., 600/9 Sriracha Industrial Park, Sukhaphiban 8 Rd, Moo 11, Nongkham, Sriracha, Chonburi 20230 Tel: 038-480766-7 Fax: 038-480828

Distributer: KASPA PHARMACEUTICAL (THAILAND) CO., LTD. 252/25 Jaransanitwong Rd., Banchanglor, Bangkoknoi Bangkok 10700, Thailand

8. Marketing authorisation number(s)

-

9. Date of first authorisation/renewal of the authorization

-

10. Date of revision of the text

-

Checklist for Summary of product characteristics (SmPC)

E-identifier No……e6400208…… Product Name……Lacasat……Active Substance……Lactulose……

Strength……Lactulose 3.3 g / 5 ml……Dosage Form……Oral solution……Co-PTL……Pornnaree Kittiwannachot……

MAH……Osoth Inter Laboratories Co., Ltd. ……Contact Person…Sakdidetch Pienkij ..E-mail : …sakdidetch.p@osi-bkc.in.th……

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Instruction **ผู้รับอนุญาต (MAH) :** 1. ผู้รับอนุญาตตรวจสอบเอกสารกำกับยา (SmPC) ว่ามีหัวข้อตามที่กำหนดหรือไม่ โดยทำเครื่องหมาย (√) หรือ (X) ในช่อง MAH SmPC หากไม่ปรากฏหัวข้อดังกล่าว (เปรียบเทียบกับเอกสารกำกับยาอ้างอิง) ให้ระบุ n/a

2. ผู้รับอนุญาตตรวจสอบข้อความในเอกสารกำกับยา (SmPC) ว่ามีเนื้อหาตรงกับเอกสารกำกับยาฉบับอ้างอิงหรือไม่ (เอกสารกำกับยาฉบับอ้างอิงระบุแหล่งที่มาของเอกสารพร้อมระบุ Revision Date) โดยทำเครื่องหมาย (√) หรือ (X) ในช่องดังกล่าว

3. เอกสารกำกับยา (SmPC) ของผู้รับอนุญาตถ้ามีหัวข้อหรือเนื้อหาไม่ตรงกับเอกสารกำกับยาอ้างอิง โปรดระบุเหตุผลและเอกสารอ้างอิงประกอบ

เจ้าหน้าที่ (Co-PTL) : ตรวจสอบข้อมูลในช่อง MAH ที่ผู้รับอนุญาตแสดงรายละเอียดว่ามีความสอดคล้องหรือไม่ โดยระบุ “สอดคล้อง” หรือ “ไม่สอดคล้อง” หากไม่ปรากฏหัวข้อดังกล่าว (เปรียบเทียบกับเอกสารกำกับยาอ้างอิง) ให้ระบุ n/a และผลพิจารณาหากพบว่า “ไม่สอดคล้อง” หรือมีข้อแก้ไขเพิ่มเติม โปรดระบุคำอธิบาย

Topic	MAH			Co-PTL	
	MAH SmPC	**SmPC Reference ☐ EMA ☐ US FDA ☑ Other(ระบุ) EMC Revision Date 11/12/2015**	**เอกสารกำกับยา<u>ไม่มี</u>หัวข้อและ/หรือเนื้อหาตรงกับเอกสารอ้างอิง (ระบุเหตุผล)**	**ผลการประเมิน**	**คำอธิบายผลการประเมิน “ไม่สอดคล้อง” และ/หรือ มีข้อแก้ไขเพิ่มเติม**
1.NAME OF THE MEDICINAL PRODUCT					
Name	<√> <x> <N/A>	<√> <x> <N/A>	<ระบุเหตุผล>	<สอดคล้อง> <ไม่สอดคล้อง> <N/A>	<ระบุคำอธิบาย>
Strength	√	√			
Pharmaceutical form*	√	√			
2 QUALITATIVE AND QUANTITATIVE COMPOSITION	√	√			
3 PHARMACEUTICAL FORM*	√	√			
4. CLINICAL PARTICULARS					
4.1 Therapeutic indications	√	√			
4.2 Posology and method of administration	√	√			
Posology	√	√			

Special populations	×	×			
Paediatric population	√	√			
Method of administration	√	√			

