CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

761369Orig1s000

Trade Name:	Hympavzi
Generic or Proper Name:	marstacimab-hncq injection
Sponsor:	Pfizer Inc.
Approval Date:	October 11, 2024
Indication:	Hympavzi is a tissue factor pathway inhibitor (TFPI) antagonist indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients 12 years of age and older with hemophilia A (congenital factor VIII deficiency) without factor VIII inhibitors, or hemophilia B (congenital factor IX deficiency) without factor IX inhibitors.

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APPLICATION NUMBER:

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APPROVAL LETTER

BLA 761369

BLA APPROVAL

Pfizer Inc.
Attention: Mary Kate Whitecavage
Director, Pfizer Global Regulatory Sciences
500 Arcola Road
Collegeville, PA 19426

Dear Mary Kate Whitecavage:

Please refer to your biologics license application (BLA) dated and received October 11, 2023, and your amendments, submitted under section 351(a) of the Public Health Service Act for Hympavzi (marstacimab-hncq) injection.

LICENSING

We have approved your BLA for Hympavzi (marstacimab-hncq) effective this date. You are hereby authorized to introduce, or deliver for introduction into interstate commerce, Hympavzi under your existing Department of Health and Human Services U.S. License No. 2001.

Hympavzi is a tissue factor pathway inhibitor (TFPI) antagonist indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients 12 years of age and older with hemophilia A (congenital factor VIII deficiency) without factor VIII inhibitors, or hemophilia B (congenital factor IX deficiency) without factor IX inhibitors.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture marstacimab drug substance at Wyeth BioPharma, Division of Wyeth Pharmaceuticals LLC in Andover, MA (FEI: 1222181). The final formulated drug product in single-dose prefilled syringe and single-dose prefilled pen will be manufactured, filled, assembled, labeled, and packaged at Pfizer Manufacturing Belgium NV at Puurs-Sint-Amands, Belgium (FEI: 1000654629). The final secondary packaging and labeling will be at Pfizer Manufacturing Belgium NV at Puurs-Sint-Amands, Belgium (FEI: 1000654629) and at (b) (4) You may label your product with the proprietary name, Hympavzi, and market it in 150 mg/mL single-dose prefilled syringe and 150 mg/mL single dose prefilled pen, injection.

DATING PERIOD

The dating period for Hympavzi prefilled syringe and prefilled pen shall be 24 months from the date of manufacture when stored at 5 ± 3°C protected from light. The date of manufacture for prefilled syringe and prefilled pen shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substace shall be (b) (4) months from the date of manufacture when stored at (b) (4) °C.

Results of ongoing stability should be submitted throughout the dating period, as they become available.

We have approved the stability protocols in your license application for the purpose of extending the expiration dating period of your drug product under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Hympavzi to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of Hympavzi, or in the manufacturing facilities, will require the submission of information to your BLA for our review and written approval, consistent with 21 CFR 601.12.

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, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert, and Instructions for Use). 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 (October 2009)*.[2]

[1] See 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 at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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, 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 BLA 761369**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for Hympavzi was not referred to an FDA advisory committee because the application did not raise significant safety or efficacy issues that were unexpected for a biologic of this class, and 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, 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

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

U.S. Food and Drug Administration
Silver Spring, MD 20993
www.fda.gov

[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]

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements at 21 CFR 600.80.

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements at 21 CFR 600.81.

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4207
Silver Spring, MD 20903

REQUESTED ENHANCED PHARMACOVIGILANCE (EPV)

We request that for Hympavzi you submit all serious and non-serious domestic and foreign cases of thromboembolic events as 15-day “Alert reports” (described under 21 CFR 600.80(c)(1)) through the 5th year following initial U.S. approval.

We request that you provide a separate narrative summary analysis of thromboembolic events reported with Hympavzi as part of your required periodic safety reports (e.g., periodic adverse experience report (PAER) required under 21 CFR 600.80(c)(2),

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

quarterly during the first 3 years post-approval and annually thereafter, through the 5th year following initial U.S. approval date.

Your analysis should include interval and cumulative data relative to the date of approval of Hympavzi. Your analysis should provide an assessment of causality, with documentation of indication (including all labeled and off-label use), temporal association, duration of therapy, associated signs and symptoms, confounders, underlying risk factors, treatment given for the event, outcome, and dechallenge/rechallenge.

POST APPROVAL FEEDBACK MEETING

New biological products 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.

If you have any questions, contact Carleveva Thompson, Regulatory Project Manager, at 301-796-1403 or Carleveva.Thompson@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Lisa Yanoff, MD
Deputy Director
Office of Cardiology, Hematology,
Endocrinology, and Nephrology
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
  - Instructions for Use
- 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/

LISA B YANOFF
10/11/2024 12:16:39 PM