August 8, 2024

Octapharma Pharmazeutika Produktionsges.m.b.H.
c/o Sergio Alegre
Octapharma USA Inc.
117 West Century Road
Paramus, NJ 07652

Dear Mr. Alegre,

This letter is in response to Octapharma Pharmazeutika Produktionsges.m.b.H.'s (Octapharma) request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of octaplasLG Powder (blood group types A and AB)[1] for U.S. military forces[2] for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3).

On June 7, 2018, pursuant to section 564(b)(1)(B) of the Act (21 U.S.C. § 360bbb-3(b)(1)(B)), the Deputy Secretary of the Department of Defense (DoD) determined that there is "a military emergency or significant potential for a military emergency, involving a heightened risk to U.S. military forces of an attack with an agent or agents that may cause, or are otherwise associated with an imminently life-threatening and specific risk to those forces."[3,4,5] Pursuant to section 564(b)(1) of the Act (21 U.S.C. § 360bbb-3(b)(1)), and on the basis of such determination, on July 9, 2018, the Secretary of the Department of Health and Human Services (HHS) then declared that circumstances exist justifying the authorization of emergency use of freeze dried

[1] Hereafter octaplasLG Powder (blood group types A and AB) will be referred to as octaplasLG Powder.
[2] For purposes of this EUA, the term "U.S. military forces" may include troops, civilians, contractors, and allied military personnel operating with Department of Defense. Also, for purposes of this EUA, it is anticipated that U.S. military medical personnel trained in the use of octaplasLG Powder will administer the authorized octaplasLG Powder to U.S. military forces. However, in the event the operational environment prevents such administration, it is possible that other trained U.S. military forces may need to administer the authorized octaplasLG Powder during an emergency as set forth in this authorization.
[3] DoD. *Letter to the HHS Secretary issuing a determination of a military emergency, or significant potential for a military emergency, and requesting a declaration under section 564 of the Federal Food, Drug, and Cosmetic Act*. June 7, 2018.
[4] Under section 564(b)(1)(B) of the Act, the Secretary of Defense may make a determination that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to United States military forces, including personnel operating under the authority of title 10 or title 50, of attack with—**(i)** a biological, chemical, radiological, or nuclear agent or agents; or **(ii)** an agent or agents that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to United States military forces.
[5] When the DoD Secretary makes such a determination, the Secretary of Health and Human Services (HHS) shall determine, within 45 calendar days of such determination, whether to make a declaration that circumstances exist to justify EUA issuance and, if appropriate, shall promptly make such a declaration.

plasma for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical.[6]

Octapharma requested this EUA so that octaplasLG Powder, which is not FDA-approved, may be acquired, distributed, and held by DoD for preparedness purposes in advance of an actual threat of agents of military combat (e.g., firearms, projectiles, and explosive devices) that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to U.S. military forces, with the intent that it may be administered by U.S. military medical personnel or other Authorized Providers[7] during an event or post-event for the treatment of hemorrhage or coagulopathy caused by exposure to agents of military combat when plasma is not available for use or when the use of plasma is not practical. An EUA is needed to facilitate DoD pre-event planning and preparedness activities related to the acquisition and use of this non-FDA approved product to enable activities to support rapid administration of treatment during an actual emergency event involving the threat of agents of military combat (e.g., firearms, projectiles, and explosive devices) that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to U.S. military forces.

This EUA is important for supporting military emergency response because it enables rapid initiation of treatment with octaplasLG Powder during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to U.S. military forces, without FDA or DoD having to take further action with respect to otherwise applicable requirements under federal law.

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act (21 U.S.C. § 360bbb-3(c)) are met, I am authorizing the emergency use of octaplasLG Powder (as described in the Scope of Authorization section of this letter (Section II)) in the specified population for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to U.S. military forces when plasma is not available for use or when the use of plasma is not practical, subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of octaplasLG Powder for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to U.S. military forces when plasma is not available for use or when the use of plasma is not practical in the specified population, when administered

[6] HHS. *Declaration that Circumstances Exist Justifying an Authorization Pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)*. July 9, 2018.

