August 13, 2020

Mr. Fortunato Aldape
Baxter Healthcare Corporation
Director, Global Regulatory Affairs, Acute Therapies
One Baxter Parkway
Deerfield, IL 60015

Dear Mr. Aldape:

This letter is in response to Baxter Healthcare Corporation's ("Baxter") request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for REGIOCIT replacement solution that contains citrate for regional citrate anticoagulation (RCA) of the extracorporeal circuit for emergency use as a replacement solution in adult patients treated with Continuous Renal Replacement Therapy (CRRT) and for whom RCA of the extracorporeal circuit is appropriate, in a critical care setting, during the Coronavirus Disease 2019 (COVID-19) pandemic, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3).

On February 4, 2020, pursuant to section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the Act), the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19.[1] Pursuant to section 564 of the Act, and on the basis of such determination, the Secretary of HHS then declared on March 27, 2020, that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, subject to the terms of the authorization issued under that section.[2]

The Agency has noted that SARS-CoV-2, the virus that causes COVID-19, has led to an increased population with critical illness and multiple organ failure, including acute kidney injury, increasing the need for CRRT. As a result, there is an insufficient supply of replacement solutions to meet the emergency need to provide CRRT in critically ill patients. Based on the totality of scientific evidence available, FDA has concluded that REGIOCIT may be effective for use as a replacement solution in adult patients treated with CRRT with suspected or confirmed

[1] U.S. Department of Health and Human Services, Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3. 85 FR 7316 (February 7, 2020).
[2] U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*, 85 FR 18250 (April 1, 2020).

COVID-19[3], and for whom RCA of the extracorporeal circuit is appropriate, in a critical care setting during the Coronavirus Disease 2019 (COVID-19) pandemic.

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act are met, I am authorizing the emergency use of your REGIOCIT product, as described in the Scope of Authorization (Section II) of this letter, subject to the terms of this authorization.

## I. Criteria for Issuance of Authorization

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

1. SARS-CoV-2, the virus that causes COVID-19, can cause a serious or life-threatening disease or condition, including severe respiratory illness and multiple organ failure, including acute kidney injury, to humans infected by this virus;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that REGIOCIT may be effective for use as a replacement solution in adult patients with suspected or known COVID-19[4] in a critical care setting who are being treated with CRRTand for whom RCA is appropriate, and that, when used under the terms and conditions described in this authorization, the known and potential benefits of REGIOCIT outweigh the known and potential risks of REGIOCIT; and

3. There is no adequate, approved, and available alternative to the emergency use of REGIOCIT due to an insufficient supply of FDA-approved alternatives to meet the emergency need during the COVID-19 pandemic.[5]

## 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:

- REGIOCIT will be used as a replacement solution only in adult patients being treated with CRRT and for whom RCA is appropriate.
- REGIOCIT will be administered only by a licensed healthcare provider in a critical care setting.

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[3] As noted in the letter of authorization, in the circumstances of this public health emergency, it would not be feasible to authorize REGIOCIT only to be used for patients with suspected or confirmed COVID-19; therefore, the authorization does not limit use to such patients.

[4] In the circumstances of this public health emergency, it would not be feasible to require healthcare providers to seek to limit REGIOCIT only to be used for patients with suspected or confirmed COVID-19; therefore, this authorization does not limit use to such patients.

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

- REGIOCIT will be available for use only in facilities that Baxter Healthcare Corporation has qualified[6] for receiving REGIOCIT.

REGIOCIT is a replacement solution that contains citrate for RCA of the extracorporeal circuit. REGIOCIT is authorized for emergency use as a replacement solution in adult patients treated with CRRT, and for whom RCA is appropriate, during the COVID-19 pandemic. REGIOCIT is intended for use in a critical care setting. REGIOCIT is intended to be used in continuous venovenous hemofiltration (CVVH), and continuous venovenous hemodiafiltration (CVVHDF) modalities.

**Authorized Product Details**

REGIOCIT is supplied as a 5000 mL sterile solution of 0.503% sodium chloride and 0.529% sodium citrate in water for injection in a polyolefin clear plastic bag.

REGIOCIT is authorized under the terms and conditions of this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

REGIOCIT is authorized to be accompanied by the following product-specific information pertaining to the emergency use, which is required to be made available to healthcare providers and patients:

- Fact Sheet for Healthcare Providers: Emergency Use of REGIOCIT during the COVID-19 Pandemic
- REGIOCIT Package Insert- EUA
- Fact Sheet for Patients and Caregivers: Emergency Use of REGIOCIT during the COVID-19 Pandemic

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 REGIOCIT, when used consistent within the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of REGIOCIT.

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 REGIOCIT may be effective for the uses described within 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 REGIOCIT, when used 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.

[6] Baxter Healthcare Corporation will determine whether an individual facility is qualified, for the purposes of receiving REGIOCIT, in accordance with the process and criteria submitted in Baxter's EUA request.

The emergency use of the authorized 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 Secretary of HHS's determination under section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the REGIOCIT, with the required labeling set forth in this section (Section II), are authorized for the uses described above.

## III. Conditions of Authorization

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

Baxter Healthcare Corporation

A. Baxter Healthcare Corporation may request changes to the authorized labeling as described in the Scope of Authorization (Section II) of this letter. Such requests will be made in consultation with, and require concurrence of, the Division of Cardiology and Nephrology (DCN)/Office of Cardiology, Hematology, Endocrinology and Nephrology (OCHEN)/Office of New Drugs (OND)/Center for Drug Evaluation and Research (CDER).

B. Baxter Healthcare Corporation may request changes to the Scope of Authorization (Section II in this letter) of the product. Such requests will be made in consultation with, and require concurrence of, the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC) and DCN/OCHEN/OND/CDER.

C. Baxter Healthcare Corporation will manufacture REGIOCIT in conformance with Current Good Manufacturing Practices.

D. Baxter Healthcare Corporation will manufacture and test REGIOCIT per the process and methods, including in-process sampling and testing and finished product testing (release and stability) to meet all specifications as referenced in Baxter's EUA request.

E. REGIOCIT will have an 18-month expiry period when stored at room temperature or refrigerated conditions.

F. Baxter Healthcare Corporation will conduct additional endotoxin testing as detailed in Baxter Healthcare Corporation's response, dated July 13, 2020, to FDA's information request, dated July 10, 2020.

G. Baxter Healthcare Corporation will not implement any changes to the description of the product, manufacturing process, facilities and equipment, and elements of the associated control strategy that assure process performance and quality of the authorized product without notification to and concurrence by the Agency.

H. Baxter Healthcare Corporation will determine whether an individual facility is qualified, for the purposes of receiving REGIOCIT, in accordance with the process and criteria submitted in Baxter Healthcare Corporation's EUA request. Baxter Healthcare Corporation will maintain documentation on its qualification activities for each individual facility.

I. Baxter Healthcare Corporation will submit information to the Agency within three working days of receipt of any information concerning any batch of REGIOCIT (whether the batch is distributed or not), as follows: (1) information concerning any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article; and (2) information concerning any bacteriological or microscopic contamination, or any significant chemical, physical, or other change in deterioration in the drug product, or any failure of one or more batches of the drug product to meet the established specifications.

J. Baxter Healthcare Corporation will report to FDA serious adverse events and all medication errors associated with the use of REGIOCIT of which they become aware during the pandemic, to the extent practicable given emergency circumstances, using either of the following options.

*Option 1*: Submit reports through the Safety Reporting Portal (SRP) as described on the FDA SRP web page.

*Option 2*: Submit reports directly through the Electronic Submissions Gateway (ESG) as described on the FAERS electronic submissions web page.

Submitted reports under both options should state: "use of REGIOCIT was under an EUA". For reports submitted under Option 1, include this language at the beginning of the question "Describe Event" for further analysis. For reports submitted under Option 2, include this language at the beginning of the "Case Narrative" field.

Baxter Healthcare Corporation and Authorized Distributors[7]

K. Baxter Healthcare Corporation will notify FDA of any authorized distributor(s) of the product, including the name, address, and phone number of any authorized distributor(s), and provide authorized distributor(s) with a copy of this EUA.

L. Baxter Healthcare Corporation and authorized distributor(s) will make REGIOCIT available with the authorized labeling as described in the Scope of Authorization (Section II) of this letter.

[7] "Authorized Distributor(s)" are identified by the sponsor in EUA requests as an entity allowed to distribute the product.

M. Baxter Healthcare Corporation and authorized distributor(s) will make available on their website(s) the Fact Sheet for Healthcare Providers, the Fact Sheet for Patients, and the REGIOCIT Package Insert for EUA.

N. Through a process of inventory control, Baxter Healthcare Corporation and authorized distributor(s) will maintain records of the healthcare settings to which they distribute REGIOCIT and the number of bags of REGIOCIT distributed.

O. Baxter Healthcare Corporation and authorized distributor(s) will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

P. Baxter Healthcare Corporation and authorized distributor(s) are authorized to make available additional information relating to the emergency use of the product that is consistent with, and does not exceed, the terms of this letter of authorization.

Hospitals and Other Healthcare Facilities to Whom the Authorized REGIOCIT Is Distributed and Healthcare Providers Administering the Authorized REGIOCIT

Q. Healthcare facilities and healthcare providers will ensure that they are aware of the letter of authorization, and the terms herein, and that the authorized labeling (as described in the Scope of Authorization (Section II) of this letter) is made available to healthcare providers and to patients and caregivers through appropriate means.

R. Through a process of inventory control, healthcare facilities will maintain records regarding the dispensed authorized REGIOCIT (i.e., lot numbers, quantity, receiving site, receipt date), and product storage.

S. Healthcare facilities will ensure that any records associated with this EUA are maintained until notified by Baxter Healthcare Corporation and/or FDA. Such records will be made available to Baxter Healthcare Corporation, HHS, and FDA for inspection upon request.

T. Healthcare facilities and prescribing health care providers or their designee receiving REGIOCIT will track all medication errors associated with the use of and all serious adverse events that are considered to be potentially attributable to REGIOCIT use and must report these to FDA in accordance with the Fact Sheet for Healthcare Providers using one of the following methods:

*Option 1:* Complete and submit a MedWatch form online (www.fda.gov/medwatch/report.htm)

*Option 2:* Complete and submit FDA Form 3500 (health professional) by fax (1-800-FDA-0178) (this form can be found via link above).

Call 1-800-FDA-1088 for questions. Submitted reports should state, "use of REGIOCIT was under an EUA" at the beginning of the question "Describe Event" for further

analysis.

Conditions Related to Printed Matter, Advertising and Promotion

U. All descriptive printed matter, including advertising and promotional material, relating to the use of REGIOCIT shall be consistent with the authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.

V. No descriptive printed matter, including advertising or promotional material, relating to the use of REGIOCIT may represent or suggest that such products are safe or effective.

W. All descriptive printed matter, including advertising and promotional material, relating to the use of REGIOCIT clearly and conspicuously shall state that:

- REGIOCIT is not FDA-approved;
- REGIOCIT has been authorized by FDA for use under an EUA;
- REGIOCIT is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

## IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of REGIOCIT during the COVID-19 pandemic is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Sincerely,

Denise M. Hinton -S3

Digitally signed by Denise M. Hinton -S3
Date: 2020.08.13 21:22:00 -04'00'

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures