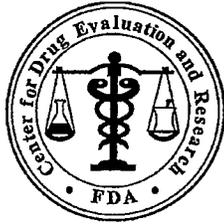


**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**22-350**

**RISK ASSESSMENT and RISK MITIGATION  
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: June 22, 2009

To: Mary Parks, M.D., Director  
Division of Metabolism and Endocrine Drug  
Products (DMEP)

Through: Jodi Duckhorn, MA, Team Leader  
Division of Risk Management

From: Jessica M. Diaz, RN, BSN  
Patient Product Information Reviewer  
Division of Risk Management

Subject: DRISK Review of Patient Labeling (Patient  
Package Insert)

Drug Name(s): ONGLYZA (saxagliptin)

Application  
Type/Number: NDA 22-350

Applicant/sponsor: Bristol-Myers Squibb Company

OSE RCM #: 2008-1199

## **1 INTRODUCTION**

Bristol-Myers Squibb Company submitted NDA 22-350 on June 30, 2008 as a new molecular entity (NME), saxagliptin. The Division of Medication Error Prevention and Analysis (DMEPA) was consulted on June 11, 2008 to review proprietary name, Onglyza. The consult was received by Division of Metabolism and Endocrine Products (DMEP) on July 23, 2008 to review the label and labeling for Onglyza.

A submission was sent by Bristol-Myers Squibb Company on April 9, 2009 for this NDA with revised labeling changes based on the comments from the review division on February 11, 2009. DMEP requested that the Division of Risk Management (DRISK) review the patient labeling that was submitted as part of the labeling for this NDA. This review is written in response to that request.

## **2 MATERIAL REVIEWED**

- ONGLYZA Patient Package Insert (PPI) revised submission from April 9, 2009
- ONGLYZA Prescribing Information (PI) revised submission from April 9, 2009, and revised by the Review Division throughout the current review cycle.

## **3 DISCUSSION**

The purpose of patient directed labeling is to facilitate and enhance appropriate use and provide important risk information about medications. Our recommended changes are consistent with current research to improve risk communication to a broad audience, including those with lower literacy.

Content and formatting revisions are made to ensure that the information is legible, clear, and patient-friendly. Patient Information that is well designed and clearly worded can help to maximize patient use and understanding of important safety information that is presented.

The draft PPI submitted by the Applicant has a Flesch Kinkaid grade level of 8.8, and a Flesch Reading Ease score of 57.3%. To enhance patient comprehension, materials should be written at a 6<sup>th</sup> to 8<sup>th</sup> grade reading level, and have a reading ease score of at least 60% (60% corresponds to an 8<sup>th</sup> grade reading level). The reading scores as submitted by the Applicant are acceptable.

In our review of the PPI, we have:

- simplified wording and clarified concepts where possible,
- ensured that the PPI is consistent with the PI,
- removed unnecessary or redundant information
- ensured that the PPI meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006).

In 2008, The American Society of Consultant Pharmacists Foundation in collaboration with The American Foundation for the Blind published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. They recommend using fonts such as Arial, Verdana, or APHont to make medical information more accessible for patients with low vision. We have reformatted the PPI document using the font APHont, which was developed by the American Printing House for the Blind specifically for low vision readers.

See the attached document for our recommended revisions to the PPI. Comments to the review division are ***bolded, underlined and italicized***.

We are providing the review division a marked-up and clean copy of the revised PPI. We recommend using the clean copy as the working document.

All future relevant changes to the PI should also be reflected in the PPI.

#### 4 CONCLUSIONS AND RECOMMENDATIONS

1. The Applicant uses both the terms "doctor," and "healthcare provider" in the proposed PPI. We recommend that one term be used consistently throughout the PPI.

In the section "What is ONGLYZA?":

- we have deleted "

**b(4)**

- we recommend moving the disease specific information to the end of the PPI or preferably address disease related information with patient individually.

2. In the section "Who should not take ONGLYZA?" we have:

- moved the section "ONGLYZA should not be used to treat:" to the section "What should I tell my doctor before taking ONGLYZA?" to be consistent with placement of this information in patient labeling.

- deleted the section C

b(4)

3. In the section "What should I tell my doctor before taking ONGLYZA?" we have:

- added "Know the medicines you take. Keep a list of your medicines and show it to your healthcare provider and pharmacist when you get a new medicine" as this is standard language in patient information.
- deleted C
- We have instead moved this information to the section "How should I take ONGLYZA?" which is typically used for drug Dosage and Administration.
- we moved the signs and symptoms that may require a need to change the patient's medication to the section "How should I take ONGLYZA?" because this section includes information from Dosage and Administration section of PI.
- we recommend not including a long list of drugs with single brand names because if the brand name of the patient's medicine is not included, they may think that their medicine is "safe".

b(4)

4. In the section "How should I take ONGLYZA?" we have:

- deleted C
- included in the section "What should I tell my healthcare provider before taking ONGLYZA?".
- added the symptoms associated with possible changes in medication dose
- added "Follow your healthcare provider's instructions for treating low blood sugar. Talk to your healthcare provider if low blood sugar is a problem for you."

b(4)

5. In the sections C

b(4)

• Patient labeling is to convey product-specific information, not disease or condition-specific information.

We recommend this information be discussed with the patient during his/her appointment with the healthcare provider.

6. In the section, "What are the possible side effects of ONGLYZA?" we have:
- added "ONGLYZA may cause serious side effects including:", which corresponds to the "Warnings and Precautions" section in PI.
  - Added "kidney problems" and "low blood sugar (hypoglycemia)" because the PI recommends dose adjustments for moderate or severe renal impairment/ESRD and a lower dose of ONGLYZA when used with sulfonylureas.
  - Under "most common side effects of ONGLYZA" added peripheral edema "swelling of hand and feet" to be consistent with the PI.
  - Removed the section that  $\ll$

**b(4)**

7. In the section, "How should I store ONGLYZA?" we have inserted the range of temperatures as listed in the PI instead of "room temperature" because it provides a quantitative range. "Room temperature" can be interpreted differently by people.

Please let us know if you have any questions.

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this page is the manifestation of the electronic signature.**  
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/s/

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Jessica Diaz  
6/22/2009 10:24:46 AM  
LABELING REVIEWER

Jodi Duckhorn  
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DRUG SAFETY OFFICE REVIEWER