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MINISTRYOFHEALTH

TANZANIAMEDICINES ANDMEDICALDEVICESAUTHORITY

PUBLIC ASSESSMENT REPORT FOR LEPTICA (PREGABALIN 150 MG) HARD GELATIN CAPSULES

Version number 01, 03/01/2023

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1. Introduction

Leptica is a generic medicine of Lyrica 300 mg hard capsules of Pfizer Limited, is an analogue of the neurotransmitter gamma-aminobutyric acid (GABA). Pregabalin decreases central neuronal excitability by binding to an auxiliary subunit (α2-δ protein) of a voltage-gated calcium channel on neurons in the central nervous system. Pregabalin reduces the release of several neurotransmitters, including glutamate, noradrenaline, and substance. Leptica is approved in Tanzania for use only in adult patients.

1.1 Product details

Registration number	TAN 21 H0485
Brand name	Leptica
Generic name, strength, and form	Each hard gelatin capsule contains 150 mg Pregabalin
ATC classification	ATC Code-N03AX16 (Anti–epileptics, other antiepileptics)
Distribution category	POM
Country of origin	Indonesia
Associated product	N/A
Marketing Authorization Holder	Bahari Pharmacy Limited Pugu Road, Industrial Area, P.O. Box 40591, Dar es Salaam Tanzania
Local Technical Representative	N/A

1.2 Assessment procedure

The application for registration of Leptica was submitted on17 January 2020.The product underwent full assessment. Assessment was completed in 3 (three) rounds of evaluation and the product was registered on 26 November 2021.

1.3 Information for users

Visual description of the finished product	Hard gelatin capsule, body and cap White Op (44.700), contain white crystalline powder. Cap printed DXM logo in black, body unmarked
Primary packing material	Aluminium – PVC Blister
Secondary packing materials	A printed carton box
Shelf-life and storage condition	24 months, Store at temperature below 30 ºC
Route of administration	Oral
Therapeutic indications	-Neuropathic pain

	Pregabalin is indicated for the treatment of peripheral and central neuropathic pain in adults. - Epilepsy Pregabalin is indicated as adjunctive therapy in adults with partial seizures with or without secondary generalization. - Generalized anxiety disorder Pregabalin is indicated for the treatment of Generalized Anxiety Disorder (GAD) in adults.

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: Leptica

Composition: Each Hard gelatin capsule contains 150 mg Pregabalin

Pack size: 3x10capsules

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

Storage conditions: Store at temperature below 30 ºC

Manufacturer address: physical address of release site

Unique identifier: Not applicable

Special warnings/precautions or instructions for use: See enclosed leaflet. The product contains lactose

The details of the primary pack include:

Brand name and strength: Leptica (Each hard gelatin capsule contains 150 mg Pregabalin)

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: PT Dexa Medica
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.

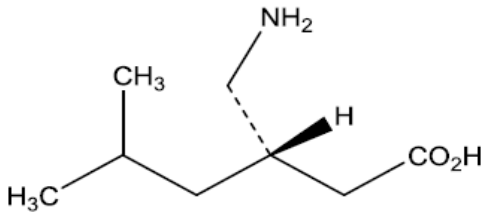
General Information

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

Molecular formula: $C_8H_{17}NO_2$

Chemical name:
(3S)-3-(Aminomethyl)-5-methylhexanoic acid

Structure:



General properties

Pregabalin is a white to off-white, non-hygroscopic, crystalline powder, slightly soluble in water and methanol. The drug substance exhibits polymorphism. Form I is manufactured. The drug substance shows isomerism. The drug substance corresponds to the S-enantiomer. A test for the enantiomeric purity is included in the drug substance specification.

Pregabalin drug substance falls into the category of BCS class I, being a highly soluble and highly permeable compound, therefore polymorphism and PSD are not critical parameters for performance of this drug product.

Manufacture

Pregabalin API manufacturer is MSN Pharmachem Private Limited, Plot No: 212 / A,B,C,D, Phase-II, IDA Pashamylaram, Pashamylaram (Village), Patancheru (Mandal), Sangareddy District, Telangana, Pincode : 502 307, India. The manufacturing complies with GMP requirements as evidenced by the GMP certificate issued by the Drugs Control Administration -Government of Telangana. Pregabalin 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

The API specifications were set as per Ph.Eur. standards and ICHQ3A. The parameters monitored during quality control are: Appearance (visual inspection), solubility, identity (IR and HPLC), assay (HPLC), related impurities (HPLC), water content (KF), and sulphated ash (Ph. Eur). Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Pregabalin API is 60 months when packed in clear low-density polyethylene bag tied with a strip then placed inside a black color low-density polyethylene bag and tied with a strip. This double polythene bag is placed inside a triple laminated bag and then this triple laminated bag is sealed and placed inside a HDPE container with storage condition ‘Store at temperature below 25^{o}C, in a closed container’.

