CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

218881Orig1s000

Trade Name:	INLURIYO tablets
Generic or Proper Name:	Imlunestrant
Sponsor:	Eli Lilly and Company
Approval Date:	September 25, 2025
Indication:	Treatment of adults with ER-positive, HER2-negative, *ESR1*-mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy

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APPROVAL LETTER

NDA 218881

NDA APPROVAL

Eli Lilly and Company
Attention: Brian Wagner
Sr. Director, Global Regulatory Affairs, NA
Lilly Corporate Center
893 Delaware St, Drop code 2543
Indianapolis, IN 46285

Dear Brian Wagner:

Please refer to your new drug application (NDA) dated October 31, 2024, received October 31, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Inluriyo (imlunestrant) Tablets.

This NDA provides for the use of Inluriyo (imlunestrant) for the treatment of adults with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, *estrogen receptor-1* (*ESR1*)-mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy.

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 (text for the Prescribing Information, Patient Package Insert) 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 via publicly available labeling repositories.

[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.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 218881**." Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Inluriyo (imlunestrant) tablets shall be 36 months from the date of manufacture when stored at 20°C to 25°C (68°F to 77°F). Excursions between 15°C to 30°C (59°F to 86°F) are permitted [see USP Controlled Room Temperature].

ADVISORY COMMITTEE

Your application for imlunestrant was not referred to an FDA advisory committee because outside expertise was not necessary; there were no controversial issues that would benefit from advisory committee discussion.

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 as breast cancer does not occur in the pediatric population.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4902-1 Complete the pre-specified, event-driven overall survival (OS) analyses comparing the imlunestrant monotherapy and standard-of-care endocrine therapy arms from the ongoing clinical trial, EMBER-3 (Study J2J-OX-JZLC), titled "A Phase 3, Randomized, Open-Label Study of Imlunestrant, Investigator's Choice of Endocrine Therapy, and Imlunestrant plus

Abemaciclib in Patients with Estrogen-Receptor Positive, HER2 Negative Locally Advanced or Metastatic Breast Cancer Previously Treated with Endocrine Therapy", to further characterize the clinical benefit of imlunestrant in patients with estrogen-receptor positive, HER2 negative *ESR1-mutated* breast cancer.

The timetable you submitted on September 9, 2025, states that you will conduct this study according to the following schedule:

Interim Report Submission:	02/2026
Trial Completion (monotherapy in the *ESR1*-mutated population):	11/2026
Final Report Submission:	05/2027

Provide the OS datasets in the interim and final report submissions.

Submit clinical protocols to your IND 145311 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients/subjects entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," **or** "**Postmarketing Commitment Correspondence**."

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]

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

[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

REPORTING REQUIREMENTS

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

POST APPROVAL FEEDBACK MEETING

New molecular entities qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standards for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website[6].

If you have any questions, contact Ja'Kaya Wilson, Regulatory Project Manager, at Jakaya.Wilson@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

R. Angelo de Claro, MD
Deputy Director (Acting)
Office of Oncologic Diseases
Center for Drug Evaluation and Research

[6] https://www.uspnf.com/

ENCLOSURES:
Content of Labeling

- Prescribing Information
- Patient Package Insert
- Carton and container labeling

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/

ROMEO A DE CLARO
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