

## PHARMACY / MEDICAL POLICY – 5.01.581


# Pharmacologic Treatment of Hemophilia

Effective Date: Mar. 7, 2024  
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Replaces: N/A

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## Introduction

When a person bleeds, the body undertakes a series of steps to stop the bleeding. The first step is that blood platelets collect at the site of injury; this sets up a temporary plug. Next, several other proteins — known as clotting factors — work together to create a permanent plug in the damaged area. There are 13 types of clotting factors. Hemophilia is a condition in which clotting factors don't work as they should. A person with hemophilia bleeds easily and the blood takes much longer to clot. Hemophilia A is the most common form, affects clotting factor VIII (factor 8), is usually inherited, and most often affects males. In some cases of hemophilia A, however, the person doesn't inherit the condition. Rather, a genetic change occurs spontaneously which results in hemophilia A. Hemlibra is a drug that can be used to prevent or reduce the number of bleeding episodes in children and adults with hemophilia A. It's used in people who have developed an immune system response against factor VIII, which is known as factor VIII inhibitors. Hemophilia B is another form, affects clotting factor IX (factor 9), is usually inherited, and also most often affects males. Hemgenix is a gene therapy that can be used to prevent or reduce the number of bleeding episodes in adults with hemophilia B. This policy describes when Hemlibra and Hemgenix may be considered medically necessary.

**Note:** The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a

service may be covered.

## Policy Coverage Criteria

Drug	Medical Necessity
<b>Hemgenix (etranacogene dezaparvovec-drlb)</b>	<p><b>Hemgenix (etranacogene dezaparvovec-drlb) may be considered medically necessary for adults when all the following criteria are met:</b></p> <ul style="list-style-type: none"><li>• Individual is 18 years of age or older</li></ul> <p><b>AND</b></p> <ul style="list-style-type: none"><li>• Individual was assigned male at birth</li></ul> <p><b>AND</b></p> <ul style="list-style-type: none"><li>• Individual has severe or moderately severe hemophilia B as defined by a plasma Factor IX (FIX) activity level of 2% or less</li></ul> <p><b>AND</b></p> <ul style="list-style-type: none"><li>• Individual meets ONE of the following:<ul style="list-style-type: none"><li>○ Current or historical life-threatening hemorrhage</li><li>○ Repeated, serious spontaneous bleeding episodes</li><li>○ Individual is currently receiving FIX prophylaxis</li></ul></li></ul> <p><b>AND</b></p> <ul style="list-style-type: none"><li>• FIX prophylaxis will be discontinued following administration of Hemgenix if the individual is currently receiving FIX prophylaxis</li></ul> <p><b>AND</b></p> <ul style="list-style-type: none"><li>• Individual does not have a history of FIX inhibitors or a positive screen result of 0.6 or greater Bethesda Units (BU) using the Nijmegen-Bethesda assay</li></ul> <p><b>AND</b></p> <ul style="list-style-type: none"><li>• Individual has received a liver health assessment including enzyme testing [alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin] AND a hepatic ultrasound and elastography</li></ul> <p><b>AND</b></p> <ul style="list-style-type: none"><li>• A hepatologist has assessed the individual if the individual has radiological liver abnormalities or sustained liver enzyme elevations</li></ul> <p><b>AND</b></p>

Drug	Medical Necessity
	<ul style="list-style-type: none"> <li>Medication is being prescribed by or in consultation with a hematologist or a prescriber who specialized in hemophilia B</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Individual does not have a history of receiving gene therapy or is under consideration for treatment for another gene therapy for hemophilia B</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Individual is human immunodeficiency virus (HIV) negative or has a controlled HIV infection</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Individual does not have an active hepatitis B or hepatitis C infection</li> </ul>
<b>Hemlibra (emicizumab-kxwh)</b>	<p><b>Hemlibra (emicizumab-kxwh) may be considered medically necessary for adults and pediatric individuals, when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>Diagnosis of hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Hemlibra is not used concurrently with high dose aPCC</li> </ul> <p><b>Note:</b> High dose aPCC is defined as greater than 100 U/kg/day administered for greater than 24 hours</p>
<b>Roctavian (valoctocogene roxaparvovec-rvox)</b>	<p><b>Roctavian (valoctocogene roxaparvovec-rvox) may be considered medically necessary when all of the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>Individual is 18 years of age or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Individual was assigned male at birth</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Diagnosis of severe hemophilia A (congenital factor VIII deficiency) with factor VIII activity &lt; 1 IU/dL</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Factor VIII prophylaxis will be discontinued following administration of Roctavian if the individual is currently receiving factor VIII prophylaxis</li> </ul> <p><b>AND</b></p>

