PROFESSIONAL INFORMATION

SCHEDULING STATUS

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1. NAME OF THE MEDICINE

DUPHALAC DRY

10 g of Duphalac Dry contains 10 g lactulose

Crystalline powder

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

10 g of DUPHALAC DRY contains 10 g lactulose (4-0-β-D-galactopyranosyl-D-fructofuranose) (a maximum of 0,25 g galactose and 0,2 g lactulose).

For the full list of excipients, see section 6 .1.

DUPHALAC DRY contains residues from the route of production with known effect, see section 4.4.

3. PHARMACEUTICAL FORM

A white to slightly yellow coloured crystalline powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

a) Constipation

Particularly when associated with laxative habituation or for those patients in whom constipation presents a special problem, e.g. children, obstetric and post-surgical patients.

b) Portal systemic encephalopathy

Hepatic coma or precoma stages where hyperammonaemia is present.

4.2 Posology and method of administration

Posology

a) Constipation

The dosage for constipation can be varied according to the individual response, but the following serves as a guide.

	Starting dose (3 days) gram per day	Maintenance dose gram per day
Adults	10-30 g	10-20 g
Children 7-14 years	10 g	10 g
Children 1-6 years	5-10 g	5-10 g

If there is no response within 48 hours the dosage can be increased and if diarrhoea occurs dosage should be decreased.

Since DUPHALAC DRY exerts its effect when it reaches the colon it may take 1-2 days before normal defaecation occurs.

b) Portal systemic encephalopathy

Starting dose 20-35 g three times a day.

Maintenance dose has to be adjusted to the individual response.

DUPHALAC DRY can be taken with breakfast cereals, or drinks such as tea, coffee, fruit juice or milk.

4.3 Contraindications

Hypersensitivity to lactulose (see section 6.1)

Galactosaemia including patients on a galactose-free diet.

Patients with intestinal obstruction.

4.4 Special warnings and precautions for use

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

DUPHALAC DRY may cause abdominal discomfort associated with flatulence or cramps. Nausea and vomiting have been reported less frequently following high doses.

From the route of synthesis, DUPHALAC DRY may contain small amounts of sugars.

Care should be taken in patients with lactose intolerance and in diabetic patients because of the presence of galactose and lactose.

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

Lactulose may contain more than 5 g lactose/galactose/epilactose depending upon the dose taken. This should be taken into account in patients with diabetes mellitus.15 ml of Lactulose contain 42,7 KJ (10,2 kcals) = 0,21 BU.

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 take lactulose for a more than 6 months period, periodic control of electrolytes is indicated.

During the therapy with laxatives it is recommended to drink sufficient amounts of fluids (1,5-2 l/day, equal to 6-8 glasses).

Prolonged use or overdosage may result in diarrhoea with excessive loss of water and electrolytes, particularly potassium.

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.

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

4.5 Interaction with other medicines and other forms of interaction

Lactulose may increase the loss of potassium induced by other drugs (e.g. thiazides, steroids and amphotericin 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 DUPHALAC DRY may be considered during pregnancy if necessary.

Breastfeeding

DUPHALAC DRY can be used during breastfeeding.

Fertility

For DUPHALAC DRY, 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

DUPHALAC DRY may cause abdominal discomfort associated with flatulence or cramps.

Nausea and vomiting have been reported less frequently following high doses.

Care should be taken in patients with lactose intolerance and in diabetic patients because of the presence of galactose and lactose.

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
Not known	cannot be estimated from the available data

Summary of the safety profile

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.

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.

System/ organ class	Frequency category		
	Very frequent (≥ 1/10):	Frequent (≥ 1/100 < 1/10):	Not known (cannot be estimated from the available data)
Immune system disorders			Hypersensitivity reactions
Gastrointestinal disorders	Flatulence, abdominal pain	Nausea and vomiting; if dosed too high, diarrhoea (sometimes including electrolyte imbalance).	
Skin and subcutaneous tissue disorders			Rash, pruritus, urticaria
Investigations		Electrolyte imbalance due to diarrhoea	

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of DUPHALAC DRY is important. It allows continued monitoring of the benefit/risk balance of DUPHALAC DRY. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

pv.south-africa@abbott.com

4.9 Overdose

If the dose is too high, the following may occur: diarrhea and abdominal pain.

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

See section 4.8. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A. 11.5 Laxatives

Pharmacotherapeutic group: Drugs for constipation. Osmotic acting laxatives

ATC code: A06AD11

Mechanism of action

DUPHALAC DRY is a synthetic disaccharide of fructose and galactose, which is not split into its monosaccharide constituents in the small intestine due to the lack of a specific enzyme. It reaches the colon unchanged where it is broken down by the saccharolytic flora into organic acids, such as lactic acid and acetic acid, acids formed in the colon under physiological conditions. Due to this local osmotic effect in the colon, water is retained, the faecal mass softened and normal colonic peristalsis restored. The mode of action differs from that of conventional laxatives.

In portal systemic encephalopathy administration of large doses of DUPHALAC DRY results in a significant reduction in the pH of the colonic contents. Lowering the pH promotes conversion of non-ionised ammonia into ionised form. The latter form being non-absorbable leads to reduction of absorption of ammonia from the intestine into the portal circulation and may even promote the excretion of ammonia from the circulation into the faeces.

In addition, the enhanced growth of saccharolytic bacteria results in a decreased formation of ammonia.

5.2 Pharmacokinetic properties

Lactulose cannot be hydrolysed in the intestine; thus very little absorption occurs. Small amounts of non hydrolysed lactulose may be absorbed, but these are readily excreted via the kidneys.

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

DUPHALAC DRY does not contain any added excipients.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

60 months.

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

Packs of 6, 10, 20 or 30 sachets of 10 g lactulose.

6.6 Special precautions for disposal and other handling

Not applicable.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Abbott Laboratories S.A. (Pty) Ltd.

Abbott Place, 219 Golf Club Terrace

Constantia Kloof 1709

South Africa

8. REGISTRATION NUMBER

28/11.5/0427

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27 May 1994

10. DATE OF REVISION OF THE TEXT

To be allocated.

NAMIBIA:

NS0 DUPHALAC DRY Sachet

Reg. No.: 04/11.5/1367

Reference:

Ref. no.	Description	Module
1.	***Summary of Product Characteristics*** Laevolac 10 g/15 ml oral solution & Lactulose 10 g/15 ml oral solution sachets MAH: Fresenius Kabi Austria GmbH	1.3.1.2.1 (stdrefs-ref-1-eu-smpc)