Topic	MAH			Co-PTL	
	MAH SmPC	SmPC Reference ☐ EMA ☐ US FDA ☑ Other(ระบุ) EMC Revision Date 11/12/2015	กรณีเอกสารกำกับยาไม่ตรงกับเอกสารอ้างอิง (ระบุเหตุผล)	MAH SmPC	SmPC Ref. ☐ EMA ☐ US FDA ☐ Other(ระบุ)..... Revision Date.....
4.3 Contraindications	√	√			
4.4 Special warnings and precautions for use	√	√			
4.5 Interaction with other medicinal products and other forms of interaction	√	√			
Additional information on special populations (i.e. Paediatric population) **(IF APPLICABLE)**	×	×			
4.6 Fertility, pregnancy and lactation	√	√			
Women of childbearing potential / Contraception in males and females	×	×			
Pregnancy	√	√			
Fertility	√	√			
4.7 Effects on ability to drive and use machines	√	√			
4.8 Undesirable effects	√	√			
4.9 Overdose	√	√			
5. PHARMACOLOGICAL PROPERTIES					
5.1 Pharmacodynamic properties	√	√			
ATC code	√	√			
Mechanism of action (if known)	√	√			
Pharmacodynamic effects	√	√			

Clinical efficacy and safety	√	√			
Paediatric population **(ถ้ามี)**	×	×			
5.2 Pharmacokinetic properties	√	√			
Paediatric population **(ถ้ามี)**	×	×			
5.3 Preclinical safety data	√	√			

Topic	MAH			Co-PTL	
	MAH SmPC	SmPC Reference ☐ EMA ☐ US FDA ☑ Other(ระบุ) EMC Revision Date 11/12/2015	กรณีเอกสารกำกับยาไม่ตรงกับเอกสารอ้างอิง (ระบุเหตุผล)	MAH SmPC	SmPC Ref. ☐ EMA ☐ US FDA ☐ Other(ระบุ)..... Revision Date.....
6.1 List of excipients	√	√			
6.2 Incompatibilities	√	√			
6.3 Shelf life	√	√			
6.4 Special precautions for storage	√	√			
6.5 Nature and contents of container	√	√			
6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product	√	√			
7. MARKETING AUTHORISATION HOLDER	√	√			
8 MARKETING AUTHORISATION NUMBER(S)	√	√			
9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION	√	√			
10 DATE OF REVISION OF THE TEXT	√	√			
11 DOSIMETRY (IF APPLICABLE)	×	×			
12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)	×	×			

หมายเหตุ * pharmaceutical dosage form ให้ระบุรูปแบบตรงตาม EDQM Standard Terms

** ผลิตภัณฑ์ดังกล่าวหากมีหลายความแรงและมีการใช้ SmPC ร่วมกันสามารถทำ Checklist รวมเป็นฉบับเดียวกันได้ (จะต้องสอดคล้องกับ SmPC Reference ด้วย)

SmPC

Reference

1

Lactulose 3.3g/5ml Oral Solution

Summary of Product Characteristics Updated 24-Jan-2022 | Tetris Pharma Ltd

1. Name of the medicinal product

Laevolac 3.3 g/5ml Oral Solution

or

Lactulose 3.3 g/5ml Oral Solution

2. Qualitative and quantitative composition

5 ml contain 3.3 g lactulose

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Oral Solution

Clear colourless to pale brownish yellow, viscous solution

4. Clinical particulars

4.1 Therapeutic indications

- Symptomatic treatment of constipation
- Treatment of portal systemic encephalopathy

4.2 Posology and method of administration

Posology

The posology should be adjusted according to the individual needs of the patient. The starting dose can be adjusted after adequate treatment effect individually (maintenance dose). Several days (2-3 days) of treatment may be needed in some patients before adequate treatment effect occurs. In case of single daily dose, this should be taken at the same time of the day, e.g. during breakfast. During the therapy with laxatives it is recommended to drink sufficient amounts of fluids (1.5- 2 l/day, equal to 6-8 glasses).

Constipation:

	Starting dose		Maintenance dose	
Adults	15-45 ml	corresponding to 10-30 g lactulose	15-30 ml	corresponding to 10-20 g lactulose

Paediatric population

	Starting dose		Maintenance dose	
Adolescents over 14 years	15-45 ml	corresponding to 10-30 g lactulose	15-30 ml	corresponding to 10-20 g lactulose
Children (7-14 years)	15 ml	corresponding to 10 g lactulose	10-15 ml	corresponding to 7-10 g lactulose
Children (1-6 years)	5-10 ml	corresponding to 3-7 g lactulose		
Babies	up to 5 ml	corresponding to up to 3 g lactulose		

If diarrhoea occurs, the dosing regimen should be reduced.

Treatment of portal systemic encephalopathy - for adults only:

Beginning with 30 - 50 ml 3 times daily (corresponding to 60 - 100 g Lactulose). The dosage has to be adopted to get 2-3 soft stools daily, pH of the stools should be between 5.0 to 5.5.

In elderly patients and patients with renal or hepatic insufficiency no special dosage recommendations exist.

Paediatric population

The safety and efficacy in children aged 0 - 18 years has not been established. No data are available.

Method of administration

The lactulose solution may be administered diluted or undiluted. The dose should be titrated according to the clinical response. Lactulose may be given as a single daily dose or up to three divided daily doses, using the measuring cup.

A single dose of lactulose should be swallowed in one and should not be kept in the mouth for an extended period of time.

The duration of treatment has to be adopted according to the symptoms.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Use in patients with galactosaemia.
- Acute inflammatory bowel disease (ulcerative colitis, Crohn's disease), gastrointestinal obstruction or subocclusive syndromes, digestive perforation or risk of digestive perforation, painful abdominal syndromes of undetermined cause.

4.4 Special warnings and precautions for use

In case of insufficient therapeutic effect after several days consultation of a physician is advised.

From the route of synthesis Lactulose may contain traces of sugars (not more than 67 mg/ml lactose, 100 mg/ml galactose, 67 mg/ml epilactose, 27 mg/ml tagatose and 7 mg/ml fructose). Lactulose should be administered with care to patients who are intolerant to lactose.

The dose normally used in constipation should not pose a problem for diabetics. However, higher doses used for treatment of portal systemic encephalopythy may need to be taken into considerations for diabetics. 15 ml of Lactulose contain 42,7 KJ (10,2 kcals) = 0,21 bu.

The defecation reflex may be altered during the treatment with lactulose.

Patients with rare hereditary problems of galactose or fructose intolerance, lactase deficiency or glucose-galactose mal-absorption should not take this medicine.

For patients with gastro-cardiac syndrome (Roemheld syndrome) lactulose should only be taken after consultation of a physician. If symptoms like meteorism or bloating occur in such patients after lactulose intake, the dose should be reduced or the treatment should be discontinued.

Chronic use of unadjusted doses and misuse can lead to diarrhoea and disturbance of the electrolyte balance.

For elderly patients or patients that are in bad general condition and who take lactulose for more than a 6 months period, periodic control of electrolytes is indicated.

In patients with portal systemic encephalopathy, concomitant administration of other laxatives should be avoided, because it hinders the individualization of drug dose. Furthermore, for the patients referred above, it should be taken into account the chance of causing electrolyte imbalance and, mainly, hypokalaemia that could aggravate encephalopathy.

During the therapy with laxatives it is recommended to drink sufficient amounts of fluids (1.5-2 l/day, equal to 6-8 glasses).

Paediatric population

Use of laxatives in children should be exceptional and under medical supervision. Lactulose should be administrated with caution in infants and small children with autosomal recessive hereditary fructose intolerance.

4.5 Interaction with other medicinal products and other forms of interaction

Lactulose may increase the loss of potassium induced by other drugs (e.g. thiazides, steroids and amphothericin B). Concomitant use of cardiac glycosides can increase the effect of the glycosides through potassium deficiency.

With increasing dosage a decrease of pH-value in the colon is found. Therefore drugs which are released in the colon pH-dependently (e.g. 5-ASA) can be inactivated.

4.6 Pregnancy and lactation

Pregnancy

Limited data on pregnant patients indicate no malformative nor foeto/neonatal toxicity. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3).

The use of lactulose may be considered during pregnancy if necessary.

Breastfeeding

Lactulose can be used during breastfeeding.

Fertility

For Lactulose no clinical data on the effects on fertility are available.

4.7 Effects on ability to drive and use machines

Lactulose has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Flatulence may occur during the first few days of treatment. As a rule it disappears after a couple of days. When dosages higher than instructed are used, abdominal pain and diarrhoea may occur. In such a case the dosage should be decreased.

Gastrointestinal disorders

Very common (≥ 1/10):	flatulence, abdominal pain.
Common (≥ 1/100 < 1/10):	nausea and vomiting; if dosed too high, diarrhoea.

Investigations

Electrolyte imbalance due to diarrhoea.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme.

Website: www.mhra.gov.uk/yellowcard.

4.9 Overdose

If the dose is too high, the following may occur:

Symptom:	diarrhoea and abdominal pain.
Treatment:	cessation of treatment or dose reduction. Extensive fluid loss by diarrhoea or vomiting may require correction of electrolyte disturbances.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Osmotically acting laxatives.

ATC code: A06A D11

Lactulose is a synthetic disaccharide formed from D-galactose and fructose. In the colon lactulose is metabolised by bacterial enzymes to short chained fatty acids mainly lactic and acetic acid as well as methane and hydrogen. This effect leads to a decrease of the pH-value and an increase of the osmotic pressure in the colon. This causes stimulation of peristalsis and an increase of the water content of the faeces.

In higher dosage lactulose causes a reduction of the pH-value, which results in an increased H+-concentration and a shift from NH3 (absorbable) to NH4+ (non- absorbable). The nitrogen excretion in the stool is accelerated. This effect may be used in the treatment of hyperammonaemia. In the treatment of hepatic encephalopathy lactulose reduces the concentration of NH3 in the blood by about 25-50 %.

Lower pH in the colon leads to suppression of proteolytic bacteria, which are involved in the formation of ammonia. Decrease in pH is caused by increasing the content of acidophilic bacteria (eg Lactobacillus). Reduced pH and the osmotic effect cleanse the colon; this stimulates the bacteria to use ammonia for bacterial protein synthesis.

5.2 Pharmacokinetic properties

Lactulose is practically not absorbed, because in man there is no corresponding disaccharidase available in the upper intestinal tract. Not being absorbed as such, it reaches the colon unchanged. There it is metabolised by the colonic bacterial flora. Metabolism is complete at doses up to 25-50 g or 40-75 ml; at higher dosages, a proportion may be excreted unchanged.

5.3 Preclinical safety data

Preclinical data based on studies of single and repeated dose toxicity reveal no special hazards for humans. A long-term animal study does not give reference to tumorigenic potential. Lactulose was not teratogenic in mice, rats and rabbits. After oral administration systemic toxicity is not to be expected due to the pharmacological and pharmacokinetic properties of lactulose.

6. Pharmaceutical particulars

6.1 List of excipients

None.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 25°C.

Keep container tightly closed.

6.5 Nature and contents of container

Glass bottles (Ph.Eur., type III), PET bottles and HDPE-bottles containing 200 ml, 300 ml, 500 ml or 1000 ml with a polyethylene screw cap.

For the bottles as measuring device a measuring cup (polypropylene) with filling marks is added.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing authorisation holder

Fresenius Kabi Austria GmbH

Hafnerstrasse 36

8055 Graz, Austria

Tel.: +43 316 249 0

Fax.:+43 316 249 1470

Info-atgr@fresenius-kabi.com

8. Marketing authorisation number(s)

PL 05061/0001

9. Date of first authorisation/renewal of the authorisation

10 March 1993 / 17 March 1998

10. Date of revision of the text

11/12/2015

Company Contact Details

Tetris Pharma Ltd

Address
14 North St, Mears Ashby, Northampton, NN6 0DW

WWW
www.tetrispharma.com

Telephone
01628 337579

Medical Information Direct Line
0330 1359533

Medical Information e-mail
medinfo@tetrispharma.com

Customer Care direct line
01628 337579

SmPC

Reference

2

Duphalac 3.335 g/5 ml Oral Solution

Mylan
contact details

Active ingredient
lactulose

Legal Category
P: Pharmacy

SmPC (/emc/product/5525/smpc) | Patient Leaflet (/emc/product/5525/pil)

Show table of contents

This information is intended for use by health professionals

1. Name of the medicinal product

Duphalac®

Lactulose 3.335g/5ml oral solution

2. Qualitative and quantitative composition

Lactulose 3.335g/5ml oral solution (as Lactulose, liquid 667 g/L)

For a full list of excipients, see 6.1

Lactulose oral solution contains residues from the route of production with known effect, see section 4.4

3. Pharmaceutical form

Oral solution.

