# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 202293Orig1s024

# OTHER REVIEW(S)

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

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

# Memorandum

**Date:** April 20, 2021

**To:** Sabry Soukehal, Sr. Regulatory Health Project Manager
Cardiology and Nephrology
Division of Regulatory Operations for Cardiology, Hematology, Endocrinology, & Nephrology

Michael Monteleone, Associate Director for Labeling
Division of Cardiology and Nephrology (DCN)

**From:** Zarna Patel, PharmD
Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

Meena Savani, PharmD
Regulatory Review Officer
OPDP

**CC:** James Dvorsky, Team Leader, OPDP
Melinda McLawhorn, Team Leader, OPDP

**Subject:** OPDP Labeling Comments for FARXIGA (dapagliflozin) tablets, for oral use

**NDA/BLA**: 202293/Supplement 24

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In response to DCN consult request dated December 18, 2020, OPDP has reviewed the proposed product labeling (PI) and the Medication Guide for FARXIGA (dapaglifozin) tablets, for oral use (Farxiga). This supplement (S24) pertains to the indication for chronic kidney disease.

**PI and Medication Guide**: OPDP's comments on the proposed labeling are based on the draft PI received by electronic mail from DCN (Sabry Soukehal) on April 8, 2021, and are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review was completed, and comments on the proposed Medication Guide were sent under separate cover on April16, 2021.

Thank you for your consult. If you have any questions, please contact Zarna Patel at zarna.patel@fda.hhs.gov or Meena Savani at meena.savani@fda.hhs.gov.

52 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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**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: | April 16, 2021 |
| To: | Sabry Soukehal, RAC<br>Senior Regulatory Health Project Manager<br>**Division of Cardiology and Nephrology (DCN)** |
| Through: | LaShawn Griffiths, MSHS-PH, BSN, RN<br>Associate Director for Patient Labeling<br>**Division of Medical Policy Programs (DMPP)** |
| From: | Sharon R. Mills, BSN, RN, CCRP<br>Senior Patient Labeling Reviewer<br>**Division of Medical Policy Programs (DMPP)**<br><br>Zarna Patel, PharmD<br>Regulatory Review Officer<br>**Office of Prescription Drug Promotion (OPDP)**<br><br>Meena Savani, PharmD<br>Regulatory Review Officer<br>**Office of Prescription Drug Promotion (OPDP)** |
| Subject: | Review of Patient Labeling: Medication Guide (MG) |
| Drug Name (established name): | FARXIGA (dapagliflozin) |
| Dosage Form and Route: | tablets, for oral use |
| Application Type/Number: | NDA 202293 |
| Supplement Number: | S-024 |
| Applicant: | AstraZeneca AB<br>c/o AstraZeneca Pharmaceuticals LP |

## 1 INTRODUCTION

On November 3, 2020, AstraZeneca AB c/o AstraZeneca Pharmaceuticals LP, submitted a Prior Approval Supplement (PAS)- Efficacy to their approved New Drug Application (NDA) 202293 for FARXIGA (dapagliflozin) tablets. With this supplement, the Applicant proposes to add, based on DAPA-CKD study and the renal data from DECLARE, the following new indications:

(b) (4)

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 Cardiology and Nephrology (DCN) on December 18, 2020, for DMPP and OPDP to review the Applicant's proposed Medication Guide (MG) for FARXIGA (dapagliflozin) tablets.

## 2 MATERIAL REVIEWED

- Draft FARXIGA (dapagliflozin) tablets MG received on November 3, 2020, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on April 8, 2021.
- Draft FARXIGA (dapagliflozin) tablets Prescribing Information (PI) received on November 3, 2020, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on April 8, 2021.
- Approved FARXIGA (dapagliflozin) tablets labeling dated May 5, 2020.

## 3 REVIEW METHODS

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

In our collaborative review of the MG we:

- simplified wording and clarified concepts where possible
- ensured that the MG is consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information
- ensured that the MG is free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the MG meets the Regulations as specified in 21 CFR 208.20
- ensured that the MG meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)

## 4 CONCLUSIONS

The MG 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 MG 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 MG.

Please let us know if you have any questions.

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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: | March 2, 2021 |
| Requesting Office or Division: | Division of Cardiology and Nephrology (DCN) |
| Application Type and Number: | NDA 202293/S-024 |
| Product Name, Dosage Form, and Strength: | Farxiga (dapagliflozin) tablets, 5 mg and 10 mg |
| Product Type: | Single Ingredient Product |
| Rx or OTC: | Prescription (Rx) |
| Applicant/Sponsor Name: | AstraZeneca AB (AZ) |
| FDA Received Date: | November 3, 2020 |
| OSE RCM #: | 2020-2566 |
| DMEPA Safety Evaluator: | Mariette Aidoo, PharmD, MPH |
| DMEPA Team Leader: | Hina Mehta, PharmD |

# 1 REASON FOR REVIEW

AstraZeneca AB (AZ) submitted a prior approval supplement for Farxiga (dapagliflozin) tablets under NDA 202293/S-024 proposing a new indication for patients with chronic kidney disease. We evaluated the proposed prescribing information (PI) and medication guide (MG) for areas of vulnerability that could lead to medication errors.

