THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR OLANGEM OD 10, OLANGEM OD 15, OLANGEM 0D 20 (OLANZAPINE 10 MG, 15 MG, 20 MG) ORODISPERSIBLE TABLETS

Version number 1.0
20 October 2023

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1. Introduction

Olangem OD is a generic medicine of Olanzapine orodispersible tablets. Olangem OD is an ntipsychotic, antimanic and mood stabilising medicine belonging to N05AH03-psycholeptics, diazepines, oxazepines, thiazepines and oxepines group. Olangem OD exerts is activity by binding to a number of receptors including serotonin 5HT2A/2C , 5HT3 , 5HT6; dopamine D1, D2 , D3, D4, D5; cholinergic muscarinic receptors M 1 -M5 ; α1 adrenergic and histamine H1 receptors. Olangem OD is approved in Tanzania for use in adults.

1.1 Product details

Registration number	Olangem OD 10 Olangem OD 15 Olangem OD 20
Brand name	Olangem OD 10 Olangem OD 15 Olangem OD 20
Generic name, strength and form	Olanzapine 10 mg Orodispersible Tablets Olanzapine 15 mg Orodispersible Tablets Olanzapine 20 mg Orodispersible Tablets
ATC classification	N05AH03-psycholeptics, diazepines, oxazepines, thiazepines and oxepines
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	Aurobindo Pharma Limited Plot No.2, Maitrivihar, Ameerpet, Hyderabad,Zip Code: 500 038, Telangana State. India E-Mail: info@aurobindo.com
Local Technical Representative	Generics & Specialties Limited P.O. Box 1469，Dar es Salaam, Tanzania

1.2 Assessment procedure

The application for registration of Olangem OD was submitted on 22/11/2018 and 09/10/201. The product underwent full assessment. Assessment was completed in 2 rounds of evaluation. Olangem OD was registered on 25/09/2020.

1.3 Information for users

Visual description of the finished product	Olangem OD 10: yellow coloured, circular, flat faced beveled edge tablets debossed with 'C' on one side and '52' on the other side.

	Olangem OD 15: yellow coloured, circular, flat faced beveled edge tablets debossed with ''C'' on one side and ''53'' on the other side. Olangem OD 20: yellow coloured, circular, flat faced beveled edge tablets debossed with ''C'' on one side and ''54'' on the other side.
Primary packing material	AL blisters
Secondary packing materials	
Shelf-life and storage condition	24 Months Do not Store above 30^0C.Store in original pack in order to protect from light and moisture
Route of administration	Oral
Therapeutic indications	**Adults:** Olanzapine is indicated for the treatment of schizophrenia. Olanzapine is effective in maintaining the clinical improvement during continuation therapy in patients who have shown an initial treatment response. Olanzapine is indicated for the treatment of moderate to severe manic episode. In patients whose manic episode has responded to Olanzapine treatment, Olanzapine is indicated for the prevention of recurrence in patients with bipolar disorder

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. Details in the secondary pack label include:
Brand name: Olangem OD 10, Olangem OD 15, Olangem OD 20
Composition: Olanzapine orodispersible tablets 10mg, 15mg, 20 mg
Pack size: 4 x 7's
Manufacturing details: batch number, manufacturing date, expiry date
Storage conditions: Store below 30^0C.Store in original pack in order to protect from light and moisture.
Manufacturer address: Aurobindo Pharma Limited, Unit VII,survey No. 411/P, 425/P, 434/P,435/P & 458/P, TSIIC, Plot No. S1, Green Industrial Park,Polepally village,Jedcherla Mandal,Mahaboob Nagar District, Telangana State, India.

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: Olangem OD 10, Olangem OD 15, Olangem OD 20
Manufacturing details: batch number, manufacturing date, expiry date
Name of manufacturer: Aurobindo Pharma Ltd, India

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.

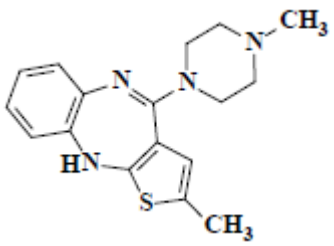
3. Scientific discussion

Quality of Active Pharmaceutical Ingredient(s)

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

General properties
Olanzapine API is compendia in BP.
Molecular formula: $C_{17}H_{20}N_4S$
Chemical name:
2-Methyl-4-(4-methylpiperazine-1-yl)-10H- thieno [2, 3-b]-[1, 5] benzodiazepine
Or 2-Methyl-4-(4-methyl-1-piperazinyl)-10H- thieno [2, 3-b]-[1, 5] benzodiazepine

Structure:



Critical physico-chemical properties of the API were freely soluble in methylene chloride, slightly soluble in methanol and ethanol (96 per cent), practically insoluble in water.It exhibits polymorphism and Olanzapine Crystalline Polymorph Form I is consistently manufactured.

Manufacture

The API manufacturing site, Aurobindo Pharma Limited, Unit - VIII, Survey No. : 10 & 13 Gaddapotharam (Village), IDA – Kazipally, Jinnaram (Mandal), Sangareddy District, Telangana state –502 319, INDIA was noted to comply with WHO GMP requirements as evidenced by the GMP certificate issued by <state the issuing authority>. Olanzapine 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 BP standards and ICHQ3A. The parameters monitored during quality control are: description, solubility, identification, water, sulphated ash, related substances, assay, residual solvents, particle size and microbial analysis. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Olanzapine API is 18 months when packed in low-density polyethylene (LDPE) bag and stored at 5±°3°C.

Quality of the Finished Pharmaceutical Product

Formulation

Olangem OD 10 is a yellow coloured, circular, flat faced beveled edge tablets debossed with ’C’ on one side and ’52’ on the other side.

Olangem OD 15 is a yellow coloured, circular, flat faced beveled edge tablets debossed with ’’C’’ on one side and ’’53’’ on the other side.

Olangem OD 20 is a yellow coloured, circular, flat faced beveled edge tablets debossed with ’’C’’ on one side and ’’54’’ on the other side.

Olangem OD contains Olanzapine and other ingredients listed here after mannitol, polacrilin potassium, crospovidone, colloidal anhydrous silica, aspartame, microcrystalline cellulose,

sodium stearylfumarate and art pineapple . 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, <excipient> is of safety concern therefore appropriate warnings were included in the product label.

Manufacture

The finished product was manufactured at Aurobindo Pharma Limited, Unit-VII (SEZ),Survey No. 411/P, 425/P, 434/P, 435/P & 458/P,TSIIC, lot. No. Sl, Green Industrial Park, Polepally village, Jedcherla Mandal, Mahaboob Nagar District, Telangana State, INDIA.The compliance of the site to TMDA GMP standards was confirmed through <site inspection/desk-review> on <date of GMP compliance>.

Specifications

The FPP is <non-compendia/compendia in BP/USP/JP/International Ph>. 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, average mass, water, disintegration time, dissolution, uniformity of dosage units, related substances, assay, fineness of dispersion and microbial contamination. 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 30°C±2°C/75%RH±5%RH for 24 months and 40°C±2°C/75%RH±5%RH for 6 months. Based on the stability data presented, the approved shelf-life is <number> months when stored in Aluminium foil at below 30°C.

Safety and efficacy information

Olangem OD 20

Safety and efficacy of Olangem OD 20 was established through bioequivalence trial. BE trial report number 392/10 was submitted.

Study title	An open label, randomized, two-treatment, two-sequence, two-period, crossover, single-dose comparative oral bioavailability study of Olanzapine Orodispersible Tablets 20 mg (Test) of Aurobindo Pharma Limited, India and Zyprexa Velotab 20 mg Oro dispersible Tablets (Reference) of Eli Lilly Nederland B.V, Nederland in 36 healthy, adult, Human subjects under fasting Conditions.
Study design	Open label, randomized, two-treatment, two-sequence, two-period, crossover, single-dose comparative oral bioavailability
Study site	AXIS Clinical Limited Plot Nos. 33-35,

