CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-456

OTHER REVIEW(S)

Department of Health and Human Services

Public Health Service

Food and Drug Administration

Center for Drug Evaluation and Research

Office of Surveillance and Epidemiology

Date:	December 2, 2009
To:	Donna Griebel, MD Director, Division of Gastroenterology Products
Through:	Kellie Taylor, PharmD, MPH, Team Leader Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Zachary Oleszczuk, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Label and Labeling Review
Drug Name(s):	Omeprazole, Sodium Bicarbonate, and Magnesium Hydroxide Tablets 20 mg/750 mg/343 mg 40 mg/750 mg/343 mg
Application Type/Number:	NDA 022456
Applicant:	GlaxoSmithKline
OSE RCM #:	2009-1559

CONTENTS

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from the Division of Gastroenterology Products (DGP) for a review of the container labels and package insert labeling for NDA 022456, for evaluation of areas that could lead to medication errors.

1.2 PRODUCT INFORMATION

Omeprazole, Sodium Bicarbonate, and Magnesium Hydroxide Tablets is a combination product indicated for short term treatment of duodenal ulcer, treatment of gastric ulcer, treatment of gastroesophageal reflux disease, and maintenance of health of erosive esophagitis. Omeprazole, Sodium Bicarbonate, and Magnesium Hydroxide Tablets will be available in two strengths. Each tablet will contain either 20 mg or 40 mg of Omeprazole and both strengths will contain 750 mg of Sodium Bicarbonate and 343 mg of Magnesium Hydroxide. The usual dose of Omeprazole, Sodium Bicarbonate, and Magnesium Hydroxide Tablets is one tablet orally once daily for four to eight weeks or as chronic therapy.

2 METHODS AND MATERIALS REVIEWED

The Division of Medication Error Prevention and Analysis used Failure Mode and Effects Analysis (FMEA)[1] in our evaluation of the Omeprazole, Sodium Bicarbonate, and Magnesium Hydroxide Tablets revised container labels (see Appendix A) and insert labeling (no image) received November 30, 2009. We also evaluated the recommendations pertaining to the label and labeling presented in OSE review #2009-1559 to see if the DMEPA recommendations had been incorporated into the labels and labeling.

3 CONCLUSIONS AND RECOMMENDATIONS

The Division of Medication Error Prevention and Analysis (DMEPA) reviewed the revised container labels and insert labeling and find the revisions acceptable. In addition to the previous label and labeling comments DMEPA requests the following recommendations in Section 3.1 be communicated to the Applicant.

The Applicant has decided to pursue approval of the proposed product without a proprietary name and mange this NDA under the established name at this time. Section 3.2 provides advice should the Applicant decided to change the name post approval.

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[1] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

3.1 COMMENTS TO THE DIVISION

1. To be consistent with the presentation of active ingredients of combination products in the United States Pharmacopeia (USP), we recommend to revise all instances of the established name to remove '/' and replace each '/' with a comma. Additionally, include the word 'and' between the second comma and before the word 'Magnesium' so the name appears as stated below:

   Omeprazole, Sodium Bicarbonate, and Magnesium Hydroxide Tablets

   Also Study Endpoint and Labeling Development (SEALD) and the Immediate Office of Pharmaceutical Science (OPS) via email on November 27, 2009, support being consistent with USP nomenclature. We acknowledge that the Office of New Drug Quality Assessment (ONDQA) chemist assigned to this product does not feel this presentation is required (via email dated November 24, 2009) and we defer to the Division of Gastrointestinal Products' assessment of the final presentation.

2. The presentation of the established name is confusing because Sodium Bicarbonate is spilt between two lines of text. We recommend that Applicant revise the presentation of the proprietary name on the container labels to ensure that the words 'Sodium' and 'Bicarbonate' appear on the same line of text. If necessary the Applicant may reduce the size of the font to achieve this revision, but ensure that the same font is used for the entire established name (i.e. do not make 'Sodium Bicarbonate' a smaller font then the rest of the established name).

We would appreciate feedback on the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Nitin Patel, Project Manager, at 301-796-5412.

3.2 COMMENTS TO THE APPLICANT REGARDING PROPRIETARY NAME

We acknowledge your decision to seek approval without a proprietary name at this time and to manage NDA 022456 under the established name. If you decided to pursue a proprietary name after the approval of this product you will need to submit a complete proprietary name submission (see Guidance for Industry Contents of a complete submission for the Evaluation of Proprietary Names[2]) and updated labels and labeling as part of a post approval labeling supplement.

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2 http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf . Guidance for Industry Contents of a complete submission for the Evaluation of Proprietary Names, November 2008.

4 REFERENCES

4.1 REVIEW

OSE Review #2009-1559 Label and Labeling Review for Zegerid ——(Omeprazole, Sodium Bicarbonate, and Magnesium Hydroxide Tablets), Oleszczuk, Z; November 5, 2009. b(4)

4.2 EMAILS

4.2.1 The Office of New Drugs Quality Assessment (ONDQA)

Rhee, Moo-Jhong, November 24, 2009, RE: NDA 22-456 Revised PI& Bottle Label: established name only.

4.2.2 Study Endpoint and Labeling Development (SEALD) and the Immediate Office of Pharmaceutical Science (OPS)

Burke, Laurie and Mille, Yana,, November 27, 2009, RE: NDA 022456 Revised PI& Bottle Label: established name only.

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_____ § 552(b)(4) Trade Secret / Confidential

✓ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22456	ORIG-1	SANTARUS INC	ZEGERID

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/s/

ZACHARY A OLESZCZUK
12/02/2009

KELLIE A TAYLOR
12/02/2009

CAROL A HOLQUIST
12/02/2009

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	November 5, 2009
To:	Donna Griebel, MD Director, Division of Gastroenterology Products
Through:	Kellie Taylor, Pharm D, MPH, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Zachary Oleszczuk, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Label and Labeling Review
Drug Name(s):	Zegerid ——(Omeprazole/Sodium Bicarbonate/Magnesium Hydroxide) Tablets b(4) 20 mg/750 mg/343 mg 40 mg/750 mg/343 mg
Application Type/Number:	NDA 022456
Applicant:	GlaxoSmithKline
OSE RCM #:	2009-1559

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1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from the Division of Gastroenterology Products (DGP) for a review of the container labels and package insert labeling for NDA 022456, for evaluation of areas that could lead to medication errors.

1.2 PRODUCT INFORMATION

b(4)

Zegerid ——— (Omeprazole/Sodium Bicarbonate/Magnesium Hydroxide) is combination product indicated for short term treatment of duodenal ulcer, treatment of gastric ulcer, treatment of gastroesophageal reflux disease, and maintenance of health of erosive esophagitis. Zegerid ——— will be available as in two strengths. Each tablet will contain either 20 mg or 40 mg of Omeprazole and both strengths will contain 750 mg of Sodium Bicarbonate and 343 mg of Magnesium Hydroxide. The usual dose of Zegerid ——— is one tablet orally once daily for four to eight weeks or as chronic therapy.

b(4)

b(4)

2 METHODS AND MATERIALS REVIEWED

b(4)

The Division of Medication Error Prevention and Analysis used Failure Mode and Effects Analysis (FMEA)[1] in our evaluation of the Zegerid ——— container labels (see Appendix A) and insert labeling (no image) received on August 24, 2009. Additionally, DMEPA reviewed the container labels and carton labeling for currently marketed Zegerid Products (see Appendix B) received on August 24, 2009.

3 CONCLUSIONS AND RECOMMENDATIONS

We request the following recommendations be communicated to the Applicant prior to approval.

3.1 COMMENTS TO THE DIVISION

1. The final determination of the proprietary name has not been completed at the time of this review. The Applicant has proposed the proprietary name 'Zegerid ——— for this product. If the approved proprietary name contains the root name 'Zegerid' the Applicant should add the statement "Do not substitute for other Zegerid Dosage Forms" to the highlights section. Section 2 contains a similar statement, however, since this proposed product is not to be interchanged with other Zegerid products, the differences of this product should be made prominent to help make healthcare providers aware of the differences and minimize the possibility of interchange. If the approved proprietary name does not contain the root name 'Zegerid', then these comments would be irrelevant and should be removed from the package insert.

b(4)

[1] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

2. Replace all the instances of 'Zegerid'——with the word 'trademark'. Since the proprietary name is still under review, we (DMEPA) would prefer to take out any reference to the proprietary name until a final determination has been reached. Once a decision has been made on the proprietary name the Applicant can revise the package insert to reflect that. b(4)

3.2 COMMENTS TO THE APPLICANT

The color scheme of gray for the 20 mg tablets and orange for the 40 mg tablets used for the proposed container labels is similar to the color scheme of the of the currently marketed product. Using a similar color scheme to differentiate the strengths of each product may introduce vulnerability to confusion that could lead to medication errors involving selection of the wrong drug. In addition to the similar color scheme, the container labels of the proposed product share overlapping numerical strengths (the 20 mg and 40 mg of Omeprazole) and two overlapping active ingredients (Omeprazole and Sodium Bicarbonate) with the currently marketed Zegerid container labels. This proposed product and the currently marketed product may be stored in close proximity to one another regardless of the final proprietary name approved for this product. Pharmacies may store medication based on the established name or active ingredients of a product. Since, both products contain omeprazole and omeprazole is the first active ingredient stated in both established names, these products may be stored in close proximity of one another. Revise the color scheme of the container labels for Zegerid —— to be different then the currently marketed Zegerid product. b(4)

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_____ § 552(b)(4) Trade Secret / Confidential

✓ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22456	ORIG-1	SANTARUS INC	ZEGERID

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/s/

ZACHARY A OLESZCZUK
11/05/2009

KELLIE A TAYLOR
11/05/2009

DENISE P TOYER
11/05/2009

CAROL A HOLQUIST
11/06/2009

SEALD LABELING REVIEW

APPLICATION NUMBER	NDA 22-456
APPLICANT	Santarus, Incorporated
DRUG NAME	ZEGRID [redacted] (omeprazole, sodium bicarbonate, and magnesium hydroxide) b(4)
SUBMISSION DATE	February 4, 2009
SEALD REVIEW DATE	October 27, 2009
SEALD REVIEWER(S)	Debbie Beitzell, BSN
	This review does not identify all guidance-related labeling issues and all best practices for labeling. We recommend the review division become familiar with those recommendations. This review does attempt to identify all aspects of the draft labeling that do not meet the requirements of 21 CFR 201.56 and 201.57.

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✓ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

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DEBRA C BEITZELL
10/28/2009

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