## 1.1 BACKGROUND INFORMATION

Farxiga (dapagliflozin) was approved on January 8, 2014 as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. On October 18, 2019 it was approved in type 2 diabetes mellitus patients to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease or multiple cardiovascular risk factors. On May 5, 2020 it was approved to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure with reduced ejection fraction (NYHA class II-IV). It is available in 5 mg and 10 mg tablets.

# 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 Review

| Material Reviewed | Appendix Section (for Methods and Results) |
|---|---|
| Product Information/Prescribing Information | A |
| Previous DMEPA Reviews | B |
| Human Factors Study | C – N/A |
| ISMP Newsletters* | D – N/A |
| 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 or ISMP Newsletters 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

AstraZeneca submitted an efficacy supplement for Farxiga (dapagliflozin) proposing a new indication for the use of Farxiga in adults with Chronic Kidney Disease (CKD):

(b) (4)

(b) (4)

We note that the newly proposed dose for Chronic Kidney disease will be the same dosage regimen as that previously approved for the indication of Heart Failure tablet (10 mg orally once daily) for renal clearance greater than 25 mL/min.

We performed a risk assessment of the proposed prescribing information (PI) and medication guide for Farxiga (dapagliflozin) to identify deficiencies that may lead to medication errors and areas for improvement.

## 4 CONCLUSION & RECOMMENDATIONS

We find the proposed medication guide acceptable from a medication error perspective. The proposed Farxiga PI may be improved to promote the safe use of this product from a medication error perspective. We provide specific recommendations in Section 4.1 below.

### 4.1 RECOMMENDATIONS FOR DIVISION OF CARDIOLOGY AND NEPHROLOGY (DCN)

A. Highlights of Prescribing Information Highlights

1. Dosage and Administration Section

a. Consider including the route of administration "orally" after the dose throughout the Highlight section and Section 2.5 of the PI. For example, revise the dosing statements in Table 1 to read: "10 mg orally once daily" and "* (b) (4) ."

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Farxiga received on November 3, 2020 from AstraZeneca AB (AZ).

| Table 2. Relevant Product Information for Farxiga | |
|---|---|
| Initial Approval Date | 01/08/2014 |
| Active Ingredient | dapagliflozin |
| Indication | FARXIGA is a sodium-glucose cotransporter 2 (SGLT2) inhibitor indicated in adults for:<br><br>Type 2 Diabetes Mellitus:<br>• as an adjunct to diet and exercise to improve glycemic control.<br>• to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease or multiple cardiovascular risk factors.<br>(PROPOSED)<br>(b) (4) |
| Route of Administration | Oral |
| Dosage Form | tablets |
| Strength | 5 mg and 10 mg |
| Dose and Frequency | (Current)<br><br>To improve glycemic control the recommended starting dose is 5 mg once daily, taken in the morning. Increase dose to 10 mg once daily in patients tolerating 5 mg who require additional glycemic control. |

| | |
|---|---|
| | To reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease or multiple cardiovascular risk factors, the recommended dose is 10 mg once daily.<br>(Proposed)<br>(b) (4) [redacted] |
| How Supplied | Yellow biconvex diamond shaped tablet |
| Storage | Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature]. |
| Container Closure | Bottles of 30 tablets |

APPENDIX B. PREVIOUS DMEPA REVIEWS

On February 17, 2021, we searched for previous DMEPA reviews relevant to this current review using the terms, dapagliflozin. Our search identified four previous reviews[a,b,c,d], and we considered our previous recommendations to see if they are applicable for this current review.

[a] Aidoo, M. Label and Labeling Review for Farxiga (NDA 202293/S-20). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 MAR 17. RCM No.: 2019-2293.

[b] Conrad A. Label and Labeling Review for Farxiga and Xigduo XR, NDA 202293/S-018 and NDA 205649/S-011. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Jun 07. RCM No.: 2018-2812.

(b) (4) [redacted]

[d] Agustin A. Label, Labeling and Packaging Review for Farxiga, NDA 202293. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2013 Nov 18. RCM No.: 2013-1640.

## 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,[e] along with postmarket medication error data, we reviewed the following Farxiga labels and labeling submitted by AstraZeneca AB (AZ).

- Prescribing Information (Image not shown) received on November 3, 2020, available from \\CDSESUB1\evsprod\nda202293\0815\m1\us\nonannotated-draft-label-ckd.docx

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

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