U.S. FOOD & DRUG ADMINISTRATION

May 20, 2020

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

Dear Mr. Aldape:

This letter is in response to Baxter Healthcare Corporation's request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the Prismaflex ST Set[1] to provide continuous renal replacement therapy (CRRT) to treat patients[2] in an acute care environment 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). The system is intended for patients who have acute renal failure, fluid overload, or both.

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.[3] Pursuant to section 564 of the Act, and on the basis of such determination,

WITHDRAWN

[1] The Prismaflex ST Set is a disposable, extracorporeal circuit for use only with the Prismaflex or PrisMax control unit. The Prismaflex ST Set has product numbers ST60, ST100, and ST150. The Prismaflex ST Set includes: AN69 (copolymer of acrylonitrile and sodium methylal sulfonate with surface treatment of polyethyleneimine) hollow fiber hemofilter/dialyzer, tubing lines, cartridge plate, and effluent bag. The Prismaflex ST Set was first CE-marked in December 2004 and is currently marketed in over 50 countries, including the European Union but it is not FDA-cleared or approved. The alternative product available in the U.S. is the Prismaflex M Set, which was cleared by FDA under K041005 (Prismaflex M60 & M100 Sets) and K080519 (Prismaflex M150 Set). The differences between the Prismaflex M Set and the subject Prismaflex ST Set are that the Prismaflex ST Set contains a polyethyleneimine surface treatment on the membrane and the ST100 and M100 models have different membrane effective surface areas ($1m^2$ for the proposed ST100 versus $0.9m^2$ for the FDA-cleared M100). For completeness, the ST60 and M60 models have the same membrane effective surface areas, and the ST150 and the M150 models have the same membrane effective surface area. This EUA authorizes use of the Prismaflex ST Set to be used as an alternative to the Prismaflex M Set.

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

[3] 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*

the Secretary of HHS then declared on March 24, 2020, that circumstances exist justifying the authorization of emergency use of medical devices, including alternative products used as medical devices, due to shortages during the COVID-19 outbreak, subject to the terms of any authorization issued under that section.[4]

Based on published data from China and preliminary reports in the U.S., it has been 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. Data in the EUA request support that a greater number of COVID-19 patients in the intensive care unit (ICU) require CRRT compared to non-COVID patients in the ICU. COVID-19 patients in the ICU need CRRT for more days than non-COVID patients. Additionally, COVID-19 patients' filters clot faster than non-COVID patients' filters, requiring more frequent filter changes. The increased number of COVID-19 patients in the hospital and ICU has caused the demand for CCRT products to rapidly increase. As a result, there is a shortage of devices and accessories to provide CRRT to critically ill patients nationwide. Prismaflex or PrisMax CRRT control units are available in the U.S. (as described in Section II). However, the Prismaflex or PrisMax CRRT control units must be used with the specific extracorporeal circuit sets manufactured by Baxter Healthcare Corporation, of which only the Prismaflex M Set described above[1] is FDA cleared. However, the supply of Prismaflex M Sets cannot meet the demand. Therefore, Prismaflex M Set is not an adequate, approved, and available alternative to Prismaflext ST Set due to shortages during the COVID-19 outbreak.

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 the Prismaflex ST Set, 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 the Prismaflex ST Set, as described in the Scope of Authorization (Section II) of this letter to provide CRRT in an acute care environment, 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 the Prismaflex ST Set may be effective to treat patients in an acute care environment during the COVID-19 pandemic,[5] and that the known and potential benefits of the

Cosmetic Act, 21 U.S.C. § 360bbb-3. 85 FR 7316 (February 7, 2020).

[4] 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 17335 (March 27, 2020).

[5] See footnote 2

WITHDRAWN

Prismaflex ST Set, when used for such use, outweigh the known and potential risks of the Prismaflex ST Set; and

3. There is no adequate, approved, and available alternative to the emergency use of the Prismaflex ST Set when there are shortages of FDA-cleared alternatives during the COVID-19 pandemic.[6]

II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of the Prismaflex ST Set to deliver CRRT to treat patients in an acute care environment during the COVID-19 pandemic. The system is intended for patients who have acute renal failure, fluid overload or both. The Prismaflex ST Set should only be used with the Prismaflex or PrisMax control unit.

