State of California—Health and Human Services Agency
Department of Health Care Services

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DATE: October 12, 2020

N.L.: 05-1020
Supersedes N.L.: 37-1292
Index: Authorizations/Benefits

TO: All County California Children's Services Program and Genetically Handicapped Persons Program Staff, Medical Consultants, Statewide Consultants, and Integrated Systems of Care Division Staff

SUBJECT: California Children's Services Program and Genetically Handicapped Persons Program Policy on Coverage of Experimental and Investigational Services

I. PURPOSE

This Numbered Letter (N.L.) updates policy on the coverage of experimental and investigational drugs, biological products, and devices under the California Children's Services (CCS) Program and the Genetically Handicapped Persons Program (GHPP).

The CCS Program publishes this N.L. under the program's authority to authorize services that are medically necessary to treat CCS-eligible conditions.[1,2,3]

II. BACKGROUND

In general, the U.S. Food and Drug Administration (FDA) must approve a new drug for general use.[4] Prior to approving a new drug for general use, the FDA may authorize its use in a clinical investigation. A clinical investigation is an experiment in which a drug is administered to one or more human subjects and consists of three phases.[5,6] A new drug under a clinical investigation is an "investigational drug."

The FDA may also authorize the use of an investigational drug to treat exceptionally ill patients under limited circumstances.[7,8] Additionally, federal law authorizes the use of investigational drugs outside of the FDA-approval process in other limited circumstances.[9]

The State of California's Right to Try Act also authorizes the use of investigational services outside of the FDA-approval process under limited circumstances.[10] Moreover, the State of California's Right to Try Act also authorizes a health care plan to cover investigational services.[10]

For the purposes of this document, the following terms are defined as follows:

A. Investigational service:

A drug, biological product, or device that has successfully completed phase one of a clinical investigation approved by the FDA, but that has not been approved for general use by the FDA and remains under investigation in an FDA approved clinical investigation.

B. Experimental services:

Drugs, equipment, procedures or services that are in a testing phase undergoing laboratory and/or animal studies prior to testing in humans. Experimental services are not undergoing a clinical investigation.[5]

III. POLICY

A. The CCS Program and GHPP will not provide coverage for experimental services unless specifically authorized by law.

B. The CCS Program and GHPP may provide coverage for an investigational service if:

1. It is approved by the FDA under any Investigational New Drug (IND) Application; or

2. It is authorized for use under the State of California's Right to Try Act; and

3. Its use is consistent with its FDA-approved IND Application or the State of California's Right to Try Act;

C. Additional criteria that will be considered in the adjudication process include:

1. Conventional therapy will not adequately treat the intended patient's condition;

2. Conventional therapy will not prevent progressive disability or premature death;

3. The provider of the proposed service has a record of safety and success with it or equivalent to that of other providers of the investigational services;

4. Other criteria (e.g., cost and availability) may be considered in the adjudication of a given request in cases in which more than one investigational service is available;

5. There is reasonable expectation that the investigational service will significantly prolong the patient's life or will maintain or restore a range of physical and social function suited to activities of daily living; and

6. The service is not being performed as part of a research study protocol. For a beneficiary with cancer who participates in a clinical trial for cancer, California Health and Safety Code (HSC) § 1370.6 requires that all routine patient care costs related to the clinical trial be covered if the beneficiary's CCS-paneled treating physician recommends participation in the clinical trial after determining that participation in the clinical trial has a meaningful potential to benefit the enrollee. The coverage does not include investigational services that have not been approved by the FDA and that are associated with the clinical trial.

D. The CCS Program and GHPP will authorize inpatient care associated with the administration of the investigational service only in situations in which the patient's underlying clinical status requires the medical necessity of acute hospital care.

E. Whole Child Model (WCM) Counties

For CCS clients who are enrolled in a Medi-Cal managed care plan (MCP) and reside in a WCM county, the client's MCP shall be responsible for authorizing, coordinating, and covering experimental and investigational services. MCPs operating in WCM counties should use the authorization guidelines described in this N.L., or utilize the MCP's existing experimental and investigational services policies, whichever is less restrictive.

