SPECIAL SUPPLEMENT TO DIRECTIONS FOR USE: EOS PMP

TEMPORARY MODIFICATION TO INDICATIONS FOR USE TO ADDRESS COVID-19

BACKGROUND

The United States Food and Drug Administration issued a guidance document ***Enforcement Policy for Extracorporeal Membrane Oxygenation and Cardiopulmonary Bypass Devices During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency*** (Monday, April 6, 2020) to expand the availability of devices used in extracorporeal membrane oxygenation (ECMO) therapy to address the Coronavirus Disease 2019 (COVID-19) Pandemic. This policy is intended to remain in effect only for the duration of the public health emergency related to COVID-19 declared by the Department of Health and Human Services (HHS), including any renewals made by the HHS Secretary.

COVID-19 can trigger acute respiratory failure and/or acute cardiopulmonary failure. Under such conditions, long-term extracorporeal oxygenation (i.e., extracorporeal oxygenation for greater than 6 hours) can be an important tool for treating patients and FDA recognizes the importance and utility of increased availability of extracorporeal oxygenation devices for patients during the COVID-19 public health emergency. Cardiopulmonary bypass devices, cleared or approved by FDA, are technologically capable of being used for ECMO therapy, providing extracorporeal oxygenation for longer than 6 hours. Therefore, to facilitate expanded availability of devices to perform ECMO therapy to treat COVID-19 patients, FDA is permitting manufacturers of cardiopulmonary bypass devices to modify the indications for use of their devices to include ECMO greater than 6 hours, without prior submission of a premarket notification to FDA (i.e. FDA clearance).

Device model	Catalogue Number
EOS PMP	050576

INDICATIONS FOR USE

FDA-Cleared Indications for Use

The device is intended for use in patients who undergo cardiopulmonary bypass surgery requiring extracorporeal circulation with a maximum blood flow rate of 5 liters /minute. It provides oxygenation and carbon dioxide removal from venous blood. The integrated heat exchanger provides blood temperature control and allows the use of hypothermia or aids in the maintenance of normothermia during surgery. The device is intended to be used for 6 hours or less.

Special Indications for Use permitted by FDA on a temporary basis to address the COVID-19 pandemic

The device can be used in an ECMO circuit to treat patients who are experiencing acute respiratory failure and/or acute cardiopulmonary failure. The device can be used in an ECMO circuit greater than 6 hours.

ADDITIONAL INFORMATION RELATED TO SPECIAL INDICATIONS FOR USE

The following information provides an addendum to the existing FDA-Cleared Directions for Use (DFU) about the device related to the Special Indications for Use.

Device Performance

Device performance is the same as that established in the IFU.

Summary of Durability Testing

Available data confirm declared performance of the device up to 5 days.

When used for longer than 5 days, continuous monitoring is required to ensure correct device operation (refer to section ***Clinical Signs and Observations that suggest device change-out is required***).

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Summary of Animal Testing

There is no additional animal testing related to use for ECMO greater than 6 hours.

Summary of Clinical Performance

There is clinical evidence relevant to the current FDA guidance for extended duration of use beyond the labelled six hours duration in the DFU.

Numerous publications have evaluated safety and performance outcomes used with LivaNova devices or in combination with other manufacturer devices to comprise the entire ECMO circuit. These studies have demonstrated adequacy of blood flow and gas exchange with complication type and frequency in keeping with current state of the art for extracorporeal cardiorespiratory support beyond the labeled six hours duration of use. [1,2] [3] [4] The published literature confirms safety and efficacy for the use of the EOS oxygenator for a wide variety of medical conditions requiring extended extracorporeal support.

Potential Risk

The following hazardous situations may arise during the use of the device in an ECMO circuit for greater than six hours:

- Gas Exchange Failure
- Fiber Leakage
- Clotting
- Pressure drop increase

In patients with viremia there is the theoretical possibility of passage of virus from blood through the fiber membrane into the exhaled gas from the oxygenator, particularly in the presence of plasma leakage across the membrane. No specific testing has been performed to evaluate the likelihood of this occurrence and clinical evidence is insufficient to quantify any associated risks. Use of polymethylpentene (PMP) membrane oxygenators may mitigate the risk of virus passage across the oxygenator membrane. Local Standard Operating Procedure (SOP) of the institution for dealing with infectious patients should be followed throughout device operation.

Clinical Signs and Observations that suggest device change-out is required

General indications are provided on Instructions for Use at paragraph "N. DEVICE CHANGE-OUT". For specific change-out clinical signs and observations refer to "Extracorporeal Life Support Organization (ELSO) General Guidelines for all ECLS Cases - August, 2017 – version 1_4":

- Per the Extracorporeal Life Support Organization (ELSO) Guidelines for Adult Respiratory Failure, a membrane oxygenator will be selected for goal rated flow based on gas transfer and surface area. ((ELSO), 2017, p. 8) These factors will contribute to maximal oxygen delivery and carbon dioxide clearance. If a membrane oxygenator is failing to provide rated flow or minimal gas transfer, or the upsaturation of inlet blood of 65% to exit saturation of 95% or less, and blood and gas flow goals are met, it may be advisable to exchange the membrane oxygenator component due to failing gas exchange. Failure of blood or gas flow goals may indicate a phase obstruction, and also warrant exchange.
- ELSO Guidelines also support the use of multiple membrane oxygenators in parallel in the event of inadequate gas exchange achieved by a single membrane. Further, water vapor can condense in the membrane lung resulting in poor CO2 clearance, and may be cleared by intermittently increasing sweep gas flow to a higher flow. ((ELSO), 2017, p. 9)
- Clotting in the circuit is detected by careful examination, using a flashlight to go over all the extracorporeal circuit. Clots are seen as very dark nonmoving areas on the surfaces. Every circuit will have some small clots at the site of connectors, infusion lines, or in areas of low flow in the pre-pump or the membrane lung. These clots are in the range of 1 to 5 mm, do not require circuit changes, and are simply observed. Clots larger than 5 mm or enlarging

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clots on the infusion side of the circuit (post membrane lung) should be removed by removing that section of the circuit or by changing the entire circuit if there are many such clots. Platelet/fibrin thrombi appear as white areas on the circuit at connectors and stagnant sections. These are clots which have not accumulated red cells, usually because they are in areas of very high flow. As with dark clots, no intervention is necessary unless the white thrombi are greater than 5 mm or growing. ((ELSO), 2017, p. 18)

- Pre and post membrane lung pressure and alarms. These measurements will determine the transmembrane lung pressure gradient. Clotting in the oxygenator is represented by increasing membrane lung pressure gradient. ((ELSO), 2017, p. 10)

In addition, the following phenomena should be monitored:

- Oxygenator fiber leaks
- Pressure drop increase and/or inability to guarantee sufficient blood flow

If any of the above conditions are observed, consider change-out of the oxygenator.

Use Conditions

The extracorporeal circulation is intended to temporarily bypass the heart and lungs function by an external circuit, where single components work independently but in synergy with each other.

When using the device in ECMO procedures, do not use in conjunction a venous reservoir and an arterial filter.

Care must be taken to monitor inflow conditions to the pumping mechanism that will feed the oxygenator. Air ingress and reduced preload conditions may impact therapeutic goals of flow delivery.

See Instructions for Use at paragraph “C. INTENDED USE” and “D. CONTRAINDICATIONS”

References

1. Kalbhenn J, Schlagenhauf A, Rosenfelder S, Schmutz A, Zieger B. Acquired von Willebrand syndrome and impaired platelet function during venovenous extracorporeal membrane oxygenation: Rapid onset and fast recovery. J Heart Lung Transplant 2018;37:985-91.
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3. Lehle K, Philipp A, Muller T, et al. Flow dynamics of different adult ECMO systems: a clinical evaluation. Artif Organs 2014;38:391-8.
4. Salazar LA, Schreuder CM, Eslava JA, et al. Extracorporeal Membrane Oxygenation in Dengue, Malaria, and Acute Chagas Disease. ASAIO J 2017;63:e71-e6.
5. Extracorporeal Life Support Organization. Guidelines for Adult Respiratory Failure.Version 1.4.

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