A clear, viscous liquid, colourless to brownish yellow.

4. Clinical particulars

4.1 Therapeutic indications

1. For the treatment of constipation.

2. For the treatment of hepatic encephalopathy (HE); hepatic coma.

4.2 Posology and method of administration

The lactulose solution may be administered diluted or undiluted. Each dose may if necessary be taken with water or fruit juices, etc.

Each dose of lactulose should be swallowed in one and should not be kept in the mouth for an extended period of time.

The posology should be adjusted according to the individual needs of the patient.

In case of single daily dose, this should be taken at the same time, e.g. during breakfast.

During the therapy with laxatives it is recommended to drink sufficient amounts of fluids (1.5–2 litres, equal to 6-8 glasses) during the day.

Dosing in constipation:

Lactulose may be given as a single daily dose or in two divided doses.

After a few days the starting dosage may be adjusted to the maintenance dose based upon treatment response. Several days (2-3 days) of treatment may be needed before treatment effect occurs.

Lactulose oral solution in bottles or 15 ml single dose sachets:

	Starting dose daily	Maintenance dose daily
Adults and adolescents	15-45 ml, corresponding to 1-3 sachets	15-30 ml, corresponding to 1-2 sachets
Children (7-14 years)	15 ml, corresponding to 1 sachet	10-15 ml, corresponding to 1 sachet*
Children (1-6 years)	5-10 ml	5-10 ml
Infants under 1 year	up to 5 ml	up to 5 ml

* If the maintenance dose is below 15 ml, lactulose in bottles should be used.

Dosing in Hepatic Encephalopathy

Adults

Starting dose: 3 to 4 times daily 30-45 ml (6-9 x 5 ml spoonfuls) or 2-3 sachets. This dose may be adjusted to the maintenance dose to achieve two or three soft stools each day.

Method of Administration

Oral use

For lactulose in bottles the measuring cup may be used.

For lactulose in 15 ml single dose sachets the corner of the sachet should be torn off and contents taken immediately.

Special populations

Paediatric population

The safety and efficacy in children (newborn to 18 years of age) with HE have not been established. No data are available.

For a precise dosing for infants and children up to 7 years lactulose in bottles should be used.

Elderly patients and patients with renal or hepatic insufficiency

No special dosage recommendations exist, since systemic exposure to lactulose is negligible.

4.3 Contraindications

• Hypersensitivity to the active substance or any of the excipients listed in section 6.1.

• Galactosaemia.

• Gastro-intestinal obstruction, -perforation or risk of perforation.

4.4 Special warnings and precautions for use

Painful abdominal symptoms of undetermined cause should be evaluated to exclude undiagnosed perforation or obstruction or undiagnosed disease/condition that predisposes to either before the treatment is started.

In case of insufficient therapeutic effect after several days the dose and/or additional measures should be re-considered.

Chronic use of unadjusted doses and misuse can lead to diarrhoea and disturbance of the electrolyte balance.

It should be taken into account that the defaecation reflex could be disturbed during the treatment.

The dose normally used in constipation should not pose a problem for diabetics.

The dose used in the treatment of HE is usually much higher and may need to be taken into consideration for diabetics.

Information on residues from manufacturing with known effect:

This product contains lactose, galactose and fructose from the route of production. Therefore, patients with rare hereditary problems of galactose or fructose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Lactulose should be administered with care to patients who are intolerant to lactose.

This product contains sulphite from the route of production.

Paediatric population

Use of laxatives in children should be exceptional and under medical supervision.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy

No effects during pregnancy are anticipated, since systemic exposure to lactulose is negligible.

Duphalac can be used during pregnancy.

Breast-feeding

No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to lactulose is negligible.

Duphalac can be used during breast-feeding.

Fertility

No effects are to be expected, since systemic exposure to lactulose is negligible.

4.7 Effects on ability to drive and use machines

Lactulose has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Flatulence may occur during the first few days of treatment. As a rule it disappears after a couple of days. When dosages higher than instructed are used, abdominal pain and diarrhoea may occur. In such a case the dosage should be decreased. See also overdose section 4.9.

If high doses (normally only associated with hepatic encephalopathy, HE) are used for an extended period of time, the patient may experience an electrolyte imbalance due to diarrhoea. Dosage should then be adjusted to obtain two or three formed stools per day.

