# marstacimab-hncq (Hympavzi™)

**Medicare Advantage Medical Policy # MA-112**
Original Effective Date: 08/01/2025
Current Effective Date: 08/01/2025

*Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

# When Services May Be Eligible for Coverage

*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Health Plan may consider marstacimab-hncq (Hympavzi™)‡ for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in patients with hemophilia A or hemophilia B to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for marstacimab-hncq (Hympavzi) will be considered when the following criteria are met:

**Initial**

- Patient is 12 years of age or older; AND
- Patient has severe hemophilia A (as defined by a baseline plasma factor VIII level ≤ 1% of normal [<1 IU/dL]) or moderately severe to severe hemophilia B (as defined by a baseline plasma factor IX level ≤ 2% of normal [≤ 2 IU/dL]); AND
- Patient does NOT have a history of factor VIII or factor IX inhibitors based on results of the Nijmegen-Bethesda assay (e.g., ≥ 0.6 Bethesda Units per mL); AND
- According to the prescriber, prophylactic use of factor VIII or IX products will NOT occur while using Hympavzi. Note that the use of factor products for the treatment of breakthrough bleeding is permitted; AND
- Patient will receive a loading dose equal to 300 mg (two 150 mg injections) by subcutaneous injection; AND
- Maintenance dose meets ONE of the following:
    - 150 mg once weekly; OR
    - 300 mg once weekly and ALL of the following:
        - Patient weight is ≥ 50 kg; AND
        - Prescriber attests that control of bleeding events is inadequate with 150 mg once weekly dose (e.g., increase in or no reduction in bleeding events or bleeding time)

**Continuation**

- Patient has received an initial authorization for Hympavzi from the plan OR has provided documentation of authorization from previous Medicare Advantage plan; AND
- Prescriber attests that the patient has responded to Hympavzi as evidenced by a decrease in bleeding episodes or bleeding time; AND
- Maintenance dose meets ONE of the following:

- 150 mg once weekly; OR
- 300 mg once weekly and ALL of the following:
  - Patient weight is ≥ 50 kg; AND
  - Prescriber attests that control of bleeding events in inadequate with 150 mg once weekly dose (e.g., increase in or no reduction in bleeding events or bleeding time).

# When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of marstacimab-hncq (Hympavzi) when the patient's hemophilia is not severe or moderately severe to be **not medically necessary.****

Based on review of available data, the Health Plan considers the continued use of marstacimab-hncq (Hympavzi) when the patient has not responded to Hympavzi to be to be **not medically necessary.****

# When Services Are Considered Investigational

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Health Plan considers the use of marstacimab-hncq (Hympavzi) when the patient selection criteria are not met (with the exception of those denoted above as **not medically necessary****) to be **investigational.***

# Background/Overview

Hympavzi is an anti-tissue factor pathway inhibitor (anti-TFPI) approved for the prophylactic treatment of patients 12 years of age and older with hemophilia A or B without inhibitors. It is an alternative to routine factor prophylaxis with the potential advantage of subcutaneous dosing that is not weight based. Hympavzi should be dosed as 150 mg injected subcutaneously once weekly following an initial loading dose of 300 mg. In patients weighing ≥ 50 kg who do not achieve an adequate response with the 150 mg weekly maintenance dose, the dose may be increased to 300 mg once weekly. In contrast to factor replacement, Hympavzi works by reducing the amount of naturally occurring TFPI. This increases the amount of thrombin that is generated, which is expected to reduce the frequency of or prevent bleeding episodes.

Hemophilia is a bleeding disorder that is caused by a deficiency or dysfunction in one of the clotting factors that enables blood to clot. Hemophilia A is caused by a deficiency in factor VIII (FVIII) and hemophilia B is caused by a deficiency in factor IX (FIX). Because the disorder is transmitted on the X-chromosome, it primarily affects males. The incidence of hemophilia is one in every 5,000 males born in the United States, approximately 80% of whom have hemophilia A. The condition is characterized by bleeding in joints, either spontaneously or in a provoked joint. Bleeding can occur

in many different body areas (e.g., muscles, central nervous system, gastrointestinal). The bleeding manifestations can lead to substantial morbidity, as well as mortality, if not properly treated.