Drug	Medical Necessity
	<ul style="list-style-type: none"> <li>Individual does not have pre-existing antibodies to adeno-associated virus serotype 5 detected by an FDA-approved test</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Individual has received a liver health assessment including enzyme testing [alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin] AND a hepatic ultrasound and elastography</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Medication is being prescribed by or in consultation with a hematologist or a prescriber who specialized in hemophilia A</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Individual is human immunodeficiency virus (HIV) negative or has a controlled HIV infection</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Individual does not have an active hepatitis B or hepatitis C infection</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Documentation is provided demonstrating that the individual received education relating to alcohol abstinence and the use of concomitant medications</li> </ul>

Drug	Investigational
<b>Hemgenix (etranacogene dezaparvovec-drlb)</b>	<p><b>All other uses of Hemgenix (etranacogene dezaparvovec-drlb) for conditions not outlined in this policy are considered investigational.</b></p> <p><b>Repeat treatment of Hemgenix (etranacogene dezaparvovec-drlb) is considered investigational.</b></p>
<b>Hemlibra (emicizumab-kxwh)</b>	<p><b>All other uses of Hemlibra (emicizumab-kxwh) for conditions not outlined in this policy are considered investigational.</b></p>
<b>Roctavian (valoctocogene roxaparvovec-rvox)</b>	<p><b>All other uses of Roctavian (valoctocogene roxaparvovec-rvox) for conditions not outlined in this policy are considered investigational.</b></p> <p><b>Repeat treatment of Roctavian (valoctocogene roxaparvovec-rvox) is considered investigational.</b></p>

Approval	Criteria
<b>Initial authorization</b>	<p><b>Hemgenix (etranacogene dezaparvovec-drlb) may be approved as a one-time infusion.</b></p> <p><b>Hemlibra (emicizumab-kxwh) can be approved for 1 year.</b></p> <p><b>Roctavian (valoctocogene roxaparvovec-rvox) may be approved as a one-time infusion.</b></p>
<b>Re-authorization criteria</b>	<p><b>Repeat treatment of Hemgenix (etranacogene dezaparvovec-drlb) is considered investigational.</b></p> <p><b>Future re-authorization of Hemlibra (emicizumab-kxwh) would depend on clinical benefit/response shown at the time of re-authorization where:</b></p> <ul style="list-style-type: none"> <li>• Chart notes documenting decreased incidence of bleeding episodes</li> </ul> <p><b>Repeat treatment of Roctavian (valoctocogene roxaparvovec-rvox) is considered investigational.</b></p>

Dosage and Quantity Limits	
Treatment	Dosage and Quantity Limit
<b>Hemlibra (emicizumab-kxwh)</b>	<ul style="list-style-type: none"> <li>• 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks, followed by a maintenance dose of: <ul style="list-style-type: none"> <li>○ 1.5 mg/kg once weekly, or</li> <li>○ 3 mg/kg once every two weeks, or</li> <li>○ 6 mg/kg once every four weeks</li> </ul> </li> </ul>

Documentation Requirements
<p><b>The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:</b></p> <ul style="list-style-type: none"> <li>• Initial approval requires chart notes documenting the diagnosis and that all criteria are met</li> <li>• Hemlibra (emicizumab-kxwh) reauthorization requires chart notes documenting progress, including decreased incidence of bleeding episodes</li> </ul>

## Coding

Code	Description
<b>HCPCS</b>	
J1411	Injection, etranacogene dezaparvovec-drlb, per therapeutic dose (Hemgenix)
J1412	Injection, valoctocogene roxaparvovec-rvox, per ml, containing nominal 2 x 10 <sup>13</sup> vector genomes (Roctavian) (new code effective 1/1/2024)
J3590	Unclassified biologics
J7170	Injection, emicizumab-kxwh (Hemlibra), 0.5 mg

## Related Information

### Benefit Application

Hemlibra (emicizumab-kxwh) and may be managed through pharmacy or medical benefits.  
Hemgenix (etranacogene dezaparvovec-drlb) is managed through the medical benefit.  
Roctavian (valoctocogene roxaparvovec-rvox) is managed through the medical benefit.

