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MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR LURATA 40 (LURASIDONE HYDROCHLORIDE 40 MG) FILM COATED TABLETS

Version number 1.0
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1. Introduction

LURATA 40 is a generic medicine of Lurasidone Hydrochloride Tablets 40 mg. LURATA 40 is an antipsychotic medicine belonging to N05AE05- Psycholeptics, antipsychotics group. LURATA 40 exerts its activity by selectively blocking dopamine and monoamine effects. LURATA 40 is approved in Tanzania for use in adults.

1.1 Product details

Registration number	TAN 20 HM 0429
Brand name	LURATA 40
Generic name, strength and form	Lurasidone Hydrochloride Tablets 40 mg
ATC classification	N05AE05- Psycholeptics, antipsychotics
Distribution category	POM
Country of origin	India
Associated product	State any other product of formulation, strength or site that is linked or associated with the product if applicable
Marketing Authorization Holder	MSN Laboratories Private Limited "MSN HOUSE", Plot No.: C-24, Industrial Estate, Sanathnagar, Hyderabad 500 018, Telangana. India
Local Technical Representative	Reddy`s Pharma Limited, P.O.Box:38083, Plot No.:12, Vingunguti, Nyerere Road, **Dar- es - Salaam**.

1.2 Assessment procedure

The application for registration of LURATA 40 was submitted on 02/01/2017. The product underwent full assessment. Assessment was completed in 2 rounds of evaluation. LURATA 40 was registered on 25/09/202.

1.3 Information for users

Visual description of the finished product	White colored, round shaped biconvex, film coated tablets debossed with "40" on one side and "ML" on other side
Primary packing material	Alu/Alu blister
Secondary packing materials	
Shelf-life and storage condition	24 Months Do not store above 30˚C
Route of administration	Oral
Therapeutic indications	Treatment of schizophrenia in adults aged 18 years and over

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 that is intended for long term use/, the package insert contains both full prescribing information as per SmPC and simplified information for patients.

Container labels
The product label information is presented in <English/Swahili>. Details in the secondary pack label include:
Brand name:
Composition: <generic name & strength, list of excipients (if applicable)>
Pack size: <primary & secondary pack>
Manufacturing details: <batch number, manufacturing date, expiry date>
Storage conditions: <state the condition as it appears on the label>
Manufacturer address: <physical address of release site>
Unique identifier: <state the unique identification used>
Special warnings/precautions or instructions for use: <include warnings or IFU if applicable>

The details of the primary pack include:
Brand name and strength:
Manufacturing details: <batch number, manufacturing date, expiry date>
Name of manufacturer: <name only>

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.
Describe any approved deviation to the requirements and the justification for the deviation.

3. Scientific discussion

Quality of Active Pharmaceutical Ingredient(s)

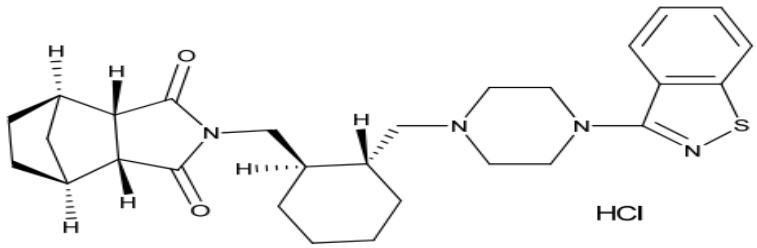
Information on quality of the API was submitted in form of full details.

General properties
Lurasidone Hydrochloride API is non-compendia.

Molecular formula: $C_{28}H_{36}N_4O_2S.HCL$
Chemical name:

(3aR,4S,7R,7aS)-2-{(1R,2R)-2-[4-(1,2-benzisothiazol-3-yl)piperazin-1-ylmethyl] cyclohexylmethyl} hexahydro-4,7-methano-2H-isoindole-1,3-dione hydrochloride

Structure:



Critical physico-chemical properties of the API were slightly soluble in aqueous solution.The crystalline polymorphic form is consistently manufactured.

Manufacture

The API manufacturing site, MSN Pharmachem Private Limited, Plot No.: 212 / A,B,C,D, Phase-II, IDA Pashamylaram, Pashamylaram (Village), Patancheru (Mandal), Medak District, Telangana, India was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by Drugs Control Administration, Government of Telangana. Lurasidone Hydrochloride 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 in-house standards and ICHQ3A. The parameters monitored during quality control are: description, solubility, identification, test for chlorides, water content, residue on ignition / sulphated ash, heavy metals, related substances, assay,chiral, diastereomer-1 content, residual solvents, amide impurity content, particle size and polymorphic identification by PXRD. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Lurasidone Hydrochloride API is 36 months when packed in polyethylene bags and stored at below 25°C.

