July 8, 2024

Jason Bennett
Director
Technology, Coding and Pricing Group
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Via Email: **jason.bennett@cms.hhs.gov**

RE: Request to establish a new HCPCS Level II code to identify Red Blood Cells, Leukocytes Reduced, Oxygen/Carbon Dioxide Reduced, Each Unit (RBCs, LR, O2/CO2 Reduced, Each Unit) (HCP231002Y5WRL)

Dear Mr. Bennett:

The Association for the Advancement of Blood & Biotherapies (AABB), America's Blood Centers (ABC) and the American Red Cross (ARC) appreciate the opportunity to submit comments in response to the Centers for Medicare & Medicaid Services' (CMS) Healthcare Common Procedure Coding System (HCPCS) Level II Code Public Meeting held on May 30, 2024. Collectively, our organizations represent the nation's blood collection establishments, transfusion services, and transfusion medicine professionals.

Our comments focus on CMS' preliminary HCPCS coding recommendation related to the establishment of a new HCPCS Level II code that identifies Red Blood Cells, Leukocytes Reduced, Oxygen/Carbon Dioxide Reduced (RBCs, LR, O2/CO2 Reduced) (request #4, HCP231002Y5WRL). We ask that your Division of Coding and Diagnosis Related Groups (DCDRG) revisit the submitted application for this product and approve the request for a new HCPCS Level II code.

RBCs, LR, O2/CO2 Reduced is a novel blood product where leukocyte reduced red blood cells are processed by the Hemanext ONE system to store and reduce the oxygen and carbon dioxide levels. Research shows that for certain populations, RBCs, LR, O2/CO2 Reduced can improve post-transfusion recovery, improve oxygen delivery for transfusion dependent patients, and potentially reduce health care costs by decreasing the number of transfusions a patient may need.[1,2,3,4,5] These important advantages of

[1] Reikvam, H., Hetland, G., Ezligini, F., et al. Safety of hypoxic red blood cell administration in patients with transfusion-dependent hematological malignancies: An interim analysis. *Transfusion and Apheresis Science* 2023 Oct;62(5):103755.
[2] Karafin MS, Field JJ, Ilich A, et al. Hypoxic storage of donor red cells preserves deformability after exposure to plasma from adults with sickle cell disease. *Transfusion* 2022 Jan;63(1):193-202.
[3] D'Alessandro A, Yoshida T, Nestheide S, et al. Hypoxic storage of red blood cells improves metabolism and post-transfusion recovery. *Transfusion* 2020 Apr;60:786-798.
[4] Williams AT, Jani VP, Nemkov T, et al. Transfusion of anaerobically or conventionally stored blood after hemorrhagic shock. *Shock* 2020 Mar;53(3):352-362.
[5] Burns JM, Yoshida T, Dumont LJ, et al. Deterioration of red blood cell mechanical properties is reduced in anaerobic storage. *Blood Transfus* 2016 Jan;14(1):80-88.

RBCs, LR, O2/CO2 Reduced in relation to any existing RBC product in the HCPCS code set were well articulated by the 15-minute and 5-minute speakers at the May 30, 2024 public meeting hosted by CMS. Additionally, in patients requiring chronic RBC transfusions (e.g., transfusion-dependent sickle cell disease and beta thalassemia), these functional advantages offer the potential to reduce transfusion requirements, reduce iron overload associated with frequent transfusion, and attenuate a multitude of pulmonary, cardiovascular, renal and other serious clinical complications associated with RBC hemolysis.[6]

The Food and Drug Administration (FDA) process for approving new blood and blood components is unique. FDA formally approves the manufacturing systems used by U.S. blood establishments to collect and manufacture blood and blood components. Following the approval of the manufacturing system, individual blood collection establishments may submit to the FDA for licensure of the blood and blood components collected and processed using the system. On September 15, 2023, FDA approved the Hemanext One container system, which permits blood establishments "to process and store Red Blood Cells, Leukocytes Reduced, O2/CO2 Reduced" and allows an appropriately licensed blood establishment to introduce the component into interstate commerce (**Addendum 1**).

Therefore, our organizations strongly support the application for a new HCPCS Level II code for FDA-approved RBCs, LR, O2/CO2 Reduced. There is a clear need for a new code for this product, which is clearly distinct from other blood components. CMS has established specific HCPCS Level II codes for other FDA device-based systems. For example, CMS recently relied on FDA's approval of a processing container device -- the INTERCEPT Blood System for Plasma -- when the Agency assigned new HCPCS codes for novel blood component products, including Pathogen Reduced Cryoprecipitated Fibrinogen Complex (P9026) and Pathogen Reduced Plasma, Cryoprecipitate Reduced (P9025).