IV. POLICY IMPLEMENTATION

A. Experimental and investigational services are not included in Service Code Grouping authorizations.[11] Providers should submit a separate Service Authorization Request (SAR) and all supporting documentation in the following manner:

1. For clients residing in a county covered by the WCM, SARs for investigational services shall be submitted to, and processed by, the MCP.

2. For clients residing in all other counties, SARs for investigational services should be submitted to the California Children's Services Network (CMS Net) for initial review. After confirming that all required supporting documents are present, county CCS personnel will notify ISCD via email at

ISCD-MedicalPolicy@dhcs.ca.gov or to secure RightFax number,

(916) 440-5768.

B. The SAR shall include the following information:

1. Documentation of each criterion listed in section III.B and III.C.

2. A complete description of the investigational service being requested:

   a. Name of service.

   b. Phase of clinical testing.

   c. Manufacturer name, contact information, and approval of product use in this beneficiary.

   d. Specific administration parameters, e.g., dosing and duration.

   e. IND letter from the FDA for individuals who have received an FDA-approved IND Application.

3. Name of CCS-paneled sub-specialist physician who will administer the investigational service.

4. Name of CCS-approved Special Care Center or facility at which administration of the investigational service will occur.

If you have any questions regarding this N.L., please contact the ISCD Medical Director or designee at ISCD-MedicalPolicy@dhcs.ca.gov.

Sincerely,

ORIGINAL SIGNED BY

Roy Schutzengel
Medical Director
Integrated Systems of Care Division

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[1] 22 Cal. Code Regs. § 41515.1 et. seq. Determination of Medical Eligibility
https://govt.westlaw.com/calregs/Document/I28E30090D4B811DE8879F88E8B0DAAAE?viewType=FullText&originationContext=documenttoc&transitionType=CategoryPageItem&contextData=%28sc.Default%29

[2] 22 Cal. Code Regs. § 41700 Availability
https://govt.westlaw.com/calregs/Document/I2F1A7E70D4B811DE8879F88E8B0DAAAE?viewType=FullText&originationContext=documenttoc&transitionType=CategoryPageItem&contextData=(sc.Default)&bhcp=1&ignorebhwarn=IgnoreWarns

[3] 22 Cal. Code Regs. § 41740 Eligibility for Treatment Services
https://govt.westlaw.com/calregs/Document/I2FDD8050D4B811DE8879F88E8B0DAAAE?viewType=FullText&origina

tionContext=documenttoc&transitionType=StatuteNavigator&contextData=%28sc.Default%29
[4] 21 U.S.C. § 355 New Drug
https://www.law.cornell.edu/uscode/text/21/355
[5] 21 C.F.R. § 312.3(b) Drugs for Human Use
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.3
[6] 21 C.F.R. § 312.21 Drugs for Human Use
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.21
[7] 21 C.F.R. § 312.23
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.23
[8] 21 C.F.R. § 312.310
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.310
[9] 21 U.S.C. § 360bbb-oa(b).
https://www.law.cornell.edu/uscode/text/21/360bbb
[10] Health & Safety Code § 111548.2
https://leginfo.legislature.ca.gov/faces/codes_displayText.xhtml?lawCode=HSC&division=104.&title=&part=5.&chapter=6.&article=4.5.
[11] Service Authorization Request Tools
https://www.dhcs.ca.gov/services/ccs/cmsnet/Pages/SARTools.aspx#service

State of California—Health and Human Services Agency
Department of Health Care Services

WILL LIGHTBOURNE
DIRECTOR

GAVIN NEWSOM
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DATE: November 17, 2020

N.L.: 07-1120
Supersedes N.L.: 01-0819
Index: Benefits

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 - Revised

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

The CCS Program publishes this N.L. under the program's authority to authorize services that are medically necessary to treat CCS-eligible conditions.[1,2,3]

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.[4] 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 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.[5,6] Reported adverse events related to emicizumab* use include thrombotic microangiopathy, thrombophlebitis, and cavernous sinus thrombosis.[7] 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 maintenances 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.

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).

C. Additional considerations for medical necessity determination:

For clients who do not meet the criteria described in sections III.A. or III.B., SCCs may demonstrate medical necessity by submitting any other clinical documentation and/or evidence that would support the initial or reauthorization of the client's Factor replacement or Emicizumab treatment. SCCs or pharmacies should submit this documentation to the Integrated Systems of Care Division (ISCD) Medical Director or designee.

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 ISCD Special Populations Unit at CCSExpeditedReview@dhcs.ca.gov; or to secure RightFax number, (916) 440-5306.

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 CCSExpeditedReview@dhcs.ca.gov; or to secure RightFax number, (916) 440-5306.

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.[8]

10. Pharmacy providers must bill by National Drug Code (NDC).

The Medi-Cal Program (including CCS/GHPP) has contracted with specific providers to supply factor replacement treatment for home use. All requests should directed to these contracted providers. The list of providers can be found on the Department of Health Care Services (DHCS) website.[9]

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[10] and the DRG frequently asked questions document.[11]

B. Emicizumab Treatment:

1. Emicizumab is 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.

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 CCSExpeditedReview@dhcs.ca.gov; or to secure RightFax number, (916) 440-5306.

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 CCSExpeditedReview@dhcs.ca.gov; or to secure RightFax number, (916) 440-5306.

6. Non-pharmacy providers must bill with HCPCS code:

   J7170, injection, emicizumab, 0.5 mg, for dates of service beginning January 1, 2019.

7. Pharmacy providers must bill by NDC.

8. Emicizumab is not carved out of DRG reimbursement.

Beginning April 1, 2021, all requests for prior authorization of medications billed by NDC and dispensed by a Medi-Cal enrolled pharmacy provider, shall be sent from the pharmacy provider to the Medi-Cal Rx vendor, Magellan Medicaid Administration, Inc. (Magellan). The Medi-Cal RX website provides guidance: https://medi-calrx.dhcs.ca.gov/home/.

If you have any questions regarding this N.L., please contact the ISCD Medical Director or designee at ISCD-MedicalPolicy@dhcs.ca.gov.

Sincerely,

ORIGINAL SIGNED BY

Roy Schutzengel
Medical Director
Integrated Systems of Care Division

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[1] 22 Cal. Code Regs. § 41515.1 et. seq. Determination of Medical Eligibility
https://govt.westlaw.com/calregs/Document/I28E30090D4B811DE8879F88E8B0DAAAE?viewType=FullText&originationContext=documenttoc&transitionType=CategoryPageItem&contextData=%28sc.Default%29
[2] 22 Cal. Code Regs. § 41700 Availability
https://govt.westlaw.com/calregs/Document/I2F1A7E70D4B811DE8879F88E8B0DAAAE?viewType=FullText&originationContext=documenttoc&transitionType=CategoryPageItem&contextData=(sc.Default)&bhcp=1&ignorebhwarn=IgnoreWarns
[3] 22 Cal. Code Regs. § 41740 Eligibility for Treatment Services
https://govt.westlaw.com/calregs/Document/I2FDD8050D4B811DE8879F88E8B0DAAAE?viewType=FullText&originationContext=documenttoc&transitionType=StatuteNavigator&contextData=%28sc.Default%29
[4] Hemophilia Facts

https://www.cdc.gov/ncbddd/hemophilia/facts.html
[5] FDA Approval
https://www.hemophilia.org/Newsroom/Medical-News/Hemlibra-Receives-Expanded-FDA-Approval-for-Hemophilia-A-Patients-Without-Inhibitors
[6] 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
[7] N Engl J Med 2017; 377:809 818 DOI: 01.1056/NEJMoa1703068
* FDA guidelines require biologic and biosimiliar 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 biosimiliar products. The active component name, without the four-digit suffix, will designate intent to address the active drug, not a specific brand or product.
[8] 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
[9] Medi-Cal Contracted Specialty Pharmacy Loctions for Blood Factors
https://www.dhcs.ca.gov/provgovpart/pharmacy/Pages/BloodFactors.aspx
[10] Diagnosis Related Group Hospital Inpatient Payment Methodology
https://www.dhcs.ca.gov/provgovpart/pages/DRG.aspx
[11] 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