### Consideration of Age

The ages stated in this policy for which Hemlibra (emicizumab-kxwh), Hemgenix (etranacogene dezaparvovec-drlb) and Roctavian (valoctocogene roxaparvovec-rvox) is considered medically necessary is based on the FDA labeling for this drug.

## Evidence Review



## Description

Hemlibra (emicizumab-kxwh) is a humanized monoclonal modified immunoglobulin G4 (IgG4) antibody with a bispecific antibody structure binding factor IXa and factor X. Emicizumab-kxwh has an approximate molecular weight of 145.6 kDa and is produced in genetically engineered mammalian (Chinese hamster ovary) cells. Emicizumab-kxwh has no structural relationship or sequence homology to FVIII and, as such, does not induce or enhance the development of direct inhibitors to FVIII.

Hemgenix (etranacogene dezaparvovec-drlb) is an adeno-associated virus (AAV) vector-based gene therapy.

Roctavian (valoctocogene roxaparvovec-rvox) is an adeno-associated virus (AAV) vector-based gene therapy.

## Background

Hemophilia is characterized as genetic mutations leading to deficiency in the factors necessary for coagulation. The most common types of hemophilia are hemophilia A, due to factor VIII deficiency, and hemophilia B, due to factor IX deficiency. The genes causing hemophilia are located on the X chromosome; therefore, most hemophiliacs are male while females are most commonly carriers. The liver produces both factors VIII and IX.

## Summary of Evidence

Hemlibra (emicizumab-kxwh) has been studied in two Phase 3 studies and a Phase 1 study with a trial extension.<sup>1-3</sup> The trials were small and of moderate to fair quality overall. The Phase 1 study was a 12-week, multicenter, open-label, dose escalation trial conducted in Japan. Individuals with severe hemophilia A, with or without inhibitors, and ages 12-59 were eligible for inclusion. Individuals were enrolled into three cohorts with varying doses of emicizumab. No primary endpoint was specified. The study was limited by very small size (n=18), nonrandomized design, and a difference in baseline ABR between cohorts (baseline ABR 15.9-37.9). Additionally, statistical comparisons were not performed. At Week 12, the median ABR decreased by 15.2-28.1 events from baseline across the cohorts. A total of 73% of individuals with inhibitors and 72% of individuals without inhibitors did not have a bleeding event during the trial. A trial extension with 27 months of follow-up in 16 individuals found the range of change in median

ABR from baseline was 15.2-31.1 events; eight individuals did not experience any bleeding during the trial extension.<sup>3</sup>

The HAVEN 1 trial was a 24-week, multicenter, multinational, open-label, randomized, Phase 3 trial in 109 individuals  $\geq 12$  years of age with hemophilia A and high FVIII inhibitor titers treated with BPAs.<sup>2</sup> Individuals receiving episodic BPAs prior to study enrollment were randomized to emicizumab prophylaxis or no prophylaxis (Groups A and B). Individuals receiving prophylactic BPAs prior to enrollment were enrolled in Group C and received emicizumab prophylaxis. Group D received prophylactic emicizumab and consisted of all individuals who did not enroll in the study before the closure of Groups A-C. Six or more bleeding events were required in the past 24 weeks for individuals on episodic BPAs prior to enrollment while  $\geq 2$  events were required for individuals on prophylactic BPAs. This difference may have led to selection bias. Controversy exists over the primary outcome measure for the HAVEN 1 trial. This was defined as the ABR for Groups A and B in [clinicaltrials.gov](https://clinicaltrials.gov) while it was described as the rate of treated bleeding events in the same groups in the published NEJM article. At 24 weeks, the annualized rate of treated bleeding events significantly decreased with prophylactic emicizumab compared to no prophylaxis (episodic BPA treatment) (2.9 vs 23.3 events, 87% decrease,  $p < 0.001$  per NEJM,  $p < 0.0001$  per manufacturer and NEJM supplement). The ABR for all bleeding events significantly decreased with prophylactic emicizumab vs episodic BPA (5.5 vs 28.3 events, 80% decrease,  $p < 0.0001$ ). Overall, 62.9% of individuals in Group A, 5.6% in Group B, and 69.4% in Group C had no bleeding events throughout the trial. Secondary endpoints including treated spontaneous bleeding events (1.3 vs 16.8 events,  $p < 0.0001$ ) and treated joint bleeds (0.8 vs 6.7,  $p = 0.0005$ ) significantly favored emicizumab prophylaxis over episodic BPA.<sup>3</sup> Of individuals in Group C who participated a previous nonintervention study ( $n = 24$ ), interindividual comparisons found bleeding events with prophylactic emicizumab were significantly less than BPA prophylaxis (3.3 vs 15.7 events, 79% decrease,  $p < 0.001$ ).<sup>2</sup> Direct clinical trial evidence comparing emicizumab with prophylactic BPAs is lacking. Additionally, all quality of life (QoL) assessments in the trial overall significantly favored emicizumab prophylaxis compared to no prophylaxis.

Hemgenix (etranacogene dezaparvovec-drlb) has been studied in the HOPE-B (NCT03569891) Phase 3, open-label clinical trial in which 54 individuals prospectively completed a lead-in period of at least 6 months with the intent to receive standard-of-care routine congenital factor IX (FIX) prophylaxis. After completing the lead-in period, participants received a single intravenous dose of Hemgenix, and were followed monthly until Month 12, then at 6-month intervals until Year 5. After a single dose of Hemgenix, increases in FIX activity were observed. For the efficacy evaluation, data up to 18 months post treatment were used. Of the 54 individuals, 53 completed at least 18 months of follow-up in the ongoing study. One individual with numerous cardiovascular and urologic risk factors, who was 75 years of age at screening, died of urosepsis and cardiogenic shock at Month 15 post dose (at 77 years of age); this death was considered to



be unrelated to treatment. Another individual received around 10% of the intended dose due to an infusion-related hypersensitivity reaction. Individuals were allowed to continue prophylaxis during Months 0 to 6. Two individuals were not able to stop routine prophylaxis after Hemgenix treatment. During Months 7 to 18, an additional individual received prophylaxis from Days 396–534 (approximately 20 weeks). Individuals were not excluded from the trial based on pre-existing neutralizing antibodies to adeno-associated virus 5 (AAV5). Some experts believe that, unlike other adeno-associated virus (AAV) vector-based gene therapies, AAV5-based products may be effective in up to 95% of individuals with hemophilia B who also carry antibodies to AAV vectors. Results from the HOPE-B trial demonstrated that Hemgenix allowed individuals to produce mean FIX activity of 39% at 6 months and 36.7% at 24 months post infusion. These factor levels correspond to mild hemophilia. Seven to 18 months post infusion, the mean adjusted annualized bleeding rate (ABR) for all bleeds was reduced by 54% compared to the 6-month lead-in period on FIX prophylactic replacement therapy (from 4.1 to 1.9). Among study participants, 74% had bleeds in the lead-in period and 37% had bleeds 7–18 months after Hemgenix treatment. In addition, 94% (51 out of 54) of individuals discontinued the use of prophylaxis and remained free of previous continuous routine prophylaxis therapy. No inhibitors to FIX were reported.

Roctavian was studied in a prospective, phase-3, open-label, single-dose, single-arm trial where 134 adult males with severe hemophilia A received a single IV dose of  $6 \times 10^{13}$  vg/kg body weight of Roctavian. These individuals were followed for a period of 5 years. The study included individuals who were previously treated with prophylactic factor VIII replacement therapy excluding emicizumab. The inclusion criteria required that individuals do not have detectable, pre-existing antibodies to AAV5 capsid. The exclusion criteria included active infection, chronic or active hepatitis B or C, HIV, current or prior history of factor VIII inhibitors, stage 3 or 4 liver fibrosis, cirrhosis, abnormal liver function test, history of thrombosis or thrombophilia, serum creatinine  $\geq 1.4$  mg/dL, and active malignancy.

The primary efficacy endpoint was a non-inferiority (NI) test of the difference in the annualized bleeding rate in the efficacy evaluation period (EEP) following the mean annualized bleeding rate (ABR) following Roctavian administration compared to the baseline.

