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GAVIN NEWSOM  
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**TO:** All County California Children's Services Program Administrators, Medical Consultants, Integrated Systems of Care Division Staff, Genetically Handicapped Persons Program Staff

**SUBJECT:** Authorization of Restricted Treatment Drugs for Bleeding Disorders

## I. PURPOSE

The purpose of this Numbered Letter (N.L.) is to establish California Children's Services (CCS) Program and Genetically Handicapped Persons Program (GHPP) policy regarding the authorization of restricted treatment products/drugs for the following specific congenital or acquired bleeding disorders and acquired inhibitor antibodies:

- Hemophilia A (Factor VIII deficiency) with and without inhibitors
- Hemophilia B (Factor IX deficiency) with and without inhibitors
- Von Willebrand Disease (VWD) with and without inhibitors
- Factor VII deficiency
- Acquired Factor XIII deficiency
- Factor X deficiency

## II. BACKGROUND

Hemophilia is a genetic disorder in which the body fails to produce proteins required for blood clotting. Depending on the severity, this can lead to excessive or prolonged bleeding episodes. Bleeding can occur spontaneously, after injury, or due to a medical procedure.

The clotting mechanism, often called the clotting cascade, involves the interaction of a series of proteins, leading to formation of a fibrin clot to plug a bleed. The clotting

cascade involves amplification via activation of clotting factors. Any decrease or absence of any of the clotting factors may disrupt the clotting process and increase bleeding time. In severe cases, spontaneous bleeding into joints and muscles may occur. These bleeds will cause pain, chronic swelling, deformity, reduced mobility, and long-term joint damage, and some bleeds are lethal.

Hemophilia A is the most well-known of the congenital bleeding disorders. Hemophilia A patients lack or have insufficient amounts of Factor VIII, a specific clotting factor. Hemophilia A mainly affects males, infrequently females.

Hemophilia B, also known as Christmas disease, is less common but causes similar bleeding as hemophilia A. Patients with hemophilia B lack or have insufficient amounts of Factor IX, another specific clotting factor. Hemophilia B mainly affects males, infrequently females.

Von Willebrand disease (VWD) can be inherited or acquired and is caused by a deficiency in von Willebrand factor (VWF). This factor is necessary to help platelets bind to the site of injury to form a clot. VWF also binds Factor VIII, extending Factor VIII's half-life circulating in the blood. VWD can occur in both males and females.

Factor VII, X, and XIII deficiencies are less common bleeding disorders caused by a deficiency in the named clotting factor. Factor VII initiates the clotting sequence when it binds to Tissue Factor upon exposure to circulating blood, upon blood vessel injury. Factor X aids in the formation of thrombin from prothrombin, in the clotting cascade. Factor XIII helps to stabilize a fibrin clot.

Current treatment of hemophilia A, hemophilia B, and VWD involves replacement of factor VIII, IX, or VWF, respectively, by intravenous infusion. A complication of this treatment is the development of inhibitors to factor VIII, IX, or VWF replacement therapies. Inhibitors are antibodies produced by the body's immune system that binds to factor VIII, IX or VWF, rendering them ineffective. Around 15 to 20 percent of individuals with hemophilia develop inhibitors.<sup>1</sup> To counteract inhibitors, higher concentrations or more frequent dosing of factor VIII, IX, or VWF therapies are often required, but this often leads to increasing inhibitor concentrations, necessitating ever-increasing factor dosing. This makes it difficult for such patients to obtain sufficient levels of factor to control bleeding. Individuals with inhibitors are therefore treated with factor VIII inhibitor-bypassing activity (FEIBA), an activated prothrombin complex concentrate (aPCC) and/or recombinant factor VIIa (NovoSeven). Dosage of bypassing agents increases over time as inhibitor concentration increases.

Hemlibra (emicizumab-kxwh), a new bispecific factor IXa and factor X-directed antibody treatment was initially approved by the Food and Drug Administration (FDA) on November 16, 2017, and expanded their approval on October 4, 2018. This is a new treatment modality for hemophilia A. It is not a factor replacement

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<sup>1</sup> <https://www.cdc.gov/ncbddd/hemophilia/facts.html>

therapy, but it is a first in class monoclonal antibody, which binds to and bridges activated factor IX and factor X, bypassing factor VIII in the body-clotting cascade.

