THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR LACTOSAN (LACTULOSE 3.35 MG/5 ML) ORAL SOLUTION

Version number 1.0
21 August, 2023

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1. Introduction

Lactosan oral solution is a pale brownish yellow colored viscous solution contains lactulose 3.35 mg/5 mL. Lactulose, a disaccharide of galactose and fructose, is an osmotic laxative. It is a synthetic disaccharide that is not digested in the small intestine and not absorbed since the specific disaccharidase is lacking in humans. It passes unchanged into the colon where it serves as an energy source for the carbohydrate- splitting bacteria. During this process short chain fatty acids are formed, the main degradation products being acetic acid, lactic acid, hydrogen and carbon dioxide. These acids lower the pH in the lumen and increase the osmolality of the intestinal contents. Stool volume is increased by moderate water retention in the intestine and intestinal peristalsis is enhanced and the passage through the colon is accelerated. Lactosan oral solution is approved in Tanzania for use in children and adults.

Product details

Registration number	TAN 23 HM 0267
Brand name	Lactosan
Generic name, strength, and form	lactulose 3.35 mg/5 mL
ATC classification	A 06A D11- Laxative
Distribution category	POM
Country of origin	India
Associated product	N/A
Marketing Authorization Holder	Core Pharma Ltd Plot No.: 22, Shop No.: 01, Congo/Lindi Street, Kariakoo, P.O. Box 21412. Tanzania.
Local Technical Representative	N/A

1.1 Assessment procedure

The application for registration of Lactosan oral solution was submitted on 06/03/2022. The product underwent full assessment. Assessment was completed in 3 (three) rounds of evaluation and the product was registered on 01/06/2023.

1.2 Information for users

Visual description of the finished product	Pale brownish yellow colored viscous solution
Primary packing material	200 mL Amber coloured PET bottle with white HDPE cap
Secondary packing materials	Printed carton box
Shelf-life and storage condition	24 months, Do not above 30°C, protect from light. Do not refrigerate or freeze.
Route of administration	Oral

Therapeutic indications	1. For the treatment of constipation. 2.For the treatment of hepatic encephalopathy (HE); hepatic coma.

2. Labelling and product information

Summary of product characteristics
The SmPC included all the relevant information to ensure correct and safe use of the medicine by healthcare providers. The complete SmPC can be accessed here.

Package insert/leaflet
The package insert is confirmed to be derived from the SmPC and contains sufficient data for the end user. Since the product is POM, the package insert contains full prescribing information as per SmPC.

Container labels
The product label information is presented in English. Details in the secondary pack label include:

Brand name: Lactosan

Composition: lactulose 3.35 mg/5 mL

Pack size: 1 bottle

Manufacturing details: batch number, manufacturing date, and expiry date

Storage conditions: Do not above 30°C, protect from light. Do not refrigerate or freeze

Manufacturer address: physical address of release site

Unique identifier: Not applicable

Special warnings/precautions or instructions for use:

The details of the primary pack include:

Brand name and strength: Lactosan

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: SANPRAS Healthcare Pvt Ltd

The content of the primary and secondary labels was aligned to the requirements of the Part V of the Compendium: Guidelines on Format and Content of Product Labels for Medicinal

products. The label contains sufficient information for proper identification of the medicine and post marketing follow up of the product.

Mock labels are appended as annex I.

3. Scientific discussion

Quality of Active Pharmaceutical Ingredients

Information on the quality of the API was submitted in form of DMF.

General Information

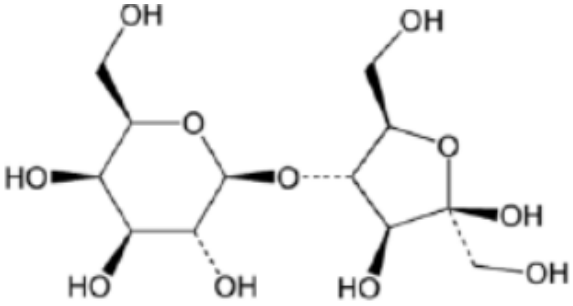
Lactulose API is compendia in USP, BP, and Ph.Eur.