	Alluri Sitaramaraju Nagar Opp. JPN Nagar, Miyapur, Hyderabad-500 049, **India**	
Study dates	26/02/2011 to 08/05/2011	
Primary objective	To compare the rate and extent of absorption of Olanzapine Orodispersible Tablets 20 mg (Test) of Aurobindo Pharma Limited, India with that of Zyprexa Ve10tab 20 mg Orodispersible Tablets (Reference) of Eli Lilly Nederland B.V., Nederland	
Secondary objective	To monitor the adverse events and to ensure the safety of the subjects.	
Number of participants	36	
Monitored parameters	C_{max}, AUC_{0-72}	
Investigational medicinal products	Test Product Olanzapine Orodispersible Tablets of Aurobindo Pharma Limited, India	Reference product Zyprexa Velotab Oro dispersible Tablets of Eli Lilly Nederland B.V
	Strength: 20 mg Batch number: ORSD10001 Expiry date: 11/2012	Strength: 20 mg Batch number: 1022180C Expiry date: 12/2012
Analytical method	LC-MS/MS	
Statistical method	SAS® software version 9.1.3	

Efficacy results are summarized as follows:

Parameter	Test	Reference	% Ratio of geometric means	90 % Confidence interval	DF	CV (%)
AUC0-72(hr.ng/ml)	1151.18	1126.72		87.01 – 119.97		37.09
AUC0-inf (units)						
Cmax (ng/ml)	38.52	38.85		85.38 – 115.14		34.39

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, Olanzapine Orodispersible Tablets of Aurobindo Pharma Limited, India is equivalent and interchangeable with Zyprexa Velotab Oro dispersible Tablets of Eli Lilly Nederland B.V under acceptable in vivo experimental conditions.

Olangem OD 15

Safety and efficacy of Olangem OD 15 was established through biowaiver application.
Comparative dissolution report number <number> was submitted.

The biowaiver was approved based on additional strength.

Olangem OD 15 fulfilled the criteriafor waiving an in-vivo bioequivalence study as per relevant TMDA guidance. Dissolution profiles of Olangem OD 15 was compared to Olangem OD 20.At least 85% of the labelled amount of Olanzapine had dissolved in all three media. Therefore, confirming similarity.

Olangem OD 10

Safety and efficacy of Olangem OD 10 was established through biowaiver application.
Comparative dissolution report number <number> was submitted.

The biowaiver was approved based on additional strength.

Olangem OD 10 fulfilled the criteriafor waiving an in-vivo bioequivalence study as per relevant TMDA guidance. Dissolution profiles of Olangem OD 10 was compared to Olangem OD 20.At least 85% of the labelled amount of Olanzapine had dissolved in all three media. Therefore, confirming similarity.

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. Olangem OD 10/15/20 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

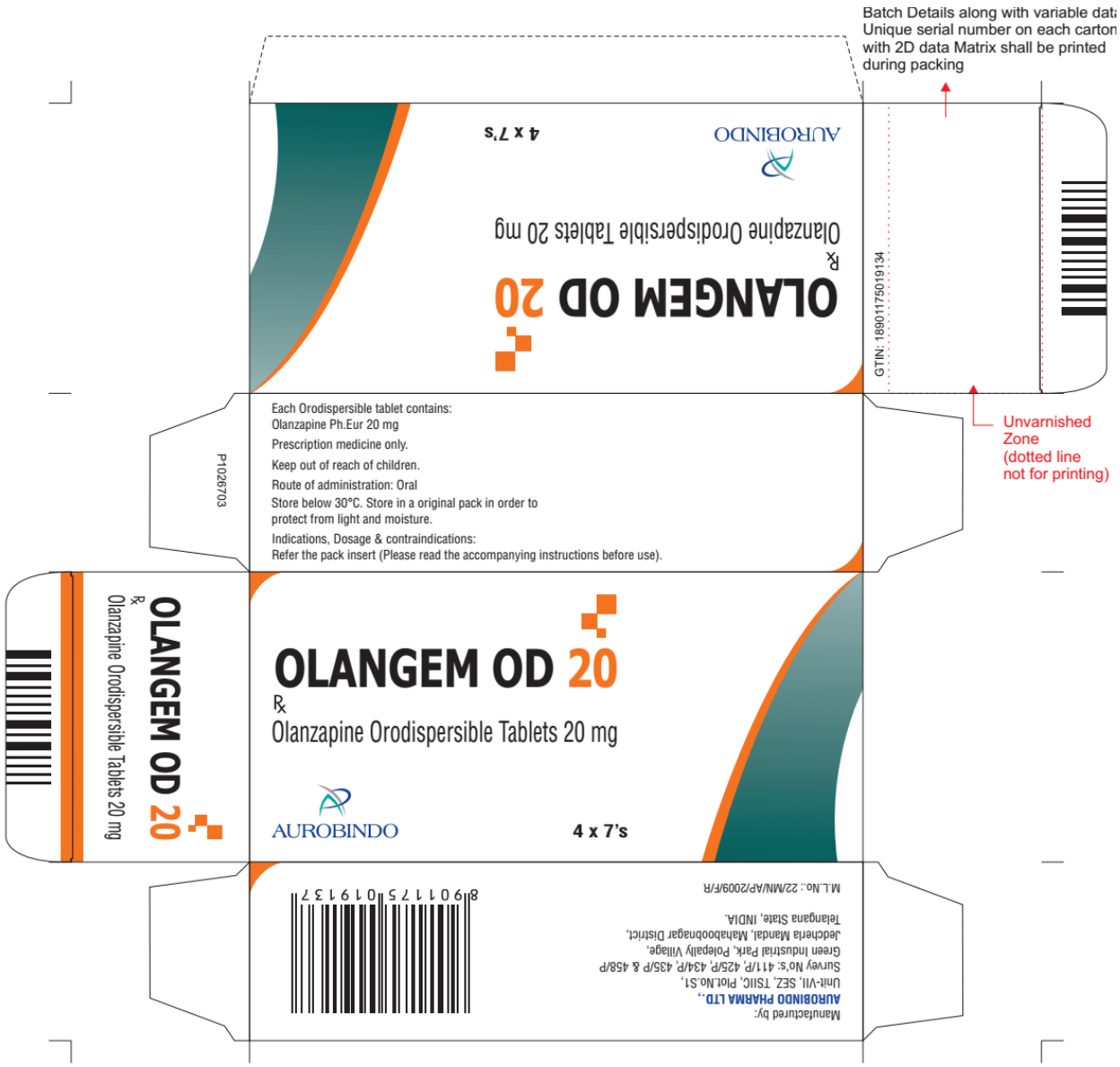
Application for renewal of registration was submitted on <DDMMYYYY>. The application was finalized in <number> rounds of evaluation. The product was confirmed to still be compliant to the standards of quality, safety and efficacy, hence registration was renewed on <DDMMYYYY>.

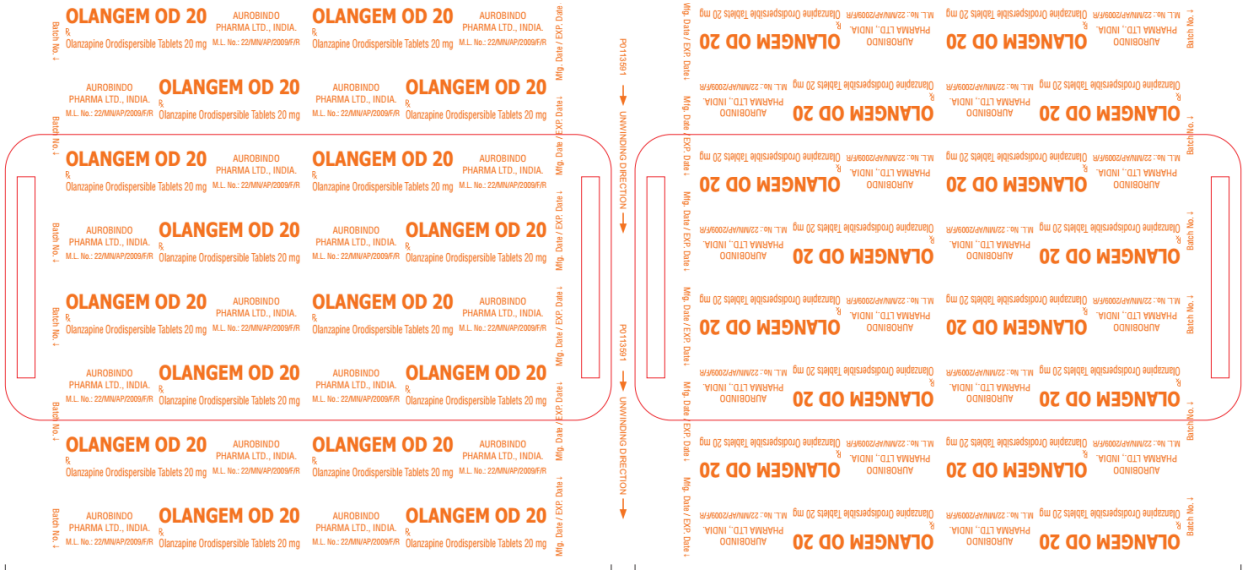
PART 5: CHANGE HISTORY

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

Annex I: Mock up label

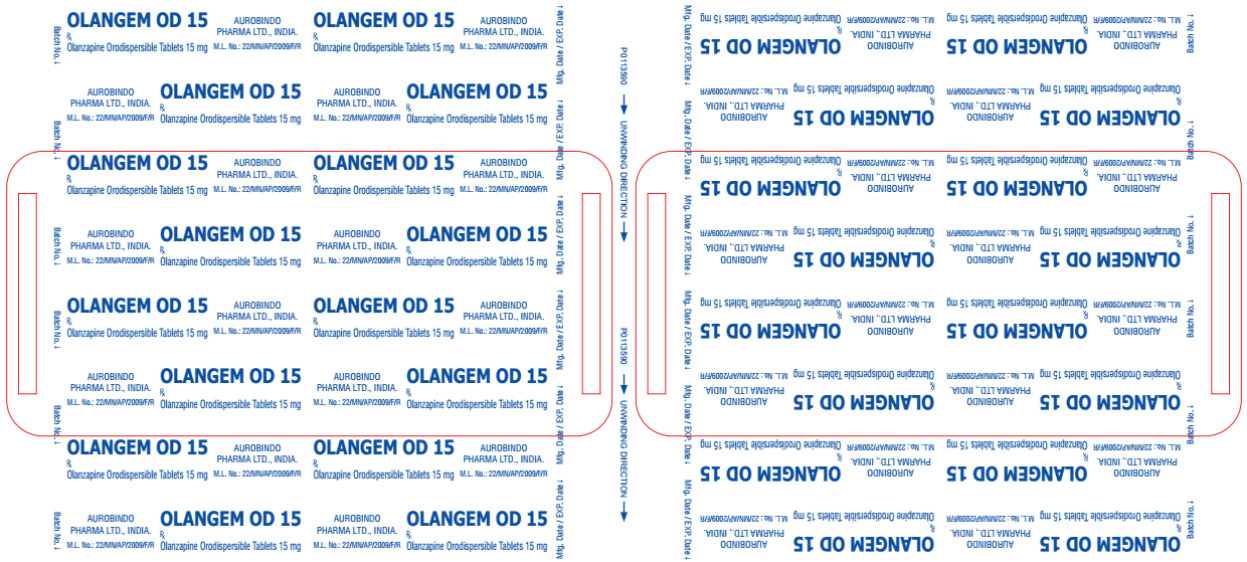
Olangem OD 20


Batch Details along with variable data
Unique serial number on each carton
with 2D data Matrix shall be printed
during packing
GTIN: 18901175019134
Unvarnished
Zone
(dotted line
not for printing)
OLANGEM OD 20
Rx
Olanzapine Orodispersible Tablets 20 mg
AUROBINDO
4 x 7's
Each Orodispersible tablet contains:
Olanzapine Ph.Eur 20 mg
Prescription medicine only.
Keep out of reach of children.
Route of administration: Oral
Store below 30°C. Store in a original pack in order to
protect from light and moisture.
Indications, Dosage & contraindications:
Refer the pack insert (Please read the accompanying instructions before use).
P1026703
OLANGEM OD 20
Rx
Olanzapine Orodispersible Tablets 20 mg
Manufactured by:
AUROBINDO PHARMA LTD.,
Unit-VII, SEZ, TSIIC, Plot.No.S1,
Survey No's: 411/P, 425/P, 434/P, 435/P & 458/P
Green Industrial Park, Polepally Village,
Jadcherla Mandal, Mahaboobnagar District,
Telangana State, INDIA.
M.L.No.: 22/MN/AP/2009/F/R



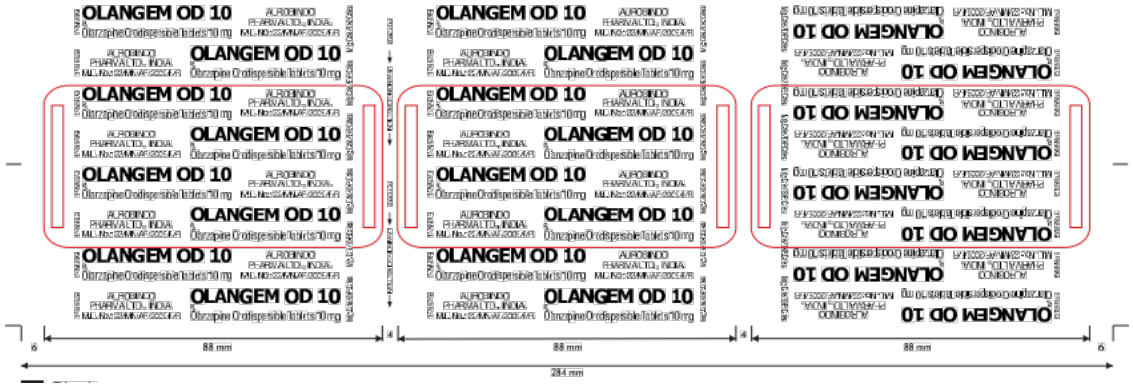
Olangem OD 15


Batch Details along with variable data & Unique serial number on each carton with 2D data Matrix shall be printed during packing
GTIN: 18901175019127
Unvarnished Zone (dotted line not for printing)
OLANGEM OD 15
Olanzapine Orodispersible Tablets 15 mg
AUROBINDO
4 x 7's
Each Orodispersible tablet contains:
Olanzapine Ph.Eur 15 mg
Prescription medicine only.
Keep out of reach of children.
Route of administration: Oral
Store below 30°C. Store in a original pack in order to protect from light and moisture.
Indications, Dosage & contraindications:
Refer the pack insert (Please read the accompanying instructions before use).
P1026702
OLANGEM OD 15
Olanzapine Orodispersible Tablets 15 mg
Manufactured by:
AUROBINDO PHARMA LTD.,
Unit-VII, SEZ, TSIIC, Plot.No.S1,
Survey No's: 411/P, 425/P, 434/P, 435/P & 458/P
Green Industrial Park, Polepally Village,
Jadcherla Mandal, Mahaboobnagar District,
Telangana State, INDIA.
M.L.No.: 22/MN/AP/2009/F/R



Olangem OD 10


during packing
AUROBINDO
4 x 7's
Olanzapine Orodispersible Tablets 10 mg
OLANGEM OD 10
GTIN: 18901175019110
Each Orodispersible tablet contains: Olanzapine Ph.Eur 10 mg
Prescription medicine only.
Keep out of reach of children.
Route of administration: Oral
Store below 30°C. Store in a original pack in order to protect from light and moisture.
Indications, Dosage & contraindications:
Refer the pack insert (Please read the accompanying instructions before use).
P1026701
Unvarnished Zone
(dotted line
not for printing)
OLANGEM OD 10
Olanzapine Orodispersible Tablets 10 mg
AUROBINDO
4 x 7's
Manufactured by:
AUROBINDO PHARMA LTD.,
Unit VII, SEZ, TSIIC, Plot. No.S1,
Survey No's:411/P, 425/P, 434/P, 435/P & 458/P
Green Industrial Park, Polepally Village,
Jadcherla Mandal, Mahaboobnagar District,
Telangana State, India.
M.L.No.: 22/MN/AP/2009/F/R
8 901175 019113


OLANGEM OD 10
AUROBINDO
PHARMA LTD., INDIA
Olanzapine Orodispersible tablets 10 mg
88 mm
284 mm