

NDA 022350/S-026
NDA 200678/S-028

SUPPLEMENT APPROVAL

AstraZeneca AB
C/O: AstraZeneca Pharmaceuticals LP
Attention: David Craig Zecher II
Regulatory Affairs Director
One MedImmune Way
Gaithersburg, MD 20878

Dear David Craig Zecher II:

Please refer to your supplemental new drug applications (sNDAs) dated and received December 12, 2023, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Onglyza (saxagliptin) tablets and Kombiglyze XR (saxagliptin and metformin hydrochloride) extended-release tablets.

These Prior Approval sNDAs provide for revisions to section 8.4 *Pediatric Use* of the Onglyza and Kombiglyze XR Prescribing Information and Medication Guides based on the results of the pediatric study D1680C00019 (CV181375) entitled, *A 26-week, multicenter, randomized, placebo-controlled, double-blind, parallel group, phase 3 trial with a 26-week safety extension period evaluating the safety and efficacy of dapagliflozin 5 and 10 mg, and saxagliptin 2.5 and 5 mg in pediatric patients with type 2 diabetes mellitus who are between 10 and below 18 years of age*. Additional edits were made throughout the Prescribing Information and Medication Guides for Onglyza and Kombiglyze XR to modernize with current labeling guidances, clarify language, improve readability and organization of information, and align with other products.

This study was conducted to address the following postmarketing requirement (PMR) established in the April 24, 2017, Acknowledge New Postmarketing Requirement letter:

- 3199-1 Conduct a 26-week randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of the monotherapies saxagliptin and dapagliflozin for the treatment of pediatric patients ages 10 to < 18 years with type 2 diabetes mellitus, followed by a 26-week site- and subject-blinded safety extension period (weeks 26 to 52). Background therapy will consist of either metformin, insulin, or metformin plus insulin. A second randomization will take place at week 14, with uptitration of dose (saxagliptin may be increased from 2.5 mg to 5 mg; dapagliflozin from 5 mg to 10 mg) for approximately half of the subjects with a hemoglobin A1C greater than or equal to 7%.

We refer to our June 12, 2024, Fulfillment of Postmarketing Requirement letter under NDA 202293/S-031 and NDA 205649/S-022, which concluded the above requirement has been fulfilled.

APPROVAL & LABELING

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effectuated” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.²

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We note that you have fulfilled the pediatric study requirement for ages 10 to 17 years for these applications.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.³

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety-related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the

³ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, contact Christine Wright, Regulatory Project Manager, at Anne.Wright@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Patrick Archdeacon, MD
Deputy Director
Division of Diabetes, Lipid Disorders, and Obesity
Office of Cardiology, Hematology, Endocrinology, and
Nephrology
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Onglyza Prescribing Information
 - Onglyza Medication Guide
 - Kombiglyze XR Prescribing Information
 - Kombiglyze XR Medication Guide

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

PATRICK ARCHDEACON
10/11/2024 03:20:27 PM