Authorized Product Details

The Prismaflex ST Set is a disposable, extracorporeal circuit for use only with the Prismaflex or PrisMax control unit. The Prismaflex ST Set has product numbers ST60, ST100, and ST150 that correlate with different membrane effective surface areas. The Prismaflex ST Set consists of:

- hollow fiber hemofilter/dialyzer
  - copolymer of acrylonitrile and sodium methylal sulfonate (AN69)
  - polyethyleneimine surface treatment
- tubing lines
- cartridge plate
- effluent bag 5LT

The fluid pathways of the Prismaflex ST Set are sterile and non pyrogenic. The Prismaflex ST Set is sterilized by Ethylene Oxide.

The following CRRT modalities are available with the Prismaflex ST Set:

- SCUF – Slow Continuous Ultra Filtration
- CVVH - Continuous Veno Venous Hemofiltration
- CVVHD - Continuous Veno Venous Hemodialysis
- CVVHDF - Continuous Veno Venous Hemodiafiltration

1. The Prismaflex ST Set mechanism of function is as follows:

Blood enters the filter via a blood inlet port where it is distributed to the hollow fibers. The patient's blood flows inside the hollow fibers and exits the device via a blood exit port.

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

WITHDRAWN

By means of hydrostatic pressure or transmembrane pressure which is created by a combination of positive and negative pressures across the membrane, plasma water along with certain lower and middle molecular weight solutes pass through the membrane and into the dialysate/filtrate compartment of the device. Considering the AN69 membrane microstructure and chemical composition, toxins having basic residues on the surface can also be adsorbed by means of ionic interactions in the bulk and/or at the blood/membrane interface.

In this device, toxins and waste products are therefore removed from the patient's blood by means of diffusion, convection and adsorption; they are eliminated via the dialysate/filtrate and the membrane during the treatment session. The dialysate/filtrate exits the devices via a dialysate outlet port.

2. The device settings that have been validated for operation of the Prismaflex ST Set are included in the authorized labeling.

   Additional treatment information has been provided in the Instructions for Use of the Prismaflex ST Set enclosed with this EUA.

The above described Prismaflex ST Set, is authorized to be accompanied with labeling entitled "IFU Insert Prismaflex ST Set" and "Prismaflex ST60 Set / ST100 Set / ST150 Set AN69 ST Membrane" Instructions for Use (available at https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations),[7] together with 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 Personnel: Emergency Use of the Prismaflex ST Set during the COVID-19 Pandemic
- Fact Sheet for Patients: Emergency Use of the Prismaflex ST Set during the COVID-19 Pandemic

The "Prismaflex ST60 Set / ST100 Set / ST150 Set AN69 ST Membrane" Instructions for Use with inserts and the two Fact Sheets are referred to as "authorized labeling." The above described Prismaflex ST Set, when accompanied with the authorized labeling is authorized to be distributed to and used under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

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 Prismaflex ST Set, when used as described in the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of this 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 Prismaflex ST Set may be

[7] As part of this authorization, the Prismaflex ST Set will be distributed with the English labeling that accompanies the product for distribution in one of the following regions: Global (non-US), South Korea, or China, as well as an insert with information specific to the emergency use.

WITHDRAWN

effective to treat patients in an acute care environment during the COVID-19 pandemic, 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 Prismaflex ST Set, 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 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 III). 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 Prismaflex ST Set described above is authorized to provide CRRT in an acute care environment.

III. Conditions of Authorization

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

Baxter Healthcare Corporation, as Sponsor of Authorized Product

A. Baxter Healthcare Corporation must comply with the labeling requirements under 21 CFR 801 Subpart A (general labeling provisions) and 21 CFR 801.109 (labeling for prescription devices), as well as those described in Section II, Scope of Authorization. As such, compliance with the unique device identification regulations (see Subpart B of 21 CFR Part 801) is not required under this EUA.

B. Baxter Healthcare Corporation must comply with applicable current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of the authorized devices.

C. Baxter Healthcare Corporation will make the Prismaflex ST Set available with authorized labeling. Baxter Healthcare Corporation may request changes to the authorized labeling. Such changes require review and concurrence from, the Division of Renal, Gastrointestinal, Obesity and Transplant Devices (DHT3)/Office of GastroRenal, ObGyn, General Hospital and Urology Devices (OHT3)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH).

D. Baxter Healthcare Corporation may request changes to the Scope of Authorization (Section II in this letter) of the authorized Prismaflex ST Set. Such requests will be made in consultation with and require concurrence from DHT3A/OHT3/OPEQ/CDRH and the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC).

WITHDRAWN

E. Baxter Healthcare Corporation may request changes to any components or materials. Such requests will be made in consultation with, and require concurrence of, DHT3A/OHT3/OPEQ/CDRH.

F. Baxter Healthcare Corporation may request the addition of other instruments and associated software for use with the product. Such requests will be made in consultation with, and require concurrence of, DHT3A/OHT3/OPEQ/CDRH.

G. Baxter Healthcare Corporation will have a process in place to collect information on the performance of Prismaflex ST Set, including from healthcare facility customers, and for reporting adverse events of which they become aware to FDA under 21 CFR Part 803.

H. Baxter Healthcare Corporation will notify FDA of any authorized distributor(s)[8] of the Prismaflex ST Set, including the name, address, and phone number of any authorized distributor(s), and provide authorized distributor(s) with a copy of this EUA and any updates.

Baxter Healthcare Corporation and Authorized Distributor(s)

I. Baxter Healthcare Corporation, and authorized distributors will distribute the authorized Prismaflex ST Set with the authorized labeling only to healthcare facilities with healthcare professionals (HCP) who are adequately equipped, trained, and capable of using the Prismaflex ST Set according to the criteria set forth by Baxter Healthcare Corporation

J. Baxter Healthcare Corporation and authorized distributor(s) will make the Prismaflex ST Set available with the authorized labeling, including fact sheets, described in the Scope of Authorization (Section II) of this letter.

K. Baxter Healthcare Corporation and authorized distributor(s) will make authorized labeling available on their website(s).

L. Authorized distributors will make Baxter Healthcare Corporation aware of any adverse events of which they become aware.

M. Through a process of inventory control, Baxter Healthcare Corporation and authorized distributor(s) will maintain records of the healthcare settings to which they distribute the Prismaflex ST Set and number of Prismaflex ST Set they distribute.

N. 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.

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

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

WITHDRAWN

be made available to FDA for inspection upon request.

Healthcare Facilities

P. Healthcare facilities using the authorized Prismaflex ST Set must make available to patients the accompanying Patient Fact Sheet and make available to HCP the accompanying Healthcare Provider Fact Sheet. Healthcare facilities using the authorized Prismaflex ST Set must also make available the other authorized labeling for the Prismaflex ST Set to patients and HCP.

Q. Healthcare facilities using the Prismaflex ST Set must make Baxter Healthcare Corporation and FDA aware of any adverse events under 21 CFR Part 803.

R. Healthcare facilities will ensure HCP using the Prismaflex ST Set are adequately equipped, trained, capable, and will maintain records of device usage.

Conditions Related to Printed Matter, Advertising and Promotion

S. All descriptive printed matter, including advertising and promotional material, relating to the use of the authorized Prismaflex ST Set 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.

T. No descriptive printed matter, including advertising or promotional material, relating to the use of the authorized Prismaflex ST Set may represent or suggest that such products are safe or effective for the delivery of CRRT in an acute care environment.

U. All descriptive printed matter, including advertising and promotional material, relating to the use of the authorized Prismaflex ST Set clearly and conspicuously shall state that:

- The Prismaflex ST Set have neither been cleared or approved to provide CRRT to treat patients in an acute care environment during the COVID-19 outbreak;
- The Prismaflex ST Set has been authorized for the above emergency use by FDA under an EUA;
- The Prismaflex ST Set has been authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of medical devices 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 is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

WITHDRAWN

Sincerely,

_____

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures

WITHDRAWN