

Hemophilia Products – Anti-Inhibitor Antibody: Hemlibra (emicizumab-kxwh) (Subcutaneous)

Effective date: 01/01/2020

Review date: 12/18/19, 1/22/20, 2/25/2021, 06/24/2021, 6/16/2022, 6/22/2023, 12/07/2023, 01/04/2024, 05/15/2024, 08/14/2024, 09/17/2025

Pharmacy Scope: Medicaid

Medical Scope: Medicaid, Commercial, Medicare

I. Length of Authorization

Unless otherwise specified*, the initial authorization will be provided for 3 months and may be renewed every 12 months thereafter.

Note: The cumulative amount of medication the patient has on-hand will be taken into account for authorizations.

** Initial and renewal authorization periods may vary by specific covered indication*

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

<u>Loading Dose:</u>
345mg weekly x 4 doses
<u>Maintenance Dose:</u>
1.5mg/kg weekly = 180mg weekly 3mg/kg every 2 weeks = 345mg every 2 weeks 6mg/kg every 4 weeks = 690mg every 4 weeks

B. Max Units (per dose and over time) [Medical Benefit]:

<u>Loading Dose:</u>
690 billable units (BU) weekly x 4 doses
<u>Maintenance Dose:</u>
1.5mg/kg weekly = 360 BU weekly 3mg/kg every 2 weeks = 690 BU every 2 weeks 6mg/kg every 4 weeks = 1380 BU every 4 weeks

Note: Patient must be dosed at a frequency that will produce the least wastage per dose based on available vial sizes of 30 mg, 60 mg, 105 mg, 150 mg, and 300mg.

III. Summary of Evidence

Hemlibra is a factor IXa and X indicated for the routine prophylaxis to prevent or reduce the frequency of bleeding episodes in patients with hemophilia A. Efficacy in patients with hemophilia A without FVIII inhibitors was established in two clinical trials, Haven 3 and Haven 4. Haven 3 was a randomized, multicenter, open-label, clinical trial in 152 patients with hemophilia A who received on-demand or prophylactic treatment. Patients received Hemlibra 3mg/kg once weekly for the first 4 weeks followed by either 1.5mg/kg once weekly or 3mg/kg once every two weeks or no prophylaxis. Hemlibra prophylaxis resulted in a statistically significant ($p < 0.0001$) 68% reduction in bleed rate for treated bleeds compared to previous FVIII prophylaxis as well as significant reductions observed in all bleeds, spontaneous bleeds, joint bleeds and target joint bleeds. Haven 4 was a single-arm, multicenter, open-label clinical trial that included 41 patients with hemophilia A, with or without FVIII inhibitors. Patients received 3mg/kg weekly for the first 4 weeks followed by 6 mg/kg once every four weeks thereafter. Results show an annualized bleed rate of 1.2 for treated bleeds with four patients experiencing zero treated bleeds, demonstrating efficacy in reducing bleed rate. Adverse effects include injection site reactions, headache and arthralgia.

IV. Initial Approval Criteria

- Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.
- Will NOT be used in combination with another agent used as prophylactic therapy for Hemophilia A (*Note: The prophylactic use of factor VIII (FVIII) products may be continued during the first week of Hemlibra prophylaxis**** See chart below;

Hemophilia A (congenital factor VIII deficiency) with inhibitors † Φ

- Diagnosis of congenital factor VIII deficiency has been confirmed by blood coagulation testing; **AND**
- Member has inhibitors to Factor VIII with a current or historical titer of ≥ 5 Bethesda Units (BU)** ; **AND**
- Must be used as routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
 - Used as primary prophylaxis in members with severe factor VIII deficiency (factor VIII level of $<1\%$); **OR**
 - Used as secondary prophylaxis in members with at least TWO documented episodes of spontaneous bleeding into joints; **AND**
- Not used in combination with Immune Tolerance Induction (ITI); **AND**
 - Member has at least two documented episodes of spontaneous bleeding into joints; **OR**
 - Member has documented trial and failure of Immune Tolerance Induction (ITI); **OR**
 - Member has documented trial and failure of or is currently on routine prophylaxis with a bypassing agent (i.e., NovoSeven, FEIBA).

****Note:** Members with inhibitor titer levels >0.6 BU to <5 BU who are not responding to or are not a candidate for standard factor replacement, will be evaluated on a case-by-case basis.

Hemophilia A (congenital factor VIII deficiency) without inhibitors † Φ

- Diagnosis of congenital factor VIII deficiency has been confirmed by blood coagulation testing; **AND**
- Used for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
- Used as treatment in one of the following:
 - Primary prophylaxis in members with severe factor VIII deficiency (factor VIII level of <1%); **OR**
 - Secondary prophylaxis in members with at least TWO documented episodes of spontaneous bleeding into joints; **AND**
- Member is not a suitable candidate for treatment with shorter half-life Factor VIII (recombinant) products at a total weekly dose of 100 IU/kg or less (as attested by the prescribing physician with appropriate clinical rationale)

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

*****Drugs to treat Hemophilia A or B**

Hemophilia A & B Drug Chart	
Factor VIIa (Hemophilia A or B)	
Novoseven RT	J7189
Sevenfact	J7212
Anti-Inhibitor Coagulant Complex (Hemophilia A or B)	
Feiba	J7198
Factor VIII (Hemophilia A)	
Advate	J7192
Kogenate FS	J7192
Helixate FS	J7192
Recombinate	J7192
Kovaltry	J7211
Eloctate	J7205

Koate / Koate-DVI	J7190
Hemofil M	J7190
Novoeight	J7182
Nuwiq	J7209
Obizur	J7188
Xyntha / Xyntha Solofuse	J7185
Afstyla	J7210
Adynovate	J7207
Jivi	J7208
Esperoct	J7204
Altuviio	J7214
Factor IX (Hemophilia B)	
AlphaNine SD	J7193
Mononine	J7193
Alprolix	J7201
Profilnine	J7194
BeneFIX	J7194
Ixinity	J7213
Rixubis	J7200
Idelvion	J7202
Rebinyn	J7203
Tissue Factor Pathway Inhibitor (Hemophilia A)	
Qfitlia	J3590

Hypnavor	J7172
----------	-------

V. Dispensing Requirements for Rendering Providers (Hemophilia Management Program)

- Prescriptions cannot be filled without an expressed need from the member, caregiver or prescribing practitioner. Auto-filling is not allowed.
- Monthly, rendering provider must submit for authorization of dispensing quantity before delivering factor product.
- The cumulative amount of medication(s) the member has on-hand should be taken into account when dispensing factor product.
- Dispensing requirements for renderings providers are a part of the hemophilia management program. This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide.

VI. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Member continues to meet criteria identified in section IV; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: thrombotic microangiopathy thromboembolic events (thromboembolism, pulmonary embolism), development of neutralizing antibodies (inhibitors), etc.; **AND**
- Any increases in dose must be supported by an acceptable clinical rationale (i.e. weight gain, half-life study results, increase in breakthrough bleeding when member is fully adherent to therapy, etc.); **AND**
- Member has demonstrated a beneficial response to therapy (i.e., the frequency of bleeding episodes has decreased from pre-treatment baseline); **AND**
- The cumulative amount of medication(s) the member has on-hand will be taken into account when authorizing.

Routine prophylaxis to prevent or reduce the frequency of bleeding episode

- Renewals will be approved for a 12 month authorization period

Dosage/Administration

Indication	Dose
Routine Prophylaxis in Congenital Hemophilia A with or without inhibitors	3 mg/kg by subcutaneous injection once weekly for the first 4 weeks, followed by 1.5 mg/kg once weekly, 3 mg/kg every two weeks, or 6 mg/kg every four weeks

VII. Billing Code/Availability Information

HCPCS Code:

- J7170 - Injection, emicizumab-kxwh, 0.5 mg; 1 billable unit = 0.5 mg

NDC:

Drug	Strength	Form	NDC
	12mg/0.4 mL	SDV	50242-0927-xx
Hemlibra	30 mg/mL	SDV	50242-0920-xx
	60 mg/0.4 mL	SDV	50242-0921- xx
	105 mg/0.7 mL	SDV	50242-0922- xx
	150 mg/mL	SDV	50242-0923- xx
	300 mg/2 mL	SDV	50242-0930-xx

VIII. References

- Hemlibra [package insert]. South San Francisco, CA; Genentech, Inc. October 2024. Accessed July 2025.
- MASAC Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Selected Disorders of the Coagulation System. Revised April 11, 2024. National Hemophilia Foundation. MASAC Document #284; April 2024. Available at: <https://www.bleeding.org>. Accessed May 2024.
- Guidelines for the Management of Hemophilia. 3rd Edition. World Federation of Hemophilia 2020. Available at: <https://www1.wfh.org/publications/files/pdf-1863.pdf>. Accessed May 2024.
- Annual Review of Factor Replacement Products. Oklahoma Health Care Authority Review Board. Updated Dec 2020. Accessed May 2024.
- Graham A1, Jaworski K. Pharmacokinetic analysis of anti-hemophilic factor in the obese patient. Haemophilia. 2014 Mar;20(2):226-9.
- Croteau SE1, Neufeld EJ. Transition considerations for extended half-life factor products. Haemophilia. 2015 May;21(3):285-8.
- Mingot-Castellano, et al. Application of Pharmacokinetics Programs in Optimization of Haemostatic Treatment in Severe Hemophilia a Patients: Changes in Consumption, Clinical Outcomes and Quality of Life. Blood. 2014 December; 124 (21).
- MASAC Recommendation Concerning Prophylaxis for Hemophilia A and B with and without Inhibitors. Revised April 27, 2022. National Hemophilia Foundation. MASAC Document #267; April 2022. Available at: <https://www.bleeding.org>. Accessed May 2024.

8. UKHCDO protocol for first line immune tolerance induction for children with severe haemophilia A: A protocol from the UKHCDO Inhibitor and Paediatric Working Parties. 2017. Available at: <http://www.ukhcdo.org/guidelines>. Accessed May 2024.
9. Oldenburg J, Mahlangu JN, Kim B, et al. Efficacy, safety, and pharmacokinetics of emicizumab prophylaxis given every 4 weeks in people with haemophilia A (HAVEN 4): a multicentre, open-label, non-randomised phase 3 study. *Lancet Haematol*. 2019 Jun;6(6):e295-e305. doi: 10.1016/S2352-3026(19)30054-7. Epub 2019 Apr 16.
10. Pipe SW, Shima M, Lehle M, et al. Efficacy, safety, and pharmacokinetics of emicizumab prophylaxis given every 4 weeks in people with haemophilia A (HAVEN 4): a multicentre, open-label, non-randomised phase 3 study. *Lancet Haematol*. 2019 Jun;6(6):e295-e305. doi: 10.1016/S2352-3026(19)30054-7. Epub 2019 Apr 16.
11. Young G, Liesner R, Chang T, et al. A multicenter, open-label phase 3 study of emicizumab prophylaxis in children with hemophilia A with inhibitors. *Blood*. 2019 Dec 12;134(24):2127-2138. doi: 10.1182/blood.2019001869. PMID: 31697801; PMCID: PMC6908828.
12. Mahlangu J, Oldenburg J, Paz-Priel I, et al. Efficacy, safety, and pharmacokinetics of emicizumab prophylaxis in Patients Who Have Hemophilia A without Inhibitors. *N Engl J Med*. 2018 Aug 30;379(9):811-822. doi: 10.1056/NEJMoa1803550. PMID: 30157389.
13. Hoots, WK. (2024). Hemophilia A and B: Routine management including prophylaxis. In Leung LLK, Tirnauer JS (Eds.), *UptoDate*. Last updated: April 16, 2024. Accessed May 13, 2024. Available from https://www.uptodate.com/contents/hemophilia-a-and-b-routine-management-including-prophylaxis?search=hemophilia%20a&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H978189854
14. First Coast Service Options, Inc. Local Coverage Article: Billing and Coding: Hemophilia Clotting Factors (A56482). Centers for Medicare & Medicaid Services Inc. Updated on 09/29/2023 with effective date 10/01/2023. Accessed May 2024.
15. Palmetto GBA. Local Coverage Article: Billing and Coding: Guidance for Anti-Inhibitor Coagulant Complex (AICC) National Coverage Determination (NCD) 110.3 (A56065). Centers for Medicare & Medicaid Services Inc. Updated on 11/14/2022 with effective date 11/24/2022. Accessed May 2024.
16. Novitas Solutions, Inc. Local Coverage Article: Billing and Coding: Hemophilia Factor Products (A56433). Centers for Medicare & Medicaid Services Inc. Updated on 09/29/2023 with effective date 10/01/2023. Accessed May 2024.

Appendix 1 – Covered Diagnosis Codes

Hemlibra

ICD-10	ICD-10 Description
D66	Hereditary factor VIII deficiency

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA):

Jurisdiction(s): N	NCD/LCD Document (s): A56482
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a56482&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP	
Jurisdiction(s): J,M	NCD/LCD Document (s): A56065
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a56065&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP	
Jurisdiction(s): H,L	NCD/LCD Document (s): A56433
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a56433&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP	

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale: Hemlibra was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Hemlibra according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.