Pharmacy Policy Bulletin: J-0697 Hemophilia Products – Commercial and Healthcare Reform	
Number: J-0697	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Injectable = Yes w/ Prior Authorization **Quantity Limits (1., 2., 3., or 4.):** **1.** Rx Mgmt Quantity Limits = Safety/Specialty **2.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt **3.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt + Watchful **4.** Rx Mgmt Performance = MRXC = Yes **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0697-019	**Original Date:** 01/31/2018
Effective Date: 10/08/2025	**Review Date:** 09/17/2025

Drugs Product(s):	• Alhemo (concizumab-mtci) • Hemlibra (emicizumab-kxwh) • Hympavzi (marstacimab-hncq) • Nuwiq [Antihemophilic Factor (Recombinant)] • Recombinate [Antihemophilic Factor (Recombinant)] • Qfitlia (fitusiran)

FDA-Approved Indication(s):	• Alhemo
	  ○ 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 [FVIII] deficiency) with or without FVIII inhibitors, or
	  ▪ Hemophilia B (congenital factor IX [FIX] deficiency) with or without FIX inhibitors
	• Hemlibra
	  ○ Routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors
	• Hympavzi

	○ 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 FVIII deficiency) without FVIII inhibitors, or ▪ Hemophilia B (congenital FIX deficiency) without FIX inhibitors • Nuwiq ○ Adults and children with Hemophilia A for: ▪ On-demand treatment and control of bleeding episodes ▪ Perioperative management of bleeding ▪ Routine prophylaxis to reduce the frequency of bleeding episodes • Recombinate ○ Hemophilia A (classical hemophilia) for the prevention and control of hemorrhagic episodes ○ Perioperative management of patients with hemophilia A (classical hemophilia) • Qfitlia ○ Routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients aged 12 years and older with hemophilia A or B with or without FVIII or FIX inhibitors

Background:	• There are multiple types of chronic, lifelong bleeding disorders that cause impaired clotting and excessive bleeding episodes. ○ Hemophilia A (classic hemophilia) is a deficiency of factor VIII. ○ Hemophilia B (Christmas disease) is a deficiency of factor IX. ○ Von Willebrand Disease (VWD) is a deficiency of von Willebrand factor. ○ Factor X deficiency (Stuart-Prower factor deficiency) is a deficiency of factor X. ○ Factor XIII deficiency is a deficiency of factor XIII. ○ Fibrinogen deficiency is a deficiency of fibrinogen (factor I). ○ Inhibitors are antibodies that form to the factor that render the factor inactive. Patients with inhibitors face a greater disease burden than patients without inhibitors. ○ The severity of hemophilia is classified based on the level of FVIII (in hemophilia A) or FIX (in hemophilia B) activity in the blood. Less than 1% of normal factor activity is characterized as severe, 1% to 5% of factor activity is characterized as moderate, and > 5% to 40% of normal factor activity is characterized as mild. • Plasma-derived factor is from human donations and purified. Recombinant factor is genetically engineered technology. • The 2020 World Federation of Hemophilia (WFH) Guidelines for the Management of Hemophilia state that there is no preference between recombinant and plasma-derived clotting factor concentrates for the treatment of hemophilia A or hemophilia B. The choice of treatment product between the classes should be based on availability, cost, and patient preferences. The plasma quality and the manufacturing process should be taken into consideration when choosing a product. The choice of treatment product for hemophilia patients with inhibitors should be based on inhibitor titer, records of clinical response to product, and site and nature of bleed.

Table 1: Clotting Products

Hemophilia A	
Plasma-derived Factor VIII Products	Hemofil M Koate
Standard Half-Life Recombinant Factor VIII Products	Advate Afstyla

