CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 202727

Name: Lansoprazole Delayed-Release Capsules USP, 15 mg (OTC)

Sponsor: Wockhardt Ltd

Approval Date: May 18, 2012

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202727

CONTENTS

Reviews / Information Included in this Review

Approval Letter	**X**
Tentative Approval Letter	
Labeling	**X**
Labeling Review(s)	**X**
Medical Review(s)	
Chemistry Review(s)	**X**
Bioequivalence Review(s)	**X**
Statistical Review(s)	
Microbiology Review(s)	
Other Review(s)	
Administrative & Correspondence Documents	**X**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202727

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 202727

Wockhardt USA LLC.
U.S. Agent for: Wockhardt Limited
Attention: Ms. Leanne Usa
20 Waterview Blvd.
Parsippany, NJ 07054

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated January 24, 2011, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Lansoprazole Delayed-Release Capsules USP, 15 mg (OTC).

Reference is also made to your amendments dated April 14, April 28, September 21, December 30, 2011; and January 5, February 21, April 16, April 20, April 27, and May 8, 2012.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for over-the-counter (OTC) use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Lansoprazole Delayed-Release Capsules USP, 15 mg (OTC) to be bioequivalent to the reference listed drug product (RLD), Prevacid® 24 HR Delayed-release Capsules, 15 mg, of Novartis Consumer Health, Inc.

Your dissolution testing should be incorporated into the stability and quality control program using the same USP method proposed in your application. The "interim" dissolution specifications are as follows:

Apparatus:	USP Apparatus II (paddle)
Speed:	75 rpm
Medium:	Acid Stage: 0.1 N HCl for one hour, followed by

	Buffer Stage: Phosphate Buffer, pH 6.8
Volume:	Acid Stage: 500 mL
	Buffer Stage: 900 mL
Temperature:	37°C ± 0.5°C

The product should meet the following "interim" specifications:

Acid stage:	Not more than 10% of the labeled amount of lansoprazole is dissolved in 60 minutes.
Buffer stage:	Not less than 80% (Q) of the labeled amount of lansoprazole is dissolved in 60 minutes.

These "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data from the first three production size batches. These data should be submitted as a "Special Supplement – Changes Being Effected" if there are no revisions to the "interim" specifications, or if the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at

http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/U_CM072392.pdf. The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

{See appended electronic signature page}

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ROBERT L WEST

05/18/2012

Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.

CENTER FOR DRUG EVALUATION AND RESEARCH

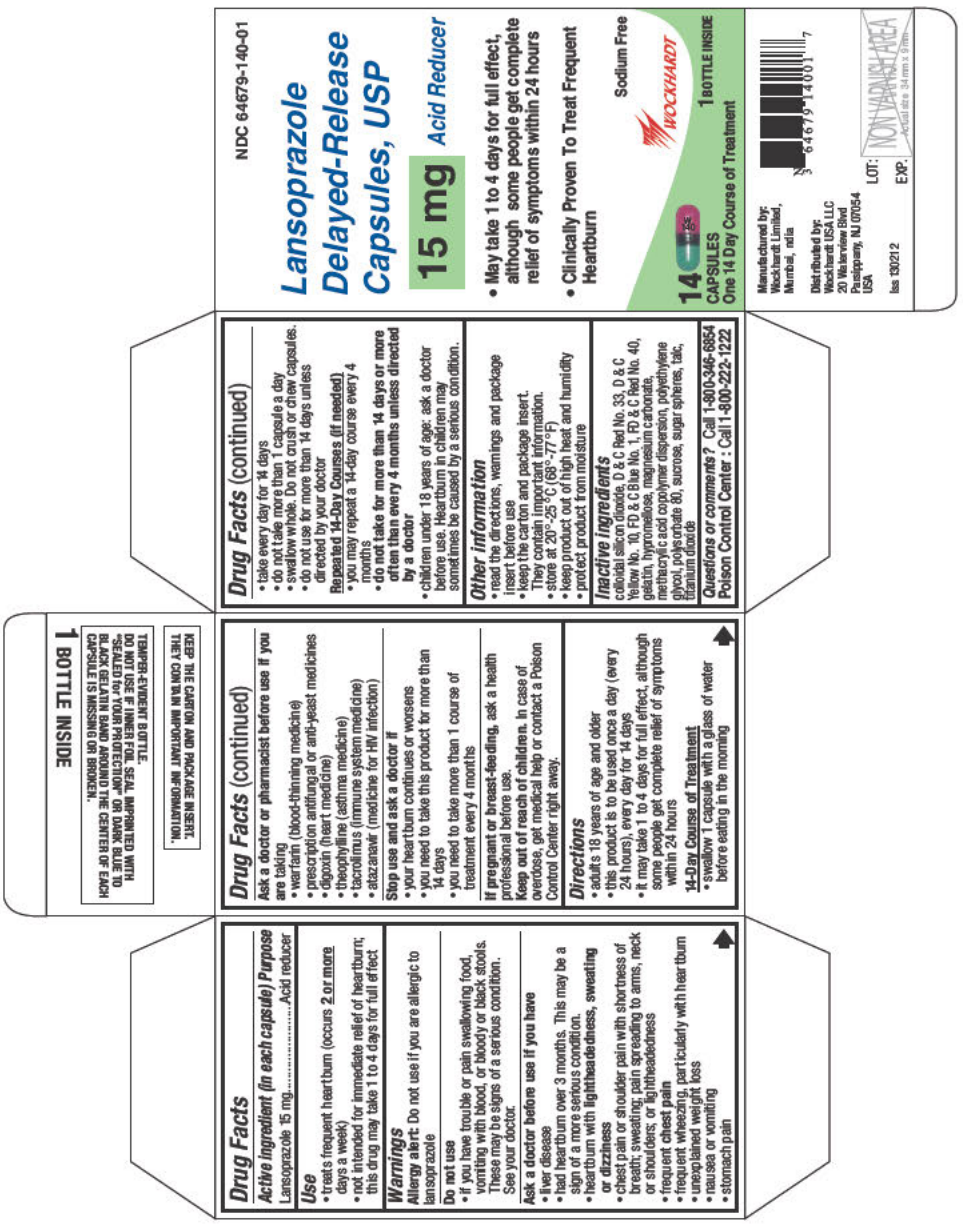
APPLICATION NUMBER:

ANDA 202727

LABELING

Lansoprazole Delayed-Release Capsules USP, 15 mg

Revised Proposed - 14 Capsules Bottle Carton



Actual size: 40 mm x 40 mm x 70 mm

Labeling Format Information:			
Fonts: Helvetica, Helvetica Narrow, bold, bold oblique			
Drug Facts:	10 pt	Leading:	6.5 pt
Headings:	8 pt	Solid Circle Bullets:	6 pt
Subheader:	6 pt	Barline:	1 pt
Body Text:	6 pt	Hairline:	0.5 pt
Drug Facts (continued):	10 pt		

Actual size: 125 mm x 42 mm x 80 mm

Drug Facts (continued)

Other information

- read the directions, warnings and package insert before use
- keep the carton and package insert. They contain important information.
- store at 20°-25°C (68°-77°F)
- keep product out of high heat and humidity
- protect product from moisture

Inactive ingredients

colloidal silicon dioxide, D & C Red No. 33, D & C Yellow No. 10, FD & C Blue No. 1, FD & C Red No. 40, gelatin, hypromellose, magnesium carbonate, methacrylic acid copolymer dispersion, polyethylene glycol, polysorbate 80, sucrose, sugar spheres, talc, titanium dioxide

Questions or comments?

Call **1-800-346-6854**

Poison Control Center :

Call **1 800 222 1222**

3 64679 14008 6

NDC 64679-140-08

Lansoprazole Delayed-Release Capsules, USP

15 mg *Acid Reducer*

- May take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours
- Clinically Proven To Treat Frequent Heartburn

28 CAPSULES

Two 14 Day Courses of Treatment

WOCKHARDT

Sodium Free

Manufactured by:
Wockhardt Limited,
Mumbai, India.

Iss.190412

Distributed by:
Wockhardt USA LLC.
20 Waterview Blvd.
Parsippany, NJ 07054
USA.

LOT:

EXP.

NON VARNISH AREA
Actual size: 42 mm x 11 mm

2 BOTTLES INSIDE

28 CAPSULES TOTAL

Lansoprazole Delayed-Release Capsules, USP

15 mg *Acid Reducer*

KEEP THE CARTON AND PACKAGE INSERT. THEY CONTAIN IMPORTANT INFORMATION.

TAMPER-EVIDENT BOTTLE.
DO NOT USE IF INNER FOIL SEAL IMPRINTED WITH "SEALED for YOUR PROTECTION" OR DARK BLUE TO BLACK GELATIN BAND AROUND THE CENTER OF EACH CAPSULE IS MISSING OR BROKEN.

Lansoprazole Delayed-Release Capsules, USP

15 mg *Acid Reducer*

2 BOTTLES INSIDE

Drug Facts

Active ingredient (in each capsule) ***Purpose***

Lansoprazole 15 mg ..... Acid reducer

Use

- treats frequent heartburn (occurs **2 or more** days a week)
- not intended for immediate relief of heartburn; this drug may take 1 to 4 days for full effect

Warnings

Allergy alert: Do not use if you are allergic to lansoprazole

Do not use

- if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor.

Ask a doctor before use if you have

- liver disease
- had heartburn over 3 months. This may be a sign of a more serious condition.
- heartburn with **lightheadedness, sweating or dizziness**
- chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent **chest pain**
- frequent wheezing, particularly with heartburn
- unexplained weight loss
- nausea or vomiting
- stomach pain

Ask a doctor or pharmacist before use if you are taking

- warfarin (blood-thinning medicine)
- prescription antifungal or anti-yeast medicines
- digoxin (heart medicine)

Drug Facts (continued)

- theophylline (asthma medicine)
- tacrolimus (immune system medicine)
- atazanavir (medicine for HIV infection)

Stop use and ask a doctor if

- your heartburn continues or worsens
- you need to take this product for more than 14 days
- you need to take more than 1 course of treatment every 4 months

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions

- adults 18 years of age and older
- this product is to be used once a day (every 24 hours), every day for 14 days
- it may take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours

14-Day Course of Treatment

- swallow 1 capsule with a glass of water before eating in the morning
- take every day for 14 days
- do not take more than 1 capsule a day
- swallow whole. Do not crush or chew capsules.
- do not use for more than 14 days unless directed by your doctor

Repeated 14-Day Courses (if needed)

- you may repeat a 14-day course every 4 months
- **do not take for more than 14 days or more often than every 4 months unless directed by a doctor**
- children under 18 years of age: ask a doctor before use. Heartburn in children may sometimes be caused by a serious condition.

Labeling Format Information:

Fonts: Helvetica, Helvetica Narrow, bold, bold oblique			
Drug Facts:	10 pt	Leading:	6.5 pt
Headings:	8 pt	Solid Circle Bullets:	6 pt
Subheader:	7 pt	Barline:	1 pt
Body Text:	6 pt	Hairline:	0.5 pt
Drug Facts (continued):	9 pt		

Lansoprazole Delayed-Release Capsules USP, 15 mg
Revised Proposed - 28 Capsules Bottle Carton

Actual size: 125 mm x 42 mm x 80 mm

Drug Facts (continued)

Other information

- read the directions, warnings and package insert before use
- keep the carton and package insert. They contain important information.
- store at 20°-25°C (68°-77°F)
- keep product out of high heat and humidity
- protect product from moisture

Inactive ingredients

colloidal silicon dioxide, D & C Red No. 33, D & C Yellow No. 10, FD & C Blue No. 1, FD & C Red No. 40, gelatin, hypromellose, magnesium carbonate, methacrylic acid copolymer dispersion, polyethylene glycol, polysorbate 80, sucrose, sugar spheres, talc, titanium dioxide

Questions or comments?

Call **1-800-346-6854**

Poison Control Center :

Call **1 800 222 1222**

3 64679 14009 3

NDC 64679-140-09

Lansoprazole Delayed-Release Capsules, USP

15 mg *Acid Reducer*

- **May take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours**
- **Clinically Proven To Treat Frequent Heartburn**

42 CAPSULES

Three 14 Day Courses of Treatment

WOCKHARDT

Sodium Free

Manufactured by:
Wockhardt Limited,
Mumbai, India.

Iss.190412

Distributed by:
Wockhardt USA LLC.
20 Waterview Blvd.
Parsippany, NJ 07054
USA.

LOT:

EXP.

NON VARNISH AREA
Actual size: 42 mm x 11 mm

3 BOTTLES INSIDE

42 CAPSULES TOTAL

Lansoprazole Delayed-Release Capsules, USP

15 mg *Acid Reducer*

KEEP THE CARTON AND PACKAGE INSERT. THEY CONTAIN IMPORTANT INFORMATION.

TAMPER-EVIDENT BOTTLE.
DO NOT USE IF INNER FOIL SEAL IMPRINTED WITH "SEALED for YOUR PROTECTION" OR DARK BLUE TO BLACK GELATIN BAND AROUND THE CENTER OF EACH CAPSULE IS MISSING OR BROKEN.

3 BOTTLES INSIDE

Lansoprazole Delayed-Release Capsules, USP

15 mg *Acid Reducer*

Drug Facts

Active ingredient (in each capsule) ***Purpose***

Lansoprazole 15 mg.....Acid reducer

Use

- treats frequent heartburn (occurs **2 or more** days a week)
- not intended for immediate relief of heartburn; this drug may take 1 to 4 days for full effect

Warnings

Allergy alert: Do not use if you are allergic to lansoprazole

Do not use

- if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor.

Ask a doctor before use if you have

- liver disease
- had heartburn over 3 months. This may be a sign of a more serious condition.
- heartburn with **lightheadedness, sweating or dizziness**
- chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent **chest pain**
- frequent wheezing, particularly with heartburn
- unexplained weight loss
- nausea or vomiting
- stomach pain

Ask a doctor or pharmacist before use if you are taking

- warfarin (blood-thinning medicine)
- prescription antifungal or anti-yeast medicines
- digoxin (heart medicine)

Drug Facts (continued)

- theophylline (asthma medicine)
- tacrolimus (immune system medicine)
- atazanavir (medicine for HIV infection)

Stop use and ask a doctor if

- your heartburn continues or worsens
- you need to take this product for more than 14 days
- you need to take more than 1 course of treatment every 4 months

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions

- adults 18 years of age and older
- this product is to be used once a day (every 24 hours), every day for 14 days
- it may take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours

14-Day Course of Treatment

- swallow 1 capsule with a glass of water before eating in the morning
- take every day for 14 days
- do not take more than 1 capsule a day
- swallow whole. Do not crush or chew capsules.
- do not use for more than 14 days unless directed by your doctor

Repeated 14-Day Courses (if needed)

- you may repeat a 14-day course every 4 months
- **do not take for more than 14 days or more often than every 4 months unless directed by a doctor**
- children under 18 years of age: ask a doctor before use. Heartburn in children may sometimes be caused by a serious condition.

Labeling Format Information:

Fonts: Helvetica, Helvetica Narrow, bold, bold oblique

Drug Facts:	10 pt	Leading:	6.5 pt
Headings:	8 pt	Solid Circle Bullets:	6 pt
Subheader:	7 pt	Barline:	1 pt
Body Text:	6 pt	Hairline:	0.5 pt
Drug Facts (continued):	9 pt		

Lansoprazole Delayed-Release Capsules USP, 15 mg
Revised Proposed - 42 Capsules Bottle Carton

Lansoprazole Delayed-Release Capsules USP, 15 mg

Revised Proposed - 14 Capsules Container Label

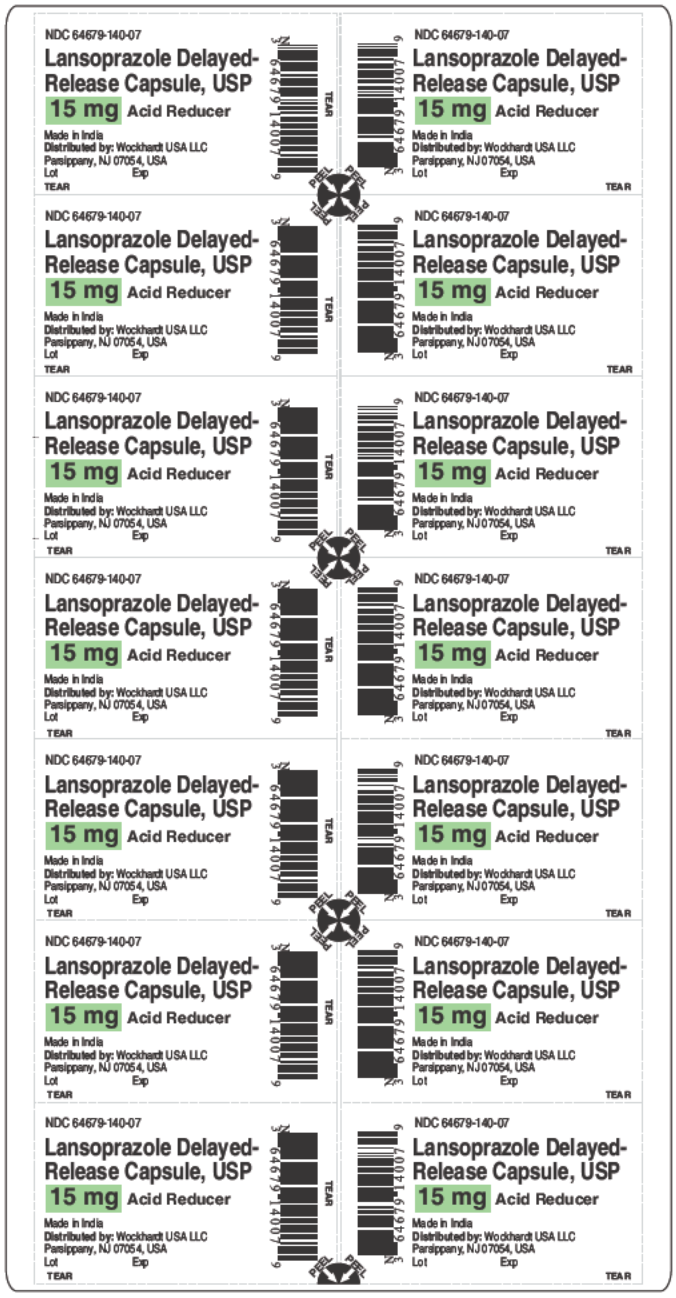
Front Panel

Back Panel

Labeling Format Information:	
Fonts: Helvetica Narrow and bold	
Headings:	8 pt
Subheader:	6 pt
Body Text:	6 pt
Leading:	5 pt
Solid Circle Bullets:	6 pt

Lansoprazole Delayed-Release Capsules USP, 15 mg

Revised Proposed - 14 Capsules Unit Dose Blister



Actual size: 88 mm x 170 mm

Lansoprazole Delayed-Release Capsules USP, 15 mg
Revised Proposed - 14 Capsules Unit Dose Carton

Drug Facts

Active ingredient (in each capsule) — **Purpose**
Lansoprazole 15 mg — Acid reducer

Use
- treats frequent heartburn (occurs 2 or more days a week)
- not intended for immediate relief of heartburn; this drug may take 1 to 4 days for full effect

Warnings
Allergy alert: Do not use if you are allergic to lansoprazole

Do not use
- if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor.

Ask a doctor before use if you have
- liver disease
- had heartburn over 3 months. This may be a sign of a more serious condition.
- heartburn with lightheadedness, sweating or dizziness
- chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent chest pain
- frequent wheezing, particularly with heartburn
- unexplained weight loss
- nausea or vomiting
- stomach pain

Ask a doctor or pharmacist before use if you are taking
- warfarin (blood-thinning medicine)
- prescription antifungal or anti-yeast medicines
- digoxin (heart medicine)
- theophylline (asthma medicine)
- tacrolimus (immune system medicine)
- atazanavir (medicine for HIV infection)

Stop use and ask a doctor if
- your heartburn continues or worsens
- you need to take this product for more than 14 days
- you need to take more than 1 course of treatment every 4 months

Drug Facts (continued)

If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions
- adults 18 years of age and older
- this product is to be used once a day (every 24 hours), every day for 14 days
- it may take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours

14-Day Course of Treatment
- swallow 1 capsule with a glass of water before eating in the morning
- take every day for 14 days
- do not take more than 1 capsule a day
- swallow whole. Do not crush or chew capsules.
- do not use for more than 14 days unless directed by your doctor

Repeated 14-Day Courses (if needed)
- you may repeat a 14-day course every 4 months
- do not take for more than 14 days or more often than every 4 months unless directed by a doctor
- children under 18 years of age: ask a doctor before use. Heartburn in children may sometimes be caused by a serious condition.

Other information
- read the directions, warnings and package insert before use
- keep the carton and package insert. They contain important information.
- store at 20°-25°C (68°-77°F)
- keep product out of high heat and humidity
- protect product from moisture

Inactive ingredients
colloidal silicon dioxide, D & C Red No. 33, D & C Yellow No. 10, FD & C Blue No. 1, FD & C Red No. 40, gelatin, hypromellose, magnesium carbonate, methacrylic acid copolymer dispersion, polyethylene glycol, polysorbate 80, sucrose, sugar spheres, talc, titanium dioxide

Questions or comments? Call 1-800-346-6854
Poison Control Center : Call 1-800-222-1222

3 64679 14007 9

Non Varnish Area

Lot Exp

KEEP THE CARTON AND PACKAGE INSERT. THEY CONTAIN IMPORTANT INFORMATION.

DO NOT USE IF INDIVIDUAL BLISTER UNIT IS TORN OR OPEN OR DARK BLUE TO BLACK GELATIN BAND AROUND THE CENTER OF EACH CAPSULE IS MISSING OR BROKEN.

Manufactured by
Wockhardt Limited, Mumbai, India.
Iss.190412

Distributed by:
Wockhardt USA LLC.
20 Waterview Blvd, Parsippany, NJ 07054, USA.

NDC 64679-140-07

Lansoprazole Delayed-Release Capsules, USP

15 mg *Acid Reducer*

- May take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours
- Clinically Proven To Treat Frequent Heartburn

Sodium Free

14 (1 x 14)
Unit-dose Capsules
One 14 Day Course of Treatment

WOCKHARDT

Size: 172 x 92 x 11 mm

Labeling Format Information:			
Fonts: Helvetica, Helvetica Narrow, bold, bold oblique			
Drug Facts:	10 pt	Leading:	6.5 pt
Headings:	8 pt	Solid Circle Bullets:	6 pt
Subheader:	7 pt	Barline:	1 pt
Body Text:	6 pt	Hairline:	0.5 pt
Drug Facts (continued):	10 pt		

Lansoprazole Delayed-Release Capsules USP, 15 mg
Revised Proposed - 28 Capsules Unit Dose Carton

Manufactured by:
Wockhardt Limited,
Mumbai, India.

Iss.190412

Distributed by:
Wockhardt USA LLC.
20 Waterview Blvd.
Parsippany, NJ 07054
USA.

N 3 64679 14010 9

Lot:
Exp.:

Non Varnish Area

Drug Facts

Active ingredient (in each capsule) — **Purpose**
Lansoprazole 15 mg ..... Acid reducer

Use
- treats frequent heartburn (occurs 2 or more days a week)
- not intended for immediate relief of heartburn; this drug may take 1 to 4 days for full effect

Warnings
Allergy alert: Do not use if you are allergic to lansoprazole

Do not use
- if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor.

Ask a doctor before use if you have
- liver disease
- had heartburn over 3 months. This may be a sign of a more serious condition.
- heartburn with **lightheadedness, sweating or dizziness**
- chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent **chest pain**
- frequent wheezing, particularly with heartburn
- unexplained weight loss
- nausea or vomiting
- stomach pain

Ask a doctor or pharmacist before use if you are taking
- warfarin (blood-thinning medicine)
- prescription antifungal or anti-yeast medicines
- digoxin (heart medicine)
- theophylline (asthma medicine)
- tacrolimus (immune system medicine)
- atazanavir (medicine for HIV infection)

Stop use and ask a doctor if
- your heartburn continues or worsens
- you need to take this product for more than 14 days
- you need to take more than 1 course of treatment every 4 months

Drug Facts (continued)

If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions
- adults 18 years of age and older
- this product is to be used once a day (every 24 hours), every day for 14 days
- it may take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours

14 Day Course of Treatment
- swallow 1 capsule with a glass of water before eating in the morning
- take every day for 14 days
- do not take more than 1 capsule a day
- swallow whole. Do not crush or chew capsules.
- do not use for more than 14 days unless directed by your doctor

Repeated 14 Day Courses (if needed)
- you may repeat a 14-day course every 4 months
- **do not take for more than 14 days or more often than every 4 months unless directed by a doctor**
- children under 18 years of age: ask a doctor before use. Heartburn in children may sometimes be caused by a serious condition.