[7] Authorized Providers are medical personnel trained in the use of octaplasLG Powder who may administer the authorized octaplasLG Powder to U.S. military forces. In the event the operational environment prevents such administration, other trained U.S. military forces may need to administer the authorized octaplasLG Powder as Authorized Providers during an emergency as set forth in this authorization.

as described in the Scope of Authorization (Section II), meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. Agents of military combat (e.g., firearms, projectiles, and explosive devices) can cause, or otherwise be associated with a serious or life-threatening disease or condition to humans exposed to these agents, specifically hemorrhage or coagulopathy during an emergency when plasma is not available for use or when the use of plasma is not practical;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that octaplasLG Powder, when used in accordance with the Scope of Authorization, may be effective for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical, and that the known and potential benefits of octaplasLG Powder for this use outweigh the known and potential risks of such product;

3. There is no adequate, approved, and available alternative to the emergency use of octaplasLG Powder; and

4. The Deputy Secretary of Defense has requested emergency use of this product for treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical.[8]

II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- Octapharma will supply octaplasLG Powder, either directly or through authorized distributor(s) to DoD as directed by DoD, for use consistent with the terms and conditions of this EUA.
- octaplasLG Powder will be used for U.S. military forces for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical.

Product Description

octaplasLG Powder is a biological product to be used for U.S. military forces for treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to U.S. military forces when plasma is not available for use or when the use of plasma is not practical.

[8] No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

octaplasLG Powder is an unapproved lyophilized plasma product created from the FDA approved, pooled, solvent/detergent treated plasma product, Octaplas. Octaplas is manufactured from human plasma collected in US licensed plasma donation centers. All plasma donations are tested for relevant transfusion-transmitted infections in accordance with U.S. federal regulations. octaplasLG Powder is presented as a powder for solution for intravenous infusion, filled into and freeze-dried in glass vials, with each product vial containing 9-14 g of A- or AB-blood group specific human plasma protein and is reconstituted with 190 ml of water for injections (WFI) solvent. Prior to reconstitution, octaplasLG Powder can be stored at +2°C to +25°C for 24 months.

octaplasLG Powder is authorized to be distributed with an FDA cleared or approved transfusion filter set.

octaplasLG Powder is authorized to be distributed as directed by DoD for storage, distribution, and administration, when packaged in the authorized packaging and with the authorized labeling (e.g., carton and container labels, fact sheets).

octaplasLG Powder is authorized to be administered without a prescription and by U.S. military medical professionals or other authorized providers under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

octaplasLG Powder is authorized for emergency use with the following information required to be made available to medical professionals or other authorized providers and recipients (to the extent practicable given the emergency circumstances) when plasma is not available for use or when the use of plasma is not practical.

- Fact Sheet for Health Care Professionals or Other Authorized Providers
- Fact Sheet for Recipients

I have concluded, pursuant to section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of the authorized octaplasLG Powder in the specified population, when used for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical, when used consistently with the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of such a product.

I have concluded, pursuant to section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that the authorized octaplasLG Powder may be effective in the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical, when used consistently with the Scope of Authorization of this letter (Section II), pursuant to section 564(c)(2)(A) of the Act.

FDA has reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, and concludes that the authorized octaplasLG Powder, when used for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical in the specified population (as described in the Scope of Authorization of this letter (Section II)), meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized octaplasLG Powder product under this EUA must be consistent with, and may not exceed, the terms of this letter, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section IV). Subject to the terms of this EUA and under the circumstances set forth in the Deputy Secretary of Defense's determination described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the octaplasLG Powder described above is authorized for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical in the specified population.

III. Conditions of Authorization

Pursuant to section 564 of the Act, I am establishing the following conditions on this authorization:

Octapharma

A. Octapharma will ensure that the authorized octaplasLG Powder will be distributed as directed by DoD, and the authorized Fact Sheet for Health Care Professionals or Other Authorized Providers, the authorized Fact Sheet for Recipients, and any other labeling that FDA may authorize, as well as any authorized amendments thereto will be made available to applicable DoD components.