Molecular formula: $C_{12}H_{22}O_{11}$

Chemical name:

- 4-O-β-D-Galactopyranosyl-D-fructofuranose
- d-Fructose, 4-O-β-d-galactopyranosyl

Structure:



General properties

Lactulose is a synthetic disaccharide. It is a reducing sugar crystallising in the; a form; it is a transparent and sweet aqueous syrup containing lactulose.

Manufacture

Lactulose API manufacturer is Danipharm A/S, Skalhuse3, DK-9240, Nibe - Denmark. The manufacturing complies with GMP requirements as evidenced by the GMP certificates issued by the state issue authority. Lactulose API is manufactured by chemical synthesis using conventional techniques. Sufficient controls of quality of materials and in-process checks were employed throughout the manufacturing process.

Specifications

Specifications

The API specifications were set as per USP standards and ICHQ3A. The parameters monitored during quality control are: description, solubility, identification test, residue on ignition, organic impurities, and assay. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The retest period of Lactulose API is 60 months when packed in original container with storage condition 'Store below 25^{o}C'.

Quality of the Finished Pharmaceutical Product

Formulation

Lactosan oral solution is a pale brownish yellow colored viscous solution.

Lactosan oral solution contains the Lactulose and other ingredients listed here after: essential oils (oil orange & oil lemon), aldehyde (C-10), propylene glycol, purified water. The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, 8th Edition in terms of function and quantities.

Manufacture

The finished product manufacturer is Sanpras Healthcare Pvt. ltd,81, S.T.I.C.E., Musalgaon, Sinnar, Tal., Sinnar, Dist. Nashik – 422112, Maharashtra, India. The compliance of the sites to TMDA GMP standards was confirmed through site inspection on 5-6/12/2018.

Specifications

The FPP is compendia. The manufacturer controls the quality of the finished product as per USP standards and ICH requirements. The parameters monitored during quality control are: appearance, identification of API, pH, weight per ml, filled volume, leak test, organic impurities, methanol, sulfites, boron and sulfated ash, assay, and microbial quality. Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system

Stability studies were conducted on 3(three) batches of the finished product stored at 30 ± 2°C & RH: 75 ± 5% RH for 24 months and 40± 2°C & RH: 75% ± 5% RH for 6 months. Based on the stability data presented, the approved shelf-life is 24 months when stored in original container with storage condition 'Do not above 30°C, protect from light. Do not refrigerate or freeze'

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After opening of bottle, the lactulose oral solution is demonstrated through in-use stability study conducted by using two (2) batches physically and chemically stable for three (3) months when store at temperature not above 30°C.

Safety and efficacy information

The quantitative and qualitative composition of the products at issue is identical to that of the innovator product Duphalac. No bio-equivalence study has been performed or is required, since the product at issue is a liquid preparation and lactulose is not intended to be absorbed.

4. Benefit-Risk Assessment and Conclusion

On basis of the data submitted, the current state of knowledge and compliance to Good Manufacturing Practice, the benefit of the product outweighs the risks associated with its use when used in accordance to the summary of product characteristics. Lactosan oral solution is recommended for registration.

5. Post-approval updates

Variation applications

Reference number	Date submitted	Change requested	Recommendation	Granting date

Feedback from pharmacovigilance, post marketing surveillance and enforcement activities