Tabulated list of adverse reactions

The following undesirable effects have been experienced with the below indicated frequencies in lactulose-treated patients in placebo-controlled clinical trials:

very common (≥1/10);

common (≥1/100 to <1/10);

uncommon (≥1/1,000 to <1/100);

rare (≥1/10,000 to <1/1,000);

very rare (<1/10,000).

MedDRA SOC	Frequency category			
	Very common	Common	Uncommon	Rare
Gastrointestinal disorders	Diarrhoea	Flatulence, abdominal pain, nausea, vomiting		
Investigations			Electrolyte imbalance due to diarrhoea	

Paediatric population

The safety profile in children is expected to be similar as in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important.It allows continued monitoring of the benefit/risk balance of the medicinal product.

Healthcare professionals are asked to report any suspected adverse reactions via the MHRA Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

If the dose is too high, the following may occur:

Symptom: diarrhoea, loss of electrolytes and abdominal pain.

Treatment: cessation of treatment or dose reduction. Extensive fluid loss by diarrhoea or vomiting may require correction of electrolyte disturbances.

No specific antidote. Symptomatic treatment should be given.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Osmotically acting laxatives, ATC code: A 06A D11

In the colon lactulose is broken down by colonic bacteria into low molecular organic acids. These acids lead to a lowering of pH in the colonic lumen and via an osmotic effect to an increase of the volume of colonic contents. These effects stimulate peristalsis of the colon and return the consistency of the stool. The constipation is cleared and the physiological rhythm of the colon is reinstated.

In hepatic encephalopathy (HE) the effect has been attributed to suppression of proteolytic bacteria by an increase of acidophilic bacteria (e.g. lactobacillus), trapping of ammonia in the ionic form by acidification of the colonic contents, catharsis due to the low pH in the colon as well as an osmotic effect, and alteration of the bacterial nitrogen metabolism by

stimulating the bacteria to utilize ammonia for bacterial protein synthesis.

5.2 Pharmacokinetic properties

Lactulose is poorly absorbed after oral administration and it reaches the colon unchanged. There it is metabolised by the colonic bacterial flora. Metabolism is complete at doses up to 25-50 g or 40-75 ml; at higher dosages, a proportion may be excreted unchanged.

5.3 Preclinical safety data

The results of acute, sub-chronic and chronic toxicity studies in various species indicate that the compound has very low toxicity. The effects observed, appear to be more related to the effect of bulk in the gastrointestinal tract than to a more specific toxic activity. In reproduction and teratology experiments in rabbits, rats or mice no adverse effects were found.

6. Pharmaceutical particulars

6.1 List of excipients

None

6.2 Incompatibilities

None known.

6.3 Shelf life

HDPE: 2 years. Other containers: 3 years.

6.4 Special precautions for storage

Do not store above 25°C. Do not refrigerate or freeze.

6.5 Nature and contents of container

Brown glass and white HDPE bottles containing 200, 300, 500 and 1000 ml; polyethylene bottles containing 5 litres; 15 ml foil sachets.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing authorisation holder

Mylan Products Ltd.

20 Station Close

Potters Bar

Herts

EN6 1TL

United Kingdom

8. Marketing authorisation number(s)

PL 46302/0032

9. Date of first authorisation/renewal of the authorisation

Date of first authorisation: 14/03/1988

Date of latest renewal: 23/07/2004

10. Date of revision of the text

Aug 2020

Company contact details

Mylan

Address
Building 4, Trident Place, Mosquito Way, Hatfield, Hertfordshire, AL10 9UL

Telephone
+44 (0)1707 853 000

Medical Information Direct Line
+44 (0)1707 853 000

Customer Care direct line
+44 (0)1707 853 000 select option 2

Stock Availability
+44 (0)1707 853 000 select option 2

WWW
http://www.mylan.com (http://www.mylan.com)

Fax
+44 (0)1707 261 803

Medical Information e-mail
info@mylan.co.uk (mailto:info@mylan.co.uk)

Medical Information Fax
+44 (0)1707 261 803

SmPC

Reference

จาก

1. https://www.medicines.org.uk/emc/product/13211/smpc

   (EMC 2015)

2. https://www.medicines.org.uk/emc/product/5525/smpc

   (EMC 2020)