	Helixate FS Kogenate FS Kovaltry Novoeight Nuwiq Obizur Recombinate Xyntha
Extended Half-Life Factor VIII Products	Altuviiio Adynovate Eloctate Esperoct Jivi
Bispecific Factor IXa- and Factor X-directed Antibody	Hemlibra
Hemophilia B	
Plasma-derived Factor IX Products	AlphaNine SD Mononine
Plasma-derived Factor IX, Factor II, Factor X and low levels Factor VII	Profilnine
Standard Half-Life Recombinant Factor IX Products	BeneFIX Ixinity Rixubis
Extended Half-Life Recombinant Factor IX Products	Alprolix Idelvion Rebinyn
Hemophilia A or B with Inhibitors	
Bypassing Agent: recombinant activated Factor VII (rFVIIa)	NovoSeven Sevenfact
Bypassing Agent: activated prothrombin complex concentrates (aPCCs)	Feiba
Tissue factor pathway inhibitor (TFPI) antagonist	Alhemo
Antithrombin (AT)-directed small interfering ribonucleic acid (siRNA)	Qfitlia
Hemophilia A with Inhibitors	
Bispecific factor IXa- and factor X-directed antibody	Hemlibra
Hemophilia A or B without Inhibitors	
TFPI antagonists	Alhemo Hympavzi
AT-directed siRNA	Qfitlia
Hemophilia A and von Willebrand Disease	
Plasma-derived Factor VIII and VWF	Alphanate Humate-P Wilate
von Willebrand Disease	
Recombinant VWF	Vonvendi
Factor X Deficiency	
Plasma-derived Factor X	Coagadex
Factor XIII Deficiency	
Plasma-derived Factor XIII	Corifact
Recombinant Factor XIII A-subunit	Tretten
Fibrinogen (Factor I) Deficiency	
Human Fibrinogen Concentrate	Fibryga RiaSTAP

- Quantity limitations are based on the Hemlibra dosing guide available at: https://www.hemlibra-hcp.com/content/dam/gene/hemlibra-hcp/pdfs/hemlibra-dosing-guide.pdf

- Prescribing Considerations:
  - Hemlibra
    - The 12 mg/0.4 mL and 30 mg/mL single dose vial do not share the same concentration as 60 mg/0.4 mL, 105 mg/0.7 mL, 150 mg/mL, or 300 mg/2 mL and cannot be combined with any other vials to achieve desired dose. Vials of the same concentration and may be combined for dosing.
    - If combining the 30 mg/mL vial with vials of different concentrations (150 mg/mL) consider the following approach: 1. Take the labeled dose from the higher-concentration vial(s) first 2. Subtract the mg used from the higher-concentration vial(s) from the total mg of Hemlibra dose 3. Use the remaining mg to calculate the mL from the 30 mg/mL vial. Do not combine Hemlibra vials of different concentrations in a single injection.
    - The recommended dose of Hemlibra is a loading dose of 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks, followed by the following three options for the maintenance dose:
      - 1.5 mg/kg once weekly or
      - 3 mg/kg once every 2 weeks or
      - 6 mg/kg once every 4 weeks
      - The selection of a maintenance dose should be based on healthcare provider preference with consideration of regimens that may increase patient adherence. The dosing of Hemlibra is weight-based (actual body weight).
      - The coded quantity level limitations optimize the number of vials used. Patient Level Authorization (PLA) will be needed for authorized quantities exceeding the coded limits. Coding of quantity level limitations is at the following:
        - 12 mg/0.4 mL is at 8 vials (20 mL) per 21 days
        - 30 mg/mL is at 4 vials (4 mL) per 21 days
        - 60 mg/0.4 mL is at 12 vials (4.8 mL) per 21 days
        - 105 mg/0.7 mL is at 8 vials (5.6 mL) per 21 days
        - 150 mg/mL is at 6 vials (6 mL) per 21 days
        - 300 mg/2 mL is at 4 vials (8 mL) per 21 days
    - The prophylactic use of factor VIII (FVIII) products may be continued during the first week of Hemlibra prophylaxis.
  - Hympavzi
    - Hympavzi was only studied in patients with severe hemophilia A (< 1% of normal factor clotting activity) and patients with moderately severe hemophilia B (≤ 2% of normal factor clotting activity). In addition, all patients studied had previously taken a factor replacement therapy.
    - The coded quantity limit for Hympavzi is four (4) prefilled syringes/pens per 28 days, which aligns with maintenance dosing in the prescribing information. Additional quantities may require patient level authorization.
    - Factor VIII and factor IX products can be administered for the treatment of breakthrough bleeds in patients receiving Hympavzi. Do not use additional doses of Hympavzi to treat breakthrough bleeds. Factor replacement products should not be used for routine prophylaxis alongside Hympavzi.
  - Alhemo
    - Dose optimization is evaluated after 4 weeks of treatment by measuring drug concentration by Enzyme-Linked Immunosorbent Assay (ELISA) prior to administration of next scheduled dose. An FDA-authorized test for the measurement of Alhemo drug concentration in plasma is not currently available.
    - Once the Alhemo concentration result is available, the maintenance dose of Alhemo is individualized.

	▪ Maintenance of Alhemo plasma concentration above 200 ng/mL is important to decrease the risk of bleeding episodes. If Alhemo plasma concentration remains below 200 ng/mL at two consecutive measurements, the benefits of continued Alhemo treatment should be evaluated versus the potential risk of bleeding events, and alternative therapies if available should be considered. ○ Qfitlia ▪ Measure AT activity using an FDA-cleared test at Weeks 4 (Month 1), 12 (Month 3), 20 (Month 5) and 24 (Month 6) following the starting dose and after any dose modification. Once the patient's target dose is identified based on AT activity 15-35%, measure AT activity annually. Ultimately, after several dose adjustments, patients with AT activity < 15% should discontinue Qfitlia. ○ Clotting factor products should be prescribed by or in consultation with a hematologist or physician who specializes in the treatment of hemophilia.

Approval Criteria

I. Factor Products (excluding monoclonal antibody products)

A. Initiation (no previous therapy)

1. Hemophilia A
When a benefit, coverage of Nuwiq or Recombinate may be approved when all of the following criteria are met **(a., b., and c.)**:
a. The member has an FDA-approved diagnosis.
b. The member is using the product for Hemophilia A (ICD-10: D66).
c. For new starts to therapy, the member has experienced therapeutic failure or intolerance to one (1) of the following plan-preferred agents, or all are contraindicated **(i. through x.)**:
i. Adynovate
ii. Advate
iii. Afstyla
iv. Altuviiio
v. Eloctate
vi. Esperoct
vii. Jivi
viii. Kogenate FS
ix. Kovaltry
x. Novoeight
xi. Xyntha

B. Maintenance (history of previous therapy)

1. Hemophilia A
When a benefit, coverage of Nuwiq or Recombinate may be approved when all of the following criteria are met **(a. and b.)**:
a. The member has received previous clotting factor product(s).
b. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(i., ii., or iii.)**:
i. Disease stability
ii. Disease improvement
iii. Delayed disease progression

II. Alhemo

A. Initial Authorization

When a benefit, coverage of Alhemo may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is 12 years of age or older.
2. The member meets one (1) of the following criteria **(a. or b.)**:
   - **a.** The member has a diagnosis of Hemophilia A (ICD-10: D66).
   - **b.** The member has a diagnosis of Hemophilia B (ICD-10: D67).
3. The member is using the product for routine prophylaxis.
4. The member meets one (1) of the following criteria **(a. or b.)**:
   - **a.** The member has a documented history of FVIII or FIX inhibitors (≥ 0.6 Bethesda units/mL).
   - **b.** The member has no documented history of FVIII or FIX inhibitors and meets all of the following criteria **(i., ii., and iii.)**:
     - **i.** The member has previously taken a factor VIII or IX replacement therapy (for example, Adynovate, Advate, Afstyla, Altuviiio, etc.).
     - **ii.** If the request is for Hemophilia A, the prescriber submits documentation that the member has severe disease (< 1% of normal factor activity).
     - **iii.** If the request is for Hemophilia B, the prescriber submits documentation that the member has moderately severe to severe disease (≤ 2% of normal factor activity).

B. Reauthorization

When a benefit, reauthorization of Alhemo may be approved when the following criteria are met **(1. and 2.)**:

1. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(a., b., or c.)**:
   - **a.** Disease stability
   - **b.** Disease improvement
   - **c.** Delayed disease progression
2. The prescriber submits documentation of Alhemo plasma concentration levels and one (1) of the following criteria are met **(a. or b.)**:
   - **a.** Alhemo plasma concentration is ≥ 200 ng/mL on consecutive measurements.
   - **b.** Alhemo plasma concentration is < 200 ng/mL on at least two (2) consecutive measurements and the provider attests to all the following criteria **(i. and ii.)**:
     - **i.** The benefits of continued Alhemo treatment outweigh potential risk of bleeding events.
     - **ii.** Alternative therapies are not clinically appropriate.