Quality of the Finished Pharmaceutical Product

Formulation

LURATA 40 is a white colored, round shaped biconvex, film coated tablets, debossed with “40” on one side and “ML” on other side. LURATA 40 contains Lurasidone Hydrochloride and other ingredients listed hereafter lactose monohydrate, mannitol 60, pregelatinized starch, croscarmellose sodium, povidone K30, purified water,citric acid anhydrous powder,magnesium stearate and opadry white 02B580001(hypromellose ,titanium dioxide, macrogol, carnauba wax). The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, Edition 8th in terms of function and quantities. Ingredient, lactose monohydrate is of safety concern therefore appropriate warnings were included in the product label.

Manufacture

The finished product was manufactured at MSN Laboratories Private Limited, Formulations Division, Unit-II, Survey Nos. 1277,1319 to 1324, Nandigama (Village), Kothur(Mandal), Mahaboob Nagar District, Telangana 509216, India.The compliance of the site to TMDA GMP standards was confirmed through site inspection on 14/12/2016.

Specifications

The FPP is non-compendia. The manufacturer controls the quality of the finished product as per in-house and ICHQ3B requirements. The parameters monitored during quality control are: description, identification, Identification of coloring agents, average weight, uniformity of weight, uniformity of dosage units, water determination, dissolution, assay, related substances and microbial evaluation. Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system

Stability studies were conducted on 3 batches of the finished product stored at 30ºC ± 2ºC/75 % ± 5 % for 36 months and 40ºC ± 2ºC/75 % ± 5 % for 6 months. Based on the stability data presented, the approved shelf-life is 36 months when stored in Alu/Alu blister at below 30ºC.

Safety and efficacy information

Safety and efficacy of LURATA 40 was established through bioequivalence trial. BE trial report number LURA-1916-13 was submitted.

Study title	An open-label, balanced, randomized, single-dose, two treatment, three-period, three-sequence, crossover, partial-replicate, reference-scaled, oral bioequivalence study of Lurasidone Hydrochloride tablets 40 mg of MSN Laboratories Pvt. Ltd, India and Latuda (Lurasidone Hydrochloride) tablets 40 mg of Sunovion pharmaceuticals inc. Marlborough, ma 01752 USA in healthy, adult, human subjects under fasting conditions

Study design	An open-label, balanced, randomized, single-dose, two-treatment, three-period, three-sequence, crossover, partial-replicate, reference-scaled, oral bioequivalence study in healthy, adult, human subjects under fasting conditions. The analyst(s) were blinded to the randomization code.	
Study site	Micro Therapeutic Research Labs Private Limited, No.6, Kamarajar Salai, Selaiyur, East Tambaram, Chennai - 600 059, Tamil Nadu, India	
Study dates	26/08/2014 to 13/10/2014 (clinical and bioanalytical phase)	
Primary objective		
Secondary objective		
Number of participants	84	
Monitored parameters	Cmax, AUC0-t, AUC0-∞, tmax, t½, Kel	
Investigational medicinal products	Test Product Lurasidone Hydrochloride tablets of MSN Laboratories Pvt. Ltd, India	Reference product LATUDA® tablets of Sunovion Pharmaceuticals Inc. Marlborough,USA
	Strength: 40 mg Batch number: DT1404015A Expiry date: 04/2016	Strength: 40 mg Batch number: K0531530 Expiry date: 06/2017
Analytical method	LC-MSIMS	
Statistical method	WinNonlin® software version 5.3	

Efficacy results are summarized as follows:

Parameter	Test	Reference	% Ratio of geometric means	90 % Confidence interval	DF	CV (%)
AUC0-t (ng.hr/ml)	232.156	221.195	104.96	98.57 – 111.75		
AUC0-inf (ng.hr/ml)	247.455	238.049	103.95	97.57 – 110.72		
Cmax (units)						

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, LURATA 40 is equivalent and interchangeable with LATUDA® 40 mg tablets under acceptable in vivo experimental conditions.

4. Benefit-Risk Assessment and Conclusion

On basis ofthe 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. LURATA 40 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 label