CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

213051Orig1s000

OTHER REVIEW(S)

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	September 3, 2019
Requesting Office or Division:	Division of Metabolism and Endocrinology Products (DMEP)
Application Type and Number:	NDA 213051
Product Name and Strength:	Rybelsus (semaglutide) tablet, 3 mg, 7 mg, and 14 mg
Applicant/Sponsor Name:	Novo Nordisk Inc. (Novo)
FDA Received Date:	August 30, 2019
OSE RCM #:	2019-643-1
DMEPA Safety Evaluator:	Ariane O. Conrad, PharmD, BCACP, CDE
DMEPA Team Leader:	Hina Mehta, PharmD

1 PURPOSE OF MEMORANDUM

Novo Nordisk submitted revised labels and labeling for Rybelsus on August 30, 2019. We reviewed the revised labels and labeling for Rybelsus (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

The Applicant implemented all of our recommendations and we have no additional recommendations at this time.

[a] Conrad A. Label and Labeling Review for Rybelsus (NDA 213051). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Aug 2 MON DD. RCM No.: 2019-643.

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/s/

ARIANE O CONRAD
09/03/2019 03:18:47 PM

HINA S MEHTA
09/04/2019 09:57:17 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Division of Pediatric and Maternal Health
Office of New Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Silver Spring, MD 20993
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Division of Pediatric and Maternal Health
PLLR Labeling Memorandum

Date: August 29, 2019 **Date consulted:** April 8, 2019

From: Jane Liedtka, M.D. Medical Officer, Maternal Health
Division of Pediatric and Maternal Health (DPMH)

Through: Lynne P. Yao, MD, OND, Director
Division of Pediatric and Maternal Health

To: Peter Franks, Regulatory Health Project Manager (RPM)
Division of Metabolic and Endocrine Products (DMEP)

Drug/NDA: Rybelsus **(**semaglutide tablet), NDA 213051

Applicant: Novo Nordisk Inc.

Subject: Pregnancy and Lactation Labeling [New drug application (NDA), priority review, contains excipient not previously approved)

Indications:

- an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM)
- an adjunct to standard treatment of cardiovascular risk factors to reduce the risk of myocardial infarction or stroke in adults with T2DM and high cardiovascular risk

Materials Reviewed:

- DPMH review of Ozempic (semaglutide) injection, NDA 209637. Jane Liedtka, MD, September 6, 2017. DARRTS Reference ID 4148940.
- Pharmacology/Toxicology review for semaglutide oral tablet, NDA 213051. Elena Braithwaite, PhD, August 23, 2019. DARRTS Reference ID 4482035.

Consult Question:

Please confirm PLLR format is acceptable.

INTRODUCTION

DMEP consulted DPMH on April 8, 2019, to provide input for appropriate labeling of the pregnancy and lactation subsections of NDA 213051 for Rybelsus, [semaglutide oral tablets formulated with an absorption enhancer, salcaprozate sodium (SNAC).] to comply with the Pregnancy and Lactation Labeling Rule (PLLR) format.

REGULATORY HISTORY AND BACKGROUND

- Ozempic [semaglutide, a human glucagon-like peptide-1 (GLP-1) receptor agonist], for injection was approved on December 5, 2017.
- On March 20, 2019, Novo Nordisk, Inc. submitted a NDA for Rybelsus, a semaglutide oral tablet via the 505 (b) 2 pathway, which contains a novel absorption enhancer, SNAC. This product is indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM and as an adjunct to standard treatment of cardiovascular risk factors to reduce the risk of myocardial infarction or stroke in adults with T2DM and high cardiovascular risk.
- The Applicant proposes dosing as a once daily oral tablet.
- The original submission included a review of the literature and a summary of the pharmacoviglance database regarding pregnancy, lactaion and effects on fertility for semaglutide.
- At the time of the original consultation, DPMH proposed to attend the labeling meeting and provide recommendations for PLLR language but did not plan to provide a written review. A previous written DPMH review for Ozempic (semaglutide for injection), NDA 209637 was to be the basis for the labeling recommendations. Labeling recommendations similar to those proposed for the previous semaglutide injection product were provided prior to the first labeling meeting. The language for labeling that was approved are reproduced below from the 2019 Ozempic label[1]. Minor modifications in the language for the first sentence of section 8.1 Risk Summary are proposed by DPMH to update the language as follows:

  > Available data with TRADENAME use in pregnant women are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes.

  OZEMPIC LABEL[1]
  Highlights of Prescribing Information (HPI)

  ·····USE IN SPECIFIC POPULATIONS·····
  Females and Males of Reproductive Potential: Discontinue OZEMPIC in women at least 2 months before a planned pregnancy due to the long washout period for semaglutide (8.3).

[1] Approved label for Ozempic, dated 4/9/2019

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