The mean EEP ABR was 2.6 bleeds/year compared to the mean baseline ABR of 5.4 bleeds/year, with the mean difference in ABR was -2.8 bleeds/year. The NI analysis met the pre-specified NI margin, indicating the effectiveness of Roctavian. Out of all individuals, a total of 1 individual did not response and 6 individuals lost response to Roctavian treatment over a median time of 3.6 years.

The most common adverse events were nausea, fatigue, infusion related reactions, headache, vomiting and abdominal pain.



## Ongoing and Unpublished Clinical Trials

The HAVEN 2 trial is an ongoing, multicenter, open-label, single-arm, Phase 3 trial which enrolled children 52-week trial.<sup>3</sup> At the time of interim analysis, 20 enrolled individuals had received treatment for >12 weeks. All individuals were treated with emicizumab 3 mg/kg SQ for 4 weeks, then 1.5 mg/kg/week. A primary endpoint was not specified. At the time of interim analysis, the mean ABR was 0.4 for treated bleeds, 3.7 for all bleeds, 0.4 for treated spontaneous bleeds, and zero for joint bleeds. No comparison with baseline ABR was provided. A total of 94.7% of individuals experienced zero treated bleeds and 63.2% had no bleeding events of any type at the time of interim analysis. Additional ongoing trials include HAVEN 3 (R, OL, MC, Phase 3, 24-week trial in 145 individuals with hemophilia A without inhibitors assessing ABR), HAVEN 4 (OL, MC, Phase 3 expansion trial in 46 individuals), and the STASEY trial (2-year, OL, MC, Phase 3b trial in 200 individuals with hemophilia A assessing AEs).<sup>3</sup>

The HAVEN 5 trial is an ongoing randomized, open-label, Phase 3 trial being conducted to compare emicizumab vs no prophylaxis in Asian adults and adolescents with any severity of hemophilia A n=16 (23%) with inhibitors and n=54 (77%) without. Interim results after 24 weeks have been reported but related subgroup results have not.

The HAVEN 6 trial is an ongoing multicenter, open-label, single-arm, Phase 3 trial being conducted to assess the safety, efficacy and PK of emicizumab in individuals with mild or moderate hemophilia A without inhibitors. At interim analysis, 71 individuals had been enrolled, 51 with moderate hemophilia and 20 with mild hemophilia. The overall annualized rate of treated bleeds was 0.8 (95% CI 0.41-1.46) and 80.3% individuals had zero bleeds.

## Safety

For Hemlibra the majority of adverse events (AEs) were described as mild to moderate. Common AEs reported in ≥ 5% of individuals from pooled clinical trials were injection-site reactions (22%), headache (15%), arthralgia (15%), pyrexia (6%), and diarrhea (6%). Serious AEs occurred in 0%-8.7% of individuals. Discontinuations due to AEs occurred in three individuals across all clinical trials. Anti-emicizumab antibodies were detected five individuals in Phase 1 trials and were suspected but not identified in two individuals in the HAVEN 1 trial.

Thromboembolic (TE) events are of concern with emicizumab. The HAVEN 1 trial identified three events of thrombotic microangiopathy (TMA) and two TE events (cavernous sinus thrombosis and skin necrosis/superficial thrombophlebitis), all occurring following activated prothrombin

complex concentrates (aPCC) administration ( $>100$  U/kg/d) for  $>1$  day. No events occurred with emicizumab alone, recombinant FVIIa (rFVIIa) alone, or aPCC x1 day. No anticoagulation was required for the TE events. The TMA events resolved in two individuals and were considered to be resolving in the third at the time of death from rectal hemorrhage following treatment with aPCC for 4 days. Treatment was restarted in one TE and one TMA individual. Overall, the HAVEN 1 authors considered there to be a potential for substantial risk with the combination of aPCC and emicizumab. This is supported by in vitro and animal evidence showing increased thrombin formation with emicizumab plus aPCC and to a lesser degree with rFVIIa.

For Hemgenix, there is no Risk Evaluation and Mitigation Strategy (REMS) program. Providers should monitor liver enzymes for hepatotoxicity, order liver testing to monitor for hepatocellular carcinogenicity, and monitor FIX activity and inhibitors for treatment efficacy. The prescribing information for Hemgenix notes that individuals who intend to receive treatment are encouraged to enroll in a study that evaluates the effect of pre-existing anti-AAV5 neutralizing antibodies on the risk of bleeding.

