Drug Coverage Policy

Effective Date……07/15/2025
Coverage Policy Number……IP0731
Policy Title……Hympavzi

Hemophilia – Hympavzi

- Hympavzi™ (marstacimab-hncq subcutaneous injection – Pfizer)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

Hympavzi, a tissue factor pathway inhibitor antagonist, is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in patients ≥ 12 years of age with 1) hemophilia A (congenital Factor VIII deficiency) without Factor VIII inhibitors, and 2) hemophilia B (congenital Factor IX deficiency) without Factor IX inhibitors.[1]

Hympavzi is recommended to be given as a 300 mg loading dose by subcutaneous injection (two 150 mg subcutaneous injections).[1] One week after the loading dose, initiate maintenance dosing of 150 mg once weekly by subcutaneous injection on the same day each week, at any time of the day. After proper training, Hympavzi may be self-administered.

Disease Overview
Hemophilia A and B are genetic bleeding disorders caused by a dysfunction or a deficiency of coagulation Factor VIII and Factor IX, respectively.[2-7] Because hemophilia is an X-linked condition, males are primarily impacted. Patients who have these types of hemophilias are not able to properly form clots in blood and may bleed for a longer time than normal following injury or surgery. Patients may also experience spontaneous bleeding in muscles, joints, and organs. Bleeds may be life-threatening. A main morbidity is hemophilic arthropathy, which limits mobility. It is estimated that 33,000 males are living with hemophilia in the US; hemophilia A accounts for around 80% of the cases (approximately 26,400 patients) and hemophilia B comprises 20% of cases (around 6,600 patients). Hemophilias are often classified as mild, moderate, or severe based on reduced Factor VIII or IX levels. Approximately 50% and 30% of patients with hemophilia A and hemophilia B, respectively, have severe disease. The formation of antibodies (or inhibitors) to factor products is a challenging complication as it causes Factor VIII and Factor IX therapies to be ineffective, which increases bleeding frequency and severity. Antibodies develop in around 30% and 10% of patients with severe hemophilia A and hemophilia B, respectively.

Coverage Policy

Policy Statement
Prior Authorization is required for benefit coverage of Hympavzi. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Hympavzi as well as the monitoring required for adverse events and long-term efficacy, approval requires Hympavzi to be prescribed by or in consultation with a hemophilia specialist.

Documentation: Documentation is required where noted in the criteria. Documentation may include, but not limited to, chart notes, laboratory tests, claims records, and/or other information.

Hympavzi is considered medically necessary when ONE of the following is met (1 or 2):

FDA-Approved Indications

1. **Hemophilia A without Factor VIII Inhibitors.** Approve for 1 year if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, iv, v, vi and vii):
      i. Patient is ≥ 12 years of age; AND
      ii. Patient is using Hympavzi for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; AND
      iii. Patient has severe hemophilia A as evidenced by a baseline (without Factor VIII replacement therapy) Factor VIII level of < 1% **[documentation required]**; AND
      iv. Patient meets ONE of the following (a or b):
         a) Patient meets BOTH of the following [(1) and (2)]:

(1) Factor VIII inhibitor titer testing has been performed within the past 30 days **[documentation required]**; AND

(2) Patient does not have a positive test for Factor VIII inhibitors of ≥ 1.0 Bethesda units/mL **[documentation required]**; OR

b) Patient has not received Factor VIII therapy in the past; AND

v. According to the prescriber, prophylactic use of Factor VIII products will not occur while using Hympavzi; AND

Note: Use of Factor VIII products for the treatment of breakthrough bleeding is permitted.

vi. The medication is prescribed by or in consultation with a hemophilia specialist; AND

vii. Preferred product criteria is met for the product(s) as listed in the below table(s) [Employer Plans]; OR

B) Patient is Currently Receiving Hympavzi. Approve if the patient meets ALL of the following (i, ii, iii, and iv):

i. Patient is using Hympavzi for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; AND

ii. According to the prescriber, prophylactic use of Factor VIII products will not occur while using Hympavzi; AND

Note: Use of Factor VIII products for the treatment of breakthrough bleeding is permitted.

iii. The medication is prescribed by or in consultation with a hemophilia specialist; AND

iv. According to the prescriber, patient experienced a beneficial response to therapy.

Note: Examples of a beneficial response to therapy include a reduction in bleeding events, in the severity of bleeding episodes, in the number of bleeding events that required treatment, and/or in the number of spontaneous bleeds.

2. Hemophilia B without Factor IX Inhibitors. Approve for 1 year if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, iv, v, and vi):

i. Patient is ≥ 12 years of age; AND

ii. Patient is using Hympavzi for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; AND

iii. Patient has moderately severe or severe hemophilia B as evidenced by a baseline (without Factor IX replacement therapy) Factor IX level ≤ 2% **[documentation required]**; AND

iv. Patient meets ONE of the following (a or b):

a) Patient meets BOTH of the following [(1) and (2)]:

(1) Factor IX inhibitor titer testing has been performed within the past 30 days **[documentation required]**; AND

(2) Patient does not have a positive test for Factor IX inhibitors of ≥ 1.0 Bethesda units/mL **[documentation required]**; OR

b) Patient has not received Factor IX therapy in the past; AND

v. According to the prescriber, prophylactic use of Factor IX products will not occur while receiving Hympavzi; AND

Note: Use of Factor IX products for the treatment of breakthrough bleeding is permitted.

vi. The medication is prescribed by or in consultation with a hemophilia specialist.

B) Patient is Currently Receiving Hympavzi. Approve if the patient meets ALL of the following (i, ii, iii, and iv):

i. Patient is using Hympavzi for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; AND

ii. According to the prescriber, prophylactic use of Factor IX products will not occur while using Hympavzi; AND
Note: Use of Factor IX products for the treatment of breakthrough bleeding is permitted.

iii. The medication is prescribed by or in consultation with a hemophilia specialist; AND

iv. According to the prescriber, patient experienced a beneficial response to therapy.
Note: Examples of a beneficial response include a reduction in bleeding events, in the severity of bleeding episodes, in the number of bleeding events that required treatment, and/or in the number of spontaneous bleeding events.

Employer Plans:

Product	Criteria
Hympavzi (marstacimab-hncq subcutaneous injection)	Patient meets ONE of the following (1 or 2): **1.** Hympavzi is being used for the treatment of Hemophilia A without inhibitors and the patient meets ONE of the following (A or B): A. Patient has tried and experienced inadequate efficacy or significant intolerance to Hemlibra **[documentation required]**; OR B. The patient has already been started on therapy with Hympavzi. **2.** Hympavzi is being used for the treatment of Hemophilia B without inhibitors.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Hympavzi for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent Use with Hemlibra (emicizumab-kxwh subcutaneous injection) in a Patient with Hemophilia A.** Hemlibra is a bispecific factor IXa- and Factor X-directed antibody indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults and pediatric patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.[8] Hympavzi has not been studied concurrently with Hemlibra.[1]

References

1. Hympavzi™ subcutaneous injection [prescribing information]. New York, NY: Pfizer; October 2024.
2. Mancuso ME, Mahlangu JN, Pipe SW. The changing treatment landscape in haemophilia: from standard half-life clotting factor concentrates to gene editing. *Lancet*. 2021;397:630-640.

3. Franchini M, Mannucci PM. The more recent history of hemophilia treatment. *Semin Thromb Hemost*. 2022;48(8):904-910.
4. Croteau SE. Hemophilia A/B. *Hematol Oncol Clin North Am*. 2022;36(4):797-812.
5. Centers for Disease Control and Prevention. Data and statistics on hemophilia. Available at: https://www.cdc.gov/hemophilia/data-research/. Accessed on November 22, 2024.
6. National Bleeding Disorders Foundation. Hemophilia A: An overview of symptoms, genetics, and treatments to help you understand hemophilia B. Available at: https://www.bleeding.org/bleeding-disorders-a-z/types/hemophilia-a. Accessed on November 22, 2024.
7. National Hemophilia Foundation. Hemophilia B. An overview of symptoms, genetics, and treatments to help you understand hemophilia B. Available at: https://www.hemophilia.org/bleeding-disorders-a-z/types/hemophilia-b. Accessed on November 22, 2024.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	05/15/2025
Selected Revision	**Preferred Product Criteria – Employer Plans:** Updated preferred product criteria Removed "Approve if, according to the prescriber, there is concern for a drug-drug interaction (e.g., drug interaction with Hemlibra and Feiba" **Added** documentation requirements throughout the policy.	07/15/2025

The policy effective date is in force until updated or retired.

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