August 10, 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 HF20 Set[1] to provide continuous renal replacement therapy (CRRT) to treat low weight (8 kilograms (kg) (18 pounds (lbs)) to 20 kg (44 lbs)) and low blood volume patients or patients[2] who have acute renal failure, fluid overload, or both, and who cannot tolerate a larger extracorporeal circuit volume 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).

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, the Secretary of HHS then declared on March 24, 2020, that circumstances exist justifying the authorization of emergency use of medical devices during the COVID-19 outbreak, pursuant to Section 564 of the FD&C Act, subject to the terms of any authorization issued under that section.[4]

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[1] The Prismaflex HF20 Set is a disposable, extracorporeal circuit for use only with the Prismaflex or PrisMax control unit. The Prismaflex HF20 Set has model number 109841. The Prismaflex HF20 Set includes: PolyAryl Ether Sulfone (PAES) hollow fiber hemofilter/dialyzer, tubing lines, cartridge plate, and effluent bag. The Prismaflex HF20 Set was first CE-marked in November 2008 in 28 countries, together with Lichtenstein, Norway and Switzerland and is currently marketed in many countries worldwide, but it is not FDA-cleared or approved.

[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 Prismaflex HF20 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 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).

There are no FDA-approved or -cleared devices for use to provide CRRT to treat low weight (8-20 kg) patients who have low blood volume and who cannot tolerate a larger extracorporeal circuit volume in an acute care environment.[5] 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 CRRT. 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, the available information indicates that COVID-19 patients' filters clot faster than non-COVID patients' filter, requiring more frequent filter changes. The use of the Prismaflex HF20 Set with the relatively low extracorporeal blood volume offers technological benefit for some smaller populations compared to current filter sets available in the United States. Currently, in the United States, low-weight patients requiring CRRT are generally treated with filter sets designed for higher weight patients. Enabling filter sets such as the HF20 set, that are designed for low-weight patients who have lower blood volume and are therefore susceptible to hemodynamic compromise with larger filter sets, would mitigate against reduced organ perfusion that occurs in patients with COVID-19 infection during the COVID-19 emergency. Based on this evidence and FDA's review of the available information including bench performance testing, clinical trial evidence, and literature data, FDA has concluded that there are no adequate, approved, and available alternatives to the Prismaflex HF20 Set and that such device may be effective in delivering CRRT to treat low weight (8-20 kg) patients who have low blood volume and who cannot tolerate a larger extracorporeal circuit volume in an acute care environment during the COVID-19 emergency.

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 Prismaflex HF20 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 HF20 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:

[5] Although a CRRT device for pediatric patients was recently granted de novo classification (the CARPEDIEM System, DEN180055), it is not considered an adequate, approved, and available alternative because: (1) the CARPEDIEM System does not offer a CRRT filter set for use with the Prismaflex and PrisMax control units which are used in the majority of hospitals in the United States; (2) the CARPEDIEM System has a different indication for use with pediatric patient weight ranges of 2.5-10 kg leaving no approved alternative for pediatric patients weighing between 10-20 kg; and (3) the Prismaflex or PrisMax CRRT control units must be used with the specific extracorporeal circuits sets manufactured by Baxter Healthcare Corporation, including the HF20 set, and only one set, the Prismaflex M Set is FDA cleared. Moreover, although another EUA product would not be considered an approved (cleared) alternative for purposes of meeting the EUA criterion, an EUA was recently issued for the Prismaflex ST Set (https://www.fda.gov/media/138254/download). Prismaflex ST Sets and Prismaflex M Sets are not indicated for patients with low weight (8-20 kg) who have low blood volume and who cannot tolerate a larger extracorporeal circuit volume, making that product likewise not adequate alternative.

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 HF20 Set (cartridge, including hemodialyzer plus tubing set) may be effective at providing CRRT to treat low weight patients who have low blood volume and who have acute renal failure, fluid overload, or both, and who cannot tolerate a larger extracorporeal circuit volume in an acute care environment during the COVID-19 emergency and that the known and potential benefits of the Prismaflex HF20 Set, when used for such use, outweigh the known and potential risks of the Prismaflex HF20 Set; and

3. There is no adequate, approved, and available alternative to the emergency use of the Prismaflex HF20 as set forth in the Scope of Authorization (Section II) of this letter, when there are no FDA-approved or -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 HF20 Set to deliver CRRT to treat patients of low weight (8-20 kg) and low blood volume who cannot tolerate a larger extracorporeal circuit volume 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 HF20 Set should only be used with the Prismaflex or PrisMax control unit.

This set is intended for use in the following veno-venous therapies: Slow Continuous Ultrafiltration (SCUF); Continuous Veno-Venous Hemofiltration (CVVH); Continuous Veno-Venous Hemodialysis (CVVHD); Continuous Veno-Venous Hemodiafiltration (CVVHDF).

The relative contraindications (individual risk/benefit to be determined by treating physician) for use of the Prismaflex HF20 Set include:

- The inability to establish vascular access
- Severe hemodynamic instability
- Known hypersensitivity to any component of the Prismaflex HF20 Set

Authorized Product Details

The Prismaflex HF20 Set is a disposable, extracorporeal circuit for use only with the Prismaflex or PrisMax control unit. The Prismaflex HF20 ST Set consists of:

- PAES hollow fiber hemofilter/dialyzer
- tubing lines
- cartridge plate

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

- effluent bag 5LT

This hollow fiber membrane is composed of PolyAryl Ether Sulfone (PAES). The Prismaflex HF20 Set is compatible with the sleeve blood warmers, which should be installed on the return line.

The fluid pathways of the Prismaflex HF20 Set are sterile and non-pyrogenic. The Prismaflex HF20 Set is sterilized by Ethylene Oxide.

1. The Prismaflex HF20 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.

   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.

   In this device, toxins and waste products are therefore removed from the patient's blood by means of diffusion and convection; 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 following device settings have been validated for operation of the Prismaflex HF20 Set:

	Prismaflex HF20
PHYSICAL CHARACTERISTICS	
Membrane effective surface area	0.2 m^2
Fiber internal diameter (wet)	215 µm
Fiber wall thickness	50 µm
Blood volume in set	58 ml
Overall dimensions • Length • Width • Height	 27 cm 22 cm 9 cm
OPERATING PARAMETERS	
Maximum TMP	500 mmHg 66.6 kPa
Maximum blood pressure	500 mmHg

	66.6 kPa
Minimum blood flow rate	20 ml/min
Maximum blood flow rate	100 ml/min

Additional treatment information has been provided in the Instructions for Use of the Prismaflex HF20 Set accompanied with this EUA.

The above described Prismaflex HF20 Set is authorized to be accompanied with labeling entitled "IFU Insert Prismaflex HF20 Set" and "Prismaflex HF20 Set" Instructions for Use (available at https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations) and operation instructions for control units compatible with the Prismaflex HF20 entitled "Prismaflex Control Unit Operator's Manual" and "PrisMax Control Unit Operator's Manual (cleared for other indications)[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 Providers: Emergency Use of the Prismaflex HF20 Set during the COVID-19 Pandemic
- Fact Sheet for Patients: Emergency Use of the Prismaflex HF20 Set during the COVID-19 Pandemic

The "Prismaflex HF20 Set" Instructions for Use with insert and the two Fact Sheets are referred to as "authorized labeling." The above described Prismaflex HF20 Set, when accompanied with the authorized labeling, is authorized to be distributed 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 HF 20 Set, when used for CRRT in an acute care environment in patients with low weight (8-20 kg) who have low blood volume and who cannot tolerate a larger extracorporeal circuit volume, and used consistently with 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 HF20 Set may be 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 HF20 Set, when used to provide CRRT in an acute care environment (as described in the Scope of

[7] Operation instructions for control units compatible with the Prismaflex HF20 entitled "Prismaflex Control Unit Operator's Manual" and "PrisMax Control Unit Operator's Manual" can be found at the Baxter Healthcare Acute Therapies website at http://www.renalacute.com.

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 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) of the Act described above and the Secretary of HHS's corresponding declaration under section 564(b)(1) of the Act, the Prismaflex HF20 Set, with the required labeling set forth in this section (Section II), are 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

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 HF20 Set available with authorized labeling. Baxter Healthcare Corporation may request changes to the authorized labeling. Such requests 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 HF20 Set. Such requests will be made in consultation with, and require concurrence of, DHT3A/OHT3/OPEQ/CDRH and the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC).

E. Baxter Healthcare Corporation may request changes to the components and 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 the Prismaflex HF20 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 HF20 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 distributor(s) will distribute the authorized the Prismaflex HF20 Set with the authorized labeling only to healthcare facilities with healthcare providers (HCP) who are equipped, trained, and capable of using the Prismaflex HF20 Set according to the criteria set forth by Baxter Healthcare Corporation. Baxter Healthcare Corporation and authorized distributor(s) must notify healthcare facility customers about the conditions of this authorization applicable to healthcare facilities prior to the use of the Prismaflex HF20 Set.

J. Baxter Healthcare Corporations and authorized distributor(s) will make the Prismaflex HF20 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 the authorized labeling available on their website(s).

L. Authorized distributor(s) 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 HF20 Set and number of Prismaflex HF20 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 be made available to FDA for inspection upon request.

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

Healthcare Facilities

P. Healthcare facilities using the authorized Prismaflex HF20 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 HF20 Set must also make available the other authorized labeling for the Prismaflex HF20 Set to patients and HCP.

Q. Healthcare facilities using the Prismaflex HF20 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 HF20 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 HF20 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 HF20 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 HF20 Set clearly and conspicuously shall state that:

- The Prismaflex HF20 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 HF20 Set has been authorized for the above emergency use by FDA under an EUA;

- The Prismaflex HF20 Set has been authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency 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.

Sincerely,

Denise M. Hinton -S3

Digitally signed by Denise M. Hinton -S3
Date: 2020.08.10 21:14:14 -04'00'

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures