ANDA 211699

ANDA APPROVAL

Mylan Pharmaceuticals Inc., a Viatris Company
3711 Collins Ferry Road
Morgantown, WV 26505
Attention: Robert Barto
Senior Director, Regulatory Affairs Officer

Dear Robert Barto:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on June 26, 2018, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Breyna (Budesonide and Formoterol Fumarate Dihydrate Inhalation Aerosol), 160 mcg/4.5 mcg/actuation and 80 mcg/4.5 mcg/actuation.

Your product is a combination product as defined by 21 CFR 3.2(e) and is comprised of drug and device constituent parts.

Reference is also made to the tentative approval letter issued by this office on March 5, 2021, and to any amendments thereafter.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug meets the requirements for approval under the FD&C Act. Accordingly, the ANDA is **approved**, effective on the date of this letter. We have determined your Breyna (Budesonide and Formoterol Fumarate Dihydrate Inhalation Aerosol), 160 mcg/4.5 mcg/actuation and 80 mcg/4.5 mcg/actuation, to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Symbicort Inhalation Aerosol, 160 mcg/4.5 mcg/actuation and 80 mcg/4.5 mcg/actuation, of AstraZeneca Pharmaceuticals LP (AstraZeneca).

The RLD upon which you have based your ANDA, AstraZeneca's Symbicort Inhalation Aerosol, 160 mcg/4.5 mcg/actuation and 80 mcg/4.5 mcg/actuation, is subject to periods of patent protection. The following patents and expiration dates (with pediatric exclusivity added) are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

U.S. Patent Number	Expiration Date
7,587,988 (the '988 patent)	October 10, 2026

7,759,328 (the '328 patent)	July 29, 2023
8,143,239 (the '239 patent)	July 29, 2023
8,387,615 (the '615 patent)	September 26, 2027
8,528,545 (the '545 patent)	April 16, 2029
8,575,137 (the '137 patent)	July 29, 2023
8,616,196 (the '196 patent)	October 7, 2029
8,875,699 (the '699 patent)	May 10, 2025
10,166,247 (the '247 patent)	July 29, 2023

Your ANDA contains paragraph IV certifications to each of the patents[1] under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Breyna (Budesonide and Formoterol Fumarate Dihydrate Inhalation Aerosol), 160 mcg/4.5 mcg/actuation and 80 mcg/4.5 mcg/actuation, under this ANDA. You have notified the Agency that Mylan Pharmaceuticals Inc., a Viatris Company (Mylan) complied with the requirements of section 505(j)(2)(B) of the FD&C Act. Litigation was initiated within the statutory 45-day period against Mylan for infringement of the '328, '239, and '137 patents in the United States District Court for the District of Delaware [AstraZeneca AB and AstraZeneca Pharmaceuticals LP v. Mylan Pharmaceuticals Inc., Mylan Laboratories Limited, Mylan Inc., and Mylan N.V., Civil Action No. 18-01562] and in the United States District Court for the Northern District of West Virginia [AstraZeneca AB and AstraZeneca Pharmaceuticals LP v. Mylan Pharmaceuticals Inc. and Kindeva Drug Delivery L.P., Civil Action No. 18-00193]. You notified the Agency that the District of Delaware case was transferred to the Northern District of West Virginia as Civil Action No. 19-00203, and that Civil Action No. 19-00203 was consolidated with Civil Action No. 18-00193. You have also notified the Agency that on March 8, 2021, the district court entered an Amended Final Judgment, stating that "[p]ursuant to 35 U.S.C. § 271(e)(4)(A), the effective date of any final approval of ANDA No. 211699 shall be a date that is not earlier than the latest date of expiration of U.S. Patent Nos. 7,759,328, 8,143,239, and 8,575,137, including any extensions or additional periods of exclusivity."[2] You have further notified the Agency that the case was appealed to the United States Court of Appeals for the Federal Circuit (Federal Circuit), and on December 8, 2021, the Federal Circuit issued a decision, vacating the stipulated judgment of infringement and remanding for further proceedings.[3] The Federal Circuit issued a mandate on March 9, 2022, in accordance with the December 8, 2021 decision.[4] Although litigation in the district court remains ongoing, the 30-month period identified in section 505(j)(5)(B)(iii) of the FD&C Act, during which FDA was precluded from approving your ANDA, has expired.

With respect to 180-day generic drug exclusivity, we note that Mylan was the first ANDA applicant for Breyna (Budesonide and Formoterol Fumarate Dihydrate Inhalation Aerosol), 160 mcg/4.5 mcg/actuation and 80 mcg/4.5 mcg/actuation, to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Mylan may be eligible for 180 days of generic drug exclusivity for Breyna (Budesonide and Formoterol Fumarate Dihydrate Inhalation Aerosol), 160 mcg/4.5 mcg/actuation and 80 mcg/4.5 mcg/actuation. This exclusivity, which is provided for under 505(j)(5)(B)(iv) of the FD&C Act, would begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). The Agency notes that Mylan failed to obtain tentative approval of this ANDA within 30 months after the date of which the ANDA was filed. See section 505(j)(5)(D)(i)(IV) of the FD&C Act (forfeiture of exclusivity for failure to obtain tentative approval). The Agency is not, however, making a formal determination at this time of Mylan's eligibility for 180-day generic drug exclusivity. It will do so only if a subsequent paragraph IV applicant becomes eligible for full approval (a) within 180 days after Mylan begins commercial marketing of Breyna (Budesonide and Formoterol Fumarate Dihydrate Inhalation Aerosol), 160 mcg/4.5 mcg/actuation and 80 mcg/4.5 mcg/actuation, or (b) at any time prior to the expiration of the '988, '328, '239, '615, '545, '137, '196, or '699 patents if Mylan has not begun commercial marketing. Please submit correspondence to this ANDA notifying the Agency within 30 days of the date of the first commercial marketing of this drug product or the RLD. If you do not notify the Agency within 30 days, the date of first commercial marketing will be deemed to be the date of the drug product's approval. See 21 CFR 314.107(c)(2).

Under section 506A of the FD&C Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Please note that if FDA requires a Risk Evaluation and Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the FD&C Act.

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Agency should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Agency in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.

Your product is a combination product as defined by 21 CFR 3.2(e) and is comprised of drug and device constituent parts; therefore, we remind you that you must comply with

the postmarketing safety reporting requirements for an approved combination product (21 CFR Part 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling materials prior to publication or dissemination. Please note that these submissions are voluntary. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert (PI), Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: https://www.fda.gov/media/128163/download).

You must also submit final promotional materials and package insert(s), 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 https://www.fda.gov/media/73013/download. Information and Instructions for completing the form can be found at https://www.fda.gov/media/132152/download. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/opdp-ectd.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions[2] with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1st of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the *Federal Register* notice announcing facility fee amounts.

All finished dosage forms or active pharmaceutical ingredients manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at https://www.fda.gov/media/71211/download. The SPL will be accessible via publicly available labeling repositories.

We remind you that you must continually monitor available labeling resources such as DRUGS@FDA for changes to your reference listed drug's labels and labeling and make any necessary revisions to your labels and labeling. More information on post-approval labeling changes may be found in the guidance for industry titled "Changes to an Approved NDA or ANDA" at https://www.fda.gov/media/71846/download.

Sincerely yours,

{See appended electronic signature page}

For Edward M. Sherwood
Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

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[1] The Agency notes that the '247 patent was submitted to the Agency after submission of your ANDA. Litigation, if any, with respect to this patent would not create a statutory stay of approval.
[2] AstraZeneca AB v. Mylan Pharmaceuticals Inc., Doc. 438, Case No. 18-00193 (N.D. W.Va. Mar. 8, 2021).
[3] AstraZeneca AB v. Mylan Pharmaceuticals Inc., Doc. 47, Case No. 21-1729 (Fed. Cir. Dec. 8, 2021).
[4] AstraZeneca AB v. Mylan Pharmaceuticals Inc., Doc. 65, Case No. 21-1729 (Fed. Cir. Mar. 9, 2022).
[5] Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

Sarah Kurtz

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