CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210308Orig1s000

OTHER REVIEW(S)

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: February 26, 2018

To: Julia Beaver, M.D., Acting Director
Division of Oncology Products 1 (DOP1)

Kim Robertson, Regulatory Project Manager, (DOP1)

William Pierce, PharmD, Associate Director for Labeling, (DOP1)

From: Kevin Wright, PharmD, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Brian Tran, PharmD, MBA, Team Leader, OPDP

Subject: OPDP Labeling Comments for Yonsa™ (abiraterone acetate) tablets, for oral use

NDA: 210308

In response to DOP1's consult request dated July 13, 2017, OPDP has reviewed the proposed product labeling (PI), patient package insert (PPI), and carton and container labeling for the original NDA submission for Yonsa™ (abiraterone acetate) tablets for oral use (Yonsa).

OPDP's comments on the proposed labeling are based on the draft PI and PPI received by electronic mail from DOP1 (Kim Robertson) on February 13, 2018, and are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review was completed, and comments on the proposed PPI were sent under separate cover on February 23, 2018.

OPDP has reviewed the attached proposed container label submitted by the Sponsor to the electronic document room on February 15, 2018, and we do not have any comments.

Thank you for your consult. If you have any questions, please contact Kevin Wright at (301) 796-3621 or kevin.wright@fda.hhs.gov.

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/s/

KEVIN WRIGHT
02/26/2018

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

PATIENT LABELING REVIEW

Date:	February 23, 2018
To:	Julia Beaver, MD Acting Director **Division of Oncology Products 1 (DOP1)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Morgan Walker, PharmD, MBA, CPH Sr. Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)**
From:	Ruth Lidoshore, PharmD Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Kevin Wright, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI)
Drug Name (established name):	YONSA (abiraterone acetate)
Dosage Form and Route:	tablets, for oral use
Application Type/Number:	NDA 210308
Applicant:	Churchill Pharmaceuticals LLC

1 INTRODUCTION

On May 19, 2017, Churchill Pharmaceuticals LLC submitted for the Agency's review a 505(b)(2) New Drug Application (NDA) 210308 for YONSA (abiraterone acetate) tablets. The Reference Listed Drug for this application is NDA 202379 for ZYTIGA (abiraterone acetate) tablets. The proposed indication for YONSA (abiraterone acetate) tablets is in combination with methylprednisolone for the treatment of patients with metastatic castration-resistant prostate cancer.

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Oncology Products 1 (DOP1) on July 13, 2017, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) for YONSA (abiraterone acetate) tablets.

2 MATERIAL REVIEWED

- Draft YONSA (abiraterone acetate) PPI received on May 19, 2017, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on February 13, 2018.
- Draft YONSA (abiraterone acetate) Prescribing Information (PI) received on May 19, 2017, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on February 13, 2018.
- Approved ZYTIGA (abiraterone acetate) comparator labeling dated February 7, 2018.

3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8th grade reading level.

Additionally, in 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss. We reformatted the PPI document using the Arial font, size 10.

In our collaborative review of the PPI we:

- simplified wording and clarified concepts where possible
- ensured that the PPI is consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information
- ensured that the PPI is free of promotional language or suggested revisions to ensure that it is free of promotional language

- ensured that the PPI meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)
- ensured that the PPI is consistent with the approved comparator labeling where applicable.

4 CONCLUSIONS

The PPI is acceptable with our recommended changes.

5 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
- Our collaborative review of the PPI is appended to this memorandum. Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the PPI.

Please let us know if you have any questions.

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/s/

RUTH I LIDOSHORE
02/23/2018

KEVIN WRIGHT
02/23/2018

MORGAN A WALKER
02/23/2018

LASHAWN M GRIFFITHS
02/23/2018

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:	February 5, 2018
Requesting Office or Division:	Division of Oncology Products 1 (DOP1)
Application Type and Number:	NDA 210308
Product Name and Strength:	Yonsa (abiraterone acetate) Tablets, 125 mg
Applicant/Sponsor Name:	Churchill Pharmaceuticals LLC
FDA Received Date:	January 29, 2018
OSE RCM #:	2017-1055-1
DMEPA Safety Evaluator:	Tingting Gao, PharmD
DMEPA Team Leader:	Chi-Ming (Alice) Tu, PharmD

1 PURPOSE OF MEMO

DOP1 requested that we review the revised Yonsa container labels (Appendix A) to determine if it is 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 revised Yonsa container labels and professional sample container labels are acceptable from a medication error perspective. We have no further recommendations at this time.

[a] Gao T. Label and Labeling Review for Yonsa (NDA 210308). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 JAN 11. RCM No.: 2017-1055.

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/s/

TINGTING N GAO
02/05/2018

CHI-MING TU
02/05/2018

LABEL AND LABELING REVIEW

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)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	January 11, 2018
Requesting Office or Division:	Division of Oncology Products 1 (DOP1)
Application Type and Number:	NDA 210308
Product Name and Strength:	Yonsa (abiraterone acetate) Tablets, 125 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Churchill Pharmaceuticals LLC
Submission Date:	September 26, 2017 and November 7, 2017
OSE RCM #:	2017-1055
DMEPA Safety Evaluator:	Tingting Gao, PharmD
DMEPA Team Leader:	Chi-Ming (Alice) Tu, PharmD
DMEPA Deputy Director (Acting):	Danielle Harris, PharmD, BCPS

1 REASON FOR REVIEW

As a part of this 505(b)(2) NDA 210308 for Yonsa, DOP1 requested DMEPA to evaluate the proposed Yonsa container labels and Prescribing Information (PI) to identify areas of vulnerability that could lead to medication errors. The listed drug is Zytiga (abiraterone acetate) Tablet, NDA 202379.

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B – N/A
Human Factors Study	C – N/A
ISMP Newsletters	D
FDA Adverse Event Reporting System (FAERS)*	E – N/A
Other	F – N/A
Labels and Labeling	G

N/A=not applicable for this review
*We do not typically search FAERS for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

3.1 PRESCRIBING INFORMATION

We reviewed the Dosage Administration section, Dosage Forms and Strength section, and How Supplied/Storage and Handling section and determined that the proposed Yonsa PI could be improved to ensure safe use of the product.

3.2 CONTAINER LABELS

We reviewed the proposed Yonsa container labels and professional sample container labels and noted the statement [redacted] (b) (4) [redacted] This statement uses the term [redacted] (b) (4) [redacted] that is typically reserved for biosimilar products. Because the proposed Yonsa product is not a biosimilar product, the use of the term [redacted] (b) (4) [redacted] is misleading.

The Applicant's external study titled "Market Research Report" evaluated the following presentations of this statements (bolded and underlined as presented in the report):[a]

A. (b) (4)

B.

C.

The external evaluation found there was no statistical difference between presentations A and B above in terms of aid in respondents' understanding of the statement (32% vs. 39%), while presentation C is least helpful (29%). Our review finds the presentation of this important statement may be improved to increase its prominence.

4 CONCLUSION & RECOMMENDATIONS

The proposed Yonsa PI, Yonsa container labels and professional sample container labels may be improved to ensure safe use. We provide specific recommendations in Section 4.1 and Section 4.2 below.

4.1 RECOMMENDATIONS FOR THE DIVISION

A. Prescribing Information
    1. Dosage and Administration, Highlights of PI
        i. Avoid the term (b) (4) because the term (b) (4) is typically reserved for use with biosimilar products. Since the proposed Yonsa Tablet is not a biosimilar product, the use of the term (b) (4) is misleading. Therefore, revise the statement (b) (4) to read "To avoid (b) (4) errors and overdose (b) (4) ." for clarity.
    2. Dosage and Administration, Full PI
        i. Avoid the term (b) (4)" because the term (b) (4)" is typically reserved for use with biosimilar products. Revise the statement Revise the statement (b) (4) to read "To avoid (b) (4) errors and overdose, (b) (4)

[a] (b) (4)

[redacted] (b) (4)
." for clarity.

4.2 RECOMMENDATIONS FOR CHURCHILL PHARMACEUTICALS

We recommend the following be implemented prior to approval of this NDA:

A. Container labels
   1. Revise the statement [redacted] (b) (4) to read [redacted] (b) (4) The term [redacted] (b) (4) is typically reserved for use with biosimilar products. Since the proposed Yonsa Tablet is not a biosimilar product, the use of the term [redacted] (b) (4) is misleading. Additionally, add a rectangular outline around the text to increase its prominence.
   2. Relocate the net quantity statement "120 tablets" to the principal display panel. The net quantity statement "120 tablets" should be displayed on the principal display panel in accordance with *Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors*. Ensure the net quantity statement is less prominent and located away from the product strength.
   3. Label the NDC number with the header "NDC" so the statement reads [redacted] (b) (4)
   4. As currently presented, the format for the expiration date is not defined. To minimize confusion and reduce the risk for deteriorated drug medication errors, identify the format you intend to use. We recommend using a format such as MMMYYYY (e.g. JAN2017) or MMMDDYYYY (e.g. JAN312017).

[redacted] (b) (4)

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for the listed drug (LD) and Yonsa that Churchill Pharmaceuticals submitted on August 17, 2017, and the listed drug (LD).

