



NDA 210496/S-019

**SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING REQUIREMENT**

Array BioPharma Inc., a wholly owned subsidiary of Pfizer Inc.
Attention: Katarzyna Kowanetz, PhD
Senior Director, Regulatory Strategy – Oncology
66 Hudson Boulevard East
New York, NY 10001

Dear Dr. Kowanetz:

Please refer to your April 24, 2025, supplemental new drug application, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Braftovi (encorafenib), capsules, for oral use.

This Prior Approval supplemental new drug application provides for updates to the Braftovi (encorafenib) Prescribing Information (PI), and the Medication Guide, with data supporting the proposed indication of Braftovi (encorafenib) in combination with cetuximab and fluorouracil-based chemotherapy for the treatment of adult patients with metastatic colorectal cancer (mCRC) with a *BRAF* V600E mutation.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

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 (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.

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

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(I)(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).

SUBPART H FULFILLED

We approved this indication under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of this supplement fulfills your commitments made under 21 CFR 314.510.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We refer to your supplemental new drug application (sNDA) submitted under section 505(b) of the FDCA for Braftovi (encorafenib), capsules.

We have received your April 8, and 24, 2025, submissions containing the final report for the following postmarketing requirement listed in the December 20, 2024, approval letter for NDA 210496/S-017.

- 4753-1 Conduct a randomized comparative clinical trial intended to verify and describe the clinical benefit of encorafenib and cetuximab in combination with mFOLFOX6 in adult patients with previously untreated BRAF V600E mutation-positive metastatic colorectal cancer by assessing progression free survival. This data may be obtained from the ongoing clinical trial, BREAKWATER (C4221015), "An open-label, multicenter, randomized Phase 3 study of EC alone (EC Arm) or in combination with chemotherapy (mFOLFOX6; EC + mFOLFOX6 Arm) versus standard-of-care chemotherapies (Control Arm: mFOLFOX6, FOLFOXIRI, or CAPOX each with or without bevacizumab) in first-line participants with BRAF V600E mutant mCRC."

We have reviewed your submissions and conclude that the above requirement was fulfilled.

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>.

This closes all of your postmarketing requirements and postmarketing commitments acknowledged in our December 20, 2024, letter. You are not required to report on the status of closed (released or fulfilled) PMRs/PMC in your annual report required under 21 CFR 314.81(b)(2)(vii).

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 are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable.

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).

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>

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).

If you have any questions, contact Gina Davis, Senior Regulatory Health Project Manager at Gina.Davis@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Steven Lemery, M.D., MHS
Director
Division of Oncology 3
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - 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/

STEVEN J LEMERY
02/24/2026 11:52:37 AM