For Roctavian, there is no Risk Evaluation and Mitigation Strategy (REMS) program. Providers should monitor liver enzymes for hepatotoxicity, factor VIII activity for thromboembolic events, and hepatocellular malignancy for hepatocellular carcinoma.

## Practice Guidelines and Position Statements

The World Federation of Hemophilia (WFH) published updated hemophilia guidelines in 2020. In regard to emicizumab, the guidelines recommend for:

- Individuals receiving emicizumab in whom confirmation of expected emicizumab levels is required, the WFH recommends use of a modified one-stage assay including an additional pre-dilution step of test plasma and assay calibration with specific emicizumab calibrators.
- Determination of FVIII activity in individuals with hemophilia A receiving emicizumab, the WFH recommends use of a chromogenic FVIII assay containing bovine FX.
- Individuals with a suspected neutralizing anti-emicizumab antibody, the WFH recommends measuring emicizumab levels using a modified one-stage assay including an additional pre-dilution step of test plasma and assay calibration with specific emicizumab calibrators.
- Individuals with severe phenotype hemophilia A without inhibitors, prophylaxis with emicizumab will prevent hemarthrosis, spontaneous, and breakthrough bleeding.



- Individuals with moderate/severe hemophilia A or B, especially those who have experienced a life-threatening bleed (e.g., intracranial hemorrhage [ICH]), the WFH recommends prophylaxis with FVIII or FIX concentrates or with a non-factor therapy (e.g., emicizumab for hemophilia A) in order to prevent a recurrent life-threatening bleed. This is particularly important during the first 3-6 months following an ICH as the risk of recurrence is highest during this period.

The guidelines also strongly recommend the use of viral-inactivated plasma-derived or recombinant clotting factor concentrates (CFCs) in preference to cryoprecipitate or fresh frozen plasma. The WFH supports the use of CFCs in preference to cryoprecipitate or FFP due to concerns about quality, safety, and efficacy. However, the WFH recognizes the reality that they are still widely used in countries around the world where they are the only available or affordable treatment options.

## **Medicare National Coverage**

There is no national coverage determination.

## **2019 Update**

A literature search from January 1, 2018, through February 28, 2019, did not identify any new evidence that would change the criteria in this policy.

## **2020 Update**

Reviewed Hemlibra prescribing information and conducted a literature search from March 1, 2019, through February 28, 2020. No new evidence was identified that would change the criteria in this policy.

## **2021 Update**

Reviewed Hemlibra prescribing information and the World Federation of Hemophilia (WFH) Guidelines for the Management of Hemophilia 3rd Edition. Added additional dose frequency for



the maintenance dose of 3 mg/kg once every two weeks and 6 mg/kg once every four weeks to the Dosage and Quantity Limit table. Updated policy with new guidelines and position statements from the WFH specific to Hemlibra.

## 2022 Update

Reviewed Hemlibra prescribing information and conducted a literature search from March 1, 2020 through October 13, 2022. Added information regarding HAVEN 5 and HAVEN 6 to the Ongoing and Unpublished Clinical Trials. No new evidence was identified that would change the criteria in this policy.

## 2023 Update

Reviewed Hemlibra prescribing information and conducted a literature search. No new evidence was identified that would change the criteria in this policy. Added criteria for Hemgenix to this policy. Updated Hemgenix criteria to state that individual meets one of the following: Current or historical life-threatening hemorrhage OR Repeated, serious spontaneous bleeding episodes OR Individual is currently receiving FIX prophylaxis. Removed separate bullet point "Individual is currently receiving FIX prophylaxis". These changes are based on the FDA approval for Hemgenix and P&T committee in February 2023. Added coverage criteria for Roctavian for the treatment of adults with severe hemophilia A without pre-existing antibodies to adeno-associated virus serotype 5.