III. Hemlibra

A. Initial Authorization

When a benefit, coverage of Hemlibra may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member has a diagnosis of Hemophilia A (ICD-10: D66).
2. The member is using the product for routine prophylaxis.

B. Reauthorization

When a benefit, reauthorization of Hemlibra may be approved when the following criterion is met **(1.)**:

1. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(a., b., or c.)**:
   - **a.** Disease stability
   - **b.** Disease improvement
   - **c.** Delayed disease progression

C. Quantity Limitations

When prior authorization is approved, Hemlibra may be authorized in quantities as follows for the loading dose only when all of the following criteria are met **(1., 2., and 3.)**:

1. There is documentation of the member's weight.
2. Based on the member's weight, the requested dose is within the FDA-approved labeled dosing for additional single-dose vial quantities of the loading dose only.
3. The following additional single-dose vial limits will be authorized if the member requires additional doses for the loading dose only **(a., b., and c.)**:
   - **a.** 60 mg/0.4 mL: 4 vials (1.6 mL)
   - **b.** 105 mg/0.7 mL: 4 vials (2.8 mL)
   - **c.** 150 mg/mL: 6 vials (6 mL)

The following are the total combined quantity limits, including both the coded limits and additional loading dose single-dose vial limits, allowed for Hemlibra.

Dose	Quantity Limit
12 mg/0.4 mL	8 vials (20 mL) per 21 days
30 mg/mL	4 vials (4 mL) per 21 days
60 mg/0.4 mL	16 vials (6.4 mL) per 21 days
105 mg/0.7 mL	12 vials (8.4 mL) per 21 days
150 mg/mL	12 vials (12 mL) per 21 days
300 mg/2 mL	4 vials (8 mL) per 21 days

IV. Hympavzi

A. Initial Authorization

When a benefit, coverage of Hympavzi may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is 12 years of age or older.
2. The member meets one (1) of the following criteria **(a. or b.)**:
   - **a.** The member has a diagnosis of Hemophilia A (ICD-10: D66) and meets all of the following criteria **(i. and ii.)**:
     - **ii.** The member does not have FVIII inhibitors
     - **iii.** The prescriber submits documentation that the member has severe disease (< 1% of normal factor activity)
   - **b.** The member has a diagnosis of Hemophilia B (ICD-10: D67) and meets all of the following criteria **(i. and ii.)**:
     - **ii.** The member does not have FIX inhibitors
     - **iii.** The prescriber submits documentation that the member has moderately severe to severe disease (≤ 2% of normal factor activity)
3. The member is using the product for routine prophylaxis.
4. The member has previously taken a factor VIII or IX replacement therapy (for example, Adynovate, Advate, Afstyla, Altuviiio, etc.).

B. Reauthorization

When a benefit, reauthorization of Hympavzi may be approved when the following criterion is met **(1.)**:

1. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(a., b., or c.)**:
   - **a.** Disease stability
   - **b.** Disease improvement
   - **c.** Delayed disease progression

C. Quantity Limitations

When prior authorization is approved, Hympavzi may be authorized in additional quantities when one (1) of the following criteria is met **(1. or 2.)**:

1. The member is requesting induction dosing within the first 28 days of therapy.

2. The member is requesting clinical exception dosing and meets all of the following criteria **(a., b., and c.)**:
   - **a.** The member has been on therapy for at least 6 months
   - **b.** The member weighs ≥ 50 kg
   - **c.** The member has experienced at least two (2) breakthrough bleeds

Dose Type	Quantity Limit
Induction Therapy	Five (5) prefilled syringes/pens within the first 28 days
Clinical Exception	Eight (8) prefilled syringes/pens per 28 days

V. Qfitlia

A. Initial Authorization

When a benefit, coverage of Qfitlia may be approved when all of the following criteria are met **(1. through 5.)**:

1. The member is 12 years of age or older.
2. The member meets one (1) of the following criteria **(a. or b.)**:
   - **a.** The member has a diagnosis of Hemophilia A (ICD-10: D66) and meets the following criterion **(i.)**:
     - **i.** The prescriber submits documentation that the member has severe disease (< 1% of normal factor activity)
   - **b.** The member has a diagnosis of Hemophilia B (ICD-10: D67) and meets the following criterion **(i.)**:
     - **i.** The prescriber submits documentation that the member has moderately severe to severe disease (≤ 2% of normal factor activity)
3. The member is using the product for routine prophylaxis.
4. The member meets one (1) of the following criteria **(a. or b.)**:
   - **a.** The member has a documented history of FVIII or FIX inhibitors (≥ 0.6 Bethesda units/mL).
   - **b.** The member has no documented history of FVIII or FIX inhibitors and meets the following criterion **(i.)**:
     - **i.** The member has previously taken a factor VIII or IX replacement therapy (for example, Adynovate, Advate, Afstyla, Altuviiio, etc.).
5. The member has documentation of antithrombin (AT) activity > 60% prior to treatment initiation and planned monitoring with AT activity to adjust dose using an FDA-cleared test.

B. Reauthorization

When a benefit, reauthorization of Qfitlia may be approved when the following criteria is met **(1. and 2.)**:

1. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(a., b., or c.)**:
   - **a.** Disease stability
   - **b.** Disease improvement
   - **c.** Delayed disease progression
2. The prescriber submits documentation of AT activity and one (1) of the following criteria are met **(a., b., or c.)**:
   - **a.** AT activity is 15%-35%
   - **b.** AT activity is < 15% and the member meets the following criterion **(i.)**:
     - **i.** The member is undergoing dose reduction.
   - **c.** AT activity is > 35% and the member meets the following criterion **(i.)**:
     - **i.** The member is undergoing dose escalation.

C. Quantity Limitations

When prior authorization is approved and benefit applies, Qfitlia may be authorized in additional quantities as follows:

Coded Quantity Limit	Approvable Reason for Quantity Limit Override **(a. or b.)**:	Approvable Override Quantity Limit
One (1) single-dose prefilled pen (50 mg) every 42 days	**a.** AT activity is > 35% after 6 months.	One (1) single-dose prefilled pen (50 mg) every 21 days
One (1) single-dose vial (20 mg) every 42 days	**b.** The member has not achieved satisfactory bleed control.	One (1) single-dose vial (20 mg) every 21 days

Note: Coding of quantity level limitations is at the starting dose interval. Claims for quantities of Qfitlia that require dose escalation for a frequency greater than every 2 months require patient level authorization (PLA) override.

VI. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

Commercial and HCR Plans:

- **Prior Authorization – Hemlibra, Hympavzi, Nuwiq, Recombinate**
  - If approved, up to a 12 month authorization may be granted.
- **Prior Authorization – Alhemo, Qfitlia**
  - Initial Authorization: If approved, up to a 6 month authorization may be granted.
  - Reauthorization: If approved, up to a 12 month authorization may be granted.
- **Quantity Limits - Hemlibra**
  - Loading Dose: If approved, up to a 4 week authorization may be granted.
- **Quantity Limits - Hympavzi**
  - Induction Dose: If approved, up to a 4 week authorization may be granted.
  - Clinical Exception: If approved, up to a 12 month authorization may be granted.
- **Quantity Limits - Qfitlia**
  - If approved, up to a 6 month authorization may be granted.

Automatic Approval Criteria

None.

References:

1. Nuwiq [package insert]. Hoboken, NJ. Octapharma AB, Inc.; June 2021.
2. Recombinate [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; March 2010.
3. Hemlibra [package insert]. San Francisco, CA: Genentech, Inc.; January 2024.

4. Hympavzi [package insert]. New York, NY: Pfizer Inc.; October 2024.
5. Alhemo [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; July 2025.
6. Qfitlia [package insert]. Cambridge, MA: Genzyme Corporation; March 2025.
7. DRUGDEX System (Micromedex 2.0). Greenwood Village, CO: Truven Health Analytics; 2024.
8. Medical and Scientific Advisory Council (MASAC). MASAC Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders. Available at: https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/MASAC-Recommendations-Concerning-Products-Licensed-for-the-Treatment-of-Hemophilia-and-Other-Bleeding-Disorders. Accessed August 08, 2024.
9. Hemlibra Dosing Guide. March 2023. Available at: https://www.hemlibra-hcp.com/content/dam/gene/hemlibra-hcp/pdfs/hemlibra-dosing-guide.pdf. Accessed August 08, 2024.
10. World Federation of Hemophilia. Guidelines for the Management of Hemophilia. Available at: https://www1.wfh.org/publications/files/pdf-1863.pdf. Accessed January 13, 2025.