B. Octapharma, in consultation with DoD, may request changes to this authorization, including the authorized Fact Sheet for Health Care Professionals or Other Authorized Providers and the authorized Fact Sheet for Recipients, the authorized labeling (e.g., carton and container labels, label on each packaged unit) and authorized packaging for the authorized octaplasLG Powder, or to the manufacturing, labeling, and packaging processes of Octapharma or its authorized agent(s) for the authorized product. Any request for changes to this EUA must be submitted to Office of Blood Research and Review (OBRR)/Center for Biologics Evaluation and Research (CBER). Such changes require appropriate authorization prior to implementation.[9]

[9] The following types of revisions may be authorized without reissuing this letter: (1) changes to the authorized labeling; (2) non-substantive editorial corrections to this letter; (3) new types of authorized labeling, including new fact sheets; (4) new carton/container labels; (5) expiration dating extensions; (6) changes to manufacturing processes, including tests or other authorized components of manufacturing; (7) new conditions of authorization to require data collection or study. All changes to the authorization require review and concurrence from OBRR. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), or (7), review and

C. Octapharma will ensure that the terms of this EUA are made available to DoD. Octapharma will provide applicable DoD components a copy of this letter of authorization and communicate to applicable DoD components any subsequent amendments that might be made to this letter of authorization and its authorized accompanying materials (e.g., Fact Sheets).

D. Octapharma will inform applicable DoD components about the need to have a process in place for performing adverse event monitoring designed to ensure that suspected adverse reactions and all medication errors associated with the use of the authorized octaplasLG Powder are reported to Octapharma. Octapharma will conduct any follow-up requested by FDA regarding adverse events, to the extent feasible given the emergency circumstances.

E. Octapharma will ensure that the authorized octaplasLG Powder is distributed within the expiry dating period.

F. Octapharma will ensure that the authorized octaplasLG Powder is distributed with an FDA cleared or approved transfusion filter set.

G. Octapharma will post on its website the following statement: "For information about the FDA-authorized emergency use of octaplasLG Powder please see: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization."

H. Octapharma will promptly notify FDA of any suspected or confirmed quality, manufacturing, distribution, and/or other issues with the authorized octaplasLG Powder of which it becomes aware.

I. Octapharma will establish a Collaborative Research and Development Agreement (CRADA) with DoD to collect data related to use of octaplasLG Powder under combat conditions. These data will be collected whenever octaplasLG Powder is transfused to patients to the extent practicable given the emergency circumstances. Collected data will include suspected adverse reactions, including serious and unexpected adverse reactions, and any medication errors associated with the use of the authorized octaplasLG Powder. Octapharma will report data to FDA on an annual basis.

J. Octapharma must submit to the Emergency Use Authorization submission file periodic safety reports annually, or at another appropriate interval determined by CBER, in accordance with a due date agreed upon with OBRR/CBER beginning after the first full calendar month after authorization. Each periodic safety report must contain descriptive information which includes:
   - A narrative summary and analysis of suspected adverse reactions submitted during the reporting interval, including interval and cumulative counts by age groups;

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concurrence is required from the Preparedness and Response Team (PREP)/Office of the Center Director (OD)/CBER.

- A narrative summary and analysis of medication errors, whether or not associated with an adverse event, that were identified since the last reporting interval;
- Newly identified safety concerns in the interval;
- Actions taken since the last report because of adverse experiences;
- Cumulative doses distributed, and doses distributed during the reporting interval.

K. Octapharma will report to FDA, as soon as possible, any serious and unexpected suspected adverse reaction that is not described under 'Risks and Adverse Events' in the authorized Fact Sheet for Health Care Professionals or Other Authorized Providers and any suspected adverse reaction resulting in death. Octapharma will conduct any follow-up requested by FDA regarding adverse events, to the extent feasible given the emergency circumstances.

L. Upon request by FDA, Octapharma will make available any records maintained in connection with this letter.

DoD

M. DoD will distribute the authorized octaplasLG Powder under its direction to the extent such decisions are consistent with and do not exceed the terms of this letter, including distribution with the authorized labeling (e.g., Fact Sheets).

N. Through a process of inventory control, DoD will maintain records regarding distribution under its direction of the authorized octaplasLG Powder (e.g., lot numbers, quantity, receiving site, receipt date).

O. DoD will ensure that the terms of this EUA are made available to applicable DoD components through applicable DoD communication channels and procedures.[10] DoD will provide applicable DoD components a copy of this letter of authorization and communicate to applicable DoD components any subsequent amendments that might be made to this letter of authorization and its authorized accompanying materials (e.g., Fact Sheets).

P. DoD will inform applicable DoD components that the authorized octaplasLG Powder may be used only by U.S. military forces for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical.

Q. DoD will be responsible for authorizing components acting as part of a DoD response to administer the authorized octaplasLG Powder in accordance with the terms of this EUA, including instructing such components about the terms of this EUA with regard to storage, distribution, and administration, and for instructing about the means through which they are to obtain and use the authorized octaplasLG Powder.

[10] For example, through pre-deployment training, hard copy, web posting, etc.

R. DoD will train applicable DoD components on the use of the authorized octaplasLG Powder in accordance with this EUA and any applicable DoD procedures or protocols.

S. DoD will make available to applicable DoD components through applicable DoD communication channels and procedures the authorized Fact Sheet for Health Care Professional or Other Authorized Providers, the authorized Fact Sheet for Recipients, and any other Fact Sheets that FDA may authorize, as well as any authorized amendments thereto.[11] U.S. military medical personnel or other authorized providers administering the authorized octaplasLG Powder will ensure that the authorized Fact Sheet for Recipients has been made available to U.S. military forces that receive octaplasLG Powder through appropriate means, to the extent feasible given the emergency circumstances. Under exigent circumstances, other appropriate means for disseminating these Fact Sheets may be used.[12]

T. DoD will inform applicable DoD components about the need to have a process in place for performing adverse event monitoring designed to ensure that suspected adverse reactions and all medication errors associated with the use of the authorized octaplasLG Powder are reported to Octapharma, to the extent practicable given emergency circumstances, in according with the conditions of the EUA. Submitted reports should state that octaplasLG Powder was used under an EUA.

U. DoD will have a process in place for recording and reporting of data, as outlined in a CRADA to be established between DoD and Octapharma. These data will be recorded whenever octaplasLG Powder is transfused to patients to the extent reasonable and practicable given the emergency circumstances. Collected data will include suspected adverse reactions and any medication errors associated with the use of the authorized octaplasLG Powder.

V. DoD will report to Octapharma, as soon as reasonably possible, any serious and unexpected suspected adverse reaction that is not described under 'Risks and Adverse Events' in the authorized Fact Sheet for Health Care Professionals or Other Authorized Providers and any suspected adverse reaction resulting in death.

W. DoD will ensure that the authorized octaplasLG Powder is distributed for use under its direction within the expiry dating on the manufacturer's labeling

X. Per the terms of the CRADA with Octapharma, DoD will work with Octapharma to ensure that any records associated with the use of this product under this EUA are maintained, to the extent practicable given the emergency circumstances, until notified by FDA. Upon request by FDA, DoD will make available these and any other records maintained in connection with this letter.

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[11] For example, through pre-deployment training, hard copy, web posting, etc.

[12] FDA recognizes that the complex environment in which octaplasLG Powder may be used may prevent dissemination of Fact Sheets at the time of use of the octaplasLG Powder. Therefore, "other appropriate means" may include activities such as DoD components sharing the Fact Sheet for Recipients with U.S. military forces in pre-deployment or other training.

Y. DoD will promptly notify FDA of any suspected or confirmed quality, manufacturing, distribution, and/or other issues with the OctaplasLG Powder of which it becomes aware.

Conditions Related to Descriptive Printed Material

Z. All descriptive printed matter relating to the use of the authorized octaplasLG Powder shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.

AA. All descriptive printed matter relating to the use of the authorized octaplasLG Powder shall clearly and conspicuously state that:

- This product has not been FDA approved or licensed;
- This product has been authorized by FDA under an EUA for use by DoD;
- This product has been authorized only for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical; and
- This product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of octaplasLG Powder for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical, under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

No descriptive printed matter relating to the use of the authorized octaplasLG Powder may represent or suggest that this product is safe or effective for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical.

V. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of octaplasLG Powder for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Sincerely,

Peter W. Marks -S

Digitally signed by Peter W. Marks -S
Date: 2024.08.08 10:34:14 -04'00'

Peter W. Marks, M.D., Ph.D.
Director
Center for Biologics Evaluation and Research

Enclosures