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## History

Date	Comments
02/01/18	New policy, approved January 16, 2018. Add to Prescription Drug section. Considered medically necessary for pediatric and adults with hemophilia A (congenital factor VIII deficiency) when criteria are met.
04/01/18	Interim Review, approved March 20, 2018. Clarified criteria language for Hemlibra, addition of definition of high dose aPCC and added history of anti-FVIII titer. Also added benefit application information.
11/01/18	Interim Review, approved October 9, 2018. Updated per expanded indication approved by FDA 10/3/18 for hemophilia A with or without Anti-Factor VIII.
11/17/18	Coding update, added HCPCS code Q9995 to policy (effective 7/1/18), removed HCPCS code J3490.
01/01/19	Coding update, added new HCPCS code J7170 (new code effective 1/1/19), replacing Q9995.
04/01/19	Annual Review, approved March 19, 2019. Literature search from 1/1/18, No changes.
01/01/20	Coding update, removed HCPCS code Q9995 as it was terminated 1/1/19.
04/01/20	Annual Review, approved March 19, 2020. Reviewed prescribing information and conducted literature search from March 1, 2019, to February 28, 2020. No changes to coverage criteria.
11/01/21	Annual Review, approved October 5, 2021. Added additional dose frequency for the maintenance dose of 3 mg/kg once every two weeks and 6 mg/kg once every four weeks to the Dosage and Quantity Limit table.
12/01/22	Annual Review, approved November 7, 2022. Reviewed prescribing information and conducted literature search from March 1, 2020, to October 13, 2022. No changes to coverage criteria. Changed the wording from "patient" to "individual" throughout the policy for standardization.
05/01/23	Annual Review, approved April 11, 2023. Changed title of medical policy from Hemlibra (emicizumab-kxwh) to Pharmacologic Treatment of Hemophilia. Reviewed



Date	Comments
	Hemlibra prescribing information and conducted a literature search. No new evidence was identified that would change the criteria in this policy. Added criteria for Hemgenix to this policy. Added HCPC code J3590 to report Hemgenix.
06/30/23	Minor correction in the policy introduction. Corrected "Hemlibra is a gene therapy that can be used to prevent, or reduce the number of bleeding episodes in adults with hemophilia B" to Hemgenix is a gene therapy that can be used to prevent or reduce the number of bleeding episodes in adults with hemophilia B".
09/01/23	Interim Review, approved August 8, 2023. Updated Hemgenix criteria to state that individual meets one of the following: Current or historical life-threatening hemorrhage OR Repeated, serious spontaneous bleeding episodes OR Individual is currently receiving FIX prophylaxis. Removed separate bullet point "Individual is currently receiving FIX prophylaxis". These changes are based on the FDA approval for Hemgenix and P&T committee in February 2023.
10/01/23	Interim Review, approved September 12, 2023. Added coverage criteria for Roctavian for the treatment of adults with severe hemophilia A without pre-existing antibodies to adeno-associated virus serotype 5. Added Roctavian to HCPCS code J3590, and added HCPCS code J1411 for Hegenix.
12/01/23	Interim Review, approved November 14, 2023, effective for dates of service on or after March 7, 2024, following 90-day provider notification. Updated coverage criteria for Hemgenix to require that FIX prophylaxis will be discontinued following administration of Hemgenix and that a hepatologist has assessed the individual if the individual has radiological liver abnormalities or sustained liver enzyme elevations. Updated the coverage criteria for Roctavian to require that FVIII prophylaxis will be discontinued following administration of Roctavian and that documentation is provided demonstrating that the individual received education relating to alcohol abstinence and the use of concomitant medications.
01/01/24	Coding update. Added new HCPCS code J1412.

**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2024 Premera All Rights Reserved.

**Scope:** Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.





## Discrimination is Against the Law

Premera Blue Cross HMO (Premera HMO) complies with applicable Federal and Washington state civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, sex, gender identity, or sexual orientation. Premera HMO does not exclude people or treat them differently because of race, color, national origin, age, disability, sex, gender identity, or sexual orientation. Premera HMO provides free aids and services to people with disabilities to communicate effectively with us, such as qualified sign language interpreters and written information in other formats (large print, audio, accessible electronic formats, other formats). Premera HMO provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, contact the Civil Rights Coordinator. If you believe that Premera HMO has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, sex, gender identity, or sexual orientation, you can file a grievance with: Civil Rights Coordinator — Complaints and Appeals, PO Box 91102, Seattle, WA 98111, Toll free: 855-332-4535, Fax: 425-918-5592, TTY: 711, Email [AppealsDepartmentInquiries@Premera.com](mailto:AppealsDepartmentInquiries@Premera.com). You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Ave SW, Room 509F, HHH Building, Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD). Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>. You can also file a civil rights complaint with the Washington State Office of the Insurance Commissioner, electronically through the Office of the Insurance Commissioner Complaint Portal available at <https://www.insurance.wa.gov/file-complaint-or-check-your-complaint-status>, or by phone at 800-562-6900, 360-586-0241 (TDD). Complaint forms are available at <https://fortress.wa.gov/oic/online-services/cc/pub/complaintinformation.aspx>.

## Language Assistance

**ATENCIÓN:** si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 844-722-4661 (TTY: 711).

**注意:** 如果您使用繁體中文，您可以免費獲得語言援助服務。請致電 844-722-4661 (TTY: 711)。

**CHÚ Ý:** Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 844-722-4661 (TTY: 711).

**주의:** 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 844-722-4661 (TTY: 711) 번으로 전화해 주십시오.

**ВНИМАНИЕ:** Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 844-722-4661 (телетайп: 711).

**PAUNAWA:** Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 844-722-4661 (TTY: 711).

**УВАГА!** Якщо ви розмовляєте українською мовою, ви можете звернутися до безкоштовної служби мовної підтримки.

Телефонуйте за номером 844-722-4661 (телетайп: 711).

**ប្រយ័ត្ន:** បើសិនជាអ្នកនិយាយ ភាសាខ្មែរ, សេវាជំនួយផ្នែកភាសា ដោយមិនគិតថ្លៃ គឺអាចមានសំរាប់អ្នក។ ចូរ ទូរស័ព្ទ 844-722-4661 (TTY: 711)។

**注意事項:** 日本語を話される場合、無料の言語支援をご利用いただけます。844-722-4661 (TTY: 711) まで、お電話にてご連絡ください。

**ማስታወሻ:** የሚናገሩት ቋንቋ ኣማርኛ ከሆነ የትርጉም ኣርዳታ ድርጅቶች፣ በኣኦ.ሊያግዝዎት ተዘጋጅተዋል። ወደ ሚከተለው ቁጥር ይደውሉ 844-722-4661 (መስማት ለተሳናቸው: 711)።

**XIYYEEFFANNAA:** Afaan dubbattu Oroomiffa, tajaajila gargaarsa afaanii, kanfaltiidhaan ala, ni argama. Bilbilaa 844-722-4661 (TTY: 711).

**ملحوظة:** إذا كنت تتحدث اذكر اللغة، فإن خدمات المساعدة اللغوية تتوافر لك بالمجان. اتصل برقم 844-722-4661 (رقم هاتف الصم والبكم: 711).

**ਧਿਆਨ ਦਿਓ:** ਜੇ ਤੁਸੀਂ ਪੰਜਾਬੀ ਬੋਲਦੇ ਹੋ, ਤਾਂ ਭਾਸ਼ਾ ਵਿੱਚ ਸਹਾਇਤਾ ਸੇਵਾ ਤੁਹਾਡੇ ਲਈ ਮੁਫਤ ਉਪਲਬਧ ਹੈ। 844-722-4661 (TTY: 711) 'ਤੇ ਕਾਲ ਕਰੋ।

**ACHTUNG:** Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 844-722-4661 (TTY: 711).

**ໂປດຊາບ:** ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ, ໂດຍບໍ່ຄ່າ, ຄ່າມີພ້ອມໃຫ້ທ່ານ. ໂທ 844-722-4661 (TTY: 711).

**ATANSYON:** Si w pale Kreyòl Ayisyen, gen sèvis èd pou lang ki disponib gratis pou ou. Rele 844-722-4661 (TTY: 711).

**ATTENTION:** Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 844-722-4661 (ATS: 711).

**UWAGA:** Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer 844-722-4661 (TTY: 711).

**ATENÇÃO:** Se fala português, encontram-se disponíveis serviços linguísticos, grátis. Ligue para 844-722-4661 (TTY: 711).

**ATTENZIONE:** In caso la lingua parlata sia l'italiano, sono disponibili servizi di assistenza linguistica gratuiti. Chiamare il numero 844-722-4661 (TTY: 711).

**توجہ:** اگر بہ زبان فارسی گفتگو می کنید، تسهیلات زبانی بصورت رایگان برای شما فراهم می باشد. با 844-722-4661 (TTY: 711) تماس بگیرید.