CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201281Orig1s000

SUMMARY REVIEW

Cross-Discipline Team Leader Review

Date	January 26, 2012
From	Jean-Marc Guettier, M.D.
Subject	Cross-Discipline Team Leader Review
NDA/BLA # Supplement#	201281/ Resubmission-Class 1
Applicant	Boehringer Ingelheim Pharmaceuticals, Inc.
Date of Submission	November 19th, 2011
PDUFA Goal Date	January 30th, 2012
Proprietary Name / Established (USAN) names	Jentadueto®/ Linagliptin and metformin hydrochloride fixed dose combination
Dosage forms / Strength	Oral tablets with the following dosage strengths: Linagliptin 2.5 mg / metformin 500 mg Linagliptin 2.5 mg / metformin 850 mg Linagliptin 2.5 mg / metformin 1000 mg
Proposed Indication(s)	To improve glycemic control in adults patients with type 2 diabetes mellitus
Recommended:	Approval

1. Introduction

Boehringer Ingelheim Pharmaceuticals, Inc. is resubmitting (class-1 resubmission) the New Drug Application #201281 under section 505(b)(2) of the Federal Food, Drug and Cosmetic Act for the fixed-dose combination product linagliptin /metformin hydrochloride. The reference listed drug is the US approved Glucophage (metformin). The applicant was issued a complete response on November 16th 2011 due to deficiencies noted at a facility (b) (4) used for the testing of metformin hydrochloride and excipients contained in the final drug product. The applicant was informed that satisfactory resolution of these deficiencies would be needed before the product could be approved. To resolve this deficiency the applicant notifies the Agency that the (b) (4) testing facility has been removed, that the testing of metformin hydrochloride will be performed by Boehringer Ingelheim Pharma GmbH & Co. KG (Ingelheim, Germany) and that the testing of excipients will be performed by (b) (4)

In addition, the applicant states that only limited new safety information for linagliptin/metformin FDC has been received since submission of the four-month safety update data and that these new data do not reveal significant changes or findings relevant to the safety profile of the product. The product is not currently marketed outside of the US. There are no clinical data in this resubmission.

2. Background

All disciplines, with the exception of CMC, involved in the first review cycle (January 19th 2011-November 19th 2011) recommended approval of the NDA. Refer to Dr. Irony's October 15th 2011 CDTL memo for details.

3. CMC/Device

The Office of Manufacturing & Product Quality (OMPQ) has determined that the new facilities employed to manufacture and test the drug substances and drug product are acceptable. Chemistry and OMPQ recommend approval.

4. Nonclinical Pharmacology/Toxicology

No new information. Refer to Dr. Irony's CDTL memo.

5. Clinical Pharmacology/Biopharmaceutics

No new information. Refer to Dr. Irony's CDTL memo.

6. Clinical Microbiology

No new information. Refer to Dr. Irony's CDTL memo.

7. Clinical/Statistical- Efficacy

No new information. Refer to Dr. Irony's CDTL memo.

8. Safety

No new information. Refer to Dr. Irony's CDTL memo.

9. Advisory Committee Meeting

No new information. Refer to Dr. Irony's CDTL memo.

10. Pediatrics

No new information. Refer to Dr. Irony's CDTL memo.

11. Other Relevant Regulatory Issues

No new information. Refer to Dr. Irony's CDTL memo.

12. Labeling

Jentadueto has been conditionally approved as the proprietary trade name by the Division of Medication Error Prevention and Analysis. Labeling discussion around the pregnancy category for metformin occurred during the last review cycle. From these discussions and review of the clinical experience with metformin published in the literature it was determined that metformin should be designated as a Pregnancy Category B drug and that language to summarize the nonclinical findings be included in section 8.1 of the label. This pregnancy category is consistent with other approved metformin labels. Refer to Dr. Irony's CDTL memo for details. Minor editing changes to the label were sent to the sponsor at the time this memorandum was written.

13. Recommendations/Risk Benefit Assessment

- Recommended Regulatory Action

APPROVAL

- Risk Benefit Assessment

Refer to Dr. Irony's CDTL memo.

- Recommendation for Postmarketing Risk Evaluation and Management Strategies

No new safety findings to trigger the need for REMS

- Recommendation for other Postmarketing Requirements and Commitments

No new safety findings to trigger the need for Postmarketing Requirements and Commitments

- Recommended Comments to Applicant

None

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/s/

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01/26/2012

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01/26/2012
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