

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

Document Number: IC-0349

Last Review Date: 06/04/2024

Date of Origin: 12/12/2017

Dates Reviewed: 12/2017, 10/2018, 03/2019, 02/2020, 04/2020, 06/2021, 06/2022, 06/2023, 03/2024, 06/2024

I. Length of Authorization

Coverage will be provided for 3 months and may be renewed every 12 months thereafter.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

<u>Loading Dose:</u>
– 345 mg weekly x 4 doses
<u>Maintenance Dose:</u>
– 6 mg/kg every 4 week dosing = 690 mg every 4 weeks

B. Max Units (per dose and over time) [HCPCS Unit]:

<u>Loading Dose:</u>
– 690 billable units (BU) weekly x 4 doses
<u>Maintenance Dose:</u>
– 6 mg/kg every 4 week dosing = 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 12 mg, 30 mg, 60 mg, 105 mg, 150 mg, and 300 mg.

III. Initial Approval Criteria ^{1-3,8,10-14}

Coverage is provided in the following conditions:

- Diagnosis of congenital factor VIII deficiency has been confirmed by blood coagulation testing;
AND

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

- Patient 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 patients with severe factor VIII deficiency (factor VIII level of <1%); **OR**
 - Used as secondary prophylaxis in patients with at least TWO documented episodes of spontaneous bleeding into joints; **AND**
- Not used in combination with Immune Tolerance Induction (ITI); **AND**
 - Patient has had at least two documented episodes of spontaneous bleeding into joints; **OR**
 - Patient had a documented trial and failure of Immune Tolerance Induction (ITI); **OR**
 - Patient had a documented trial and failure of, or is currently on, routine prophylaxis with a bypassing agent (i.e., NovoSeven, Feiba)

***Note: Patients 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

- Must be 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 patients with severe factor VIII deficiency (factor VIII level of <1%); **OR**
 - Secondary prophylaxis in patients with at least TWO documented episodes of spontaneous bleeding into joints; **AND**
- Patient 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

IV. Renewal Criteria ^{1-3,8}

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **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**
- Patient has demonstrated a beneficial response to therapy (i.e., the frequency of bleeding episodes has decreased from pre-treatment baseline)

V. Dosage/Administration ¹

Indication	Dose
Routine Prophylaxis in Congenital Hemophilia A with or without inhibitors	<u>Loading Dose:</u> Administer 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks <u>Maintenance Dose:</u> <ul style="list-style-type: none">Administer 1.5 mg/kg once weekly; ORAdminister 3 mg/kg every two weeks; ORAdminister 6 mg/kg every four weeks

VI. Billing Code/Availability Information

HCPCS Code:

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

NDC:

Drug	Strength	Form	NDC
Hemlibra	12 mg/0.4 mL	SDV	50242-0927-xx
	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

VII. References

- Hemlibra [package insert]. South San Francisco, CA; Genentech, Inc. January 2024. Accessed May 2024.
- 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.

7. 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).
8. 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.
9. 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.
10. Oldenburg J, Mahlangu JN, Kim B, et al. Efficacy, safety, and pharmacokinetics of emicizumab prophylaxis in Hemophilia A with Inhibitors. *N Engl J Med*. 2017 Aug 31;377(9):809-818. doi: 10.1056/NEJMoa1703068. Epub 2017 Jul 10.
11. 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.
12. 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.
13. 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.
14. 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
15. 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.
16. 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.
17. 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

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

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes		
Jurisdiction	NCD/LCA/LCD Document (s)	Contractor
H,L	A56433	Novitas Solutions, Inc.
J,M	A56065	Palmetto GBA
N	A56482	First Coast Service Options, Inc.

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
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC