SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product
Osmowin
(Lactulose solution USP)

2. Qualitative and quantitative composition
Each 15 ml contains Lactulose concentrate USP equivalent to Lactulose……. 10 gm
Aqueous base……..... q.s

For the full list of excipients, see section 6.1.

3. Pharmaceutical form
Oral solution

Description: Colourless or Pale Yellow to Amber Coloured Syrup Liquid with Sweet taste having Lemon Flavour.

4. Clinical particulars
4.1 Therapeutic indications

i) For the treatment of acute and the prevention and treatment of chronic portal systemic encephalopathy including the stages of hepatic pre-coma and coma.
ii) For the treatment of chronic and habitual constipation.
iii) Where a soft stool is considered of medical benefit (haemorrhoids, post colonic / anal surgery.

4.2 Posology and method of administration
Posology
The lactulose solution may be administered diluted or undiluted. The dose should be titrated according to the clinical response. A single dose of lactulose should be swallowed in one and should not be kept in the mouth for an extended period of time.

Portal systemic Encephalopathy
The usual dosage is 30 to 45 ml three to four times daily. The dosage may be adjusted every day or two to produce two or three soft stools daily.

Hourly doses of 30 to 40 ml of Osmowin may be used to induce rapid laxation indicated in the initial phase of the therapy of Portal systemic Encephalopathy. When the laxative effect has been achieved, the dose of Osmowin may then be reduced to the usual daily dosage.

Improvement in the patient's condition may take 24-28 hours to occur. Continuous long-term therapy is indicated to lessen the severity and prevent the recurrence of Portal systemic Encephalopathy. The dose of Osmowin for this purpose id the same as the usual daily dose.

In the treatment of acute episodes of Portal systemic Encephalopathy, a rapid response is desirable. In such cases it is important to avoid under dosage, and 50 ml every 1-2 hours can be given, if necessary, until two loose bowel actions have occurred.

Thereafter doses may be reduced to usual doses (30 to 45 ml three to four times daily. The administration of Osmowin as a retention enema is an alternative technique. This can be done by diluting Osmowin and is of considerable value especially in the unconscious patient. In such cases 300 ml of Osmowin may be mixed with 700 ml of water or normal saline to be used as a retention enema, the enema is to be retained for 30-60 minutes, and repeated every 4-6 hours until the patient is able to take oral medication.

Chronic constipation

Lactulose may be given as a single daily dose or in two divided doses, using the measuring cup. All dosages should be adjusted to the needs of the individual. In case of single daily dose, this should be taken at the same time, e.g., during breakfast.

More serious constipation, and or constipation such as caused by chemotherapy agent may require higher dosages.

	Osmowin oral solution	
	Starting dose (3 days)	**Maintenance dose**
Adults	15 – 45 ml	15 – 30 ml
Children (7 – 14 years)	15 ml	10 – 15 ml
Children (1 – 6 years)	5 – 10 ml	5 – 10 ml
Infants under 1 year	5 ml	5 ml

When experiencing constipation patients should be advised to drink plenty of water, and increase the fibre content in their diet.

4.3 Contraindications

Contraindicated in patients with hypersensitivity to the active substance or to any of the excipients
- Galactosaemia.
- Bowel obstruction

4.4 Special warnings and precautions for use

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

A theoretical hazard may exist for patients treated with lactulose who may be required to undergo electrocautery procedures during proctoscopy or colonoscopy. If sugars reach the colon, then bacterial breakdown causes Hydrogen production.

Accumulation of hydrogen gas in significant concentration in the presence of an electrical spark may result in explosive reaction. Although this complication has not been reported

with lactulose, patients on lactulose therapy undergoing such procedures should have a thorough bowel cleansing with non-fermentable solution.

Osmowin contains galactose (1.5 g or less per 15 ml) and lactose (0.9 g or less per 15 ml) and should be used with caution in diabetics as blood glucose levels may be elevated, usually after extended use.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. Lactulose should be administered with care to patients who are intolerant to lactose.

Chronic misuse of laxatives may result in electrolyte imbalance in particular serum potassium levels may be decreased. Elderly debilitated patients who receive Osmowin for more than six months should have serum electrolytes measured periodically.

In the overall management of Portal systemic Encephalopathy, it should be recognized that there is a pre-existing liver disease and efforts should be made to identify and treat the precipitating cause of hepatic coma. Thus, the overall management of hepatic encephalopathy should include dietary protein restriction bowel cleansing and sterilization, correction of electrolytes and fluid imbalance, provision of caloric and nutritional needs and treatment of underlying liver diseases.

Paediatric use

It is recommended that if Osmowin is given to infants and children this should be done under medical supervision. The defaecation reflex may be altered during the treatment with lactulose. This alteration is considered to improve bowel habits during constipation and can be seen as a normalization of stool frequency.