Emicizumab-kxwh was initially indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients with hemophilia A with factor VIII inhibitors. FDA's expanded approval includes patients of all ages with hemophilia A who do not have inhibitors.<sup>2,3</sup> Reported adverse events related to emicizumab\* use include thrombotic microangiopathy, thrombophlebitis, and cavernous sinus thrombosis.<sup>4</sup> Prophylactic use of bypassing agents must be discontinued the day before starting emicizumab prophylaxis. Loading doses of the drug are given weekly for four weeks, followed by maintenance doses weekly, every two weeks, or every four weeks.

### III. POLICY

#### A. Factor Replacement Treatment:

Treatment of hemophilia factor deficiencies, acquired inhibitors, and VWD are a benefit for CCS Program/GHPP clients when the following criteria are met:

1. Client meets program eligibility.
2. Diagnosis of hemophilia A, B, and VWD, any factor deficiency, or documented development of factor inhibitors.
3. Client is under the care of a federally approved Hemophilia Treatment Center (HTC) or a CCS approved Hemophilia Special Care Center (SCC).

#### B. Emicizumab Treatment:

1. Client meets program eligibility.
2. Client must have congenital hemophilia A with or without Factor VIII inhibitors and currently be prescribed clotting factor or bypassing agents on either prophylaxis or episodic regimens, or be deemed eligible for prophylaxis based on disease severity or bleeding history.

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<sup>2</sup> <https://www.hemophilia.org/Newsroom/Medical-News/Hemlibra-Receives-Expanded-FDA-Approval-for-Hemophilia-A-Patients-Without-Inhibitors>

<sup>3</sup> On November 21, 2018, The Medical and Scientific Advisory Council of the National Hemophilia Foundation released RECOMMENDATION ON THE USE AND MANAGEMENT OF EMICIZUMABKXWH (HEMLIBRA®) FOR HEMOPHILIA A WITH AND WITHOUT INHIBITORS.

<https://www.hemophilia.org/sites/default/files/document/files/255Emicizumab.pdf>

<sup>4</sup> N Engl J Med 2017; 377:809-818 DOI: 01.1056/NEJMoa1703068

\* FDA guidelines require biologic and biosimilar products contain a four-letter suffix following the active component of the product. This four-letter FDA assigned suffix has no clinical significance and is to differentiate between competing biologic and biosimilar products. The active component name, without the four-digit suffix, will designate intent to address the active drug, not a specific brand or product.

3. Client is under the care of a federally approved Hemophilia Treatment Center (HTC) or a CCS approved Hemophilia Special Care Center (SCC).
4. Prophylactic use of clotting factor should be discontinued after the first week of emicizumab prophylaxis. Prophylactic use of bypassing agents should be discontinued before starting emicizumab prophylaxis.
5. Use of on-demand clotting factor and bypassing agents, such as Recombinant Factor VIIa (NovoSeven), or Factor VIII Inhibitor Bypassing Activity (FEIBA) should follow guidance of prescribing hematologist. Patients may receive Factor VIII with emicizumab for Immune Tolerance Induction (ITI).

If the criteria described above are not met, but the requesting provider has clinical documentation and/or scientific evidence that may be relevant to the request, the provider may submit this additional documentation to the Integrated Systems of Care Division (ISCD) Medical Director or designee for consideration during the eligibility determination.

#### **IV. POLICY IMPLEMENTATION**

##### **A. Factor Replacement Treatment:**

1. Hemophilia factor replacement products are not covered by a Service Code Grouping authorization and a separate authorization is needed.
2. Requesting CCS Program/GHPP providers must submit the following items to their Independent CCS program county office, Special Populations Authorization Unit, or GHPP:
  - a. CCS Program/GHPP Service Authorization Request (SAR).
  - b. Copy of prescription.
  - c. If requesting replacement of (as needed) factor, the client's bleed log or confirmation of bleeding from the client's HTC.
3. Authorization of factor products for regular factor replacement prophylaxis is limited to a one-month supply.
4. Authorization is limited to dispensing total factor within ten percent of prescribed monthly dose (+/- 10 percent).
5. Authorization of factor replacement for (as needed) use is limited to the initial prescribed supply and then only replacement of amounts used, as documented by client's bleed log or confirmation from the client's HTC.