Below, please find examples of HCPCS code descriptor terms identifying specific blood component processing methods, associated existing HCPCS codes including pathogen reduction and irradiation, and how these processing methods clinically differentiate each product. In a number of instances, individual HCPCS-coded blood products incorporate multiple processing methods that differentiate their functionality in multiple ways for use in specific clinical situations.

[6] Kato GJ, Steinberg MH and Gladwin MT. Intravascular hemolysis and pathophysiology of sickle cell disease. *J Clin Invest* 2017 Mar 1;127(3):750-760.

P Code Descriptor Term	HCPCS Level II Codes	Processing Method	Clinical Differentiation
Pheresis	P9034-P9037, P9055, P9073	Collected on apheresis platform	Limits donor platelet exposures
Leukocytes reduced	P9016, P9031, P9033, P9035, P9037, P9040, P9051-P9058	Filtered to remove contaminating leukocytes	Reduced risk of febrile reactions
Irradiated	P9032, P9033, P9036-P9038, P9040, P9053, P9056-P9058	Exposed to specific dose of irradiation	Reduced risk of transfusion-associated graft-versus-host disease (TA-GVHD)
CMV-negative	P9051, P9053, P9055, P9058	Screened with serological methods for presence of CMV antibodies	Reduced CMV infection risk
HLA-matched	P9052	Typed with serological methods for HLA on platelets	Reduced HLA alloimmunization risk
Frozen within X hours of collection	P9017, P9059	Time to freezing of plasma component after production	Corresponds with differing levels of key coagulation factors
Pathogen reduced	P9025, P9026, P9070, P9071, P9073	Treated with amotosalen/UVA light	Reduced risk of transfusion-transmitted infections and TA-GVHD

AABB, ABC, and ARC believe that CMS' policies should uniformly support patients' access to novel products, which are often differentiated based on the processing method. We request that CMS reconsider the request for establishment of a HCPCS Level II code specifically identifying RBCs, LR, O2/CO2 Reduced. If you have any questions, please contact Susan Leppke (301-547-3962, sleppke@aabb.org), Diane Calmus (202-654-2988, dcalmus@americasblood.org), or Julie Manes (202-417-5147, julie.manes@redcross.org).

Sincerely,

Debra BenAvram
Chief Executive Officer
AABB

Kate Fry
Chief Executive Officer
America's Blood Centers

J. Chris Hrouda
President, Biomedical Services
American Red Cross

cc: Marge Watchorn (Division of Coding & Diagnosis Related Groups)

Addendum 1

U.S. FOOD & DRUG ADMINISTRATION

GRANT – DE NOVO
September 15, 2023

Hemanext, Inc.
Attention: Laura Daniels
99 Hayden Avenue, Suite 620
Lexington, MA 02421

Re: BR220665

Trade/Device Name:	Hemanext One
Regulation Number:	21 CFR 864.9115
Regulation Name:	Container system for the processing and storage of Red Blood Cell components under reduced oxygen conditions
Regulatory Class:	Class II
Product Code:	QYC
Dated:	December 30, 2021
Received:	January 5, 2022

Dear Laura Daniels:

The Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration (FDA) has completed its review of your De Novo request for classification of the Hemanext One, a prescription device under 21 CFR Part 801.109 with the following indications for use:

> Blood container set used to process and store Red Blood Cells Leukocytes Reduced, O2 /CO2 Reduced.
>
> HEMANEXT ONE is intended to process and store CP2D/AS-3 Red Blood Cells, Leukocytes Reduced (LR RBC) that have been prepared within the standard 8-hour hold time. Processing of Red Blood Cells with the HEMANEXT ONE system must be initiated within 8 hours of collection and completed within 12 hours of collection. The Red Blood Cells must be processed at room temperature (20-26 °C). The HEMANEXT ONE system limits O2 and CO2 levels in the storage environment. Red Blood Cells Leukocytes Reduced, O2 /CO2 Reduced may be stored for up to 42 days at 1-6 °C. HEMANEXT ONE is used for volumes no greater than 350 mL of LR RBC.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the Hemanext One, and substantially equivalent devices of this generic type, into Class II under the generic name Container system for the processing and storage of Red Blood Cells under reduced oxygen conditions.