Quality of the Finished Pharmaceutical Product

Formulation

Lepticais a hard gelatin capsule, body and cap White Op (44.700), contain white crystalline powder. Cap printed DXM logo in black, body unmarked.

Lepticacontains the Pregabalin and other ingredients listed here after: Lactose, Corn starch, Talc,Capsule shells (Gelatin and Titanium dioxide (E171)). The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, 8thEdition in terms of function and quantities.

Manufacture

The finished product manufacturer is PT Dexa Medica, Jl. Jend. Bambang Utoyo No.138, Palembang.The compliance of the site to TMDA GMP standards was confirmed through desk-review

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Specifications

The FPP is compendia in BP. The manufacturer controls the quality of the finished product as per in-house standards and ICH requirements. The parameters monitored during quality control are: appearance (visual inspection), identification (HPLC, IR), identification of Titanium oxide, disintegration, dissolution, uniformity of weight, weight of capsule content, assay (HPLC), impurities (HPLC), water content (KF.), microbial content, and leakage test of blister pack. Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system

Stability studies were conducted on a 3(three)batches of the finished productstored at 30 ± 2°C & RH: 75 ± 5% RH for 24months 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 Aluminum-PVC blisterswith storage condition ‘Store at temperature below 30 ºC.

Safety and efficacy information

Safety and efficacy of Leptica was established through a bioequivalence trial.

BE trial report number BE. 293/EQL/2013was submitted.

Study title	BIOEQUIVALENCE STUDY OF PREGABALIN 150 MG CAPSULES PRODUCED BY PT DEXA MEDICA, IN COMPARISON WITH THE COMPARATOR PRODUCT LYRICA CAPSULE 150 MG, MANUFACTURED BY PFIZER MANUFACTURING DEUTSCHLAND GMBH GERMANY
Study design	Randomized open label, two treatments, two periods, two sequence, crossover bioequivalence on 26 healthy adult human subjects, with a washout period of 7 days between two periods with test product- Pregabalin 150 mg capsules produced by PT Dexa Medica, against Reference product- Lyrica capsule 150 mg, Pfizer Manufacturing Deutschland GmbH Germany.
Study site	PT Equilab International, JI. RS. Fatmawati Persil 33, Jakarta 12430, Indonesia

Study dates	17-06-2016 up to 27-06-2016	
Primary objective	To assess whether the test product is bioequivalent to reference product	
Secondary objective	Assessment of safety and tolerability of the subjects.	
Number of participants	Subjects Enrolled: 26 Total number of subjects completed the study: 20 Drop-out / withdrawn: 6 Included subjects in statistical analysis: 20	
Monitored parameters	Tmax, Cmax, AUC0→t, AUC0→∞, AUC% Extrapolation Kel and T1/2	
Investigational medicinal products	Test Product	Reference product
	Strength: 150 mg Batch number: K-10311-00-F-PSC-1 Expiry date: 02/2015	Strength: 150 mg Batch number: 0538111 Expiry date: 10/2014
Analytical method	LC-MS/MS method was used for the determination of plasma concentrations of analyte	
Statistical method	SAS® procedure PROC GLM Software (SAS Institute Inc., USA)	

Efficacy results are summarized as follows:

Parameter	**Test**	**Reference**	**90 % Confidence interval**	**DF**	**CV (%)**
AUC0-t (hr.µg/mL)	10.35	10.31	98.75-104.41	18	Complete
AUC0-inf (µg.hr/mL)	13.92	13.78	98.66-104.11	18	Complete
Cmax (µg/mL)	2.10	2.15	98.75-109.93	18	Complete

The acceptance limits of 80 – 125% are met by the AUC and Cmax values. Furthermore, the safety profile of the test product is similar to that of reference product. Therefore, Leptica(Pregabalin 150 mg) capsules produced by Pt Dexa Medica is equivalent and interchangeable withLyrica 150 mg capsule, manufactured by Pfizer Manufacturing Deutschland Gmbh, Germanyunder acceptable in vivo experimental conditions.

