

NDA 204629/S-063
 NDA 206111/S-046
 NDA 208658/S-034
 NDA 206073/S-044
 NDA 212614/S-029

SUPPLEMENT APPROVAL

Boehringer Ingelheim Pharmaceuticals, Inc.
 Attention: Agnieszka Abeyta, Pharm.D.
 Senior Associate Director, Regulatory Affairs
 Andrew Gee, Ph.D.
 Director, Regulatory Affairs, Established Products
 Crystal Lloyd, Pharm.D.
 Post Doctoral Medical Fellow, United States Product Chemistry, Manufacturing, and
 Controls Regulatory Affairs
 900 Ridgebury Road, PO Box 368
 Ridgefield, CT 06877

Dear Dr. Abeyta, Dr. Gee, and Dr. Lloyd:

Please refer to your supplemental new drug applications (sNDAs), dated and received March 12, 2025, and your amendments, submitted under section 505(b) and pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA or the Act) for the following:

Application Number	Supplement Number	Product Name
NDA 204629	063	Jardiance (empagliflozin) tablets
NDA 206111	046	Synjardy (empagliflozin and metformin hydrochloride tablets)
NDA 208658	034	Synjardy XR (empagliflozin and metformin hydrochloride extended-release tablets)
NDA 206073	044	Glyxambi (empagliflozin and linagliptin tablets)
NDA 212614	029	Trijardy XR (empagliflozin, linagliptin, and metformin hydrochloride extended-release tablets)

These Prior Approval sNDAs provide for updates to section 5 *Warnings and Precautions* of the Prescribing Information regarding the risk of Fournier’s gangrene in patients without diabetes mellitus. These Prior Approval sNDAs also provide for combining the genitourinary infections into a single Warning and Precaution subsection

NDA 204629/S-063
NDA 206111/S-046
NDA 208658/S-034
NDA 206073/S-044
NDA 212614/S-029
Page 2

titled, *Genitourinary Infections, including Urosepsis, Pyelonephritis, Necrotizing Fasciitis of the Perineum (Fournier's Gangrene), and Genital Mycotic Infections*, with corresponding changes made to the Highlights section, Table of Contents, Section 6 *Adverse Reactions* and Section 17 *Patient Counseling Information*. The Medication Guides were revised to align with the changes in the Prescribing Information.

Additional edits were made throughout the Jardiance, Glyxambi, and Trijardy Prescribing Informations for alignment with recent labeling changes made with empagliflozin products.

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 with a minor editorial revision listed below and reflected in the enclosed labeling.

Updated the cross-reference for Warning and Precaution 5.2 to 5.3 in subsection 8.6 *Renal Impairment* of the Synjardy/Synjardy XR Prescribing Information for consistency with other empagliflozin products.

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 Effected" (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

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>.

NDA 204629/S-063
NDA 206111/S-046
NDA 208658/S-034
NDA 206073/S-044
NDA 212614/S-029
Page 3

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).

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.

Because none of these criteria apply to your supplemental applications, you are exempt from this requirement.

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

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>

NDA 204629/S-063
NDA 206111/S-046
NDA 208658/S-034
NDA 206073/S-044
NDA 212614/S-029
Page 4

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 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).

NDA 204629/S-063
NDA 206111/S-046
NDA 208658/S-034
NDA 206073/S-044
NDA 212614/S-029
Page 5

If you have any questions, call Michael Oyewole, Regulatory Project Manager, at (301) 796-3897.

Sincerely,

{See appended electronic signature page}

Monika Houstoun, Pharm.D., M.P.H.
Deputy Director for Safety
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
 - Jardiance Prescribing Information and Medication Guide
 - Synjardy and Synjardy XR Prescribing Information and Medication Guide
 - Glyxambi Prescribing Information and Medication Guide
 - Trijardy XR Prescribing Information and 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/

MONIKA A HOUSTOUN
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