Disease severity is usually defined by plasma levels of factor VIII or IX (depending on hemophilia type) and has been classified as follows:

- Severe: levels less than 1% of normal
- Moderate: levels 1-5% of normal
- Mild: levels > 5 to 40% of normal

The main treatment strategy for both types of hemophilia is factor replacement therapy in which administration of the deficient clotting factor is given to achieve adequate hemostasis. Depending on individual patient characteristics such as disease severity and number of bleeds, patients may receive prophylactic factor replacement therapy or only receive treatment in response to a bleed ("on demand therapy"). Many different factor VIII and IX replacement therapies are FDA approved. An alternative to factor prophylaxis in patients with hemophilia A is emicizumab (Hemlibra®)‡, a bispecific factor IXa and factor X-directed antibody that is administered subcutaneously.

# FDA or Other Governmental Regulatory Approval

**U.S. Food and Drug Administration (FDA)**

Hympavzi was approved in October 2024 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.

# Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Hympavzi was established in 116 adult and pediatric patients (Aged 12 years and older and $\geq$ 35 kg) with severe hemophilia A without FVIII inhibitors or severe hemophilia B without FIX inhibitors enrolled in the BASIS study, an open-label, multi-center, two-phase study. Severe hemophilia is defined as factor activity less than 1%. Patients with a history of coronary artery disease, venous or arterial thrombosis or ischemic disease were excluded from the study.

Following screening, patients entered a 6-month observation phase and were enrolled to two cohorts based on the factor replacement treatment they were receiving prior to study entry: on-demand or routine prophylaxis. Patients who completed the observation phase were to receive 12 months of Hympavzi. Of the 116 patients who received Hympavzi, 33 patients were in the on-demand

treatment cohort and 83 were in the prophylactic treatment with FVIII or FIX cohort during the observation phase. Patients who completed the 12-month BASIS study were eligible to enroll in an open-label extension study.

Patients received an initial 300 mg loading dose of Hympavzi followed by maintenance doses of 150 mg once weekly for 12 months. Dose escalation to 300 mg of Hympavzi once weekly was permitted after 6 months of treatment in patients weighing ≥ 50 kg and experiencing ≥ 2 breakthrough bleeds. Fourteen (12%) underwent dose escalation.

The mean annualized bleeding rates (ABRs) for treated bleeds were 38 and 7.85 in the observational phase for the on-demand and prophylaxis cohorts, respectively. All patients in the on-demand cohort had one or more target joints at study entry and 36% had 3 or more target joints at study entry. In the routine prophylaxis cohort, 57% of the patients had one or more target joints at study entry and 16% had 3 or more target joints at study entry.

The efficacy of Hympavzi for each cohort was based upon the ABR of treated bleeds during treatment with Hympavzi compared to ABR during the observational phase. Other objectives of the study included evaluation of Hympavzi prophylaxis on the incidences of spontaneous bleeds, joint bleeds, target joint bleeds, and total bleeds.

In the cohort receiving on-demand factor therapy (n = 33), the ABR during the 6-month observation phase was 38.00 and it was reduced to 3.18 during the 12-month active treatment phase ($p < 0.0001$). Similar reductions were seen in the number of spontaneous bleeds, joint bleeds, total bleeds (treated and untreated), and joint bleeds.

In the cohort receiving routine prophylactic factor-based therapy (n = 83), the ABR during the 6-month observation phase was 7.85 and it was reduced to 5.08 during the 12-month active treatment phase. Similar reductions were seen in the number of spontaneous bleeds, joint bleeds, target joint bleeds, and total bleeds (treated and untreated). This reduction met the criteria for non-inferiority compared to routine factor prophylaxis.

# References

1. Hympavzi [package insert]. Pfizer Laboratories Div Pfizer Inc. New York, NY. Updated February 2025.
2. Hympavzi (marstacimab-hncq) New Drug Review. IPD Analytics. Updated November 2024.

# Policy History

Original Effective Date: 08/01/2025
Current Effective Date: 08/01/2025
05/20/2025 UM Committee review. New policy
Next Scheduled Review Date: 05/2026

# Coding

*The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.*

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

| Code Type | Code |
|---|---|
| CPT | No codes |
| HCPCS | C9304 |
| ICD-10 Diagnosis | All related diagnoses |

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

**NOTICE:** If the Patient's health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

**NOTICE:** Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

**NOTICE:** Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

## Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link:

https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.