Other information
- read the directions, warnings and package insert before use
- keep the carton and package insert. They contain important information.
- store at 20°-25°C (68°-77°F)
- keep product out of high heat and humidity
- protect product from moisture

Inactive ingredients
colloidal silicon dioxide, D & C Red No. 33, D & C Yellow No. 10, FD & C Blue No. 1, FD & C Red No. 40, gelatin, hypromellose, magnesium carbonate, methacrylic acid copolymer dispersion, polyethylene glycol, polysorbate 80, sucrose, sugar spheres, talc, titanium dioxide

Questions or comments? Call **1-800-346-6854**
Poison Control Center : Call **1-800-222-1222**

KEEP THE CARTON AND PACKAGE INSERT. THEY CONTAIN IMPORTANT INFORMATION.

DO NOT USE IF INDIVIDUAL BLISTER UNIT IS TORN OR OPEN OR DARK BLUE TO BLACK GELATIN BAND AROUND THE CENTER OF EACH CAPSULE IS MISSING OR BROKEN.

NDC 64679-140-10

Lansoprazole Delayed-Release Capsules, USP

15 mg *Acid Reducer*

- **May take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours**
- **Clinically Proven To Treat Frequent Heartburn**

Sodium Free

28 (2 x 14)
Unit-dose Capsules
Two 14 Day Course of Treatment

WOCKHARDT

Size: 172 x 92 x 22 mm

Labeling Format Information:			
Fonts: Helvetica, Helvetica Narrow, bold, bold oblique			
Drug Facts:	10 pt	Leading:	6.5 pt
Headings:	8 pt	Solid Circle Bullets:	6 pt
Subheader:	7 pt	Barline:	1 pt
Body Text:	6 pt	Hairline:	0.5 pt
Drug Facts (continued):	10 pt		

Lansoprazole Delayed-Release Capsules USP, 15 mg
Revised Proposed - 42 Capsules Unit Dose Carton

Manufactured by:
Wockhardt Limited,
Mumbai, India.

Iss.190412

Distributed by:
Wockhardt USA LLC.
20 Waterview Blvd.
Parsippany, NJ 07054
USA.

N 3 64679 14011 6

Lot:
Exp.:

Non Varnish Area

Drug Facts

Active ingredient (in each capsule) — **Purpose**
Lansoprazole 15 mg ..... Acid reducer

Use
- treats frequent heartburn (occurs 2 or more days a week)
- not intended for immediate relief of heartburn; this drug may take 1 to 4 days for full effect

Warnings
Allergy alert: Do not use if you are allergic to lansoprazole

Do not use
- if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor.

Ask a doctor before use if you have
- liver disease
- had heartburn over 3 months. This may be a sign of a more serious condition.
- heartburn with **lightheadedness, sweating or dizziness**
- chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent **chest pain**
- frequent wheezing, particularly with heartburn
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- nausea or vomiting
- stomach pain

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- warfarin (blood-thinning medicine)
- prescription antifungal or anti-yeast medicines
- digoxin (heart medicine)
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- atazanavir (medicine for HIV infection)

Stop use and ask a doctor if
- your heartburn continues or worsens
- you need to take this product for more than 14 days
- you need to take more than 1 course of treatment every 4 months

Drug Facts (continued)

If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions
- adults 18 years of age and older
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14 Day Course of Treatment
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Other information
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- protect product from moisture

Inactive ingredients
colloidal silicon dioxide, D & C Red No. 33, D & C Yellow No. 10, FD & C Blue No. 1, FD & C Red No. 40, gelatin, hypromellose, magnesium carbonate, methacrylic acid copolymer dispersion, polyethylene glycol, polysorbate 80, sucrose, sugar spheres, talc, titanium dioxide

Questions or comments? Call **1-800-346-6854**
Poison Control Center : Call **1-800-222-1222**

KEEP THE CARTON AND PACKAGE INSERT. THEY CONTAIN IMPORTANT INFORMATION.	DO NOT USE IF INDIVIDUAL BLISTER UNIT IS TORN OR OPEN OR DARK BLUE TO BLACK GELATIN BAND AROUND THE CENTER OF EACH CAPSULE IS MISSING OR BROKEN.

NDC 64679-140-11

Lansoprazole Delayed-Release Capsules, USP

15 mg *Acid Reducer*

- **May take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours**
- **Clinically Proven To Treat Frequent Heartburn**

Sodium Free

42 (3 x 14)
Unit-dose Capsules
Three 14 Day Course of Treatment

WOCKHARDT

Size: 172 x 92 x 33 mm

Labeling Format Information:			
Fonts: Helvetica, Helvetica Narrow, bold, bold oblique			
Drug Facts:	10 pt	Leading:	6.5 pt
Headings:	8 pt	Solid Circle Bullets:	6 pt
Subheader:	7 pt	Barline:	1 pt
Body Text:	6 pt	Hairline:	0.5 pt
Drug Facts (continued):	10 pt		

Lansoprazole Delayed-Release Capsules USP, 15 mg

- **May take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours**

Please read the entire package insert before taking lansoprazole delayed-release capsules, Save for future reference.

How Lansoprazole Delayed-Release Capsules Treats Your Frequent Heartburn

Lansoprazole delayed-release capsules stops acid production at the source – the **pumps** that release acid into the stomach. Lansoprazole delayed-release capsule is taken once a day (every 24 hours), every day for 14 days.

What You Can Expect When Taking Lansoprazole Delayed-Release Capsules

Frequent heartburn can occur anytime during the 24-hour period (day or night). Take lansoprazole delayed-release capsules in the morning before eating. Lansoprazole delayed-release capsule is clinically proven to treat frequent heartburn. Although some people get complete relief of symptoms within 24 hours, it may take 1 to 4 days for full effect. Make sure you take lansoprazole delayed-release capsule every day for 14 days to treat your frequent heartburn.

Who Should Take Lansoprazole Delayed-Release Capsules

Adults (18 years and older) with **frequent heartburn** – when you have heartburn 2 or more days a week.

Who Should NOT Take Lansoprazole Delayed-Release Capsules

People who have one episode of heartburn a week or less, or who want immediate relief of heartburn.

How to Take Lansoprazole Delayed-Release Capsules 14-DAY Course of Treatment

- Swallow 1 capsule with a glass of water before eating in the morning.
- Take every day for 14 days.
- Do not take more than 1 capsule a day.
- Do not use for more than 14 days unless directed by your doctor.

When to Take Lansoprazole Delayed-Release Capsules Again

You may repeat a 14-day course of therapy every 4 months.

When to Talk to Your Doctor

Do not take for more than 14 days or more often than every 4 months unless directed by a doctor.

Warnings and When to Ask Your Doctor

Allergy alert: Do not use if you are allergic to lansoprazole

Do not use

- If you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor.

Ask a doctor before use if you have

- liver disease
- had heartburn over 3 months. This may be a sign of a more serious condition.
- heartburn with **lightheadedness, sweating or dizziness**
- chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent **chest pain**
- frequent wheezing, particularly with heartburn
- unexplained weight loss
- nausea or vomiting
- stomach pain

Ask a doctor or pharmacist before use if you are taking

- warfarin (blood-thinning medicine)
- prescription antifungal or anti-yeast medicines
- digoxin (heart medicine)

- theophylline (asthma medicine)
- tacrolimus (immune system medicine)
- atazanavir (medicine for HIV infection)

Stop use and ask a doctor if

- your heartburn continues or worsens
- you need to take this product for more than 14 days
- you need to take more than 1 course of treatment every 4 months

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach children. In case of overdose, get medical help or contact a Poison Control Center right away.

Tips for Managing Heartburn

- Avoid foods or drinks that are more likely to cause heartburn, such as rich, spicy, fatty and fried foods, chocolate, caffeine, alcohol and even some acidic fruits and vegetables.
- Eat slowly and do not eat big meals.
- Do not eat late at night or just before bedtime.
- Do not lie flat or bend over soon after eating.
- Raise the head of your bed.
- Wear loose-fitting clothing around your stomach.
- If you are overweight, lose weight.
- If you smoke, quit smoking.

Clinical studies prove Lansoprazole Delayed-Release Capsule effectively treats frequent heartburn

In three clinical studies, lansoprazole delayed-release capsule was shown to be significantly better than placebo in treating frequent heartburn.

How Lansoprazole Delayed-Release Capsule is Sold

Lansoprazole delayed-release capsule is available in 14 (1 x 14) capsules, 28 (2 x 14) capsule, (3 x 14) 42 capsule sizes and 14 capsules, 28 capsule, 42 capsule unit dose blisters. These sizes contain one, two and three 14-day courses of treatment, respectively. Do not use for more than 14 days in a row unless directed by your doctor. For the 28 count (two 14-day courses) and the 42 count (three 14-day courses), you may repeat a 14-day course every 4 months.

For Questions or Comments About Lansoprazole Delayed-Release Capsules

Call 1-800-346-6854

Poison Control Center: Call 1-800-222-1222

Manufactured by:
Wockhardt Limited
Mumbai, India.

Distributed by:
Wockhardt USA LLC.
20 Waterview Blvd.
Parsippany, NJ 07054
USA.

Iss.130212

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202727

LABELING REVIEWS

(APPROVAL SUMMARY)
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 202727 Date of Submission: April 20, 2012

Applicant's Name: Wockhardt Limited

Established Name: Lansoprazole Delayed-Release Capsules USP, 15 mg (OTC)

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

REMS Check Boxes
RISK EVALUATION AND MITIGATIONSTRATEGY

REMS required? No

MedGuides and/or PPIs (505-1(e)) ☐ Yes ☒ No

Communication plan (505-1(e)) ☐ Yes ☒ No

Elements to assure safe use (ETASU) (505-1(f)(3)) ☐ Yes ☒ No

Implementation system if certain ETASU (505-1(f)(4)) ☐ Yes ☒ No

Timetable for assessment (505-1(d)) ☐ Yes ☒ No

ANDA REMS acceptable?
☐ Yes ☐ No ☒ n/a

	FPL	DATE SUBMITTED	RECOOMENDATION
CONTAINER – 14s	yes	4/20/2012	AC FOR AP
CARTON – 1 x 14	yes	4/20/2012	
CARTON –2 x 14, & 3 x 14	yes	4/20/2012	AC FOR AP
BLISTER – 14s	yes	4/20/2012	AC FOR AP
BLISTER CARTON – 1 x14, 2 x 14, & 3 x 14	yes	4/20/2012	AC FOR AP
INSERT	yes	4/20/2012	AC FOR AP
SPL		4/20/2012	AC FOR AP

NOTE/QUESTION TO CHEMIST:

From: Park, Chan H
Sent: **Friday, April 13, 2012 3:27 PM**
To: Maldonado, Damaris
Cc: Park, Chan H
Subject: ANDA 202727 (Lansoprazole D-R Capsules, 15 mg (OTC)
Importance: High

Hi Damaris,

This is FYI. I am forwarding the following comments to the sponsor in response to their labeling amendment of 2/21/2012. Thanks,

Chan

1. We acknowledge that you are withdrawing the packaging of [redacted] (b) (4), and instead you are proposing packaging for the 14 days, 28 days and 42 days regimen in both bottle and blister packaging.

2. We acknowledge that your blister packaging is not child-resistant. Please be advised that OTC drug products that used to be available by prescription only must all have child-resistant closure per 16 CFR 1700.14(a)(30). We ask you that you revise your blister packaging accordingly and submit all related CMC information as an amendment or you withdraw your proposal for the blister packaging. Please respond.

From: Park, Chan H
Sent: **Tuesday, May 01, 2012 2:00 PM**
To: Maldonado, Damaris
Cc: Park, Chan H
Subject: ANDA 202727 (Lansoprazole Capsules, OTC)
Importance: High

Hi Damaris,

This is to inform you that the sponsor submitted CMC information regarding child-resistant blister packaging in the amendment of 4/20/2012. The submission was made in response to the labeling deficiency in which we asked the sponsor to employ the CRC for blister packaging **as required by the regulation**. I would appreciate your attention to this matter. Thanks,

Chan

FOR THE RECORD:

1. MODEL LABELING – Prevacid® 24 hours Capsules (NDA 022327/S-017), approved 10/31/2011. The approval letter, not the labeling, was posted for the S-019 (approved 4/23/2012) at the FDA website. The approval was for the addition of an instant redeemable coupon (IRC).
   As for the PI, the Prevacid® 24 Hours, which was last approved on 4/19/2011 (NDA 22327/S-013), was used for review.

2. Prevacid® 24 Hours Capsules is available for both Rx (NDA 020406) and OTC (NDA 022327). However, these two drug products have different indications.

3. This drug product is the subject of a USP monograph. There is no new information posted in the PF as of the 4/13/2012.

4. The listing of inactive ingredients in the DESCRIPTION section of the carton appears to be consistent with the listing of inactive ingredients found in the statement of composition in the CMC section.

LANSOPRAZOLE DELAYED RELEASE CAPSULES, USP 15mg (OTC)

S.No.	Ingredients	Reference	Function
[redacted] (b) (4)			

Following this page, 1 Page Withheld in Full as (b)(4)

SHADE & COMPOSITION APPROVAL OF HARD GELATIN CAPSULE SHELL

Colour Shade Ref.No	(b) (4)	Size of the Capsule	3
CAP		**BODY**	
Colour Description	OP DK PINK	Colour Description	OP GREEN
Average Weight	(b) (4)	Average Weight	(b) (4)
SAP Colour Code		SAP Colour Code	

Colourants	E.No	%	mg	Colourants	E.No	%	mg
(b) (4)							

5. PATENTS/EXCLUSIVITIES

There are no unexpired patents for this product in the Orange Book Database.

Exclusivity Data

Appl No	Prod No	Exclusivity Code	Exclusivity Expiration	Labeling Impact
N022327	001	NP	May 18, 2012	None

6. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON RLD

RLD - Store at 20 to 25°C (68 to 77°F).

ANDA: Store at 20 to 25°C (68 to 77°F). [see USP Controlled Room Temperature]

USP - Preserve in tight containers, and store at controlled room temperature.

7. PACKAGING CONFIGURATIONS

RLD – Bottle of 1 x 14, 2 x 14, and 3x 14
ANDA – Bottle of 1 x 14, 2 x 14, and 3x 14
Blister – 14 (1 x 14), (b) (4) (2 x 14), and 42 (3 x 14) Unit-dose Capsules

The sponsor added bottle of 14s in the CMC amendment of 12/30/2011. In addition, the sponsor added a "Dark Blue to Black Band" to the center of the capsule in the amendment of 12/30/2011.

*** The container/closure system employs a tamper-evident printed seal printed with SEALED for YOUR PROTECTION". See below:

*** The sponsor revised the blister to be CRC as required and submitted related CMC information in the amendment of 4/20/2012. It was notified to the chemist. See NOTE/QUESTIONS TO CHEMIST above.

8. The description of the capsules from the CMC information:

Opaque dark pink cap and opaque dark green body, size '3' empty hard gelatin capsules imprinted with W on cap with 140 black ink and containing dark blue to black gelatin band around the centre of capsule. The capsules are filled with white to off white pellets

***The sponsor submitted revised CMC information on 12/30/2011 reflecting the inclusion of dark blue to black band around the center of the capsules .

***This drug product meets the requirement for the tamper-evident band for the hard gelatin capsules per 21 CFR 211.132.

*** The pictorial of the capsule on the container and carton reflects the actual description of the finished drug product.

9. CONTAINER/CLOSURE

S.NO.	PACKAGING COMPONENTS	MANUFACTURER/SUPPLIER
	14's Count Bottle Pack	
	(b) (4)	
	Unit dose Blister Pack -	
	(b) (4)	

10. Manufacturer

Wockhardt Limited
L1, M.I.D.C. Area, Jalgaon Road Chikalthana, Aurangabad Maharashtra - 431 210
INDIA.

11. Font size of the Container, Carton and PI for OTC:

21 CFR 201.66 states as follows: The term

"Drug Facts" – 8 pts.
Questions and Comments with a phone Number – 6 pts
Text – 6 pts
Bullet Point Statement – 5 pts.

ANDA – The sponsor's proposed font size meets the requirements of 21 CFR 201.66.

Labeling Format Information:			
Fonts: Helvetica, Helvetica Narrow, bold, bold oblique			
Drug Facts:	10 pt	Leading:	6.5 pt
Headings:	8 pt	Solid Circle Bullets:	6 pt
Subheader:	6 pt	Barline:	1 pt
Body Text:	6 pt	Hairline:	0.5 pt
Drug Facts (continued):	10 pt		

12. The font size of the final printed INSERT is 10 pts.

13. MedWatch – checked 5/2/2012:

Current Safety Information

- FDA Drug Safety Communication: Clostridum difficile - associated diarrhea can be associated with stomach acid drugs known as proton pump inhibitors (PPIs)[1]
  2/8/2012

- FDA Drug Safety Podcast for Healthcare Professionals: *Clostridium difficile*-associated diarrhea can be associated with stomach acid drugs known as proton pump inhibitors (PPIs)[2]
  2/8/2012

Date of Review: 5/2/2012 **Date of Submission: 4/20/2012**

Primary Reviewer: Chan Park

Team Leader: Koung Lee

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

CHAN H PARK
05/07/2012

KOUNG U LEE
05/08/2012
For Wm. Peter Rickman

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 202727 Date of Submission: February 21, 2012

Applicant's Name: Wockhardt Limited

Established Name: Lansoprazole Delayed-Release Capsules USP, 15 mg

Labeling Deficiencies:

1. GENERAL COMMENT

   We acknowledge that you are withdrawing the packaging of (b) (4) (b) (4), and instead you are proposing packaging for the 14days, 28 days and 42 days regimen in both bottle and blister packaging.

2. CONTAINER – 14s

   Satisfactory in FPL as of the 2/21/2012 submission

3. CARTON – 1 x 14s, 2 x 14s, and 3 x 14s ,

   We note that you included the following (b) (4) statement on the carton for the 2 bottles and 3 bottles. Please delete this and/or comment.

   (b) (4)

4. BLISTER CARD – (b) (4) and 14s

   a. If space permits, we recommend that you include the test “Made in India”.

   b. We acknowledge that your blister packaging is not child-resistant. Please be advised that OTC products that used to be available by prescription only must all have child-resistant closure per 16 CFR 1700.14(a)(30). We ask you that you revise your blister packaging accordingly and submit all related CMC information as an amendment or you withdraw your proposal for the blister packaging. Please respond.

5. BLISTER CARTON – 14 (1 x 14), 28 (2 x 14), and 42 (3 x 14) Unit-dose Capsules

   a. Delete the statement (b) (4) (b) (4)

   b. See comment 4(b) above.

6. INSERT – How Lansoprazole Delayed-Release Capsules is Sold:

   See comment 4(b) above.

Revise the labeling as described above and submit final printed labeling electronically. Please provide the labeling in the Structured Product Labeling (SPL) as well as pdf. format.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -

http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

To facilitate review of your next submission please provide a side-by-side comparison of your proposed labeling with your last labeling submission with all differences annotated and explained.

If you have any questions, please call Chan Park at 240-276-8951 or send e-mail to chan.park@fda.hhs.gov

{See appended electronic signature page}

_____

William Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

NOTE/QUESTION TO CHEMIST:

_____

From: Park, Chan H
Sent: Friday, April 13, 2012 3:27 PM
To: Maldonado, Damaris
Cc: Park, Chan H
Subject: ANDA 202727 (Lansoprazole D-R Capsules, 15 mg (OTC)
Importance: High

Hi Damaris,

This is FYI. I am forwarding the following comments to the sponsor in response to their labeling amendment of 2/21/2012. Thanks,

Chan

1. We acknowledge that you are withdrawing the packaging of (b) (4) (b) (4), and instead you are proposing packaging for the 14 days, 28 days and 42 days regimen in both bottle and blister packaging.

2. We acknowledge that your blister packaging is not child-resistant. Please be advised that OTC drug products that used to be available by prescription only must all have child-resistant closure per 16 CFR 1700.14(a)(30). We ask you that you revise your blister packaging accordingly and submit all related CMC information as an amendment or you withdraw your proposal for the blister packaging. Please respond.

FOR THE RECORD:

1. MODEL LABELING – Prevacid® 24 hours Capsules (NDA 022327/S-017), approved 10/31/2011. As for the PI, the Prevacid® 24 Hours, which was last approved on 4/19/2011 (NDA 22327/S-013), was used for review.

2. Prevacid® 24 Hours Capsules is available for both Rx (NDA 020406) and OTC (NDA 022327). However, these two drug products have different indications.

3. This drug product is the subject of a USP monograph. There is no new information posted in the PF as of the 4/13/2012.

4. The listing of inactive ingredients in the DESCRIPTION section of the carton appears to be consistent with the listing of inactive ingredients found in the statement of composition in the CMC section.

LANSOPRAZOLE DELAYED RELEASE CAPSULES, USP 15mg (OTC)

S.No.	Ingredients	Reference	Function

(b) (4)

SHADE & COMPOSITION APPROVAL OF HARD GELATIN CAPSULE SHELL

Colour Shade Ref.No	(b) (4)			Size of the Capsule	3		
CAP				**BODY**			
Colour Description	OP DK PINK			Colour Description	OP GREEN		
Average Weight	(b) (4)			Average Weight	(b) (4)		
SAP Colour Code				SAP Colour Code			
Colourants	E.No	%	mg	Colourants	E.No	%	mg
(b) (4)							

5. PATENTS/EXCLUSIVITIES

There are no unexpired patents for this product in the Orange Book Database.

Exclusivity Data

Appl No	Prod No	Exclusivity Code	Exclusivity Expiration	Labeling Impact
N022327	001	NP	May 18, 2012	None

6. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

RLD - Store at 20 to 25°C (68 to 77°F).

ANDA: Store at 20 to 25°C (68 to 77°F). [see USP Controlled Room Temperature]

USP - Preserve in tight containers, and store at controlled room temperature.

7. PACKAGING CONFIGURATIONS

RLD – Bottle of 1 x 14, 2 x 14, and 3x 14
ANDA – Bottle of 1 x 14, 2 x 14, and 3x 14
Blister – 14 (1 x 14), (b) (4) (2 x 14), and 42 (3 x 14) Unit-dose Capsules

The sponsor added bottle of 14s in the CMC amendment of 12/30/2011. In addition, the sponsor added a "Dark Blue to Black Band" to the center of the capsule in the amendment of 12/30/2011.

*** The container/closure system employs a tamper-evident printed seal printed with SEALED for YOUR PROTECTION". See below:

8. The description of the capsules from the CMC information:

Opaque dark pink cap and opaque dark green body, size '3' empty hard gelatin capsules imprinted with W on cap with 140 black ink and containing dark blue to black gelatin band around the centre of capsule. The capsules are filled with white to off white pellets

***The sponsor submitted revised CMC information on 12/30/2011 reflecting the inclusion of dark blue to black band around the center of the capsules .

***This drug product meets the requirement for the tamper-evident band for the hard gelatin capsules per 21 CFR 211.132.

*** The pictorial of the capsule on the container and carton reflects the actual description of the finished drug product.

9. CONTAINER/CLOSURE

S.NO.	PACKAGING COMPONENTS	MANUFACTURER/SUPPLIER
	14's Count Bottle Pack	
	(b) (4)	
	Unit dose Blister Pack -	
	(b) (4)	

10. Manufacturer

Wockhardt Limited
L1, M.I.D.C. Area, Jalgaon Road Chikalthana, Aurangabad Maharashtra - 431 210 INDIA.

11. Font size of the Container, Carton and PI for OTC:

21 CFR 201.66 states as follows:

The term "Drug Facts" – 8 pts.
Questions and Comments with a phone Number – 6 pts

Text – 6 pts
Bullet Point Statement – 5 pts.

ANDA – The sponsor's proposed font size meets the requirements of 21 CFR 201.66.

Labeling Format Information:			
Fonts: Helvetica, Helvetica Narrow, bold, bold oblique			
Drug Facts:	10 pt	Leading:	6.5 pt
Headings:	8 pt	Solid Circle Bullets:	6 pt
Subheader:	6 pt	Barline:	1 pt
Body Text:	6 pt	Hairline:	0.5 pt
Drug Facts (continued):	10 pt		

12. The font size of the final printed INSERT is 10 pts.

13. MedWatch – checked 4/13/2012:

Current Safety Information

- FDA Drug Safety Communication: Clostridum difficile - associated diarrhea can be associated with stomach acid drugs known as proton pump inhibitors (PPIs)[1]
  2/8/2012

- FDA Drug Safety Podcast for Healthcare Professionals: *Clostridium difficile*-associated diarrhea can be associated with stomach acid drugs known as proton pump inhibitors (PPIs)[2]
  2/8/2012

Date of Review: 4 /13/2012 **Date of Submission: 2/21/2012**

Primary Reviewer: Chan Park **Date:**

Team Leader: Koung Lee **Date:**

C:\Documents and Settings\parkc\My Documents\202727.NA2.L.doc

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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

CHAN H PARK
04/16/2012

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 202727 Date of Submission: January 24, 2011 and January 5, 2012

Applicant's Name: Wockhardt Limited

Established Name: Lansoprazole Delayed-Release Capsules USP, 15 mg

Labeling Deficiencies:

1. CONTAINER – 14s, (b) (4)

   a. We believe that the term (b) (4) for the reference listed drug, Prevacid® 24 HR. Please delete this term from your labels.

   b. Please enhance the prominence the text “Delayed-Release Capsules, USP” to appear commensurate to the term “Lansoprazole” as “Delayed-Release Capsules”” is part of the established name for this drug product.

   c. It is preferable to relocate the boxed statement “DO NOT USE…MISSING OR BROKEN.” close to the principal display panel. We refer you to the Prevacid® 24HR label for guidance.

   d. Please confirm that your container/closure system employs a tamper-evident printed seal printed with SEALED for YOUR PROTECTION”.

   e. We note that you include a pictorial of your drug product. Please ensure that this pictorial reflects the accurate description of your drug product. Please revise and/or comment.

   f. Include the statement “one 14 Day Course of Treatment” in association with the net quantity statement for the bottle of 14s.

   g. Include the following boxed statement in proximity to the principal display panel:

IMPORTANT: THIS BOTTLE DOES NOT CONTAIN FULL PRODUCT INFORMATION. SEE CARTON FOR COMPLETE LABELING. READ ALL WARNINGS ON CARTON BEFORE USE. DO NOT DISCARD CARTON.

   h. The font sizes used for the label appear that they do not meet requirements stipulated in 21 CFR 201.66. Please ensure that the font size on all labeling piece meet the requirement. Please revise accordingly and/or comment.

   i. (b) (4)

   j.

(b) (4)

2. CARTON – 1 x 14s and (b) (4)

   a. See comments under CONTAINER, whichever applicable.

   b. You listed “D & C Red. No. 33” and “D & C Yellow No. 10” as inactive ingredients contained in your drug product while these are not found in the Description and Composition of the Drug Product section in the CMC. Please delete these and/or comment.

   c. We recommend that you include the phone number of the Poison Control Center.

3. BLISTER CARD – (b) (4) and 14s

   a. See comment 1(a) above.

   b. The Poison Prevention Packaging Act notes that special packaging (child-resistant closures) should be the responsibility of the manufacturer when the container is clearly intended to be utilized in dispensing (unit-of-use packaging). We believe that this packaging should comply with the Act. Please confirm that your blister packaging is child-resistant and/or comment.

   c. Please ensure that the strength appears sufficiently prominent with sufficient background color contrast.

4. BLISTER CARTON – 14 (1 x 14) and (b) (4) Unit-dose Capsules

   a. See comments under CARTON, whichever applicable.

   b. Please refer to the comment 1(i) above. As this drug product has 14 day course of treatment, please explain the rational for proposing (b) (4). It would be desirable to propose 14s, 28s, or 42s blister tablets. Please revise the packaging configuration and/or comment.

5. INSERT

   a. It appears that the labeling you submitted may not be a final printed labeling (FPL). Please submit the FPL in artwork and/or comment.

   b. See comment 1(a) above.

   c. Please include the strength “15 mg” in association with the drug product name.

   d. Please delete the (b) (4) as it is not appearing in the updated labeling for the “Prevacid 24 Capsules.

   e. We recommend that you include the phone number for the Poison Control Center.

   e. Please delete a reference to the (b) (4) (b) (4) and/or comment.

Revise the labeling as described above and submit final printed labeling electronically. Please provide the labeling in the Structured Product Labeling (SPL) as well as pdf. format.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

To facilitate review of your next submission please provide a side-by-side comparison of your proposed labeling with your last labeling submission with all differences annotated and explained.

If you have any questions, please call Chan Park at 240-276-8951 or send e-mail to chan.park@fda.hhs.gov

{See appended electronic signature page}

_____

William Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

FOR THE RECORD:

1. MODEL LABELING – Prevacid®24 hours Capsules (NDA 022327/S-017), approved 10/31/2011. As for the PI, the Prevacid®24 Hours, which was last approved on 4/19/2011 (NDA 22327/S-013), was used for review.

2. Prevacid® 24 Hours Capsules is available for both Rx (NDA 020406) and OTC (NDA 022327). However, these two drug products have different indications.

3. This drug product is the subject of a USP monograph.

4. The listing of inactive ingredients in the DESCRIPTION section of the carton appears to be consistent with the listing of inactive ingredients found in the statement of composition in the CMC section.

LANSOPRAZOLE DELAYED RELEASE CAPSULES, USP 15mg (OTC)

S.No.	Ingredients	Reference	Function
	(b) (4)		

5. PATENTS/EXCLUSIVITIES

There are no unexpired patents for this product in the Orange Book Database.

Exclusivity Data

Appl No	Prod No	Exclusivity Code	Exclusivity Expiration	Labeling Impact
N022327	001	NP	May 18, 2012	None

6. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

RLD - Store at 20 to 25^{O}C (68 to 77^{O}F).

ANDA: Store at 20 to 25^{O}C (68 to 77^{O}F). [see USP Controlled Room Temperature]

USP - Preserve in tight containers, and store at controlled room temperature.

7. PACKAGING CONFIGURATIONS

RLD – Bottle of14s, 28s, and 48s

ANDA – Bottle of 14s, (b) (4)
Blister – 14 (1 x 14) and (b) (4) Unit-dose
Capsules

The sponsor added bottle of 14s in the CMC amendment of 12/30/2011. In addition, the sponsor added a “Dark Blue to Black Band” to the center of the capsule in the amendment of 12/30/2011.

8. The description of the capsules from the CMC information:

Opaque dark pink cap and opaque dark green body, size ‘3’ empty hard gelatin capsules imprinted with W on cap with 140 black ink and containing dark blue to black gelatin band around the centre of capsule. The capsules are filled with white to off white pellets

***The sponsor submitted revised CMC information on 12/30/2011 reflecting the inclusion of dark blue to black band around the center of the capsules .

***This drug product meets the requirement for the tamper-evident band for the hard gelatin

capsules per 21 CFR 211.132.

9. CONTAINER/CLOSURE

S.NO.	PACKAGING COMPONENTS	MANUFACTURER/SUPPLIER
14's Count Bottle Pack		
(b) (4)		

S.NO.	PACKAGING COMPONENTS	MANUFACTURER/SUPPLIER
(b) (4)		
Unit dose Blister Pack		
(b) (4)		

10. Manufacturer

Wockhardt Limited
L1, M.I.D.C. Area, Jalgaon Road Chikalthana, Aurangabad Maharashtra - 431 210 INDIA.

11. Font size of the Container, Carton and PI for OTC:

21 CFR 201.66 states as follows:

The term “Drug Facts” – 8 pts.
Questions and Comments with a phone Number – 6 pts
Text – 6 pts
Bullet Point Statement – 5 pts.

ANDA
See comment 1(h) above.

Date of Review: 2/7/2012 **Date of Submission: 1/24/2011 and 1/5/2012**

Primary Reviewer: Chan Park **Date:**

Team Leader: Koung Lee **Date:**

C:\Documents and Settings\parkc\My Documents\202727.NA1.L.doc

---

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

CHAN H PARK
02/07/2012

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202727

CHEMISTRY REVIEWS

ANDA 202-727

Lansoprazole Delayed-Release Capsules, USP
15 mg (OTC)

Wockhardt Limited

Damaris Maldonado
Chemistry Division II

Table of Contents

Chemistry Review Data Sheet

1. ANDA: 202-727

2. REVIEW: # 3

3. REVIEW DATE: May 8, 2012.

4. REVIEWER: Damaris Maldonado

5. PREVIOUS DOCUMENTS:

Acknowledgement letter	5/12/2011
Original	1/26/2011
Amendment	4/14/2011
Amendment	4/28/2011
Major Amendment	12/30/2011

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Major Amendment	4/17/2012
CMC and Labeling Amendment	4/23/2012
Amendment	4/30/2012
Telephone Amendment	5/08/2012

7. NAME & ADDRESS OF APPLICANT:

Name:	Wockhardt Limited Wockhardt Towers Bandra-Kurla Complex Bandra (East), Mumbai - 400051
Address:	Maharashtra, India
Representative:	Ms. Leanne Usa Wockhardt USA LLC., 20 Waterview Blvd, 3rd floor, Parsippany, NJ 07054 Phone # 973-257-4998, Fax # 973-257-4999

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: NA

b) Non-Proprietary Name (USAN): Lansoprazole Delayed-Release Capsules, USP

9. LEGAL BASIS FOR SUBMISSION:
The basis for this ANDA submission is the RLD Prevacid® 24 hours (NDA 22-327) manufactured by Novartis.
Per electronic OB, there are no unexpired patents claimed for the drug product. There is an exclusivity NP listed for the drug product, which will expire on May 18, 2012. A statement is provided that Wockhardt Limited will not market their product until these exclusivities expire.

10. PHARMACOLOGICAL CATEGORY: Anti-ulcer.

11. DOSAGE FORM: Delayed-Release Capsules

12. STRENGTH/POTENCY: 15 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: ___ Rx __X__ OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____ SPOTS product – Form Completed

__X__ Not a SPOTS product

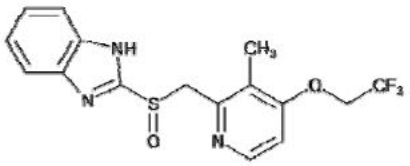
15b. NANOTECHNOLOGY PRODUCT TRACKING:
_____NANO product – Form Completed (See Appendix R.4)

__X__Not a NANO product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name(s): 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl] methyl] sulfinyl]-1H-Benzimidazole.
2-(2-Benzimidazolylsulfinylmethyl)-3-methyl-4-(2,2,2-trifluoroethoxy)pyridine.

Chemical Structure:



Molecular Formula: $C_{16}H_{14}F_3N_3O_2S$

Molecular Weight: 369.37

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
21605	II	Wockhardt	Lansoprazole	1	Adequate	May 8, 2012	Amendment reviewed

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or NA (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
ANDA & Review	ANDA 202-176	Prescription for 15 mg and 30 mg

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EES	Pending	10/31/2011	
Methods Validation	NA		
Labeling	Acceptable	5/8/2012	Chan Park
Bioequivalence	Acceptable	4/20/2012	Li Xia
EA	Categorical Exclusion		

Chemistry Review Data Sheet

Application:	ANDA202727/000	**Action Goal:**	
Stamp Date:	26-JAN-2011	**District Goal:**	26-JAN-2013
Regulatory:			
Applicant:	WOCKHARDT	**Brand Name:**	
	20 WATERVIEW BLVD 3RD FL	**Estab. Name:**	LANSOPRAZOLE
	PARSIPPANY, NJ 07054	**Generic Name:**	
Priority:		**Product Number; Dosage Form; Ingredient; Strengths**	
Org. Code:	600	001; CAPSULE, DELAYED ACTION; LANSOPRAZOLE; 15MG	
Application Comment:			

FDA Contacts:	L. PARK	Project Manager	(HFD-617)	2402768536
	B. WU	Team Leader	(HFD-640)	2402768437

Overall Recommendation: PENDING on 31-OCT-2011 by EES_PROD

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the order assigned by the Office according to patent expiration.

The Chemistry Review for ANDA 202-727

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Approvable based on the CMC review

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance, Lansoprazole is compendial. It is a white to brownish, odorless crystalline powder that is freely soluble in dimethylformamide and soluble in methanol. Stability and water solubility increase with pH. There are several reported polymorphs of lansoprazole. Wockhardt employs (b) (4)

The drug product, Lansoprazole Delayed-Release is compendial too. The process of drug manufacturing consists of

(b) (4)

B. Description of How the Drug Product is Intended to be Used

Directions

- adults 18 years of age and older
- this product is to be used once a day (every 24 hours), every day for 14 days
- it may take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours

14-Day Course of Treatment

- swallow 1 capsule with a glass of water before eating in the morning
- take every day for 14 days
- do not take more than 1 capsule a day
- swallow whole. Do not crush or chew capsules.
- do not use for more than 14 days unless directed by your doctor

Repeated 14-Day Courses (if needed)

- you may repeat a 14-day course every 4 months
- do not take for more than 14 days or more often than every 4 months unless directed by a doctor
- children under 18 years of age: ask a doctor before use. Heartburn in children may sometimes be caused by a serious condition.

C. Basis for Approvability or Not-Approval Recommendation

The firm addressed all deficiencies and comments.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

DAMARIS C MALDONADO
05/10/2012

BINGYUAN WU
05/10/2012
Acting TL

LINDA M PARK
05/10/2012

ANDA 202-727

Lansoprazole Delayed-Release Capsules, USP
15 mg (OTC)

Wockhardt Limited

Damaris Maldonado
Chemistry Division II

Table of Contents

Chemistry Review Data Sheet

1. ANDA 202-727

2. REVIEW: # 2

3. REVIEW DATE: March 30, 2012.

4. REVIEWER: Damaris Maldonado

5. PREVIOUS DOCUMENTS:

Acknowledgement letter	5/12/2011
Original	1/26/2011
Amendment	4/14/2011
Amendment	4/28/2011

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Major Amendment	12/30/2011

7. NAME & ADDRESS OF APPLICANT:

Name:	Wockhardt Limited Wockhardt Towers Bandra-Kurla Complex Bandra (East), Mumbai - 400051
Address:	Maharashtra, India
Representative:	Ms. Leanne Usa Wockhardt USA LLC., 20 Waterview Blvd, 3rd floor, Parsippany, NJ 07054 Phone # 973-257-4998, Fax # 973-257-4999

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: NA
b) Non-Proprietary Name (USAN): Lansoprazole Delayed-Release Capsules, USP

9. LEGAL BASIS FOR SUBMISSION:

The basis for this ANDA submission is the RLD Prevacid® 24 hours (NDA 22-327) manufactured by Novartis.
Per electronic OB, there are no unexpired patents claimed for the drug product. There is an exclusivity NP listed for the drug product, which will expire on May 28, 2012. A statement is provided that Wockhardt Limited will not market their product until these exclusivities expire.

10. PHARMACOLOGICAL CATEGORY: Anti-ulcer.

11. DOSAGE FORM: Delayed-Release Capsules

12. STRENGTH/POTENCY: 15 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: ____ Rx __X__ OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
____ SPOTS product – Form Completed

__X__ Not a SPOTS product

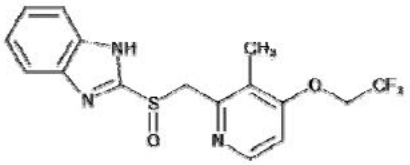
15b. NANOTECHNOLOGY PRODUCT TRACKING:
____NANO product – Form Completed (See Appendix R.4)

__X__Not a NANO product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name(s): 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl] methyl] sulfinyl]-1H-Benzimidazole.
2-(2-Benzimidazolylsulfinylmethyl)-3-methyl-4-(2,2,2-trifluoroethoxy)pyridine.

Chemical Structure:



Molecular Formula: $C_{16}H_{14}F_3N_3O_2S$
Molecular Weight: 369.37

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
21605	II	Wockhardt	Lansoprazole	1	Inadequate	4/5/2012	Amendment reviewed

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or NA (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
ANDA & Review	ANDA 202-176	Prescription for 15 mg and 30 mg

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EES	Pending	10/31/2011	
Methods Validation	NA		
Labeling	Deficient	2/22/2012	Chan Park
Bioequivalence	Pending		
EA	Categorical Exclusion		

Chemistry Review Data Sheet

Application:	ANDA202727/000	**Action Goal:**	
Stamp Date:	26-JAN-2011	**District Goal:**	26-JAN-2013
Regulatory:			
Applicant:	WOCKHARDT	**Brand Name:**	
	20 WATERVIEW BLVD 3RD FL	**Estab. Name:**	LANSOPRAZOLE
	PARSIPPANY, NJ 07054	**Generic Name:**	
Priority:		**Product Number; Dosage Form; Ingredient; Strengths**	
Org. Code:	600	001; CAPSULE, DELAYED ACTION; LANSOPRAZOLE; 15MG	
Application Comment:			

FDA Contacts:	L. PARK	Project Manager	(HFD-617)	2402768536
	B. WU	Team Leader	(HFD-640)	2402768437

Overall Recommendation: PENDING on 31-OCT-2011 by EES_PROD

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the order assigned by the Office according to patent expiration.

The Chemistry Review for ANDA 202-727

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Not Approvable

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance, Lansoprazole is compendial. It is a white to brownish, odorless crystalline powder that is freely soluble in dimethylformamide and soluble in methanol. Stability and water solubility increase with pH. There are several reported polymorphs of lansoprazole. Wockhardt employs (b) (4)

(b) (4)

B. Description of How the Drug Product is Intended to be Used

Lansoprazole delayed-release capsules are available in 15 mg and 30 mg strengths. Directions for use specific to the route and available methods of administration for each of these dosage forms is presented below. Lansoprazole delayed-release capsules should be taken before eating. Lansoprazole delayed-release capsules SHOULD NOT BE CRUSHED OR CHEWED. In the clinical trials, antacids were used concomitantly with lansoprazole.

2.1 Recommended Dose

Indication	Recommended Dose	Frequency
Duodenal Ulcers		
Short-Term Treatment	15 mg	Once daily for 4 weeks
Maintenance of Healed	15 mg	Once daily
H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence*		
Triple Therapy:		
Lansoprazole	30 mg	Twice daily (q12h) for 10 or 14 days

†Controlled studies did not extend beyond indicated duration.

‡For patients who do not heal with lansoprazole for 8 weeks (5 to 10%), it may be helpful to give an additional 8 weeks of treatment. If there is a recurrence of erosive esophagitis, an additional 8 week course of lansoprazole may be considered.

¶Varies with individual patient. Recommended adult starting dose is 60 mg once daily. Doses should be adjusted to individual patient needs and should continue for as long as clinically indicated. Dosages up to 90 mg twice daily have been administered. Daily dose of greater than 120 mg should be administered in divided doses. Some patients with Zollinger-Ellison Syndrome have been treated continuously with lansoprazole for more than 4 years.

Lansoprazole Delayed-Release Capsules – Nasogastric Tube (≥16 French) Administration

- For patients who have a nasogastric tube in place, Lansoprazole Delayed-Release Capsules can be administered as follows:
  - Open capsule.
  - Mix intact granules into 40 mL of apple juice. DO NOT USE OTHER LIQUIDS.
  - Inject through the nasogastric tube into the stomach.
  - Flush with additional apple juice to clear the tube.

C. Basis for Approvability or Not-Approval Recommendation

Not Approvable

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 202727 APPLICANT: Wockhardt Limited

DRUG PRODUCT: Lansoprazole Delayed-Release Capsules, USP, 15 mg (OTC)

The deficiencies presented below represent **MINOR** deficiencies.

A. Deficiencies:

1. (b) (4)
2.
3.
4.
5.
6.
7.
8.
9.

(b) (4)

10.

11.

12.

13.

14.

15.

16. Please provide updated stability results.

Sincerely yours,

{See appended electronic signature page}

Glen J. Smith
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

DAMARIS C MALDONADO
04/19/2012

BINGYUAN WU
04/19/2012
Acting TL

LINDA M PARK
04/19/2012

ANDA 202-727

Lansoprazole Delayed-Release Capsules, USP
15 mg (OTC)

Wockhardt Limited

Damaris Maldonado
Chemistry Division II

Table of Contents

Chemistry Review Data Sheet

1. ANDA 202-727

2. REVIEW: # 1

3. REVIEW DATE: July 9, 2011.

4. REVIEWER: Damaris Maldonado

5. PREVIOUS DOCUMENTS:

Acknowledgement letter	5/12/2011

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	1/26/2011
Amendment	4/14/2011
Amendment	4/28/2011

7. NAME & ADDRESS OF APPLICANT:

Name:	Wockhardt Limited Wockhardt Towers Bandra-Kurla Complex Bandra (East), Mumbai - 400051
Address:	Maharashtra, India
Representative:	Ms. Leanne Usa Wockhardt USA LLC., 20 Waterview Blvd, 3rd floor, Parsippany, NJ 07054 Phone # 973-257-4998, Fax # 973-257-4999

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: NA
b) Non-Proprietary Name (USAN): Lansoprazole Delayed-Release Capsules, USP

9. LEGAL BASIS FOR SUBMISSION:
The basis for this ANDA submission is the RLD Prevacid® 24 hours (NDA 22-327) manufactured by Novartis.

Per electronic OB, there are no unexpired patents claimed for the drug product. There is an exclusivity NP listed for the drug product, which will expire on May 28, 2012. A statement is provided that Wockhardt Limited will not market their product until these exclusivities expire.

10. PHARMACOLOGICAL CATEGORY: Anti-ulcer.

11. DOSAGE FORM: Delayed-Release Capsules

12. STRENGTH/POTENCY: 15 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: ____ Rx __X__ OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

____ SPOTS product – Form Completed

__X__ Not a SPOTS product

15b. NANOTECHNOLOGY PRODUCT TRACKING:

_____NANO product – Form Completed (See Appendix R.4)

__X__Not a NANO product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name(s): 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl] methyl] sulfinyl]-1H-Benzimidazole.
2-(2-Benzimidazolylsulfinylmethyl)-3-methyl-4-(2,2,2-trifluoroethoxy)pyridine.

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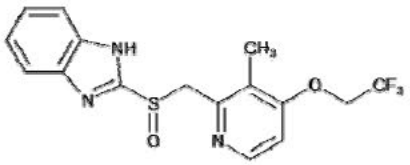

Molecular Formula: $C_{16}H_{14}F_3N_3O_2S$
Molecular Weight: 369.37

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
21605	II	Wockhardt	Lansoprazole	1	Inadequate	5/23/2011	Original

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or NA (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
ANDA & Review	ANDA 202-176	Prescription for 15 mg and 30 mg

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EES	Pending	4/25/2011	
Methods Validation	NA		
Labeling	Pending		
Bioequivalence	incomplete	9/10/2011	
EA	Categorical Exclusion		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of assignment to the reviewer.

The Chemistry Review for ANDA 202-727

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Not Approvable

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance, Lansoprazole is compendial. It is a white to brownish, odorless crystalline powder that is freely soluble in dimethylformamide and soluble in methanol. Stability and water solubility increase with pH. There are several reported polymorphs of lansoprazole. Wockhardt employs (b) (4)

The drug product, Lansoprazole Delayed-Release is compendial too. The process of drug manufacturing consists of

(b) (4)

B. Description of How the Drug Product is Intended to be Used

Lansoprazole delayed-release capsules are available in 15 mg and 30 mg strengths. Directions for use specific to the route and available methods of administration for each of these dosage forms is presented below. Lansoprazole delayed-release capsules should be taken before eating. Lansoprazole delayed-release capsules SHOULD NOT BE CRUSHED OR CHEWED. In the clinical trials, antacids were used concomitantly with lansoprazole.

2.1 Recommended Dose

Indication	Recommended Dose	Frequency
Duodenal Ulcers		
Short-Term Treatment	15 mg	Once daily for 4 weeks
Maintenance of Healed	15 mg	Once daily
H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence*		
Triple Therapy:		
Lansoprazole	30 mg	Twice daily (q12h) for 10 or 14 days

†Controlled studies did not extend beyond indicated duration.

‡For patients who do not heal with lansoprazole for 8 weeks (5 to 10%), it may be helpful to give an additional 8 weeks of treatment. If there is a recurrence of erosive esophagitis, an additional 8 week course of lansoprazole may be considered.

¶Varies with individual patient. Recommended adult starting dose is 60 mg once daily. Doses should be adjusted to individual patient needs and should continue for as long as clinically indicated. Dosages up to 90 mg twice daily have been administered. Daily dose of greater than 120 mg should be administered in divided doses. Some patients with Zollinger-Ellison Syndrome have been treated continuously with lansoprazole for more than 4 years.

Lansoprazole Delayed-Release Capsules – Nasogastric Tube (≥16 French) Administration

- For patients who have a nasogastric tube in place, Lansoprazole Delayed-Release Capsules can be administered as follows:
  - Open capsule.
  - Mix intact granules into 40 mL of apple juice. DO NOT USE OTHER LIQUIDS.
  - Inject through the nasogastric tube into the stomach.
  - Flush with additional apple juice to clear the tube.

C. Basis for Approvability or Not-Approval Recommendation

Not Approvable

Following this page, 54 Pages Withheld in Full as (b)(4)

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 202-727 APPLICANT: Wockhardt Limited

DRUG PRODUCT: Lansoprazole Delayed-Release Capsules, USP, 15 mg (OTC)

The deficiencies presented below represent MAJOR deficiencies.

A. Deficiencies:

(b) (4)

1.

2.

3.

4.

5.

6.

7.

8.

17. (b) (4)

18.

19.

20.

21.

22.

23.

24.

25.

26.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. The labeling and bioequivalence portions of your application are under review. Deficiencies, if any, will be conveyed to you under separate cover. In addition, a satisfactory cGMP compliance evaluation from the Office of Compliance is required in order for this ANDA to be approved.

2. Please provide updated stability data for the exhibit batches.

3. Please be advised that the section corresponding to the excipients in your QOS provided the following statement: (b) (4)

Sincerely yours,

{electronic signature on file}

Glen Smith
Division Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

DAMARIS C MALDONADO
10/31/2011

LINDA M PARK
10/31/2011

BINGYUAN WU
10/31/2011
Acting TL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202727

BIOEQUIVALENCE REVIEWS

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	202727		
Drug Product Name	Lansoprazole Delayed Release Capsules, USP (OTC)		
Strength(s)	15 mg		
Applicant Name	Wockhardt Limited		
Address	Wockhardt Towers, Bandra Kurla Complex, Bandra (East) Mumbai - 400051 Maharashtra - INDIA		
Applicant's Point of Contact	Ms. Leanne Usa 20 Waterview Blvd, 3rd Floor, Parsippany, NJ 07054.		
Contact's Telephone Number	973-257-4998		
Contact's Fax Number	973-257-4999		
Original Submission Date(s)	January 26, 2011		
Submission Date(s) of Amendment(s) Under Review	September 22, 2011 (response to dissolution deficiency) January 3, 2012 (response to CMC's deficiency regarding band seal of capsules for 15 mg OTC)		
Reviewer	Li Xia, Ph.D.		
Study Number (s)	CPB-101-2010		
Study Type (s)	Fasting		
Strength (s)	15 mg		
Clinical Site	Clinical Pharmacokinetics & Biopharmaceutics Department		
Clinical Site Address	Wockhardt Limited, Mulund-Goregaon Link Road, Bhandup (West), Mumbai – 400 078, India.		
Analytical Site	Clinical Pharmacokinetics & Biopharmaceutics Department		
Analytical Site Address	Wockhardt Limited, Mulund-Goregaon Link Road, Bhandup (West), Mumbai – 400 078, India.		
OVERALL REVIEW RESULT	**ADEQUATE**		
WAIVER REQUEST RESULT	**ADEQUATE** (waiver request for the fed study)		
OSI REPORT RESULT	**ADEQUATE**		
BIOEQUIVALENCE STUDY TRACKING/SUPPORTING DOCUMENT #	**STUDY/TEST TYPE**	**STRENGTH**	**REVIEW RESULT**
1	**FASTING**	**15 mg**	**ADEQUATE**
1	**DISSOLUTION**	**15 mg**	**ADEQUATE**

1 EXECUTIVE SUMMARY

This application contains the results of a fasting bioequivalence (BE) study comparing a test product, Wockhardt Limited's Lansoprazole Delayed Release Capsules, 15 mg (OTC) to the corresponding reference listed drug (RLD), Novartis ' Prevacid® 24 HR (Lansoprazole) Delayed Release Capsule, 15 mg (OTC). The fasting BE study was designed as a single-dose, 4-way crossover fully replicate study in healthy male subjects. The firm's fasting BE study is acceptable. The results are summarized in the table below.

Lansoprazole DR Capsules, 15 mg (OTC)
Fasting Bioequivalence Study No. (CPB-101-2010), N=50 (Male)
Least-Square Geometric Means, Point Estimates and 90% Confidence Intervals

Parameter (units)	Test	Reference	Ratio	90% C.I.	
AUC0-t (ng·hr/mL)	1577.2538	1734.3179	0.91	85.676	96.535
AUC∞ (ng·hr/mL)	1619.7304	1780.0345	0.91	85.749	96.560
Cmax (ng/mL)	512.213	571.26299	0.90	83.688	96.066

This application contains a request for waiver of in vivo bioequivalence study requirement for Lansoprazole Delayed Release Capsules, USP 15 mg (OTC) under fed condition. The firm has referenced fasting, fed and sprinkled fasting BE studies conducted on its Lansoprazole Delayed-Release Capsules, 30 mg (Rx) strength in its sister ANDA 202176, which were found acceptable by the Division of Bioequivalence (DB). However, ANDA 202176 is incomplete pending the in vitro test for nasogastric (NG) tube administration[1,2]. Please note that in vitro NG tube testing is not required for Lansoprazole DR Capsules (OTC).

As per DB's control correspondence review (#90520) for Lansoprazole Delayed-Release Capsules, 15 mg (OTC)[3], fasting and fed studies are recommended to establish bioequivalence to the RLD, Novartis ' Prevacid® 24 HR (Lansoprazole) Delayed Release Capsule, 15 mg (OTC). If the firm will market both Rx and OTC product lines, the firm may cross reference the acceptable BE studies on the 30 mg strength of Rx product. The DB may deem the 15 mg strength of Lansoprazole Delayed-Release Capsules (to be marketed as an OTC product) bioequivalent to the corresponding strength of the reference product under CFR 320.24(b)(6) provided that the following criteria are met (1) acceptable *in vivo* BE studies on 30 mg (Rx); (2) acceptable dissolution testing across all strengths (both OTC and Rx product); and (3) the formulation of the 15 mg strength (OTC) is proportionally similar to that of the 30 mg strength (to be marketed as a Rx product). Per the DB's biomanagement meeting minutes on 3/27/2012[4], the waiver request for the fed study is deemed adequate.

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[1] DARRTS: REV-BIOEQ-01(General Review) for ANDA 202176, final date 2/2/2012.
[2] Per the RLD labeling of Prevacid® 24 HR (OTC), there is no statement "the product may be administered by a nasogastric (NG) tube". Therefore, in vitro NG tube testing is not required for Lansoprazole DR Capsules (OTC).
[3] Control correspondence #90520 at V:\ (b) (4) \controls\090520c1009.doc.
[4] V:\DIVISION\BIO\BIO2\BIO Management Meeting Minutes\2012 Meeting Minutes

The firm has conducted comparative dissolution testing on the 15 mg (OTC) and 30 mg (Rx) strengths using the USP method (500 mL of 0.1 N HCl at the acid stage in one hour followed by 900 mL of pH 6.8 Phosphate Buffer at 37ºC ± 0.5ºC using USP apparatus II at 75 rpm). The firm's dissolution testing data met the USP specifications at A1 level (acid stage: NMT 10% in 60 minutes) and B1 level [buffer stage: NLT 80% (Q) in 60 minutes]. However, the test product batches used in dissolution testing were not fresh and were stored for approximately 15 months after manufacturing date, the DB considered these specifications as interim, the firm was asked to conduct dissolution data from 3 fresh production lots[5]. In its amendment dated 9/22/2011, the firm acknowledged to conduct this test as a **post-approval commitment.** The final specifications will be determined upon review of these dissolution data.

The strength of 15 mg OTC in the test product is proportional similar to the strength of 30 mg Rx. The reviewer notes that the firm's 15 mg Rx submitted in ANDA 202176 and 15 mg OTC have the same formulation and the same batch number. The DB deems the 15 mg strength of Lansoprazole Delayed-Release Capsules (OTC) bioequivalent to Novartis's Prevacid® 24 HR (Lansoprazole) Delayed-Release Capsules, 15 mg (OTC) under 21 CFR 320.24(b)(6) based on acceptable BE studies submitted in the sister ANDA 202176 for the 30 mg strength (Rx), the comparative dissolution data and formulation proportionality between 15 mg (OTC) and 30 mg (Rx) test products[6].

Routine Office of Scientific Investigations (OSI) inspections of the analytical and clinical site (Clinical Pharmacokinetics & Biopharmaceutics Department,Wockhardt Limited, Mulund-Goregaon Link Road, Bhandup (West), Mumbai – 400 078, India) were completed on 07/08/2009 for ANDA078701 with the outcomes of VAI. No significant findings were reported following the inspection of the clinical site. Form 483 was issued for the analytical portion for the fasting and fed BE studies. The OSI inspection report was reviewed and found to be adequate on 09/14/2009 by the DB for ANDA078701[7]. The OSI findings are not relevant to the current application. Therefore, no OSI inspection is pending or necessary for the analytical and clinical site.

The application is acceptable with no deficiencies.

[5] DARRTS: REV-BIOEQ-02(Dissolution Review) for ANDA 202727, final date 8/30/2011.
[6] Historically, the DB deemed 15 mg (OTC) of Lansoprazole DR Capsules bioequivalent to Novartis's Prevacid® 24 HR (Lansoprazole) DR Capsules, 15 mg (OTC) under CFR 320.24(b)(6) for ANDA 202194 and ANDA (b) (4), which did not contain fasting and fed bioequivalence studies.
[7] DARRTS: REV-BIOEQ-01 (General Review) for ANDA078701, final date 09/14/2009.

2 TABLE OF CONTENTS

3 SUBMISSION SUMMARY

3.1 Drug Product Information

Test Product	Lansoprazole Delayed Release Capsule USP, 15 mg (OTC)
Reference Product	Prevacid® 24 HR (Lansoprazole) Delayed Release Capsule, 15 mg (OTC)
RLD Manufacturer	Novartis
NDA No.	022327
RLD Approval Date	May 18, 2009
Indication	Over-the-counter (OTC) use. Short-term treatment of frequent heartburn (occurs 2 or more days a week) in adults aged 18 years and older.

3.2 PK/PD Information[8]

Bioavailability	Delayed-Release Oral Capsules contain an enteric-coated granule formulation of lansoprazole. Absorption of lansoprazole begins only after the granules leave the stomach. Absorption is rapid and relatively complete with absolute bioavailability over 80 %.
Food Effect	Both Cmax and AUC are diminished by about 50 % to 70% if the drug is given 30 minutes after food as opposed to the fasting condition. There is no significant food effect if the drug is given before meals.
Tmax	1.7 hrs
Metabolism	Lansoprazole is extensively metabolized in the liver through the cytochrome P450 system. Two metabolites have been identified in measurable quantities in plasma (the hydroxylated sulfinyl and sulfone derivatives of lansoprazole). These metabolites have very little or no antisecretory activity. Lansoprazole is thought to be transformed into two active species which inhibit acid secretion by (H+,K+)-ATPase within the parietal cell canaliculus, but are not present in the systemic circulation.
Excretion	Following single-dose oral administration of lansoprazole, virtually no unchanged lansoprazole was excreted in the urine. Approximately two-third of Lansoprazole metabolites may be excreted by biliary system.
Half-life	1.5 hrs
Drug Specific Issues (if any)	Animal study demonstrated that Lansoprazole produced dose-related gastric enterochromaffin-like cell (ECL) hyperplasia and ECL cell carcinoids in both sexes. No patients showed evidence of ECL cell effects similar to these observed in animal studies.

3.3 OGD Recommendations for Drug Product[9]

Number of studies recommended:	2, fasting and fed

[8] RLD label for PREVACID® (LANSOPRAZOLE) Delayed- Release Capsule, Rx
[9] Control Correspondence #090520 at V:\ (b) (4) \controls\090520c1009.doc

1.	**Type of study:**	Fasting
	Design:	Single-dose, two-treatment, two-period crossover in-vivo
	Strength:	15 mg OTC [RLD: Prevacid® 24 HR (Lansoprazole) Delayed-Release Capsules, 15 mg, manufactured by Novartis Consumer Health, Inc.]
	Subjects:	Normal healthy males and non-pregnant females, general population
	Additional Comments:	Applicants may consider using a reference-scaled average bioequivalence approach for this drug product. If using this approach, the applicant should provide evidence of high variability in the bioequivalence parameters AUC and/or Cmax (i.e., within-subject variability $\geq$30%). For general information on this approach, please refer to Haidar et al., Bioequivalence Approaches for Highly Variable Drugs and Drug Products, Pharm. Res. 25:237-241(2008).

2.	**Type of study:**	Fed
	Design:	Single-dose, two-treatment, two-period crossover in-vivo
	Strength:	15 mg OTC (see above)
	Subjects:	Normal healthy males and non-pregnant females, general population
	Additional Comments:	See above

Analytes to measure (in plasma/serum/blood):	Only the parent drug, lansoprazole, be measured in plasma for bioequivalence studies
Bioequivalence based on:	90% CI of Lansoprazole (Cmax and AUC)
Waiver request of in-vivo testing:	If the firm will market both Rx and OTC product lines, the firm may cross reference the acceptable BE studies on the 30 mg strength of Rx product. The DB II may deem the 15 mg strength of Lansoprazole Delayed-Release Capsules (to be marketed as an OTC product) bioequivalent to the corresponding strength of the reference product (OTC) under CFR 320.24(b)(6) provided that the following criteria are met (1) acceptable in vivo BE studies on the 30 mg strength (to be marketed as a prescription drug product); (2) acceptable dissolution testing across all strengths; and (3) the formulation of the 15 mg strength (OTC) is proportionally similar to that of the 30 mg strength.
Source of most recent recommendations:	Control review: CD#90520 ((b) (4)). As per the DB control review (CD#090520), the formulation of the 15 mg (OTC) reference product is the same as that of the 15 mg (Rx) reference product except minor changes in the composition of the two-piece gelatin capsules and the addition of a gelatin tamper evidence band.

Summary of OGD or DB History (for details, see Appendix):	Presently, there is no generic product approved for the OTC lansoprazole DR capsules. The Office of Generic Drugs (OGD) has received following ANDAs for Lansoprazole Delayed-Release Capsules (OTC): 202727, Wockhardt Ltd; 202319, Perrigo; (b) (4) (b) (4); 202194, Dr. Reddys; (b) (4) (b) (4)
Additional Comments	Since the OTC label does not mention sprinkled and nasogastric tube administration, the sprinkled fasting and in vitro NJ tube studies are not necessary for this product.

3.4 Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	Yes	1
Single-dose fed	No	
Steady-state	No	
In vitro dissolution	Yes	1
Waiver requests	Yes	Waiver request for fed study
BCS Waivers	No	
Clinical Endpoints	No	
Failed Studies	No	
Amendments	Yes	9/22/2011 (response to dissolution deficiency) January 3, 2012 (response to CMC's deficiency regarding band seal of capsules for 15 mg OTC)

3.5 Pre-Study Bioanalytical Method Validation

Information Requested	Data	
Bioanalytical method validation report location	**Study Report Location: Appendix 16.2.5.3, Page No. 676-812**	
Analyte / IS	**Lansoprazole** [redacted] (b) (4)	
Method description	Estimation of Lansoprazole in human plasma using [redacted] (b) (4) as an Internal Standard (IS) was performed using High Performance Liquid Chromatography Mass Spectrometric Method.	
Lower Limit of Quantification (ng/mL)	2.00	N/AP
Average recovery (%)	75.17	83.06 %
Standard curve concentrations (ng/mL)	2.00 to 1506.72	N/AP
QC concentrations (ng/mL)	2.01 to 1250.08	N/AP
QC Intra-day precision range (%)	1.98 to 7.14	N/AP
QC Intra-day accuracy range (%)	90.50 to 96.26	N/AP
QC Inter-day precision range (%)	2.58 to 10.89 %	N/AP
QC Inter-day accuracy range (%)	96.32 to 98.18	N/AP
Bench-top stability (5 hrs) Precision (%) Accuracy (%)	 2.27 to 2.40 95.92 to 97.15	N/AP
Stock stability Room Temperature for 11 hrs (%) Room Temperature IS Dilution for 28 hrs (%) Refrigerated for 6 days (%)	 100.37 N/AP 105.89	 102.62 99.06 107.10
Processed stability (46 hrs) Precision (%) Accuracy (%)	 1.78 to 12.65 96.03 to 99.92	N/AP
Freeze-thaw stability (3 cycles) Precision (%) Accuracy (%)	 1.22 to 2.59 97.30 to 98.37	N/AP
Long-term storage stability (6 days) **Below -50°C** Precision (%) Accuracy (%) **Below -20°C** Precision (%) Accuracy (%)	 1.38 to 2.10 98.08 to 98.24 1.31 to 2.29 98.18 to 99.80	N/AP
Long-term storage stability (50 days) **Below -50°C** Precision (%) Accuracy (%) **Below -20°C** Precision (%) Accuracy (%)	 0.48 to 0.78 96.27 to 98.13 0.84 to 1.10 95.68 to 98.23	N/AP
Long-term storage stability (120 days) **Below -50°C** Precision (%) Accuracy (%) **Below -20°C** Precision (%) Accuracy (%)	 1.19 to 3.79 98.40 to 102.05 1.64 to 3.47 98.18 to 104.52	N/AP

Information Requested	Data	
Analyte / IS	**Lansoprazole**	(b) (4)
Dilution integrity **Four times dilution** Precision (%) Accuracy (%) **Two times dilution** Precision (%) Accuracy (%)	 2.41 96.55 0.85 96.30	 N/AP
Selectivity	No significant interference from endogenous components was observed at retention time of analyte and IS in all the human plasma batches screened.	
Sensitivity Precision (%) Accuracy (%)	 3.47 99.35	 N/AP
Precision & Accuracy (b) (4)		
Linearity Range (ng/mL) Precision range (%) Accuracy range (%)	2.00 to 1506.72 1.91 to 5.91 90.88 to 102.34	N/AP N/AP N/AP
Precision & Accuracy (b) (4)		
Linearity Range Precision range (%) Accuracy range (%)	2.00 to 1506.72 1.39 to 8.82 95.81 to 112.29	N/AP N/AP N/AP

SOPs submitted	CPB-AM-050-00 High Performance Liquid Chromatography Mass Spectrometric Method for Estimation of Lansoprazole in Human Plasma Using (b) (4) as an Internal Standard	CPB-AP-005-03 Preparation of Calibration Curve Standards and Quality Control Samples
	CPB-AP-009-03 Bioanalytical Method Validation	CPB-AP-011-03 Reporting of Bioanalytical Results
	CPB-AP-021-01 Incurred Samples Reanalysis	
Bioanalytical method is acceptable		

Comments on the Pre-Study Method Validation:

- In its addendum 1 & 2 to Method Validation Report, the firm provided partial validation on the precision & accuracy batch using different instrument of same make ((b) (4) and (b) (4)) besides the instrument (b) (4) used for the quantitative determination of lansoprazole in human plasma.

- In its addendum 4, the firm provided long term stability data of Lansoprazole for 120 days below -50°C and -20°C, which is sufficient to cover the sample storage for fasting study (42 days).

Firm's pre-study method validation is **acceptable**.

3.6 In Vivo Studies

Table 1. Summary of all in vivo Bioequivalence Studies

Study Ref. No.	Study Objectives	Study Design	Treatments (Dose, Dosage Form, Route) [Product ID]	Subjects (No. (M/F) Type Age: mean (Range)	Formulation	Mean Parameters						Study Report Location
						C_{max} (ng/mL)	T_{max} (hr)	AUC_{0-t} (ng.hr/mL)	$AUC_{0-\infty}$ (ng.hr/mL)	$T_{½}$ (hr)	K_{el} (hr^{-1})	
Fasted Bioequivalence Study (Study No. CPB-101-2010)												
CPB-101-2010	**Efficacy:** To assess bioavailability on new formulation of Lansoprazole Delayed Release 15 mg capsule of Wockhardt Limited, India compared with Prevacid® 24 HR Delayed Release capsule (containing enteric-coated granules consisting of 15 mg of Lansoprazole) of Novartis Consumer Health Inc., USA in 52 normal, adult, human subjects under fasting condition. **Safety:** To monitor adverse events and ensure safety of the subjects.	A single center, randomized, single dose, open-label, analyst-blind, two-treatment, four-period, two-sequence, replicate, crossover comparative bioavailability study under fasting condition.	**Test Product (A):** Lansoprazole DR 15 mg Capsule USP (Manufactured by Wockhardt Limited, India) Oral **Batch No:** LJ10534 **Reference Product (B):** Prevacid® 24 HR (containing Lansoprazole) DR 15 mg capsule (Distributed by: Novartis Consumer Health Inc., USA.) Oral **Batch No:** 10074797	**Participated Subjects:** 52 male healthy subjects **Mean age:** 27.0 ± 4.24 (20 - 41) **Clinical Phase Completed Subjects:** 50 male healthy subjects **Mean age:** 27.1 ± 4.27 (20 - 41) **Considered for PK & Statistical Analyses:** 50 male healthy subjects **Mean age:** 27.1 ± 4.27 (20 - 41)	**Lansoprazole (Combined)**							**Section 11.4 of Clinical Study Report. Page No 44**
					Test (A)	548.13 (33.37)	2.00 (1.00 – 4.50)	1940.37 (65.78)	2036.06 (71.27)	2.18 (54.17)	0.40 (43.93)	
					Reference (B)	614.67 (34.08)	1.50 (0.75 – 4.00)	2112.23 (64.13)	2218.80 (70.14)	2.16 (57.67)	0.41 (45.21)	

Arithmetic mean values (% CV) have been reported for all the parameters except T_{max} for which median (min-max) values have been reported.

Table 2. Statistical Summary of the Comparative Bioavailability Data Calculated by the Reviewer

Lansoprazole DR Capsules, OTC, 15 mg Fasting Bioequivalence Study No. (CPB-101-2010), N=50 (Male) Least-Square Geometric Means, Point Estimates and 90% Confidence Intervals					
Parameter (units)	**Test**	**Reference**	**Ratio**	**90% C.I.**	
AUC0-t (ng·hr/mL)	1577.2538	1734.3179	0.91	85.676	96.535
AUC∞ (ng·hr/mL)	1619.7304	1780.0345	0.91	85.749	96.560
Cmax (ng/mL)	512.213	571.26299	0.90	83.688	96.066

Table 3. Reanalysis of Study Samples

Study No. CPB-101-2010 Study Report Location: Appendix 16.2.5.1, Section 12.3, Page No. 620 and 654								
Lansoprazole								
Reason why assay was repeated	**Number of samples reanalyzed**				**Number of recalculated values used after reanalysis**			
	Actual number		**% of total assays**		**Actual number**		**% of total assays**	
	T	**R**	**T**	**R**	**T**	**R**	**T**	**R**
Pharmacokinetic	0	0	0.00	0.00	0	0	0.00	0.00
ISV (Internal Standard Variation)	1	3	0.02	0.07	1	3	0.02	0.07
Total	**1**	**3**	**0.02**	**0.07**	**1**	**3**	**0.02**	**0.07**
Note:	1 sample of test product and 3 sample of Reference product were reanalyzed. Total no. of samples analyzed: 4004 (excluding 200 PD & 200 PD+IS samples, as these cannot be assigned to either test or reference formulation)							

Did use of recalculated plasma concentration data change study outcome?

N/A.

Comments from the Reviewer:

Repeat Analysis

Out of total 4404 samples analyzed, 4 samples were repeated due to ISV (Internal Standard Variation). The original and repeat values are similar, the repeats are acceptable.

Incurred Sample Reanalysis

Out of total 4400 subject samples analysed, 236 samples were reanalysed in 3 different batches as Incurred sample reanalysis and 97.03 % of the incurred samples were found with in ± 20 % as per SOP CPB-AP-021-01.

3.7 Formulation

Location in appendix	Section 4.2, Page 31
If a tablet, is the RLD scored?	No
If a tablet, is the test product biobatch scored	No
Is the formulation acceptable?	**ACCEPTABLE**
If not acceptable, why?	

3.8 In Vitro Dissolution

Location of DBE Dissolution Review	DARRTS: REV-BIOEQ-02(Dissolution Review) for ANDA 202727, final date 8/30/2011.
Source of Method (USP, FDA or Firm)	USP
Medium	Acid Resistance Stage: 0.1 N HCl Buffer Stage: pH 6.8 Phosphate Buffer
Volume (mL)	Acid Resistance Stage: 500 mL Buffer Stage: 900 mL
USP Apparatus type	USP Apparatus Type II (Paddle)
Rotation (rpm)	75 rpm
USP specifications	Acid Resistance Stage: NMT 10% dissolved in 60 min. Buffer Stage: NLT 80% (Q) dissolved in 60 min.
If a modified-release tablet, was testing done on ½ tablets?	No
F2 metric calculated?	Yes
If no, reason why F2 not calculated	
Is method acceptable?	The dissolution specifications are considered as interim since the data were not generated from fresh batch.
If not then why?	

	F2 metric
15 mg OTC (test) vs. 15 mg OTC (RLD)	50.19
15 mg OTC (test) vs. 30 mg Rx (test)	54.85

Reviewer's Comments:

- There is a USP method for this product. The firm's dissolution testing data with the USP method (500 mL of 0.1 N HCl at the acid stage in one hour followed by 900 mL of pH 6.8 Phosphate Buffer at 37ºC ± 0.5ºC using USP apparatus II at 75 rpm) meet the USP specifications at the A1 level [Acid Stage: *NMT 10% in 60 minutes*] and the B1 level [Buffer Stage: *NLT 80%* (Q) *in 60 minutes*]. However,

the batches used in dissolution testing were not fresh and were stored for approximately 15 months after manufacturing date. Since in the chemistry section, the firm has provided 12 month drug-product-stability data at room temperature, the DB considered these specifications as interim. The specifications will be finalized after evaluation of dissolution data from 3 fresh production lots[5].

- In response to DB's dissolution deficiency letter issued on 9/10/2011, in its amendment dated 9/22/2011, the firm accepted the interim specifications and acknowledged to conduct dissolution test for 3 fresh production lots as a **post-approval commitment.** The final specifications will be determined upon review of these dissolution data. The firm should complete these studies within 6 months of approval.

- The in-vitro dissolution profile of Wockhardt's Lansoprazole Delayed Release Capsules, USP 15 mg (OTC) and 30 mg (Rx) are also similar ($F2 \geq 50$) and comparable to each other. The in vitro dissolution profile of Wockhardt's Lansoprazole DR Capsules 15 mg is also similar ($F2 \geq 50$) to that of the reference listed drug product (PREVACID ® 24 HR) for the OTC product line.

3.9 Waiver Request(s)

Waiver requested	Request waiver for the fed BE study
BE for lower strength under CFR 320.24(b)(6) ?	Wockhardt conducted acceptable fasting study comparing its 15 mg (OTC) to the RLD (OTC), PREVACID® 24 HR. The DB deems the 15 mg strength of Lansoprazole Delayed-Release Capsules (OTC) bioequivalent to Novartis's Prevacid® 24 HR (Lansoprazole) Delayed-Release Capsules, 15 mg (OTC) under CFR 320.24(b)(6) based on acceptable BE studies submitted in the sister ANDA 202176 for the 30 mg strength (Rx), the comparative dissolution data and formulation proportionality between 15 mg (OTC) and 30 mg (Rx) test products.

3.10 Deficiency Comments

None.

3.11 Recommendations

1. The Division of Bioequivalence (DB) **accepts** the fasting bioequivalence (BE) study No. CPB-101-2010 conducted by Wockhardt Limited on its Lansoprazole Delayed Release Capsules, 15 mg (OTC), batch # LJ10534, comparing it to the

corresponding reference listed drug (RLD), Novartis ' Prevacid® 24 HR (Lansoprazole) Delayed Release Capsule, 15 mg (OTC), batch #10074797.

- The firm's dissolution testing data with the USP method (500 mL of 0.1 N HCl at the acid stage in one hour followed by 900 mL of pH 6.8 Phosphate Buffer at 37ºC ± 0.5ºC using USP apparatus II at 75 rpm)) meet the USP specifications at the A1 level [Acid Stage: *NMT 10% in 60 minutes*] and the B1 level [Buffer Stage: *NLT 80%* (Q) *in 60 minutes*]. However, the data were generated from the test products that had been stored for approximately 15 months at the time of testing, the DB considered these specifications as interim. The firm gave **a post approval commitment** to submit the dissolution data to the FDA using the USP method for 3 fresh commercial scale batches. The final specifications will be determined upon review of these dissolution data. The firm should complete these studies within 6 months of approval.

2. The firm has conducted acceptable in vivo BE studies (submitted in a separate ANDA 202176 dated on 08/06/2010) comparing Lansoprazole Delayed-Release Capsules USP, 30 mg, to PREVACID® Capsules (Lansoprazole Delayed-Release) Capsule, 30 mg, manufactured by Takeda Pharms. The formulation for the strength of 15 mg OTC is proportionally similar to the 30 mg strength of the test product which underwent bioequivalence testing. The DB deems the 15 mg strength of Lansoprazole Delayed-Release Capsules (to be marketed as an OTC product) bioequivalent to Novartis's Prevacid® 24 HR (Lansoprazole) Delayed-Release Capsules, 15 mg (OTC) under 21 CFR 320.24(b)(6).

3.12 Comments for Other OGD Disciplines

Discipline	Comment
All	Wockhardt conducted acceptable fasting study comparing its 15 mg (OTC) to the RLD (OTC), PREVACID® 24 HR. This application contains a request for waiver of in vivo bioequivalence study requirements for Lansoprazole Delayed Release Capsules, USP 15 mg (OTC) under fed condition. It does not have stand alone fed study. The firm has referenced fasting, fed and sprinkle fasting bioequivalence (BE) studies conducted on the 30 mg (Rx) strength in its sister ANDA 202176. The Division of Bioequivalence (DB) has reviewed ANDA 202176 and found the fasting, fed, and sprinkled fasting BE studies on the 30 mg strength capsule to be acceptable. However, ANDA 202176 is incomplete pending the in vitro test for nasogastric (NG) tube administration. Please note that in vitro NG tube testing is not required for Lansoprazole DR Capsules (OTC).

4 APPENDIX

4.1 Individual Study Reviews

4.1.1 Single-dose Fasting Bioequivalence Study

4.1.1.1 Study Design

Table 4 Study Information

Study Number	CPB-101-2010
Study Title	A randomized, single dose, open-label, two-treatment, four-period, two-sequence, replicate, crossover comparative bioavailability study on new formulation of Lansoprazole Delayed Release 15 mg capsule of Wockhardt Limited, India compared with Prevacid® 24 HR Delayed Release capsule (containing enteric-coated granules consisting of 15 mg of Lansoprazole) of Novartis Consumer Health Inc., USA in 52 normal, adult, human subjects under fasting condition.
Clinical Site (Name, Address, Phone #)	Clinical Pharmacokinetics & Biopharmaceutics Department, Wockhardt Limited, Mulund-Goregaon Link Road, Bhandup (West), Mumbai – 400 078, India. Tel: +91-22-6652 4444, Fax: +91-22-6652 4545
Principal Investigator	Dr. Ilesh Changela
Dosing Dates	Period-I: 27/08/2010, Period-II: 07/09/2010, Period-III: 14/09/2010 & Period-IV: 21/09/2010
Analytical Site (Name, Address, Phone #)	Clinical Pharmacokinetics & Biopharmaceutics Department, Wockhardt Limited, Mulund-Goregaon Link Road, Bhandup (West), Mumbai – 400 078, India. Tel: +91-22-6652 4444, Fax: +91-22-6652 4545
Analysis Dates	23/09/2010 to 07/10/2010
Bioanalytical Investigator	(b) (6)
Storage Period of Biostudy Samples (no. of days from the first day of sample collection to the last day of sample analysis)	27/08/2010 to 07/10/2010 (42 days)

Table 5. Product information

Product	Test	Reference
Treatment ID	**A**	**B**
Product Name	Lansoprazole Delayed Release Capsules USP, 15 mg (OTC)	Prevacid® 24 HR (containing Lansoprazole) DR
Manufacturer	Wockhardt Limited, India	Distributed by: Novartis Consumer Health Inc., USA.
Batch/Lot No.	LJ10534	10074797
Manufacture Date	April 2009	Not Available
Expiration Date	April 2011	March 2011
Strength	15 mg	15 mg
Dosage Form	Capsule	Capsule
Bio-batch Size	(b) (4) Capsules	Not Available
Production Batch Size	Capsules	Not Available
Potency	104.9 %	101.1 %
Content Uniformity (Individual values & % RSD)	104.5,105.1,105.0,105.2,106.2,105.7,105.7,106.0,105.8,105.8 % % RSD: 0.5	---
Dose Administered	15 mg	15 mg
Route of Administration	Oral	Oral

Table 6. Study Design, Single-Dose Fasting Bioequivalence Study

Number of Subjects	52 subjects were dosed, 50 subjects completed and included in the analysis
No. of Sequences	2
No. of Periods	4
No. of Treatments	2
No. of Groups	1
Washout Period	11 days between Period I and II 7 days between Period II and III and IV
Randomization Scheme	ABAB: 1, 3, 6, 7, 9, 12, 13, 16, 17, 19, 22, 23, 25, 27, 29, 32, 33, 36, 38, 39, 41, 44, 45, 47, 49, 52 BABA: 2, 4, 5, 8, 10, 11, 14, 15, 18, 20, 21, 24, 26, 28, 30, 31, 34, 35, 37, 40, 42, 43, 46, 48, 50, 51
Blood Sampling Times	Pre-dose (0.0 hr) and at 0.5,0.75, 1.0, 1.25, 1.5, 1.75, 2.0, 2.25, 2.5, 2.75, 3.0, 3.5, 4.0, 4.5, 5.0, 6.0, 8.0,10.0, 12.0 and 16.0 hours post-dose in each period.

Blood Volume Collected/Sample	A total of 84 blood samples (4 mL each except pre dose samples for which 10 mL) were collected from each subject in K2EDTA vacutainer (Containing 80 ul. of 1M sodium bicarbonate) in all the four periods (21 samples in each period) as per the above schedule specified in study protocol.
Blood Sample Processing/Storage	After collection of blood samples from the subjects at each time point, the designated study personnel centrifuged the blood samples at 3000 ± 50 RPM for a period of 10 minutes at a temperature of 4 ± 3°C to separate plasma. Plasma separation was done under subdued light. All such separated plasma samples were transferred in duplicates to pre-labeled storage vials (labeled with project number, subject number, period number, sampling time point & aliquot number). The plasma vials were stored upright in deep freezers at a temperature of -50°C or colder from the date of first blood sample collection (27/08/2010) to the date of completion of analysis (07/10/2010).
IRB Approval	August 19, 2010
Informed Consent	August 19, 2010
Length of Fasting	Overnight fasting for minimum 10.0 hrs before dosing
Length of Confinement	All the subjects who met the eligibility criteria as per protocol were admitted into the CPU at least 11.0 hrs before dosing.
Safety Monitoring	Safety measurements were conducted at periodic intervals, throughout the course of the study. Physician and nursing staff were available for medical check-up of the subjects starting from screening of the volunteers to completion of clinical phase of the study (render medical care, if required). The safety measurements evaluated were of clinical laboratory parameters, vital signs and also adverse event monitoring.

Comments on Study Design:

The study design is acceptable.

4.1.1.2 Clinical Results

Table 7. Demographics Profile of Subjects Completing the Bioequivalence Study

Study No. CPB-101-2010			
		Treatment Groups	
		Test Product N = 50	Reference Product N = 50
Age (years)	Mean ± SD	27.1 ± 4.27	27.1 ± 4.27
	Range	20 - 41	20 - 41
Age Groups	< 18	0	0
	18 – 40	49 (98.00 %)	49 (98.00 %)
	41 – 65	1 (2.00 %)	1 (2.00 %)
	66 – 75	0	0
	> 75	0	0
Sex	Male	50 (100 %)	50 (100 %)
	Female	0	0
Race	Asian	50 (100 %)	50 (100 %)
	Black	0	0
	Caucasian	0	0
	Hispanic	0	0
	Other	0	0
BMI (kg/m^2)	Mean ± SD	22.08 ± 1.902	22.08 ± 1.902
	Range	18.7 – 25.0	18.7 – 25.0
Other Factors		Nil	Nil

Table 8. Dropout Information, Fasting Bioequivalence Study

Study No. CPB-101-2010				
Subject No	Reason for dropout/replacement	Period	Replaced?	Replaced with
07	Withdrawn from the study, as he found positive in Breath Alcohol test during check-in of period-III.	III	N/AP	N/AP
13	Did not report to study site for the check-in of period-III hence dropped out from the study	III	N/AP	N/AP

Table 9. Study Adverse Events, Fasting Bioequivalence Study

Body System / Adverse Event	Reported Incidence by Treatment Groups	
	Fasted Bioequivalence Study Study No.: CPB-101-2010	
	Test	Reference
Body as a whole	Nil	
Cardiovascular	Nil	
Gastrointestinal	Nil	
Nervous System	Nil	
Respiratory system	Nil	
Others	Nil	
Post Study Assessment		
Decrease in RBC count	1 (1.92 %)*	
Rise in Lymphocyte count	1 (1.92 %)*	
Rise in Eosinophil count	1 (1.92 %)*	
Rise in Alkaline Phosphatase level	1 (1.92 %)*	
Rise in GGTP level	3 (5.77 %)	
Rise in SGOT level	2 (3.85 %)*	
Rise in SGPT level	2 (3.85 %)*	
Total	**11 (21.15 %)**	

Note:
52 subjects participated in this study.
*- Adverse event is mild and related unlikely to studied drug.

Percentage values are rounded off.

Table 10. Protocol Deviations, Fasting Bioequivalence Study

Study No. CPB-101-2010		
Type	**Subject #s (Test)**	**Subject #s (Ref.)**
Blood sampling time point deviations	04 & 27	16
Deviation during bioanalytical phase of the study	For data acquisition and processing, Analyst software version 1.4.2 was used instead of analyst software version 1.4.1 for (b) (4).	

Comments on Dropouts/Adverse Events/Protocol Deviations:

Dropouts
Subjects #7 and #13 dropped out of the study from Period III. The samples from these subjects in period I and II were not analyzed and were not included in reviewer and firm's PK and statistical analysis.

Adverse Events
There were no serious or unexpected AEs reported during the study. There were 11 adverse events reported in the study, which were abnormal clinical laboratory value observed during post study safety assessment.

Protocol Deviations
There were 3 blood sampling time deviations (< 5 min) observed during the study, the time deviations were considered unlikely to affect the PK analysis or overall PK conclusions. The actual time points and scheduled time points were used in firm and reviewer's PK and statistical analysis, respectively.

4.1.1.3 Bioanalytical Results

Table 11. Assay Validation – Within the Fasting Bioequivalence Study

Bioequivalence Study No. CPB-101-2010								
Parameter	**Standard Curve Samples**							
Concentration (ng/mL)	**2.00**	**6.58**	**21.92**	**62.62**	**178.93**	**511.22**	**1278.05**	**1503.59**
Inter day Precision (%CV)	1.31	4.42	3.98	3.06	2.73	3.69	3.84	3.27
Inter day Accuracy (%Actual)	99.70	100.47	101.69	101.66	100.28	100.10	97.78	98.44
Linearity (range of r^2)	0.992 to 1.000							
Linearity Range (ng/mL)	2.00 to 1503.59							
Sensitivity (ng/mL)	2.00							

Study Report Location: Appendix 16.2.5.1, Section 12.1 Page No. 619 and 625-633

Parameter	**Quality Control Samples**			
Concentration (ng/mL)	**5.99**	**150.62**	**627.58**	**1255.15**
Inter day Precision (%CV)	6.69	5.91	5.55	6.35
Inter day Accuracy (%Actual)	101.27	101.93	100.39	100.71

Comments on Study Assay Validation:

Acceptable.

Any interfering peaks in chromatograms?	No
Were 20% of chromatograms included?	Yes
Were chromatograms serially or randomly selected?	Serially (subjects #1, 2, 3, 4, 5, 6, 8, 9, 10, and 11)

Comments on Chromatograms:

Acceptable.

Table 12. SOP's Dealing with Bioanalytical Repeats of Study Samples

SOP No.	Effective Date of SOP	SOP Title
CPB-AP-011-03	30/11/2009	Reporting of Bioanalytical Results

Table 13. Additional Comments on Repeat Assays

Were all SOPs followed?	Yes
Did recalculation of PK parameters change the study outcome?	N/A
Does the reviewer agree with the outcome of the repeat assays?	Yes
If no, reason for disagreement	

Summary/Conclusions, Study Assays:

Acceptable.

4.1.1.4 Pharmacokinetic Results

Table 14. Arithmetic Mean Pharmacokinetic Parameters

Mean plasma concentrations are presented in Table 18 and Figure 1

Fasting study

ARITHMETIC MEANS AND RATIOS - REPLICATE 1 (PERIODS 1 AND 2)

		Test				Reference				Ratio
Parameter	**Unit**	**Mean**	**CV %**	**Min**	**Max**	**Mean**	**CV %**	**Min**	**Max**	**(T/R)**
AUCT	ng hr/mL	1854.360	66.12	378.06	5319.78	2023.986	64.54	279.13	6799.59	0.92

		Test				Reference				Ratio
Parameter	Unit	Mean	CV %	Min	Max	Mean	CV %	Min	Max	(T/R)
AUCINF	ng hr/mL	1947.577	71.48	385.81	6226.71	2119.874	70.33	287.84	7930.40	0.92
CMAX	ng/mL	539.845	36.05	119.68	917.49	592.597	34.01	106.70	1049.54	0.91
TMAX	hr	1.750	.	1.00	4.50	1.500	.	0.75	4.00	1.17
KEL	hr-1	0.400	43.39	0.13	0.88	0.413	46.70	0.12	0.99	0.97
THALF	hr	2.169	55.31	0.79	5.53	2.131	55.50	0.70	5.75	1.02

ARITHMETIC MEANS AND RATIOS - REPLICATE 2 (PERIODS 3 AND 4)

		Test				Reference				Ratio
Parameter	Unit	Mean	CV %	Min	Max	Mean	CV %	Min	Max	(T/R)
AUCT	ng hr/mL	2026.389	65.71	271.58	6442.49	2200.483	64.02	444.23	6039.36	0.92
AUCINF	ng hr/mL	2124.539	71.38	273.87	7377.81	2317.733	70.24	447.46	7026.70	0.92
CMAX	ng/mL	556.414	30.91	199.82	1018.65	636.747	34.07	180.67	1314.53	0.87
TMAX	hr	2.000	.	1.00	3.50	1.625	.	1.00	4.00	1.23
KEL	hr-1	0.396	44.91	0.12	0.90	0.404	44.05	0.12	0.89	0.98
THALF	hr	2.186	53.56	0.77	5.69	2.198	60.13	0.78	5.93	0.99

ARITHMETIC MEANS AND RATIOS - ALL PERIODS (PERIODS 1, 2, 3, AND 4)

		Test				Reference				Ratio
Parameter	Unit	Mean	CV %	Min	Max	Mean	CV %	Min	Max	(T/R)
AUCT	ng hr/mL	1940.374	65.78	271.58	6442.49	2112.234	64.13	279.13	6799.59	0.92
AUCINF	ng hr/mL	2036.058	71.27	273.87	7377.81	2218.804	70.14	287.84	7930.40	0.92
CMAX	ng/mL	548.130	33.37	119.68	1018.65	614.672	34.08	106.70	1314.53	0.89
TMAX	hr	2.000	.	1.00	4.50	1.500	.	0.75	4.00	1.33

		Test				Reference				Ratio
Parameter	Unit	Mean	CV %	Min	Max	Mean	CV %	Min	Max	(T/R)
KEL	hr-1	0.398	43.93	0.12	0.90	0.409	45.21	0.12	0.99	0.97
THALF	hr	2.178	54.17	0.77	5.69	2.164	57.67	0.70	5.93	1.01

* Tmax values are presented as median, range.

Table 15. Geometric Means and 90% Confidence Intervals - Firm Calculated

Drug: Lansoprazole Dose (15 mg) Least Squares Geometric Means, Ratio of Means, and 90% Confidence Intervals				
Fasted Bioequivalence Study (Study No. CPB-101-2010) Study Report Location: Section 11.4 of Clinical Study Report. Page No. 45				
Lansoprazole				
Parameter	Test	Reference	Ratio	90% C.I.
AUC_{0-t} (ng.hr/mL)	1577.2538	1734.3179	90.94 %	85.68 % - 96.54 %
$AUC_{0-\infty}$ (ng hr/mL)	1619.7304	1780.0345	90.99 %	85.75 % - 96.56 %
C_{max} (ng/mL)	512.2130	571.2630	89.66 %	83.69 % - 96.07 %

Table 16. Geometric Means and 90% Confidence Intervals- Reviewer Calculated

Lansoprazole DR Capsules, OTC, 15 mg Fasting Bioequivalence Study No. (CPB-101-2010), N=50 (Male) Least-Square Geometric Means, Point Estimates and 90% Confidence Intervals					
Parameter (units)	Test	Reference	Ratio	90% C.I.	
AUC0-t (ng·hr/mL)	1577.2538	1734.3179	0.91	85.676	96.535
AUC∞ (ng·hr/mL)	1619.7304	1780.0345	0.91	85.749	96.560
Cmax (ng/mL)	512.213	571.26299	0.90	83.688	96.066

Table 17. Additional Study Information, Fasting Study No. CPB-101-2010

Root mean square error, AUC0-t	0.2437045	
Root mean square error, AUC∞	0.2418293	
Root mean square error, Cmax	0.315418	
	Test (replicate 1 and 2)	Reference (replicate 1 and 2)

Kel and AUC∞ determined for how many subjects?	50	50
Do you agree or disagree with firm's decision?	agree	agree
Indicate the number of subjects with the following:		
measurable drug concentrations at 0 hr	No	No
first measurable drug concentration as Cmax	No	No
Were the subjects dosed as more than one group?	No	No

Comments on Pharmacokinetic and Statistical Analysis:

The fasting study is a 4 way crossover replicate design study. Subjects #7 and #13 dropped out of the study from Period III. Yet, the firm did not propose the reference-scaled average bioequivalence approach in its fasting BE study protocol. Thus, only the average bioequivalence method was used to perform bioequivalence statistics for AUC and Cmax in these studies.

Per firm's protocol, "*Pharmacokinetic and Statistical analysis for plasma concentration versus time profile of Lansoprazole will be performed on the data obtained from all subjects who have* ***completed*** *clinical phase and bioanalytical phase of the study successfully*". The samples from these two subjects in period I and II were not analyzed and were not included in reviewer and firm's PK and statistical analysis. The data from 50 subjects who completed all 4 periods of the study were included in PK and statistical analysis.

Summary and Conclusions, Single-Dose Fasting Bioequivalence Study:

In summary, the 90% confidence intervals for lnAUC0-t, lnAUC∞ and lnCmax are within the acceptable limits of 80-125%.

The fasting study is acceptable.

Table 18. Mean Plasma Concentrations, Single-Dose Fasting Bioequivalence Study

Replicate 1

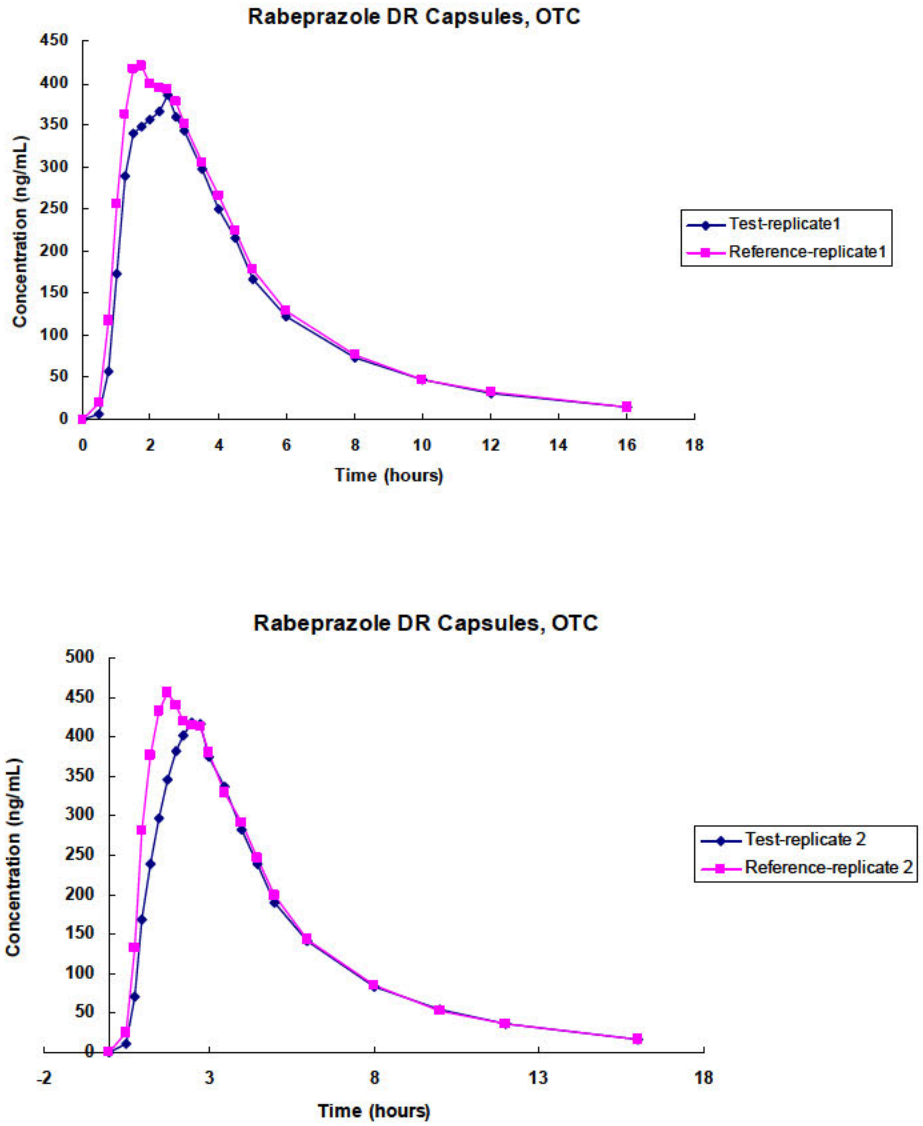
	Treatment A		Treatment B	
Time	Mean (ng/mL)	CV%	Mean (ng/mL)	CV%
0	0.00	.	0.00	.
0.5	6.16	372.64	19.28	368.34
0.75	57.20	186.38	117.69	161.17
1.0	173.32	129.17	256.16	110.92
1.25	289.06	94.32	363.40	82.86
1.5	340.19	82.98	417.49	73.45
1.75	348.76	75.58	419.75	64.72
2.0	356.69	67.51	399.96	58.32
2.25	367.23	56.79	394.41	52.84
2.5	386.79	49.22	392.96	50.02
2.75	360.80	49.91	377.62	49.16
3	344.23	47.46	352.39	49.86
3.5	298.10	54.11	306.52	54.77
4.0	250.94	61.41	267.16	59.05
4.5	215.51	69.39	224.31	72.16
5.0	167.72	75.43	178.51	76.17
6.0	123.22	89.69	129.41	87.52
8.0	74.19	117.26	76.66	118.23
10.0	47.17	142.30	48.16	142.91
12	31.10	164.27	32.44	167.64
16	13.95	204.52	14.62	208.93

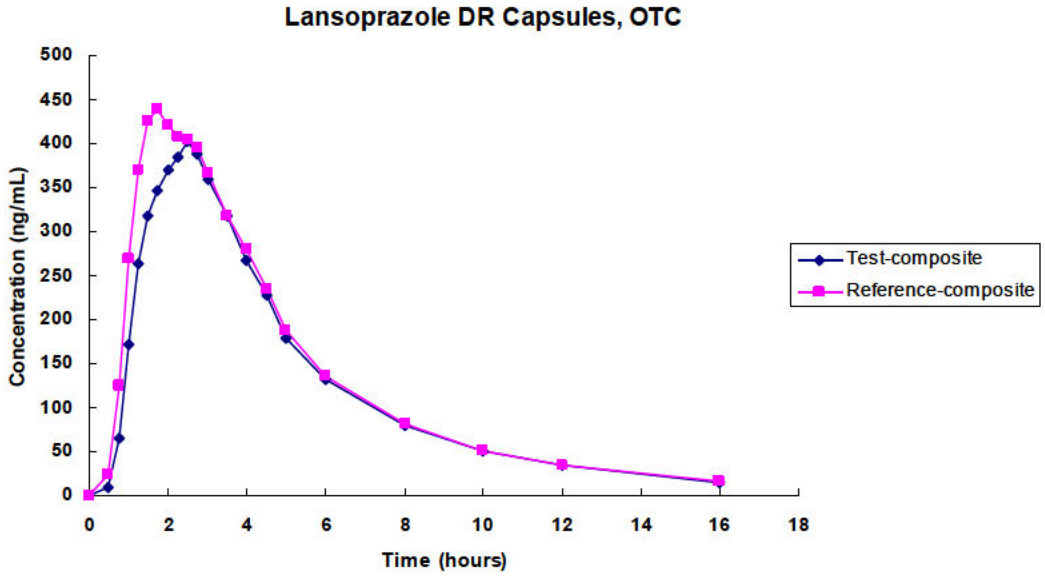
Replicate 2

	Treatment A		Treatment B	
Time	Mean (ng/mL)	CV%	Mean (ng/mL)	CV%
0	0.00	.	0.00	.
0.5	10.13	352.77	26.20	357.92

	Treatment A		Treatment B	
Time	Mean (ng/mL)	CV%	Mean (ng/mL)	CV%
0.75	71.48	176.12	132.15	147.05
1.0	169.02	133.70	281.05	102.16
1.25	238.51	109.38	377.40	89.12
1.5	296.78	84.85	433.24	72.92
1.75	345.73	73.94	457.35	64.48
2.0	381.75	65.02	439.79	61.91
2.25	401.31	59.77	420.27	58.03
2.5	418.80	47.90	415.04	51.92
2.75	416.47	46.05	412.40	48.00
3	374.20	49.17	380.42	48.37
3.5	337.45	53.68	329.13	51.72
4.0	283.14	56.74	291.15	57.48
4.5	239.89	63.73	246.70	60.18
5.0	190.09	71.32	198.64	66.34
6.0	141.27	81.74	142.80	79.26
8.0	83.63	106.54	84.50	108.90
10.0	53.58	133.02	51.76	134.92
12	36.37	158.86	35.87	159.10
16	15.75	195.37	16.66	198.19

Figure 1. Mean Plasma Concentrations, Single-Dose Fasting Bioequivalence Study




Lansoprazole DR Capsules, OTC
Concentration (ng/mL)
500
450
400
350
300
250
200
150
100
50
0
0
2
4
6
8
10
12
14
16
18
Time (hours)
Test-composite
Reference-composite

4.2 Formulation Data

LANSOPRAZOLE DELAYED RELEASE CAPSULES, USP 15 mg (OTC)

S. No	Ingredients	Function	Quantity/ Capsule (mg)		Quantity/ Capsule (%)
			15 mg (OTC)	30 mg (Rx)	
(b) (4)					

Following this page, 7 Pages Withheld in Full as (b)(4)

Is there an overage of the active pharmaceutical ingredient (API)?	No
If the answer is yes, has the appropriate chemistry division been notified?	N/A
If it is necessary to reformulate to reduce the overage, will bioequivalence be impacted?	N/A
Comments on the drug product formulation:	Comments below

Reviewer's Comments:

- The formulation of 15 mg OTC is exactly the same as that of 15 mg Rx product previously submitted in ANDA # 202176, and the formulation of 15 mg product (OTC) is proportionally similar to the formulation of the 30 mg strength product with respect to both API and excipients. In ANDA 202176, Wockhardt has conducted acceptable bioequivalence studies under fasting, fed and fasting sprinkled-over-applesauce condition on its Lansoprazole Delayed Release Capsules USP 30 mg (Rx) against reference listed drug product PREVACID® 30 mg (Rx) capsules.

- The addition of the band for the commercial batch is considered as Level I change, which is unlikely to have any detectable impact on formulation quality and performance. As per the Guidance for Industry: SUPAC-MR, for level 1 change, there is no dissolution documentation beyond application/compendial requirements.

- Quantities of all excipients in Lansoprazole Delayed-Release Capsules, 15 mg (OTC), fall well below the IIG limits for this oral route of administration. Color additives of FD & C Red , FD & C Blue # 1 and D & C Red # 33 are acceptable as per 21CFR Sec. 74 which states that the color may be safely used for coloring ingested drugs in amounts consistent with current good manufacturing practice.

- [redacted] (b) (4)

Therefore, the formulation is acceptable.

4.3 Dissolution Data

Dissolution Review Path	DARRTS: REV-BIOEQ-02(Dissolution Review) for ANDA 202727, final date 8/30/2011.

Table 19. Dissolution Data

Dissolution conditions:	
Apparatus:	USP Apparatus II (Paddle)
Speed of Rotation:	75 RPM
Medium:	Acid stage: 0.1N HCl ; Buffer stage: pH 6.8 Phosphate Buffer
Volume:	500 mL and 900 ml
Temperature:	37 ± 0.5° C
Firm's proposed specification:	
Acid stage at 1 Hour	Not more than 10 %
Buffer stage at 60 Minutes	Not less than 80% (Q) of labeled amount of Lansoprazole
Site of testing : Wockhardt Limited, Aurangabad, Maharashtra, India	

Study Ref No.	**Product ID \ Batch No. (Test – Manufacture Date) (Reference – Expiration Date)**	**Dosage Form& Strength**	**No. of Dosage Units Tested**		**Collection Times (Minutes)**					
					Acid stage (60 Min)	**Buffer stage**				
						15 Min	**20 Min**	**30 Min**	**45 Min**	**60 Min**
Study Report #:NA	Lansoprazole Delayed Release Capsules,15 mg /LJ10534 Manufacturing Date:April 2009	15 mg Capsules	12	Mean	0	60	73	88	100	102
				Range	[redacted] (b) (4)					
				%CV	106	14	11	13	8	3
Study Report #:NA	PREVACID ® 24 HR Delayed Release Capsules,15 mg / 10074797 Expiry Date: March 2011	15 mg Capsules	12	Mean	1	72	82	78	92	94
				Range	[redacted] (b) (4)					
				%CV	127	16	6	10	6	2

Date of testing (Test Product): July 2010
Date of testing (Reference Product): August 2010

Note: The %CV for the test product during the acid phase is reported as 106% in the summary table; however, after reviewing the raw data of the 12 units the %RSD is 0%. Thus, the reviewer has concluded the %CV of 106 as an error by the firm.

Dissolution Conditions	**Apparatus:**	USP Apparatus II (Paddle)
	Speed of Rotation:	75 RPM
	Medium:	Acid stage: 0.1N HCl ; Buffer stage: pH 6.8 Phosphate Buffer
	Volume:	500 mL and 900 ml
	Temperature:	37 ± 0.5° C
Firm's Proposed Specifications	Acid stage: Not more than 10 % in 60 min; Buffer stage: Not less than 80% (Q) of labeled amount of Lansoprazole.	
Dissolution Testing Site (Name, Address)	Wockhardt Limited, Aurangabad, Maharashtra, India	

Study Ref No.	**Testing Date**	**Product ID \ Batch No. (Test - Manufacture Date) (Reference – Expiration Date)**	**Dosage Strength & Form**	**No. of Dosage Units**		**Acid stage**	**Buffer stage**					**Study Report Location**
						60 min	**15 min**	**20 min**	**30 min**	**45 min**	**60 min**	
Study Report #:		Lansoprazole Delayed Release Capsules,30 mg /LJ10538 Manufacturing Date: April 2009	30 mg Capsules	12	Mean	1	45	70	85	97	100	
					Range	(b) (4)						
					%CV	111	14	8	4	1	1	
Study Report #:		PREVACID ® Delayed Release Capsules,30 mg / 771822E21 Expiry Date: October 2012	30 mg Capsules	12	Mean	1	61	66	71	79	85	
					Range	(b) (4)						
					%CV	109	2	3	3	3	3	

4.4 SAS Output

4.4.1 Fasting Study Data

(b) (4)

Project Manager: Please hold the letter

BIOEQUIVALENCE COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 202727

APPLICANT: Wockhardt Limited

DRUG PRODUCT: Lansoprazole Delayed-Release Capsules USP, 15 mg (OTC)

The Division of Bioequivalence II (DBII) has completed its review and has no further questions at this time.

We acknowledge that you will conduct dissolution testing using the USP dissolution method for your Lansoprazole Delayed-Release Capsules USP, 15 mg (OTC).

We acknowledge your acceptance of the interim specifications [*Acid Stage: NMT 10% in 60 minutes; Buffer Stage: NLT 80%* (Q) *in 60 minutes*] for your dissolution testing using the USP dissolution method. Please submit dissolution data using the USP method for 3 fresh production lots when they become available as your **post approval commitment**. The final specifications will be determined upon review of these dissolution data. Please complete these studies within 6 months of approval.

Please note that the bioequivalence comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

{See appended electronic signature page}

Barbara M. Davit, Ph.D., J.D.
Director
Division of Bioequivalence II
Office of Generic Drugs
Center for Drug Evaluation and Research

4.5 Outcome Page

ANDA: 202727

Completed Assignment for 202727 ID: 16541

Reviewer: Xia, Li **Date Completed:**

Verifier: **Date Verified:**

Division: Division of Bioequivalence

Description: Lansoprazole Delayed Release Capsules, USP (OTC), 15 mg

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Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
16541	1/26/2011	Bioequivalence Study	Fasting Study	1	1
16541	9/22/2011	Other	Study Amendment	1	1
16541	1/3/2012	Other	Study Amendment	1	1
				Bean Total:	3

DBE2 Complexity Points:

Typical BE Study Applications

BE Study Fasting	
Clinical (Common to all APIs)	1
Bioanalytical (API 1)	1
Statistical Analysis (API 1)	1
Bioanalytical (API 2)	0
Statistical Analysis (API 2)	0
Metabolite	0
Fasting Study Total	*3*
Study Amendment (s)	
Study Amendment	2
Study Amendment Total	*2*
Study Total	*5*

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LI XIA
04/12/2012

XIAOJIAN JIANG
04/12/2012

ETHAN M STIER on behalf of BARBARA M DAVIT
04/20/2012

DIVISION OF BIOEQUIVALENCE DISSOLUTION REVIEW

ANDA No.	202727
Drug Product Name	Lansoprozole Delayed Release Capsules (OTC)
Strength (s)	15 mg
Applicant Name	Wockhardt Limited
Address	Wockhardt Towers, Bandra Kurla Complex, Bandra (East) Mumbai – 400051 Maharashtra - INDIA
Applicant's Point of Contact	Leanne Usa U.S. Agent 20 Waterview Blvd, 3rd Floor, Parsippany, NJ 07054.
Contact's Phone Number	973-257-4998
Contact's Fax Number	973-257-4999
Submission Date(s)	January 26, 2011
First Generic	No
Reviewer	Li Gong, Ph.D.
Study Number (s)	CPB-101-2010
Study Type (s)	Fasting
Strength(s)	15 mg
Clinical Site	Wockhardt Limited
Clinical Site Address	Clinical Pharmacokinetics & Biopharmaceutics Department Mulund-Goregaon Link Road, Bhandup (West), Mumbai - 400 078, India
Analytical Site	Wockhardt Limited
Analytical Address	Clinical Pharmacokinetics & Biopharmaceutics Department Mulund-Goregaon Link Road, Bhandup (West), Mumbai - 400 078, India
Dissolution Method	**Correct**
OVERALL REVIEW RESULT	**INADEQUATE**

BIOEQUIVALENCE STUDY TRACKING/SUPPORTING DOCUMENT #	**STUDY/TEST TYPE**	**STRENGTH**	**REVIEW RESULT**
1	**Dissolution**	**15 mg**	**Adequate**

I. EXECUTIVE SUMMARY

This is a review of the dissolution testing data only. This ANDA references NDA 022327 for OTC Prevacid® 24 hr from Novartis.

There is a USP method for this product. The firm's dissolution testing data with the USP method (Acid Stage: 500 mL of 0.1 N HCl at 37°C, using USP Apparatus II at 75 rpm; Buffer Stage: 900 mL of phosphate buffer, pH 6.8 at 37°C, using USP Apparatus II at 75 rpm) meet the USP specifications [Acid Stage: *Not more than 10% of the labeled amount of lansoprazole is dissolved in 60 minutes;* Buffer Stage *Not less than 80%* (Q) *of the labeled amount of lansoprazole is dissolved in 60 minutes*]. However, the batches used in dissolution testing were not fresh and were stored for approximately 15 months after manufacturing date. Since in the chemistry section, the firm has provided 12 month drug-product-stability data at room temperature, the DBE will consider these specifications as interim. The specifications will be finalized after evaluation of dissolution data from 3 fresh production lots (**see the Note below**).

The Long Term Storage Stability (LTSS) data were sufficient to cover the maximum storage duration of the fasting bioequivalence (BE) study samples.

In addition, the firm submitted the DBE's eCTD Summary Tables in PDF format only.

The DBE will review the firm's fasting BE study at a later date. The firm is cross referencing fed BE study and sprinkle BE study from its ANDA 202176.

Note:
The firm has submitted a separate ANDA 202176 for Lansoprazole ER Capsules, 15 mg and 30 mg (for prescription; Rx). The DBE has conducted a "dissolution only" review on that ANDA 202176 [see DARTS for ANDA 20176 JOHNSON, GLENDOLYNN S 03/17/2011 N/A 03/17/2011 REV-BIOEQ-02(Dissolution Review) Original-1 (Not Applicable) Archive]. **For the ANDA 202176 the DBE made the similar recommendation of interim specifications**.

Table 1: SUBMISSION CONTENT CHECKLIST

Information			YES	NO	N/A
Did the firm use the FDA-recommended dissolution method			☐	☐	☒
Did the firm use the USP dissolution method			☒	☐	☐
Did the firm use 12 units of both test and reference in dissolution testing			☒	☐	☐
Did the firm provide complete dissolution data (all raw data, range, mean, % CV, dates of dissolution testing)			☒	☐	☐
Did the firm conduct dissolution testing with its own proposed method			☐	☐	☒
Is FDA method in the public dissolution database (on the web)			☐	☐	☒
SAS datasets submitted to the electronic document room (edr)	Fasting BE study*	PK parameters	☒	☐	☐
		Plasma concentrations	☒	☐	☐
	Fed BE study	PK parameters	☐	☐	☒
		Plasma concentrations	☐	☐	☒
	Other study	PK parameters	☐	☐	☒
		Plasma concentrations	☐	☐	☒
Are the DBE Summary Tables present an in either PDF and/or MS Word Format?**			☒	☐	☐
If any of the tables are missing or incomplete please indicate that in the comments and request the firm to provide the complete DBE Summary Tables 1-16.					
Is the Long Term Storage Stability (LTSS) sufficient to cover the maximum storage time of the study samples?			☒	☐	☐
If the LTSS is NOT sufficient please request the firm to provide the necessary data.					

*The firm conducted only one BE study under fasting condition.

**The firm provided the DBE eCTD Summary Tables in PDF format only. The firm will be asked to provide the DBE eCTD Summary Tables in MS Word format.

Lansoprazole ER Capsule (USP Method)

Acid Stage

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: *75 rpm*

Times and Tolerances— Not more than 10% of the labeled amount of lansoprazole is dissolved in 60 minutes.

Buffer Stage

Medium: either phosphoric acid or sodium hydroxide to a pH of 6.8; 900 mL

Apparatus 2: *75 rpm*

Times and Tolerances— Not less than 80% (Q) *of the labeled amount of lansoprazole is dissolved in 60 minutes.*

Table 2: Summary of In Vitro Dissolution Studies

Dissolution conditions:	
Apparatus:	USP Apparatus II (Paddle)
Speed of Rotation:	75 RPM
Medium:	Acid stage: 0.1N HCl ; Buffer stage: pH 6.8 Phosphate Buffer
Volume:	500 mL and 900 ml
Temperature:	37 ± 0.5° C
Firm's proposed specification:	
Acid stage at 1 Hour	Not more than 10 %
Buffer stage at 60 Minutes	Not less than 80% (Q) of labeled amount of Lansoprazole
Site of testing : Wockhardt Limited, Aurangabad, Maharashtra, India	

Study Ref No.	**Product ID \ Batch No. (Test – Manufacture Date) (Reference – Expiration Date)**	**Dosage Form& Strength**	**No. of Dosage Units Tested**		**Collection Times (Minutes)**					
					Acid stage (60 Min)	**Buffer stage**				
						15 Min	**20 Min**	**30 Min**	**45 Min**	**60 Min**
Study Report #:NA	Lansoprazole Delayed Release Capsules,15 mg /LJ10534 Manufacturing Date:April 2009	15 mg Capsules	12	Mean	0	60	73	88	100	102
				Range						(b) (4)
				%CV	106	14	11	13	8	3
Study Report #:NA	PREVACID ® 24 HR Delayed Release Capsules,15 mg / 10074797 Expiry Date: March 2011	15 mg Capsules	12	Mean	1	72	82	78	92	94
				Range						(b) (4)
				%CV	127	16	6	10	6	2

Date of testing (Test Product): July 2010
Date of testing (Reference Product): August 2010
Note: The %CV for the test product during the acid phase is reported as 106% in the summary table; however, after reviewing the raw data of the 12 units the %RSD is 0%. Thus, the reviewer has concluded the %CV of 106 as an error by the firm.

II. COMMENTS:

1. The firm's dissolution testing data with the USP method (Acid Stage: 500 mL of 0.1 N HCl at 37°C, using USP Apparatus II at 75 rpm; Buffer Stage: 900 mL of phosphate buffer, pH 6.8 at 37°C, using USP Apparatus II at 75 rpm) meet the USP specifications (Acid Stage: *Not more than 10% of the labeled amount of lansoprazole is dissolved in 60 minutes;* Buffer Stage *Not less than 80%* (Q) *of the labeled amount of lansoprazole is dissolved in 60 minutes*) at L_1 level. However, the batches used in dissolution testing were not fresh and were stored for approximately 15 months. Therefore, the specifications should be considered as interim. The specifications will be finalized after evaluation of dissolution data from 3 fresh production lots.

2. The Long Term Storage Stability (LTSS) data were sufficient to cover the maximum storage duration of the fasting BE study samples.

3. The firm did not submit the DBE eCTD Summary Tables in MS Word format. The firm submitted the DBE Summary Tables in PDF format only.

III. DEFICIENCY COMMENTS:

1. The firm should acknowledge the following USP dissolution method and interim specifications: The dissolution testing should be conducted using the USP method (Acid Stage: 500 mL of 0.1 N HCl at 37°C, using USP Apparatus II at 75 rpm; Buffer Stage: 900 mL of phosphate buffer, pH 6.8 at 37°C, using USP Apparatus II at 75 rpm). The test product should meet the following specifications:

   Acid Stage: Not more than 10% *(Q)* of the labeled amount of lansoprazole is dissolved in 60 minute.

   Buffer Stage: Not less than 80% *(Q)* of the labeled amount of lansoprazole is dissolved in 60 minutes.

   Since the dissolution testing was performed on batches stored for at least 15 months, the DBE recommended specifications should be considered as interim. The specifications will be finalized after evaluation of dissolution data from 3 fresh production lots when they become available.

2. The firm did not provide the DBE eCTD Summary Tables in MS Word format.

IV. RECOMMENDATIONS:

The *in-vitro* dissolution testing conducted by Wockhardt Limited on its test product, Lansoprazole Delayed Release Capsules USP, 15 mg (Batch #LJ10534), comparing it

with Novartis' PREVACID ® 24 HR Delayed Release Capsules, 15 mg (Batch #10074797), is **incomplete** due to the above deficiencies.

The DBE acknowledges that the firm will conduct dissolution testing with the USP method (Acid Stage: 500 mL of 0.1 N HCl at 37°C, using USP Apparatus II at 75 rpm; Buffer Stage: 900 mL of phosphate buffer, pH 6.8 at 37°C, using USP Apparatus II at 75 rpm). The test product should meet the following specifications:

> **Acid Stage:** Not more than 10% (Q) of the labeled amount of lansoprazole is dissolved in 60 minutes.
>
> **Buffer Stage:** Not less than 80% (Q) of the labeled amount of lansoprazole is dissolved in 60 minutes.

Since the dissolution testing was performed on batches stored for at least 15 months, the DBE recommended specifications should be considered as interim. The firm should acknowledge the dissolution testing method and the interim specifications. The specifications will be finalized after evaluation of dissolution data from 3 fresh production lots when they become available.

BIOEQUIVALENCE DEFICIENCIES

ANDA: 202727

APPLICANT: Wockhardt Limited

DRUG PRODUCT: Lansoprazole Delayed Release Capsules, USP 15 mg (OTC)

The Division of Bioequivalence (DBE) has completed its review of the dissolution testing portion of your submission acknowledged on the cover sheet. The review of the bioequivalence study and your waiver request will be done at a later date. The following deficiencies have been identified:

1. Your dissolution testing using the method specified in USP 34 monograph for Lansoprazole Delayed Release Capsules is incomplete. The data provided were generated from the test products that had been stored for approximately 15 months at the time of testing. Since data from stored batches should not be considered for setting the specifications, the DBE recommends interim specifications for the 15 mg DR Capsule (OTC).

   The dissolution testing should be conducted with the USP method (Acid Stage: 500 mL of 0.1 N HCl at 37°C, using USP Apparatus II at 75 rpm; Buffer Stage: 900 mL of phosphate buffer, pH 6.8 at 37°C, using USP Apparatus II at 75 rpm) The test product should meet the following interim specifications:

   Acid Stage: *Not more than 10% of the labeled amount of lansoprazole is dissolved in 60 minutes*

   Buffer Stage: *Not less than 80%* (Q) *of the labeled amount of lansoprazole is dissolved in 60 minutes.*

   Please acknowledge your acceptance of the interim specifications. We ask that you submit dissolution data using the USP method for 3 fresh production lots when they become available. The final specifications will be determined upon review of these dissolution data.

2. Please provide the DBE eCTD Summary Tables in MS Word format.

Sincerely yours,

{See appended electronic signature page}

Barbara M. Davit, Ph.D., J.D.
Acting Director
Division of Bioequivalence II
Office of Generic Drugs
Center for Drug Evaluation and Research

VI. OUTCOME

ANDA: 202727

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
14760	1/26/2011	Dissolution Data	Dissolution Review	1	1
				Bean Total:	1

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LI GONG
08/29/2011

SHRINIWAS G NERURKAR
08/29/2011

ETHAN M STIER on behalf of BARBARA M DAVIT
08/30/2011

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202727

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

ROUTING SHEET

☒ **APPROVAL** ☐ **TENTATIVE APPROVAL** ☐ **SUPPLEMENTAL APPROVAL (NEW STRENGTH)** ☐ **CGMP**

Division: II	**Team: 24**	**PM: Linda Park**

Electronic ANDA: Yes ☒ No ☐

ANDA #:202727
Firm Name:Wockhardt Limited
ANDA Name:Lansoprazole Delayed-Release Capsules USP, 15 mg (OTC)
RLD Name:Prevacid® 24HR (lansoprazole) delayed-release capsules, 15 mg, of Novartis Consumer Health, Inc.

Electronic AP Routing Summary Located:
V:\Chemistry Division II\Team 24\AP Summary

AP/TA Letter Located:
V:\Chemistry Division II\Team 24\AP LTR

Project Manager Evaluation: **Date: 5-14-12 Initials:** LP

☐ Previously reviewed and tentatively approved --- Date _____
☐ Previously reviewed and CGMP Complete Response issued -- Date _____

Original Rec'd date 1-26-11	Date of Application 1-24-11	Date Acceptable for Filing 5-12-11
Patent Certification (type) PIII	Date Patent/Excl. expires 5/18/12	Citizens' Petition/Legal Case? Yes☐ No ☒ (If YES, attach email from PM to CP coord)
First Generic Yes ☒ No ☐ **DMF#:** _____ (provide MF Jackets)	Priority Approval (Top 100, PEPFAR, etc.)? Yes ☐ No ☐ Comment: Prepared Draft Press Release sent to Cecelia Parise Yes ☐ No ☐ Date:	
☐ Suitability Petition/Pediatric Waiver	Pediatric Waiver Request: Accepted ☐ Rejected ☐ Pending ☐	

EER Status: ☐ Pending ☒ Acceptable ☐ OAI *EES Date Acceptable: PN* ☐ Warning Letter Issued; Date:
Has there been an amendment providing for a Major change in formulation since filling? Yes ☐ No ☒ Comment:
Date of Acceptable Quality (Chemistry) 5-10-12 Addendum Needed: Yes ☐ No ☒ Comment:
Date of Acceptable Bio 4-20-12 Bio reviews in DARRTS: Yes ☒ No ☐ (Volume location:)
Date of Acceptable Labeling 5-8-12 Attached labeling to Letter: Yes ☐ No ☐ Comment:
Date of Acceptable Sterility Assurance (Micro) na

Methods Val. Samples Pending: Yes ☐ No ☒; Commitment Rcvd. from Firm: Yes ☐ No ☐

Post Marketing Agreement (PMA): Yes ☐ No ☒ (If yes, email PM Coordinator) Comment:

Modified-release dosage form: Yes ☒ No ☐ (If yes, enter dissolution information in Letter)

Routing:
☒ Labeling Endorsement, Date emailed: _____ REMS Required: Yes ☐ No ☐ REMS Acceptable: Yes ☐ No ☐

☒ Regulatory Support

☐ Paragraph 4 Review (Dave Read, Susan Levine), Date emailed: _____

☒ Division

☒ 1st Generic Review

☒ Bob West / Peter Rickman
☐ Keith Webber

☒Filed AP Routing Summary in DARRTs	☒Notified Firm and Faxed Copy of Approval Letter	☒ Sent Email to "CDER-OGDAPPROVALS" distribution list

OGD APPROVAL ROUTING SUMMARY

1. ***Regulatory Support Branch Evaluation***

Martin Shimer **Date: 5/15/2012**

Chief, Reg. Support Branch **Initials:** MHS

Contains GDEA certification: Yes ☒ No ☐	Determ. of Involvement? Yes ☐ No ☒
(required if sub after 6/1/92)	Pediatric Exclusivity System
	RLD =Prevacid-24 HR NDA# 22-327 Date Checked N/A Nothing Submitted ☐ Written request issued ☐ Study Submitted ☐
Patent/Exclusivity Certification: Yes ☒ No ☐ If Para. IV Certification- did applicant: Notify patent holder/NDA holder Yes ☐ No ☐ Was applicant sued w/in 45 days:Yes ☐ No ☐ Has case been settled: Yes ☐ No ☐ Date settled: Is applicant eligible for 180 day	
Generic Drugs Exclusivity for each strength: Yes ☐ No ☒	
Date of latest Labeling Review/Approval Summary _____	
Any filing status changes requiring addition Labeling Review Yes ☐ No ☒	
Type of Letter: ☒ APPROVAL ☐ TENTATIVE APPROVAL ☐ SUPPLEMENTAL APPROVAL (NEW STRENGTH) ☐CGMP ☐ OTHER:	
Comments:ANDA submitted on 1/26/2011, BOS=Prevacid 24 NDA 22-327, no relevant patents statement, NP exp. 5/18/2012. ANDA ack for filing on 1/26/2011 (LO dated 5/12/2011). The only barrier to the approval of this ANDA is the NP exclusivity which will expire in 3 days. ANDA will be eligible for Full Approval on or after 5/18/2012.	

2. ***Labeling Endorsement***

Reviewer, : Labeling Team Leader, :

Date_____ Date 5/18/12

Initials_____ Initials rlw/for

REMS required? REMS acceptable?

☐Yes ☒No ☐Yes ☐No ☐n/a

Comments:

Final-printed labeling (FPL) found acceptable for approval 5/8/12. No REMS is required.

3. ***Paragraph IV Evaluation*** **PIV's Only**

David Read **Date 5/18/12**

OGD Regulatory Counsel **Initials rlw/for**

Pre-MMA Language included ☐

Post-MMA Language Included ☐

Comments:N/A. There are no paragraph IV certifications associated with this NDA.

4. ***Quality Division Director /Deputy Director Evaluation*** **Date 5/16/2012**

Chemistry Div. **II (Smith)** **InitialsGJS**

Comments:CMC Acceptable.

5. ***First Generic Evaluation*** **First Generics Only**

Frank Holcombe **Date5/18/12**

Assoc. Dir. For Chemistry **Initials rlw/for**

Comments: (First generic drug review)

N/A. Multiple ANDAs for Lansoperazole Delayed-release Capsules USP, 15 mg and 30 mg have been

approved (Rx).

OGD Office Management Evaluation

6. Peter Rickman **Date 5/18/12**
Director, DLPS **Initials rlw/for**

Para.IV Patent Cert: Yes☐ No☐
Pending Legal Action: Yes ☐ No ☐
Petition: Yes☐ No☐
Comments: Bioequivalence studies (fasting) found acceptable. Wockhardt also referenced fasting, non-fasting and sprinkle studies from their pending ANDA 200176 for Lansoprazole Delayed-release Capsules USP, 15 mg and 30 mg (Rx). These studies have been reviewed under that ANDA and found acceptable. In-vitro dissolution testing found acceptable. Waiver granted for the non-fasting study for the OTC formulation under 21 CFR 320.24(b)(6). Bio study sites have acceptable OSI inspection histories. Office-level bio endorsed 4/20/12.

Final-printed labeling (FPL) found acceptable for over-the-counter use 5/8/12. No REMS is required.

CMC found acceptable for approval (Chemistry Review #3) 5/10/12.

AND/OR

7. Robert L. West **Date 5/18/12**
Deputy Director, OGD **Initials RLWest**

Para.IV Patent Cert: Yes☐ No☒
Pending Legal Action: Yes☐ No☒
Petition: Yes☐ No☒
Press Release Acceptable ☐
Date PETS checked for first generic drug _____

Comments: Acceptable EES dated 5/16/12 (Verified 5/18/12). No "OAI" Alerts noted.

There are no patents listed in the current "Orange Book" for this OTC drug product. Wockhardt has addressed the new product exclusivity (NP) that expired on May 18, 2012.

The agency has issued a response to the previously pending "Q" Citizen Petition.

This ANDA is recommended for approval with over-the-counter labeling.

8. ***OGD Director Evaluation***
Keith Webber
Deputy Director, OPS

Comments: RLWest for Keith Webber, Ph.D. 5/18/12.
First Generic Approval ☒
PD or Clinical for BE ☐
Special Scientific or Reg.Issue ☐
Press Release Acceptable ☐

Comments:

9. Project Manager
Date 5-18-12
Initials lp

Check Communication and Routing Summary into DARRTS

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

- 
-  [1]
-  [2]

- FDA Home[3]
- Drug Databases[4]
- Orange Book[5]

-

Patent and Exclusivity Search Results from query on Appl No 022327 Product 001 in the OB_OTC list.

Patent Data

There are no unexpired patents for this product in the Orange Book Database.

Exclusivity Data

Appl No	Prod No	Exclusivity Code	Exclusivity Expiration
N022327	001	NP	May 18, 2012

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LINDA M PARK
05/22/2012

QUALITY DEFICIENCY - MINOR

ANDA 202727

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North VII
7620 Standish Place
Rockville, Maryland 20855

TO: Wockhardt Limited

TEL: 973-257-4998

ATTN: Leanne Usa

FAX: 973-257-4999

FROM: Linda Park

FDA CONTACT PHONE: (240) 276-8536

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated January 24, 2011, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lansoprazole Delayed-Release Capsules USP, 15 mg (OTC).

Reference is also made to your amendment dated December 30, 2011.

The Division of Chemistry has completed its review of the submission(s) referenced above and has identified deficiencies which are presented on the attached ____ pages. This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

Your amendment should respond to all of the deficiencies listed. **Facsimiles or partial replies will not be considered for review**, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. Your cover letter should clearly indicate that the response is a ***QUALITY MINOR AMENDMENT*** and should appear prominently in your cover letter.

We also request that you include a copy of this communication with your response. Please direct any questions concerning this communication to the project manager identified above.

SPECIAL INSTRUCTIONS:

*Effective **01-Aug-2010**, the new mailing address for Abbreviated New Drug Application (ANDA) Regulatory Documents will be:*

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North VII
7620 Standish Place
Rockville, Maryland 20855

All ANDA documents will only be accepted at the new mailing address listed above. For further information, please refer to the following websites prior to submitting your ANDA Regulatory documents: Office of Generic Drugs (OGD): http://www.fda.gov/cder/ogd or Federal Register: http://www.gpoaccess.gov/fr/

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 202727 APPLICANT: Wockhardt Limited

DRUG PRODUCT: Lansoprazole Delayed-Release Capsules, USP, 15 mg (OTC)

The deficiencies presented below represent **MINOR** deficiencies.

A. Deficiencies:

1. (b) (4)
2.
3.
4.
5.
6.
7.
8.

9. (b) (4)

10.

11.

12.

13.

14.

15.

16. Please provide updated stability results.

Sincerely yours,

{See appended electronic signature page}

Glen J. Smith
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

BINGYUAN WU
04/19/2012
Acting TL

** Please email me at chan.park@fda.hhs.gov to confirm that you have received this labeling comment.

Telephone Fax
ANDA 202727

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773
240-276-8951

TO: Wockhardt Limited TEL: 973-257-4998

ATTN: Leanne Usa FAX: 973-257-4999

FROM: Chan Park

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lansoprazole D-R Capsules USP, 15 mg (OTC).

Pages (including cover): 4

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 202727 Date of Submission: February 21, 2012

Applicant's Name: Wockhardt Limited

Established Name: Lansoprazole Delayed-Release Capsules USP, 15 mg

Labeling Deficiencies:

1. GENERAL COMMENT

   We acknowledge that you are withdrawing the packaging of (b) (4) (b) (4), and instead you are proposing packaging for the 14days, 28 days and 42 days regimen in both bottle and blister packaging.

2. CONTAINER – 14s

   Satisfactory in FPL as of the 2/21/2012 submission

3. CARTON – 1 x 14s, 2 x 14s, and 3 x 14s ,

   We note that you included the following (b) (4) statement on the carton for the 2 bottles and 3 bottles. Please delete this and/or comment.

   (b) (4)

4. BLISTER CARD – (b) (4) and 14s

   a. If space permits, we recommend that you include the test “Made in India”.

   b. We acknowledge that your blister packaging is not child-resistant. Please be advised that OTC products that used to be available by prescription only must all have child-resistant closure per 16 CFR 1700.14(a)(30). We ask you that you revise your blister packaging accordingly and submit all related CMC information as an amendment or you withdraw your proposal for the blister packaging. Please respond.

5. BLISTER CARTON – 14 (1 x 14), 28 (2 x 14), and 42 (3 x 14) Unit-dose Capsules

   a. Delete the statement (b) (4) (b) (4)

   b. See comment 4(b) above.

6. INSERT – How Lansoprazole Delayed-Release Capsules is Sold:

   See comment 4(b) above.

Revise the labeling as described above and submit final printed labeling electronically. Please provide the labeling in the Structured Product Labeling (SPL) as well as pdf. format.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -

http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

To facilitate review of your next submission please provide a side-by-side comparison of your proposed labeling with your last labeling submission with all differences annotated and explained.

If you have any questions, please call Chan Park at 240-276-8951 or send e-mail to chan.park@fda.hhs.gov

{See appended electronic signature page}

_____

William Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

CHAN H PARK
04/16/2012

** Please email me at chan.park@fda.hhs.gov to confirm that you have received this labeling comment.

Telephone Fax

ANDA 202727

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773
240-276-8951

TO: Wockhardt Limited TEL: 973-257-4998

ATTN: Leanne Usa FAX: 973-257-4999

FROM: Chan Park

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lansoprazole Delayed-Release Capsules USP, 15 mg.

Pages (including cover): 5

SPECIAL INSTRUCTIONS:

*Effective **01-Aug-2010**, the new mailing address for Abbreviated New Drug Application (ANDA) Regulatory Documents has become:*

Office of Generic Drugs
Document Control Room
7620 Standish Place
Rockville, Maryland 20855

ANDAs will only be accepted at the new mailing address listed above. For further information, please refer to the following websites prior to submitting your ANDA Regulatory documents: Office of Generic Drugs (OGD): http://www.fda.gov/cder/ogd or Federal Register: http://www.gpoaccess.gov/fr/

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 202727 Date of Submission: January 24, 2011 and January 5, 2012

Applicant's Name: Wockhardt Limited

Established Name: Lansoprazole Delayed-Release Capsules USP, 15 mg

Labeling Deficiencies:

1. CONTAINER – 14s, (b) (4)

   a. We believe that the term (b) (4) for the reference listed drug, Prevacid® 24 HR. Please delete this term from your labels.

   b. Please enhance the prominence the text “Delayed-Release Capsules, USP” to appear commensurate to the term “Lansoprazole” as “Delayed-Release Capsules”” is part of the established name for this drug product.

   c. It is preferable to relocate the boxed statement “DO NOT USE…MISSING OR BROKEN.” close to the principal display panel. We refer you to the Prevacid® 24HR label for guidance.

   d. Please confirm that your container/closure system employs a tamper-evident printed seal printed with SEALED for YOUR PROTECTION”.

   e. We note that you include a pictorial of your drug product. Please ensure that this pictorial reflects the accurate description of your drug product. Please revise and/or comment.

   f. Include the statement “one 14 Day Course of Treatment” in association with the net quantity statement for the bottle of 14s.

   g. Include the following boxed statement in proximity to the principal display panel:

IMPORTANT: THIS BOTTLE DOES NOT CONTAIN FULL PRODUCT INFORMATION. SEE CARTON FOR COMPLETE LABELING. READ ALL WARNINGS ON CARTON BEFORE USE. DO NOT DISCARD CARTON.

   h. The font sizes used for the label appear that they do not meet requirements stipulated in 21 CFR 201.66. Please ensure that the font size on all labeling piece meet the requirement. Please revise accordingly and/or comment.

   i. (b) (4)

   j.

(b) (4)

2. CARTON – 1 x 14s and (b) (4)

   a. See comments under CONTAINER, whichever applicable.

   b. You listed “D & C Red. No. 33” and “D & C Yellow No. 10” as inactive ingredients contained in your drug product while these are not found in the Description and Composition of the Drug Product section in the CMC. Please delete these and/or comment.

   c. We recommend that you include the phone number of the Poison Control Center.

3. BLISTER CARD – (b) (4) and 14s

   a. See comment 1(a) above.

   b. The Poison Prevention Packaging Act notes that special packaging (child-resistant closures) should be the responsibility of the manufacturer when the container is clearly intended to be utilized in dispensing (unit-of-use packaging). We believe that this packaging should comply with the Act. Please confirm that your blister packaging is child-resistant and/or comment.

   c. Please ensure that the strength appears sufficiently prominent with sufficient background color contrast.

4. BLISTER CARTON – 14 (1 x 14) and (b) (4) Unit-dose Capsules

   a. See comments under CARTON, whichever applicable.

   b. Please refer to the comment 1(i) above. As this drug product has 14 day course of treatment, please explain the rational for proposing (b) (4). It would be desirable to propose 14s, 28s, or 42s blister tablets. Please revise the packaging configuration and/or comment.

5. INSERT

   a. It appears that the labeling you submitted may not be a final printed labeling (FPL). Please submit the FPL in artwork and/or comment.

   b. See comment 1(a) above.

   c. Please include the strength “15 mg” in association with the drug product name.

   d. Please delete the (b) (4) as it is not appearing in the updated labeling for the “Prevacid 24 Capsules.

   e. We recommend that you include the phone number for the Poison Control Center.

   e. Please delete a reference to the (b) (4) (b) (4) and/or comment.

Revise the labeling as described above and submit final printed labeling electronically. Please provide the labeling in the Structured Product Labeling (SPL) as well as pdf. format.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

To facilitate review of your next submission please provide a side-by-side comparison of your proposed labeling with your last labeling submission with all differences annotated and explained.

If you have any questions, please call Chan Park at 240-276-8951 or send e-mail to chan.park@fda.hhs.gov

{See appended electronic signature page}

_____

William Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

CHAN H PARK
02/07/2012

QUALITY DEFICIENCY - MAJOR

ANDA 202727

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North VII
7620 Standish Place
Rockville, Maryland 20855

APPLICANT: Wockhardt USA LLC.
U.S. Agent for: Wockhardt Limited

ATTN: Leanne Usa

FROM: Linda Park

TEL: 973-257-4998

FAX: 973-257-4999

FDA CONTACT PHONE: (240) 276-8536

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated January 24, 2011, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lansoprazole Delayed Release Capsules, 15 mg (OTC).

Reference is also made to your amendments dated April 14, and April 28, 2011.

The Division of Chemistry has completed its review of the submission(s) referenced above and has identified deficiencies which are presented on the attached ____ pages. This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

Your amendment should respond to all of the deficiencies listed. **Facsimiles or partial replies will not be considered for review**, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. Your cover letter should clearly indicate that the response is a ***QUALITY MAJOR AMENDMENT*** and should appear prominently in your cover letter.

We also request that you include a copy of this communication with your response. Please direct any questions concerning this communication to the project manager identified above.

SPECIAL INSTRUCTIONS:

*Effective **01-Aug-2010**, the new mailing address for Abbreviated New Drug Application (ANDA) Regulatory Documents will be:*

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North VII
7620 Standish Place
Rockville, Maryland 20855

All ANDA documents will only be accepted at the new mailing address listed above. For further information, please refer to the following websites prior to submitting your ANDA Regulatory documents: Office of Generic Drugs (OGD): http://www.fda.gov/cder/ogd or Federal Register: http://www.gpoaccess.gov/fr/

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 202727 APPLICANT: Wockhardt Limited

DRUG PRODUCT: Lansoprazole Delayed-Release Capsules USP, 15 mg (OTC)

The deficiencies presented below represent **MAJOR** deficiencies.

A. Deficiencies:

1. (b) (4)

2.

3.

4.

5.

6.

7.

Following this page, 2 Pages Withheld in Full as (b)(4)

26. [redacted] (b) (4)

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. The labeling and bioequivalence portions of your application are under review. Deficiencies, if any, will be conveyed to you under separate cover. In addition, a satisfactory cGMP compliance evaluation from the Office of Compliance is required in order for this ANDA to be approved.

2. Please provide updated stability data for the exhibit batches.

3. Please be advised that the section corresponding to the excipients in your QOS provided the following statement: [redacted] (b) (4)

Sincerely yours,

{See appended electronic signature page}

Glen Smith
Division Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

BINGYUAN WU
10/31/2011
Acting TL

BIOEQUIVALENCE AMENDMENT

ANDA 202727

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Wockhardt Limited

TEL: (973) 257-4998

ATTN: Leanne Usa

FAX: (973) 257-4999

FROM: Chitra Mahadevan

FDA CONTACT PHONE: (240) 276-8782

Dear Madam:

This facsimile is in reference to the bioequivalence data submitted on January 26, 2011, pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lansoprazole Delayed Release Capsules (OTC), 15 mg.

The Division of Bioequivalence II has completed its review of the submission referenced above and has identified deficiencies which are presented on the attached **3** pages. This facsimile is to be regarded as an official FDA communication and unless requested, a hard-copy will not be mailed.

You should submit a response to these deficiencies in accord with 21 CFR 314.96. Your amendment should respond to all the deficiencies listed. **Facsimiles or partial replies will not be considered for review.** Your cover letter should clearly indicate:

Bioequivalence Response to Information Request
Bioequivalence Bioequivalence Summary Tables
Bioequivalence Dissolution Acknowledgement

If applicable, please clearly identify any new studies (i.e., fasting, fed, multiple dose, dissolution data, waiver or dissolution waiver) that might be included for each strength. We also request that you include a copy of this **communication with your response.**
Please submit a copy of your amendment in an archival (blue) jacket and unless submitted electronically through the gateway, a review (orange) jacket. Please direct any questions concerning this communication to the project manager identified above.

Please remember that when changes are requested to your proposed dissolution methods and/or specifications by the Division of Bioequivalence, an amendment to the Division of Chemistry should also be submitted to revise the release and stability specification. We also recommend that supportive dissolution data or scientific justification be provided in the CMC submission to demonstrate that the revised dissolution specification will be met over the shelf life of the drug product.

SPECIAL INSTRUCTIONS:

Effective 01-Aug-2010, the new mailing address for Abbreviated New Drug Application (ANDA) Regulatory Documents will be:

Office of Generic Drugs
Document Control Room
7620 Standish Place
Rockville, Maryland 20857

After the effective date, 01-Aug-2010, ANDAs will only be accepted at the new mailing address listed above. DO NOT submit your ANDA Regulatory documents to this address prior to 01-Aug-2010. For further information, please refer to the following websites prior to submitting your ANDA Regulatory documents: Office of Generic Drugs (OGD): http://www.fda.gov/cder/ogd or Federal Register: http://www.gpoaccess.gov/fr/

Please submit your response in electronic format. This will improve document availability to review staff.

BIOEQUIVALENCE DEFICIENCIES

ANDA: 202727

APPLICANT: Wockhardt Limited

DRUG PRODUCT: Lansoprazole Delayed Release Capsules, USP 15 mg (OTC)

The Division of Bioequivalence II (DB II) has completed its review of the dissolution testing portion of your submission acknowledged on the cover sheet. The review of the bioequivalence (BE) study and your waiver request will be done at a later date. The following deficiencies have been identified:

1. Your dissolution testing using the method specified in the USP 34 monograph for Lansoprazole Delayed Release Capsules is incomplete. The data provided were generated from test products that had been stored for approximately 15 months at the time of testing. Since data from stored batches should not be considered for setting the specifications, the DB II recommends interim specifications for the 15 mg DR Capsule (OTC).

   The dissolution testing should be conducted with the USP method - Acid Stage: 500 mL of 0.1 N HCl at 37°C, using USP Apparatus II at 75 rpm; Buffer Stage: 900 mL of phosphate buffer, pH 6.8 at 37°C, using USP Apparatus II at 75 rpm. The test product should meet the following interim specifications:

   Acid Stage: Not more than 10% of the labeled amount of lansoprazole is dissolved in 60 minutes

   Buffer Stage: Not less than 80% *(Q)* of the labeled amount of lansoprazole is dissolved in 60 minutes

   Please acknowledge your acceptance of the interim specifications. Please submit dissolution data using the USP method for 3 fresh production lots when they become available. The final specifications will be determined upon review of these dissolution data.

2. Please provide the eCTD BE Summary Tables in MS Word format.

Sincerely yours,

{See appended electronic signature page}

Barbara M. Davit, Ph.D., J.D.
Acting Director
Division of Bioequivalence II
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

BARBARA M DAVIT
09/10/2011

ANDA FILING CHECKLIST

(CTD or eCTD FORMAT)

FOR COMPLETENESS AND ACCEPTABILITY of an APPLICATION

ANDA: 202727
APPLICANT: WOCKHARDT LIMITED
RELATED APPLICATION(S): NA

DRUG NAME: LANSOPRAZOLE
DOSAGE FORM: DELAYED-RELEASE CAPSULES USP, 15 MG **(OTC)**

LETTER DATE: **JANUARY 24, 2011**
RECEIVED DATE: JANAUARY 26, 2011

☐ P-IV
☐ FIRST GENERIC
☐ EXPEDITED REVIEW REQUEST (Approved/Denied)
☐ PEPFAR

Electronic or Paper Submission: Mixed Type II DMF# 21605

BASIS OF SUBMISSION:
NDA/ANDA: 22-327
FIRM: NOVARTIS
RLD: PREVACID 24HR

****Document Room Note: for New Strength amendments and supplements, if specific reviewer(s) have already been assigned for the original, please assign to those reviewer(s) instead of the default random team(s).**

Review Team:

CHEM Team: **DC2 TM 21** ☒ **Activity**	Bio Team: **DBE 2 TM7: Xiaojian Jiang** ☒ **Activity**
CHEM Team Leader: Radhika Rajagopalan ☒ **No Assignment Needed in DARRTS**	Bio PM: Chitra Mahadevan ☐ **FYI**
CHEM RPM: **Frank J. Nice** ☒ **FYI**	Clinical Endpoint Team: **(No)** ☐ **Activity**
DMF Review Team Leader: **Aloka Srinivasan** ☒ **FYI**	
Labeling Reviewer: **Park, Sarah** ☒ **Activity**	Micro Review: **(No)** ☐ **Activity**

Regulatory Reviewer: Rebekah Granger Date: **4/25/2011**	Recommendation: ☒ **FILE** ☐ **REFUSE to RECEIVE**

Comments: EC - 1 YES
Therapeutic Code: 8019000 MISCELLANEOUS ULCER AGENT
On Cards: YES
Archival copy: **ELECTRONIC (GATEWAY)**
Sections: I

- **For More Information on Submission of an ANDA in Electronic Common Technical Document (eCTD) Format please go to: http://www.fda.gov/cder/regulatory/ersr/ectd.htm**
- **For a Comprehensive Table of Contents Headings and Hierarchy please go to: http://www.fda.gov/cder/regulatory/ersr/5640CTOC-v1.2.pdf**
- **For more CTD and eCTD informational links see the final page of the ANDA Checklist**
- **A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage http://www.fda.gov/cder/ogd/**

1. Edit Application Property Type in DARRTS where applicable for

a. First Generic Received
☐ Yes ☒ No
b. Market Availability
☐ Rx ☒ OTC
c. Pepfar
☐ Yes ☒ No
d. Product Type
☐ Small Molecule Drug (usually for most ANDAs except protein drug products)
e. USP Drug Product (at time of filing review)
☒ Yes ☐ No

2. Edit Submission Patent Records
   ☒ Yes
3. Edit Contacts Database with Bioequivalence Recordation where applicable
   ☒ Yes
4. Requested EER
   ☒ Yes

ADDITIONAL COMMENTS REGARDING THE ANDA:

Additional information can also be located in Wockhardt's separate Rx ANDA of Lansoprazole Delayed Release Capsule USP 15 mg and 30 mg ANDA 202176

4/1 – Leanne Usa 973-257-4998

Provide email address for API and DP contact person. For future submission please include in EES form
Remove qualifier phrase in your EIA statement
Provide DBE Tables 1-8 in Module 2.7
Provide a retest date or expiration date of API
Submit schematic diagram for blister packs

4/28 – Leanne Usa 973-257-4998

Please provide a statement of commitment that Wockhardt will carry out banding of the capsules around the intersection of the two capsules halves.

DBE Contact entered 4/25

Per correspondence submitted by sponsor dated 4/14 the above is adequate for filing

MODULE 1: ADMINISTRATIVE

		COMMENT (S)
1.1	**Signed and Completed Application Form (356h)** (Rx/OTC Status) YES (original signature)	
1.1.2	**Establishment Information:** YES 1. Drug Substance Manufacturer 2. Drug Product Manufacturer 3. Outside Testing Facility(ies)	
1.2	**Cover Letter** YES	
1.2.1	**Form FDA 3674** **(PDF)** YES – Box B	
*	**Table of Contents** (paper submission only) YES	
1.3.2	**Field Copy Certification** (N/A for E-Submissions) YES (original signature)	
1.3.3	**Debarment Certification-GDEA** (Generic Drug Enforcement Act)/Other: (no qualifying statement) 1. Debarment Certification (original signature) YES 2. List of Convictions statement (original signature) YES	
1.3.4	**Financial Certifications** Bioavailability/Bioequivalence Financial Certification (Form FDA 3454) YES Disclosure Statement (Form FDA 3455)	
1.3.5	**Patent Information** Patents listed for the RLD in the Electronic Orange Book Approved Drug Products with Therapeutic Equivalence Evaluations **Patent Certification** 1. Patent number(s) 2. Paragraph: (Check all certifications that apply) MOU ☐ PI ☒ PII ☐ PIII ☐ PIV ☐ (Statement of Notification) ☐ 3. Expiration of Patent(s): NA a. Pediatric exclusivity submitted? b. Expiration of Pediatric Exclusivity? YES 4. Exclusivity Statement: Marketing intentions? Will not market until after expiration **Patent and Exclusivity Search Results from query on Appl No 022327 Product 001 in the OB_OTC list.** --- <> **There are no unexpired patents for this product in the Orange Book Database.** <> **Appl No** **Prod No** **Exclusivity Code** **Exclusivity Expiration** **N022327** **001** **NP** **May 18, 2012**	

1.4.1	**References** Letters of Authorization 1. DMF letters of authorization a. Type II DMF authorization letter(s) or synthesis for Active Pharmaceutical Ingredient YES b. Type II DMF# 21605 c. Type III DMF authorization letter(s) for container closure YES 2. US Agent Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) YES	
1.12.11	**Basis for Submission** NDA#: 22-327 Ref Listed Drug: PREVACID 24HR Firm: CONSUMER HEALTH INC. **ANDA suitability petition required?** If Yes, provide a copy of approved suitability petition and number **ANDA Citizen's Petition Required?** If Yes, provide petition number and copy of petition	

MODULE 1: ADMINISTRATIVE (Continued)

		COMMENT (S)
1.12.12	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use SAME 2. Active ingredients SAME 3. Inactive ingredients JUSTIFIED 4. Route of administration SAME 5. Dosage Form SAME 6. Strength SAME	
1.12.14	**Environmental Impact Analysis Statement** **(**cite 21CFR 25.31, if applicable) YES	
1.12.15	**Request for Waiver** Request for Waiver of In-Vivo BA/BE Study(ies)	
1.14.1	**Draft Labeling** (Multi Copies N/A for E-Submissions) **1.14.1.1** 4 copies of draft (each strength and container) YES **1.14.1.2** 1 side by side labeling comparison of containers and carton with all differences annotated and explained YES **1.14.1.3** 1 package insert (content of labeling) submitted electronically YES **1.14.1.4** SPL YES **1.14.1.5** Proprietary name requested NO If Yes, did the firm provide the request as a separate electronic amendment labeled "Proprietary Name Request" at initial time of filing 1. Yes 2. No - contact the firm to submit the request as a separate electronic amendment **HOW SUPPLIED** Lansoprazole delayed-release capsule is available in (b) (4) (b) (4) and 14 capsules unit dose blister packs	
1.14.3	**Listed Drug Labeling** **1.14.3.1** 1 side by side labeling (package and patient insert) comparison with all differences annotated and explained YES **1.14.3.3** RLD package insert, 1 RLD label and 1 RLD container label YES	

MODULE 2: SUMMARIES

		COMMENT (S)
2.3	**Quality Overall Summary (QOS)** **E-Submission: PDF** YES **Word Processed e.g., MS Word** YES A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage http://www fda.gov/cder/ogd/ **Question based Review (QbR)** YES **2.3.S Drug Substance (Active Pharmaceutical Ingredient)** YES 2.3.S.1 General Information 2.3.S.2 Manufacture 2.3.S.3 Characterization 2.3.S.4 Control of Drug Substance 2.3.S.5 Reference Standards or Materials 2.3.S.6 Container Closure System 2.3.S.7 Stability **2.3.P Drug Product** YES 2.3.P.1 Description and Composition of the Drug Product 2.3.P.2 Pharmaceutical Development 2.3.P.2.1 Components of the Drug Product 2.3.P.2.1.1 Drug Substance 2.3.P.2.1.2 Excipients 2.3.P.2.2 Drug Product 2.3.P.2.3 Manufacturing Process Development 2.3.P.2.4 Container Closure System 2.3.P.3 Manufacture 2.3.P.4 Control of Excipients 2.3.P.5 Control of Drug Product 2.3.P.6 Reference Standards or Materials 2.3.P.7 Container Closure System 2.3.P.8 Stability	
2.7	**Clinical Summary (Bioequivalence)** Model BE Data Summary Tables **E-Submission: PDF** YES **Word Processed: e.g., MS Word** YES **2.7.1 Summary of Biopharmaceutic Studies and Associated Analytical Methods** **2.7.1.1 Background and Overview** Table 1. Submission Summary YES Table 4. Bioanalytical Method Validation YES Table 6. Formulation Data YES **2.7.1.2 Summary of Results of Individual Studies** Table 5. Summary of In Vitro Dissolution YES **2.7.1.3 Comparison and Analyses of Results Across Studies** Table 2. Summary of Bioavailability (BA) Studies YES Table 3. Statistical Summary of the Comparative BA Data YES **2.7.1.4 Appendix** **2.7.4.1.3 Demographic and Other Characteristics of Study Population** Table 7. Demographic Profile of Subjects Completing the Bioequivalence Study YES **2.7.4.2.1.1 Common Adverse Events** Table 8. Incidence of Adverse Events in Individual Studies YES	

MODULE 3: 3.2.S DRUG SUBSTANCE

<table>
<tr><th></th><th></th><th>COMMENT (S)</th></tr>
<tr><td>3.2.S.1</td><td>General Information (Do not refer to DMF) YES
3.2.S.1.1 Nomenclature
3.2.S.1.2 Structure
3.2.S.1.3 General Properties</td><td></td></tr>
<tr><td>3.2.S.2</td><td>Manufacturer
Drug Substance (Active Pharmaceutical Ingredient)
1. Name and Full Address(es)of the Facility(ies) YES
2. Contact name, phone and fax numbers, email address YES
3. Specify Function or Responsibility YES
4. Type II DMF number for API 21605
5. CGMP Certification YES
6. CFN or FEI numbers</td><td></td></tr>
<tr><td>3.2.S.3</td><td>Characterization YES
Provide the following in tabular format:
1. Name of Impurity(ies)
2. Structure of Impurity(ies)
3. Origin of Impurity(ies)</td><td></td></tr>
<tr><td>3.2.S.4</td><td>Control of Drug Substance (Active Pharmaceutical Ingredient)
3.2.S.4.1 Specification YES
Testing specifications and data from drug substance manufacturer(s)
3.2.S.4.2 Analytical Procedures YES
3.2.S.4.3 Validation of Analytical Procedures
(API that is USP or reference made to DMF, must provide verification of USP or DMF procedures) YES
1. Spectra and chromatograms for reference standards and test samples YES
2. Samples-Statement of Availability and Identification of:

DRUG SUBSTANCE (Lansoprazole)

We hereby state that adequate quantity of Drug substance (Lansoprazole) is available with Wockhardt Limited, Aurangabad and is kept under controlled and recommended storage condition. The drug substance (Lansoprazole) can be made available to FDA on request.

Identified control numbers for Drug substance

<table><tr><th>Drug substance</th><th>Wockhardt's Control number</th></tr><tr><td>Lansoprazole</td><td>LJS10723</td></tr></table>
3.2.S.4.4 Batch Analysis
1. COA(s) specifications and test results from drug substance mfgr(s) YES
2. Applicant certificate of analysis YES
3.2.S.4.5 Justification of Specification YES</td><td></td></tr>
<tr><td>3.2.S.5</td><td>Reference Standards or Materials (Do not refer to DMF) YES</td><td></td></tr>
<tr><td>3.2.S.6</td><td>Container Closure Systems Refer to DMF</td><td></td></tr>
<tr><td>3.2.S.7</td><td>Stability
1. Retest date or expiration date of API YES – (b)(4) months</td><td></td></tr>
</table>

MODULE 3: 3.2.P DRUG PRODUCT

		COMMENT (S)
3.2.P.1	**Description and Composition of the Drug Product** 1. Unit composition YES 2. Inactive ingredients and amounts are appropriate per IIG (per/dose justification) YES 3. Conversion from % to mg/dose values for inactive ingredients (if applicable) N/A 4. Calculation of daily elemental iron or provide statement of adherence to 21CFR73.1200 N/A 5. Injections: If the reference listed drug is packaged with a drug specific diluent then the diluent must be Q1/Q2 and must be provided in the package configuration N/A	
3.2.P.2	**Pharmaceutical Development** Pharmaceutical Development Report YES	
3.2.P.3	**Manufacture** **3.2.P.3.1 Drug Product** (Finished Dosage Manufacturer and Outside Contract Testing Laboratories) 1. Name and Full Address(es)of the Facility(ies) YES 2. Contact name, phone and fax numbers, email address YES 3. Specify Function or Responsibility YES 4. CGMP Certification YES 5. CFN or FEI numbers **3.2.P.3.2 Batch Formula** YES **3.2.P.3.3 Description of Manufacturing Process and Process Controls** 1. Description of the Manufacturing Process YES 2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch) with equipment specified YES 3. Packaging records required if the package is part of manufacturing process YES 4. If sterile product N/A 5. Reprocessing Statement (cite 21CFR 211.115) YES **3.2.P.3.4 Controls of Critical Steps and Intermediates** YES **3.2.P.3.5 Process Validation and/or Evaluation** 1. Microbiological sterilization validation 2. Filter validation (if aseptic fill) PROPOSED COMMERCIAL BATCH SIZE: **STRENGTH** / **EXHIBIT BATCH SIZE** / **COMMERCIAL BATCH SIZE** (b) (4) **15 mg** / (b) (4) Capsules / (b) (4) Capsules	
3.2.P.4	**Controls of Excipients** (Inactive Ingredients) **Also refer to ANDA 202176** Source of inactive ingredients identified YES **3.2.P.4.1 Specifications** 1. Testing specifications (including identification and characterization) YES 2. Suppliers' COA (specifications and test results) YES **3.2.P.4.2 Analytical Procedures** YES **3.2.P.4.3 Validation of Analytical Procedures** (verification of USP procedure) USP/NF Testing **3.2.P.4.4 Justification of Specifications:** 1. Applicant COA YES	

MODULE 3: 3.2.P DRUG PRODUCT (Continued)

<table>
<tr><th></th><th></th><th>COMMENT (S)</th></tr>
<tr><td>3.2.P.5</td><td>
Controls of Drug Product
3.2.P.5.1 Specification(s) YES
3.2.P.5.2 Analytical Procedures (if USP, see Validation of Analytical Procedures section) YEs
3.2.P.5.3 Validation of Analytical Procedures
(if using USP procedure, must provide verification of USP procedure) YES
Samples - Statement of Availability and Identification of:
1. Finished Dosage Form YES
2. Lot number(s) and strength of Drug Product(s) YES

FINISHED DOSAGE FORM (Lansoprazole Delayed Release Capsules)

We hereby state that adequate samples of Lansoprazole Delayed Release Capsules USP, 15 mg (OTC) manufactured are kept at controlled storage condition. The samples can be made available to FDA on request.

Identification of lot numbers:
<table>
<tr><th>Drug product</th><th>Batch number</th></tr>
<tr><td>Lansoprazole Delayed Release Capsules USP, 15 mg (OTC)</td><td>LJS10917</td></tr>
</table>
3.2.P.5.4 Batch Analysis
Certificate of Analysis for Finished Dosage Form YES
3.2.P.5.5 Characterization of Impurities YES
3.2.P.5.6 Justification of Specifications YES
</td><td></td></tr>
<tr><td>3.2.P.7</td><td>
Container Closure System
1. Summary of Container/Closure System (if new resin, provide data) YES
2. Components Specification and Test Data YES
3. Packaging Configuration and Sizes YES
4. Container/Closure Testing (water permeation, light transmission, extractables and leachables when applicable) YES
5. Source of supply and suppliers address YES
</td><td></td></tr>
<tr><td>3.2.P.8</td><td>
3.2.P.8.1 Stability (Finished Dosage Form)
1. Stability Protocol submitted YES
2. Expiration Dating Period YES – (b) (4) MONTHS
3.2.P.8.2 Post-approval Stability and Conclusion
Post Approval Stability Protocol and Commitments YES
3.2.P.8.3 Stability Data
1. 3 month accelerated stability data
a. four (4) time points 0,1,2,3 YES
-OR-
b. three (3) time points 0,3,6 *
2. Batch numbers on stability records the same as the test batch YES – Lot # LJS10917

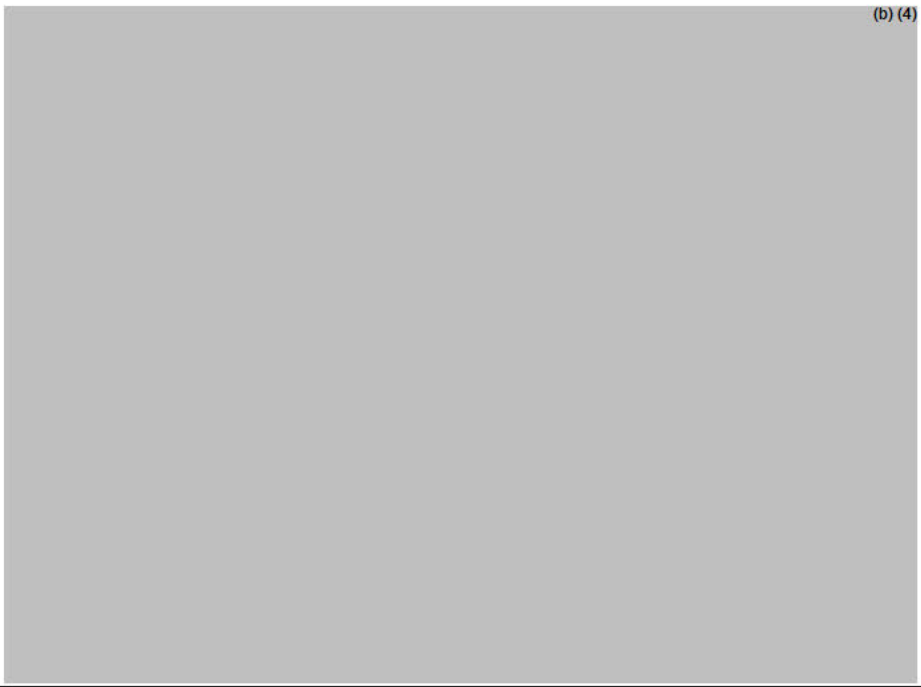
Note: * The Capsules of the parent ANDA exhibit batches are assigned separate batch numbers after packaging into different packs which are then taken for stability studies.
</td><td></td></tr>
</table>

**must provide 3 exhibit batches with 12 months of room temperature stability data (Refer to Guidance for Industry: Q1A(R2) Stability Testing of New Drug Substances and Products November 2003, Section B.)*

MODULE 3: 3.2.R REGIONAL INFORMATION (Drug Substance)

		COMMENT (S)
3.2.R Drug Substance	**3.2.R.1.S Executed Batch Records for drug substance (if available)** Refer to DMF **3.2.R.2.S Comparability Protocols** Refer to DMF **3.2.R.3.S Methods Validation Package** Refer to Module 3.2.S.4.3 Methods Validation Package (3 copies for paper and N/A for E-Submissions) (Required for Non-USP drugs)	

MODULE 3: 3.2.R REGIONAL INFORMATION (Drug Product)

		COMMENT (S)
3.2.R Drug Product	**3.2.R.1.P.1** **Executed Batch Records** Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures) Batch Reconciliation and Label Reconciliation YES **Lansoprazole Delayed Release Capsules, USP 15 mg** (b) (4) 	

Identification of Batch Numbers of Test Batch

Lansoprazole Delayed Release Capsules, USP 15 mg

(b) (4)

Yield Reconciliation of Lansoprazole Delayed Release Capsules, USP 15 mg

(b) (4)

3.2.R.1.P.2 Information on Components Refer to Module 3.2.P.4 and Module 3.2.P.7

3.2.R.2.P Comparability Protocols N/A

3.2.R.3.P Methods Validation Package Refer to Module 3.2.P.5.3

Methods Validation Package (3 copies for paper and N/A for E-Submissions)
(Required for Non-USP drugs)

MODULE 5: CLINICAL STUDY REPORTS

		COMMENT (S)
5.2	**Tabular Listing of Clinical Studies** YES	
5.3.1 (complete study data)	**Bioavailability/Bioequivalence** **1. Formulation data same?** a. Comparison of all Strengths (check proportionality of multiple strengths) YES b. Parenterals, Ophthalmics, Otics and Topicals (21 CFR 314.94 (a)(9)(iii)-(v) **2. Lot Numbers and strength of Products used in BE Study(ies)** RLD: Lot # 10074797 ANDA: Lot # LJ10534 **3. Study Type: IN-VIVO PK STUDY(IES)** (Continue with the appropriate study type box below)	
	5.3.1.2 Comparative BA/BE Study Reports 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) YES 2. Summary Bioequivalence tables: Table 10. Study Information YES Table 12. Dropout Information YES Table 13. Protocol Deviations YES **5.3.1.3 In Vitro-In-Vivo Correlation Study Reports** 1. Summary Bioequivalence tables: Table 11. Product Information YES Table 16. Composition of Meal Used in Fed Bioequivalence Study N/A **5.3.1.4 Reports of Bioanalytical and Analytical Methods for Human Studies** 1. Summary Bioequivalence table: Table 9. Reanalysis of Study Samples YES Table 14. Summary of Standard Curve and QC Data for Bioequivalence Sample Analyses YES Table 15. SOPs Dealing with Bioanalytical Repeats of Study Samples YES **5.3.7** **Case Report Forms and Individual Patient Listing**	
5.4	**Literature References**	
	Possible Study Types:	
Study Type	**IN-VIVO BE STUDY(IES) with PK ENDPOINTS** (i.e., fasting/fed/sprinkle) 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) YES 2. EDR Email: Data Files Submitted YES 3. In-Vitro Dissolution YES – In Module 5.3.1.2	
Study Type	**IN-VIVO BE STUDY with CLINICAL ENDPOINTS** 1. Properly defined BE endpoints (eval. by Clinical Team) Select 2. Summary results meet BE criteria: 90% CI of the proportional difference in success rate between test and reference must be within (-0.20, +0.20) for a binary/dichotomous endpoint. For a continuous endpoint, the test/reference ratio of the mean result must be within (0.80,1.25) Select 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) Select 4. EDR Email: Data Files Submitted Select	

Study Type	**IN-VITRO BE STUDY(IES)** (i.e., in vitro binding assays) Select 1. Study(ies) meets BE criteria (90% CI of 80-125) Select 2. EDR Email: Data Files Submitted Select 3. In-Vitro Dissolution Select	
Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** **1. Solutions (Q1/Q2 sameness)** Select a. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming) Select **2. Suspensions (Q1/Q2 sameness):** a. In-Vivo PK Study Select 1. Study(ies) meets BE Criteria (90% CI of 80-125, C max, AUC) Select 2. EDR Email: Data Files Submitted Select b. In-Vivo BE Study with Clinical End Points Select 1. Properly defined BE endpoints (eval. by Clinical Team) Select 2. Summary results meet BE criteria (90% CI within +/- 20% of 80-125) Select 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) Select 4. EDR Email: Data Files Submitted Select c. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming) Select	
Study Type	**IN-VIVO BE STUDY(IES) with PD ENDPOINTS** (e.g., topical corticosteroid vasoconstrictor studies) 1. Pilot Study (determination of ED50) Select 2. Pivotal Study (study meets BE criteria 90%CI of 80-125) Select	
Study Type	**TRANSDERMAL DELIVERY SYSTEMS** 1. In-Vivo PK Study Select a. Study(ies) meet BE Criteria (90% CI of 80-125, C max, AUC) Select b. In-Vitro Dissolution Select c. EDR Email: Data Files Submitted Select 2. Adhesion Study Select 3. Skin Irritation/Sensitization Study Select	

Updated 12/14/2010

Table 3 Statistical Summary of the Comparative Bioavailability Data

Drug: Lansoprazole Dose (15 mg) Least Squares Geometric Means, Ratio of Means, and 90% Confidence Intervals				
Fasted Bioequivalence Study (Study No. CPB-101-2010) Study Report Location: Section 11.4 of Clinical Study Report. Page No. 45				
Lansoprazole				
Parameter	**Test**	**Reference**	**Ratio**	**90% C.I.**
C_{max} (ng/mL)	512.2130	571.2630	89.66 %	83.69 % - 96.07 %
AUC_{0-t} (ng.hr/mL)	1577.2538	1734.3179	90.94 %	85.68 % - 96.54 %
$AUC_{0-\infty}$ (ng.hr/mL)	1619.7304	1780.0345	90.99 %	85.75 % - 96.56 %

Acceptance Criteria of BE Limit for Lansoprazole for C_{max}, AUC_{0-t} & $AUC_{0-\infty}$: 80.00% to 125.00 %.

Following this page, 2 Pages Withheld in Full as (b)(4)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

REBEKAH P GRANGER
05/09/2011

MARTIN H Shimer
05/12/2011

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 202727

Wockhardt USA LLC
US Agent for Wockhardt Limited
Attention: Leanne Usa
20 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to the telephone conversation dated April 1 and April 28, 2011 and your correspondence dated April 14 and April 28, 2011.

NAME OF DRUG: Lansoprazole Delayed-release Capsules, 15 mg

DATE OF APPLICATION: January 24, 2011

DATE (RECEIVED) ACCEPTABLE FOR FILING: January 26, 2011

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Frank J. Nice
Project Manager
240-276-8555

Sincerely yours,

{See appended electronic signature page}

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MARTIN H Shimer
05/12/2011
Signing for Wm Peter Rickman