6. For non-Whole Child Model (WCM) independent counties, requests for initial and continuing treatment will be reviewed and authorized by county CCS Programs.
7. For dependent counties, requests for initial and continuing treatment will be reviewed and authorized by the Integrated Systems of Care Division (ISCD) Special Populations Unit at [CCS\\_Operations@dhcs.ca.gov](mailto:CCS_Operations@dhcs.ca.gov), or to secure RightFax number, (916) 440-5768.
8. For WCM counties, requests for initial and continuing treatment will be reviewed and authorized by the Integrated Systems of Care Division (ISCD) Special Populations Unit at [CCS\\_Operations@dhcs.ca.gov](mailto:CCS_Operations@dhcs.ca.gov), or to secure RightFax number, (916) 440-5768.
9. Non-pharmacy providers must bill with Healthcare Common Procedure Coding System (HCPCS) codes. Acceptable hemophilia factor replacement codes to use may be found in the Blood and Blood Derivatives section of the Medi-Cal provider manual.<sup>5</sup>
10. Pharmacy providers must bill by National Drug Code.

The Medi-Cal Program (including CCS/GHPP) has contracted with specific providers to supply factor replacement treatment for home use. All requests should be directed to these contracted providers. The list of providers can be found on the Department of Health Care Services (DHCS) website.<sup>6</sup>

Select factor replacement products are carved out of Diagnosis Related Group (DRG) inpatient reimbursement. Review CCS Information Notice # 13-06 for more information. Additional information can be found at the DHCS DRG website<sup>7</sup> and the DRG frequently asked questions document.<sup>8</sup>

#### B. Efficizumab Treatment:

1. Efficizumab is not covered by a Service Code Grouping authorization and a separate authorization is needed.

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<sup>5</sup> Blood and Blood Derivatives Section of the Medi-Cal provider manual:  
[http://files.medi-cal.ca.gov/pubsdoco/publications/masters-mtp/part2/blood\\_m01o03o04p00.doc](http://files.medi-cal.ca.gov/pubsdoco/publications/masters-mtp/part2/blood_m01o03o04p00.doc)

<sup>6</sup> Medi-Cal Contracted Specialty Pharmacy Locations for Blood Factors  
<https://www.dhcs.ca.gov/provgovpart/pharmacy/Pages/BloodFactors.aspx>

<sup>7</sup> Diagnosis Related Group Hospital Inpatient Payment Methodology  
<https://www.dhcs.ca.gov/provgovpart/pages/DRG.aspx>

<sup>8</sup> Medi-Cal Diagnosis Related Group Payment Method Frequently Asked Questions For State Fiscal Year 2018-19  
[https://www.dhcs.ca.gov/provgovpart/Documents/DRG/SFY18-19Medi-Cal\\_DRG\\_FAQ.pdf](https://www.dhcs.ca.gov/provgovpart/Documents/DRG/SFY18-19Medi-Cal_DRG_FAQ.pdf)

2. Requesting CCS Program/GHPP providers must submit the following items to their Independent CCS program county office, Special Populations Authorization Unit, or GHPP:
  - a. CCS Program/GHPP Service Authorization Request (SAR).
  - b. Copy of prescription.
3. For non-Whole Child Model (WCM) independent counties, requests for initial and continuing emicizumab treatment will be reviewed and authorized by county CCS Programs.
4. For dependent counties, requests for initial and continuing emicizumab treatment will be reviewed and authorized by the Integrated Systems of Care Division (ISCD) Special Populations Unit at [CCS\\_Operations@dhcs.ca.gov](mailto:CCS_Operations@dhcs.ca.gov), or to secure RightFax number, (916) 440-5768.
5. For WCM counties, requests for initial and continuing emicizumab treatment will be reviewed and authorized by the Integrated Systems of Care Division (ISCD) Special Populations Unit at [CCS\\_Operations@dhcs.ca.gov](mailto:CCS_Operations@dhcs.ca.gov), or to secure RightFax number, (916) 440-5768.
6. Non-pharmacy providers must bill with HCPCS code:
  - a. J7170, injection, emicizumab, 0.5 mg, for dates of service beginning January 1, 2019.
7. Pharmacy providers must bill by National Drug Code.
8. Emicizumab is not carved out of DRG reimbursement.

Please send any questions about the content of this letter to the ISCD Medical Director or designee at ISCD.

Sincerely,

**ORIGINAL SIGNED BY**

Roy Schutzengel  
Medical Director  
Integrated Systems of Care Division