NDA 219469

NDA APPROVAL

Bayer HealthCare Pharmaceuticals Inc.
Attention: Harpreet Sandhu, Ph.D., MBA
Director, Global Regulatory Affairs Strategist, Women's Health Care
100 Bayer Boulevard
P.O. Box 915
Whippany, NJ 07981

Dear Dr. Sandhu:

Please refer to your new drug application (NDA) received July 26, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Lynkuet (elinzanetant) capsules.

We acknowledge receipt of your major amendment dated July 22, 2025, which extended the goal date by three months.

This NDA provides for the use of Lynkuet (elinzanetant) capsules for the treatment of moderate to severe vasomotor symptoms due to menopause.

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 and Patient Package Insert) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling **and** carton and container labeling submitted on June 13, 2025, 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 219469**." 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 Lynkuet (elizanetant) capsules shall be 30 months from the date of manufacture when stored at 20°C to 25°C (68°F to 77°F).

ADVISORY COMMITTEE

Your application for Lynkuet (elinzanetant) capsules 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.

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

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]

REPORTING REQUIREMENTS

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

REQUESTED ENHANCED PHARMACOVIGILANCE (EPV)

We request that you submit all serious and non-serious, domestic and foreign cases of hepatic adverse events, including liver injury, as defined below, as 15-day "Alert reports" (described under 21 CFR 314.80(c)(1)) through the 3rd year following the initial U.S. approval date.

Cases of hepatic adverse events, including liver injury, to be reported as 15-day "Alert reports" and to be included in the summary analysis should meet the following criteria:

1. Alanine Aminotransferase (ALT)/Aspartate Aminotransferase (AST) > 8x upper limit of normal (ULN) OR

2. ALT/AST > 3x ULN and total bilirubin >2x ULN OR

[3] For the most recent version of a guidance document, 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

3. ALT/AST > 3x ULN associated with symptoms suggestive of hepatic disease (e.g., anorexia, dark urine, new onset fatigue, fever, jaundice, nausea, vomiting, pruritus, abdominal pain) OR

4. Any hepatic adverse event leading to discontinuation OR

5. Any hepatic event preferred term (PT) denoting diagnosis, jaundice, liver injury, or non-infectious hepatitis

As described in 21 CFR 314.80(c)(1)(ii), we request that you investigate all reports of serious and non-serious hepatic adverse events, including liver injury, which meet the above criteria (1-5) and, when applicable, obtain the data elements (a-h) included below. When you receive new information about a report of a serious or non-serious hepatic adverse event, including liver injury, that has been previously reported, submit a follow-up Individual Case Safety Report containing the new information and using the same unique case identification number as the initial report (as described in 21 CFR 314.80(f)(5)(viii)).

Provide a narrative summary including analysis of hepatic adverse events, including liver injury, as part of your required periodic safety reports (e.g., periodic adverse drug experience report (PADER) required under 21 CFR 314.80(c)(2)), through the 3rd year following the initial U.S. approval date.

Your analysis should include interval and cumulative data relative to the date of U.S. approval of Lynkuet and include the following:

1. A medical literature review of case reports/case series of hepatic adverse events, including liver injury, obtained or otherwise received with Lynkuet

2. A discussion of worldwide and domestic trends in reporting of hepatic adverse events including liver injury, including global drug utilization data in terms of an estimated number of patients exposed to Lynkuet (total and stratified by U.S. versus foreign).

3. Causality assessment

Your summary analysis should be in a separate dedicated section of the periodic safety report and include line listings of the cases in addition to your synthesized summary.

The line listings for the cases of hepatic adverse events, including liver injury, should include the following information, if available:

a. Case ID

b. Patient's age and sex

c. Body Mass Index (BMI)

d. Concomitant medications (including prescription and over-the-counter medications, herbal/dietary supplements, illicit substances, and their respective indications, dosages, and dates taken)

e. Relevant investigations (e.g., albumin, autoimmune markers, coagulation parameters, endoscopic retrograde cholangiopancreatography, eosinophil count, liver biopsy, liver enzymes, liver imaging, viral serology)

f. Relevant medical history (e.g., alcohol consumption, autoimmune disease, biliary tract disorders, blood transfusion, cardiac disorders – specifically right heart failure or hypotension, cirrhosis, connective tissue disease, family history of liver disease, recent tattoos, recent travel, viral illness, viral or alcoholic hepatitis)

g. Event outcome (e.g., liver transplant, lost to follow-up, not resolved, resolved with or without sequelae, unknown)

h. Documentation of indication, temporal association, duration of therapy, associated signs and symptoms of the hepatic adverse event, treatment given for the event, serious outcome (i.e., death, life-threatening, hospitalization, disability, congenital anomaly, important medical event), and dechallenge/rechallenge

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 Samantha Bell, Regulatory Project Manager, at (301) 796-9687 or samantha.bell@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Janet Maynard, M.D., M.H.S.
Director
Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- Carton and Container Labeling

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

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/

JANET W MAYNARD
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