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RESEARCH**

*APPLICATION NUMBER:*

**201281Orig1s000**

**SUMMARY REVIEW**

## Cross-Discipline Team Leader Review

<b>Date</b>	January 26, 2012
<b>From</b>	Jean-Marc Guettier, M.D.
<b>Subject</b>	Cross-Discipline Team Leader Review
<b>NDA/BLA #</b>	201281/ Resubmission-Class 1
<b>Supplement#</b>	
<b>Applicant</b>	Boehringer Ingelheim Pharmaceuticals, Inc.
<b>Date of Submission</b>	November 19 <sup>th</sup> , 2011
<b>PDUFA Goal Date</b>	January 30 <sup>th</sup> , 2012
<b>Proprietary Name / Established (USAN) names</b>	Jentaducto®/ Linagliptin and metformin hydrochloride fixed dose combination
<b>Dosage forms / Strength</b>	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
<b>Proposed Indication(s)</b>	To improve glycemic control in adults patients with type 2 diabetes mellitus
<b>Recommended:</b>	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 16<sup>th</sup> 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 19<sup>th</sup> 2011-November 19<sup>th</sup> 2011) recommended approval of the NDA. Refer to Dr. Irony's October 15<sup>th</sup> 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**

Jentaducto 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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