Table 2. Relevant Product Information for listed drug and Yonsa

Product Name	**Zytiga**	**Yonsa**
Initial Approval Date	4/28/2011	N/A
Active Ingredient	abiraterone acetate	abiraterone acetate
Indication	indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer.	indicated in combination with methylprednisolone for the treatment of patients with metastatic castration-resistant prostate cancer.
Route of Administration	Oral	Oral
Dosage Form	Tablets Film-Coated Tablets	Tablets
Strength	Tablets: 250 mg Film-Coated Tablets: 250 mg and 500 mg	125 mg
Dose and Frequency	1,000 mg (two 500 mg tablets or four 250 mg tablets) administered orally once daily in combination with prednisone 5 mg administered orally twice daily. • For patients with baseline moderate hepatic impairment (Child-Pugh Class B), reduce the ZYTIGA starting dose to 250 mg once daily. • For patients who develop hepatotoxicity during treatment, hold ZYTIGA until recovery. Retreatment may be initiated at a reduced dose.	500 mg (four 125 mg tablets) administered orally once daily in combination with methylprednisolone 4 mg administered orally twice daily. • For patients with baseline moderate hepatic impairment (Child-Pugh Class B), reduce the YONSA starting dose to 125 mg once daily. • For patients who develop hepatotoxicity during treatment, hold YONSA until recovery. Retreatment may be initiated at a reduced dose.

Table 2. Relevant Product Information for listed drug and Yonsa		
Product Name	**Zytiga**	**Yonsa**
How Supplied	ZYTIGA 500 mg film-coated Tablets: high-density polyethylene bottles containing 60 tablets. ZYTIGA 250 mg film-coated Tablets: high-density polyethylene bottles containing 120 tablets. ZYTIGA 250 mg uncoated Tablets: high-density polyethylene bottles containing 120 tablets.	YONSA 125 mg Tablets are available in high-density polyethylene (HDPE) (b) (4) bottles of 120 tablets.
Storage	Store at 20°C to 25°C (68°F to 77°F)	Store at 20°C to 25°C (68°F to 77°F)
Container Closure	White, opaque 150-mL highdensity polyethylene (HDPE) bottle with (b) (4)) closure with induction seal liner.	**High density polyethylene (HDPE) configuration** 120-count, 150 cc round HDPE bottle with a 38 mm child-resistant lined closure (b) (4)

APPENDIX D. ISMP NEWSLETTERS

D.1 Methods

On September 14, 2017, we searched the Institute for Safe Medication Practices (ISMP) newsletters using the criteria below, and then individually reviewed each newsletter. We limited our analysis to newsletters that described medication errors or actions possibly associated with the label and labeling.

ISMP Newsletters Search Strategy	
ISMP Newsletter(s)	Acute Care and Community
Search Strategy and Terms	Match Exact Word or Phrase: Abiraterone

D.2 Results

The search retrieved no articles.

APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[b] along with postmarket medication error data, we reviewed the following Yonsa labels and labeling submitted by Churchill Pharmaceuticals.

- Container labels submitted on November 7, 2017
- Professional Sample Container labels submitted on November 7, 2017
- Prescribing Information (Image not shown) submitted on September 26, 2017

G.2 Label and Labeling Images

Container label

HDPE Bottle

(b) (4)

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

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/s/

TINGTING N GAO
01/11/2018

CHI-MING TU
01/11/2018

DANIELLE M HARRIS
01/12/2018

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 8/16/2017

TO: Office of New Drugs
Division of Oncology Products (DOP1)

FROM: Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Decline to Conduct Biopharmaceutical Inspection**

RE: NDA 210308

The Division of New Drug Bioequivalence Evaluation (DNDBE) within the Office of Study Integrity and Surveillance (OSIS) declines to conduct a biopharmaceutical inspection for the site specified below.

Rationale

OSIS received a bopharmaceuitcal inspection request from the Division of Oncology Products 1 dated July 6, 2017. An inspection of study CHL-AA-201 at the site below was requested.

The site did not enroll study subjects. OSIS determined that the site is the location of coordinating investigator that oversaw the overall clinical conduct of the 18 clinical sties that ranodmzed subjects. Therefore, OSIS declines to conduct a bioequivalence inspection at the site listed below.

Inspection Site

Facility Type	Facility Name	Facility Address
Clinical	City of Hope Hospital	1500 East Duarte Road, Duarte, CA

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/s/

ANGEL S JOHNSON
08/21/2017

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 8/16/2017

TO: Office of New Drugs
Division of Oncology Products (DOP1)

FROM: Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Recommendation to accept data without on-site inspection**

RE: NDA 210308

The Division of New Drug Bioequivalence Evaluation (DNDBE) within the Office of Study Integrity and Surveillance (OSIS) recommends accepting data without on-site inspection. The rationale for this decision is noted below.

Rationale

OSIS recently inspected the sites listed below. The inspectional outcome from the inspections was classified as No Action Indicated (NAI).

Inspection Sites

Facility Type	Facility Name	Facility Address
Clinical	PAREXEL Early Phase Clinical Unit	MedStar Harbor Hospital, 3001 South Hanover Street, 7th Floor, Baltimore, MD
Analytical	(b) (4)	
Analytical		

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/s/

ANGEL S JOHNSON
08/21/2017