4.5 Interaction with other medicinal products and other forms of interaction

There have been conflicting reports about the concomitant use of Neomycin and lactulose although in some situations the two drugs administered together are more effective than either one alone.

Theoretically, the elimination of certain colonic bacteria Neomycin and possibly other anti-infective agents may interfere with the desired degradation of lactulose and thus prevent the acidification of colonic content.

There have been some reports that lactulose-fermenting bacteria are relatively resistant to neomycin, which might explain why a combination could work in some cases. Thus, the status of the lactulose-treated patient should be closely monitored (including stool pH) in the event of concomitant oral antibiotic therapy.

4.6 Fertility, pregnancy and lactation

Use in Pregnancy

Lactulose has been shown to be effective for the treatment of constipation associated with pregnancy when administered to women at different stages of pregnancy.

Reproduction studies with daily oral doses of lactulose (50% w/w) up to 12 ml per kg in mice and rats and 6 ml per kg in rabbits have not revealed any evidence of an increased occurrence of foetal damage or other deleterious effects.

Use in Lactation
There are no data on the secretion of Lactulose in breast milk or the effect on the breast-fed infant. Risk-benefit should be considered.

Fertility
There is 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
Initial dosing may produce gaseous distension with flatulence and intestinal cramps in about 20% of patients. These effects are usually mild and transient.

Excessive dosage can lead to diarrhoea. If untreated potential complications of diarrhoea may include fluid loss, and electrolyte disturbances such as hypokalaemia and hypernatraemia.

Loss frequently, nausea, vomiting, anorexia and increased thirst have been reported.

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 providers are asked to report any suspected adverse reactions to the marketing authorization holder or if available via the national reporting system (See details below);

Paper based reporting: TMDA yellow card
Online reporting: https://sqrt.tmda.go.tz/
*USSD reporting: send a simple short text message to report any suspected Adverse Drug Reaction by dialing *152*00# and follow the instructions*.

4.9 Overdose
Symptoms:
If the dose is too high, the following may occur: diarrhoea and abdominal pain.

Management: 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: Drugs for constipation. Osmotically acting laxatives.
ATC code: A06A D11.

Lactulose is a synthetic disaccharide formed from D-galactose and fructose. Lactulose as a prebiotic substance strengthens the growth of bifidobacteria and lactobacilli, whereas Clostridium and Escherichia coli may be suppressed.

In the colon lactulose is metabolised by bacterial enzymes to short chain 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.

5.2 Pharmacokinetic properties

Experiments data on lactulose given orally to man indicate that lactulose is poorly absorbs from the gastrointestinal tract and no enzymes capable of hydrolysis of lactulose into it component monosaccharides are known to be present in human gastrointestinal tissue.

Lactulose reaches the colon virtually unchanged. There it is metabolised by colonic bacteria to low molecular weight acids i.e., lactic acid and other short chain carboxylic acids. Metabolism is complete at doses up to 25-50 g or 40-75 ml; at higher dosages, a proportion may be excreted unchanged.

Lactulose given orally to man results in only small amounts reaching the blood by absorption through the small intestine probably by a non-mediated diffusion mechanism.

Otherwise, small increases in blood sugar levels are probably attributable to the small amounts of galactose and lactose also present in Duphalac.

Urinary excretion has been determined to be 3% or less and is essentially complete within 24 hours. A small quantity of lactulose is probably hydrolysed in the colon into its constituent monosaccharides, galactose and fructose. The end result is a change in osmotic pressure and acidification of the colonic contents resulting in an increase in stool water-content with resultant distention and softening of the stools, which in turn promotes increased peristalsis and bowel evacuation.

In patients with chronic constipation, lactulose increases the number of bowel movements per day and the number of days when bowel movements occur.

5.3 Preclinical safety data

The results of acute, sub-chronic and chronic toxicity studies in various species indicated 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

Lemon flavour
Purified water q.s

6.2 Incompatibilities
Non incompatibilities have been reported.

6.3 Shelf life
24 months

6.4 Special precautions for storage
Store below or at 30˚C. Do not freeze.
Under recommended storage condition, a normal darkening of colour may occur. Such darkening is characteristic of sugar solutions and does not affect therapeutic actions.

6.5 Nature and contents of container
Amber Coloured PET Bottle of 100 ml & 200 ml with ROPP caps with coextruded polyethylene wads.

6.6 Special precautions for disposal and other handling
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorisation holder
Win-Medicare Pvt Ltd
1311, Modi Tower, 98, Nehru Place, New Delhi 110019
India.

8. Marketing authorisation number(s)
TAN 20 HM 0416

9. Date of first authorisation/renewal of the authorisation
25/09/2020

10. Date of revision of the text