Type of feedback	Impact	Response

Re-registration applications

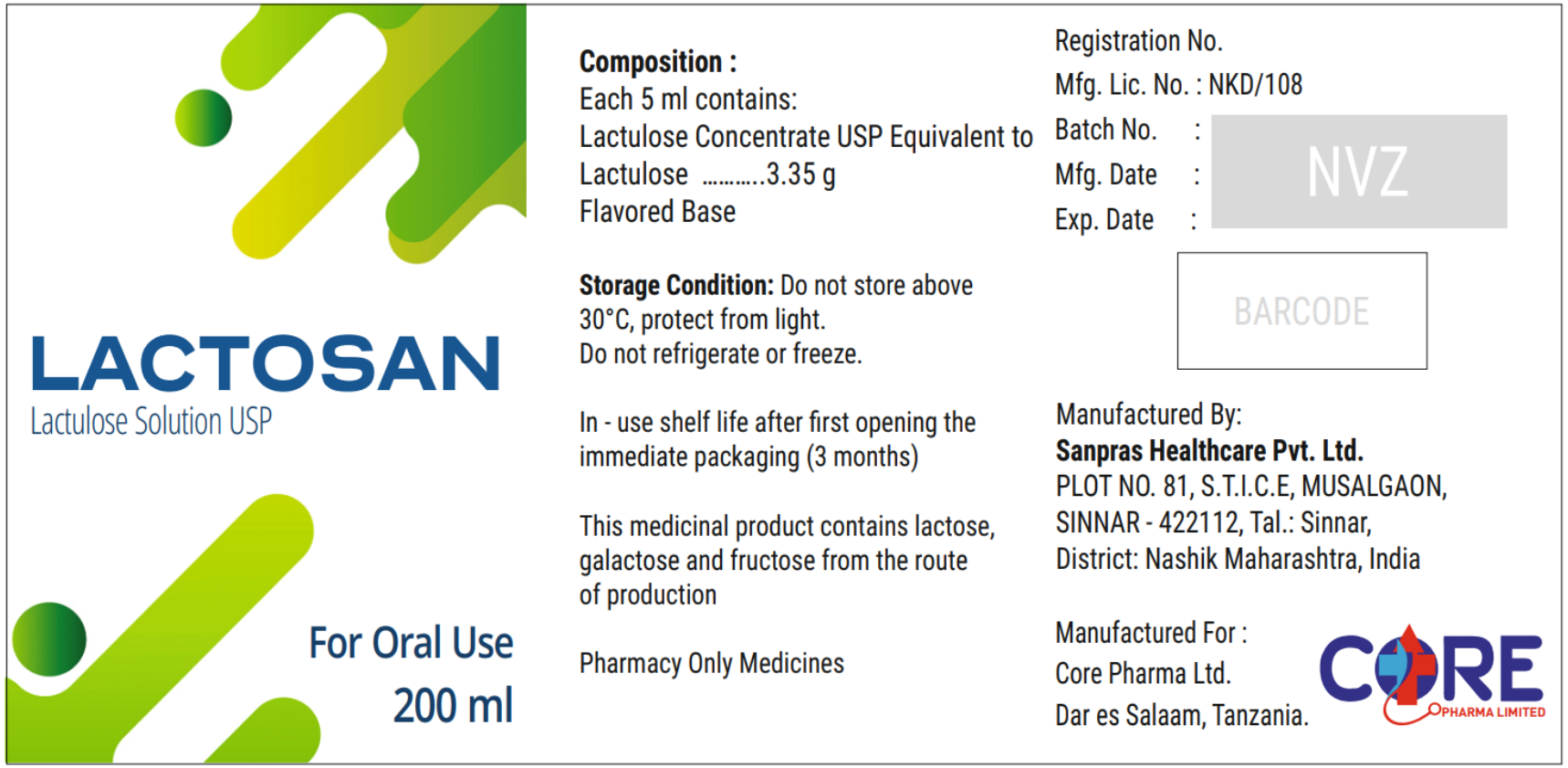
Application for renewal of registration was submitted on <DDMMYYYY>. The application was finalized in <number> rounds of evaluation. The product was confirmed to still be compliant to the standards of quality, safety and efficacy, hence registration was renewed on <DDMMYYYY>.

PART 5: CHANGE HISTORY

Version number	Date	Description of update	Section(s) Modified	Approval date

Annex I: Mock up labels;

Primary pack label;



Secondary pack label:

Effective date: 03/10/2022