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. Leptica 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

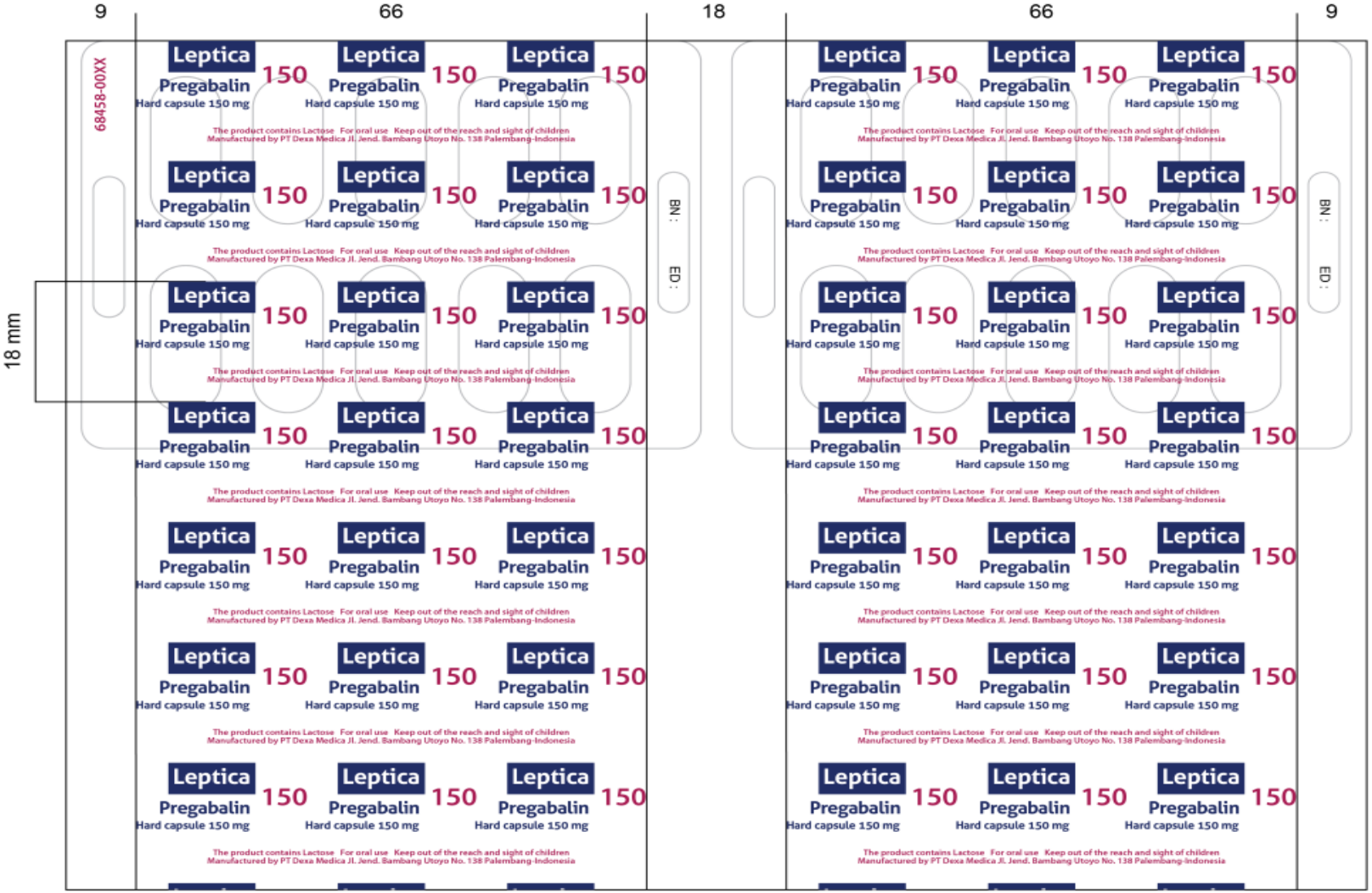
Application for renewal of registration was submitted on <DDMMYYYY>. The application was finalized in <number> rounds of evaluation. The product was confirmed to still be compliant to the standards of quality, safety and efficacy, hence registration was renewed on <DDMMYYYY>.

PART 5: CHANGE HISTORY

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

Annex I: Mock up labels;

Primary pack label;



Effective date: 03/10/2022

Secondary pack label;