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Efferon® LPS

Extracorporeal blood adsorber

The Instructions for use

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Efferon® LPS

1. INTENDED PURPOSE

Device is intended for the extracorporeal purification of blood by selective adsorption of lipopolysaccharides and non-selective adsorption of cytokines, myoglobin, cellular debris, endogenous and exogenous toxic substances. Efferon® LPS is a non-pyrogenic, gamma-sterilized, single-use device.

2. DESCRIPTION OF THE DEVICE

Efferon® LPS is a sealed polycarbonate cylinder with two dialysis-type connectors at the edges, filled with a suspension of polymeric adsorbent beads in an isotonic (0,9 %) sodium chloride solution. Efferon® LPS is used in intensive care units, departments of hemodialysis departments, and for extracorporeal treatment methods.

3. INDICATIONS

- Sepsis of verified or suspected gram-negative aetiology, including septic shock
- Elevated levels of endotoxin in blood, critical endotoxemia
- Elevated levels of cytokines in blood, “cytokine storm” syndrome

Therapy protocol:

- First treatment for 6-12 hours;
- Second treatment for another 6-12 hours.

Clinical assessment to be made after second treatment to determine if the patient is receiving clinical benefit for continuation of therapy.

4. CONTRAINDICATIONS

- Uncorrected hypovolemia
- Uncontrolled bleeding
- Anaphylactic or nonspecific reaction to the components of the extracorporeal circuit
- Pregnancy

5. TARGET PATIENT GROUP AND INTENDED USERS

- Efferon® LPS is intended for use in adult patients ≥18 years old.
- Efferon® LPS should only be used by qualified intensivists, perfusionists, anesthesiologists, nephrologists, transfusion specialists.

6. LIMITATIONS

- Efferon® LPS should only be administered by personnel who have been properly trained in administration of extracorporeal therapies.
- Efferon® LPS is used in the Intensive care units (ICUs), departments of hemodialysis departments, and for extracorporeal treatment methods.
- Access and Resource Requirements.Hemoperfusion typically requires specialized equipment including the availability of suitable hemoperfusion devices and extracorporeal circuits. Access to hemoperfusion may be limited in certain healthcare settings or regions, which can restrict its widespread use and availability.
- Hemoperfusion therapy can be costly due to the specialized equipment, consumables, and expertise required. The cost-effectiveness of hemoperfusion compared to alternative treatments or supportive care approaches should be carefully evaluated in each specific clinical case.

7. WARNINGS

- Patients with disseminated intravascular coagulation, thrombocytopenia and low body weight should undergo the treatment with extra caution.
- Efferon® LPS should only be removed from the sterile vacuum pouch immediately before use and under aseptic conditions.
- The extracorporeal circuit should be monitored continuously during treatment for blood leaks.
- Inlet pressures above 300 mmHg may be indicative of circuit clotting and can yield to hemolysis.
- Vital functions should be continuously monitored during hemoperfusion.
- The timing and duration of hemoperfusion therapy can significantly impact its effectiveness. It is crucial to initiate treatment at the right time and continue it for an appropriate duration to maximize the potential benefits. Determining the optimal timing and duration can be complex, and it may vary based on the specific conditions, patient characteristics, and disease progression.

8. GENERAL PRECAUTIONS

Efferon® LPS should only be used by qualified personnel experienced in extracorporeal therapy.

Common risks of extracorporeal therapy include:

- Hypovolemia
- Bleeding
- Catheter infection
- Air embolism
- Individual intolerance to components of the extracorporeal circuit
- Increased clearance of drugs
- Hemolysis
- Decrease in platelets level
- Premature circuit clotting (insufficient dose of hemoperfusion, economic losses)

The extracorporeal circuit should be monitored continuously during treatment to prevent complications associated with extracorporeal therapies such as blood loss caused by leaks, hypothermia, dyspnea, hypotension, and death caused by air embolism. No hypersensitivity reactions during the use of Efferon® LPS have been previously reported. However, the possibility of such reactions cannot be excluded. Should hypersensitivity reaction be suspected hemoperfusion should be terminated immediately.

Efferon® LPS is a single-use device. Reuse may result in device clotting, hemolysis, and secondary intoxication/infection.

9. POTENTIAL SIDE EFFECTS

- Short-term hemodynamic disorders (increased need for vasopressor support, a decrease in cardiac output) due to the partial withdrawal of circulating blood volume into the extracorporeal circuit
- Risks associated with anticoagulation (bleeding, allergic reactions, heparin-induced thrombocytopenia)
- Unintended removal of other blood substances, unwanted loss of medicinal substances, nutrients and heat
- Hemolysis
- Thrombocytopenia, leukopenia
- Clotting in the extracorporeal circuit
- Blood loss and air embolism due to decompression of the extracorporeal circuit
- Risks related to vascular access placement (e.g. infection, blood loss, thrombosis, tissue/organ injury)

10. CLINICAL BENEFITS

The most recent clinical data obtained using Efferon® LPS and analogous hemoperfusion devices suggest the following clinical benefits:

- successful resolution of septic shock and restoration of systemic hemodynamic function (65 % proportion of responders);
- multiple Organ Failure Syndrome faster resoluton (reduce of SOFA score by ≥2 points within 3 days) (75 % proportion of responders);
- decrease of vasopressor drugs dosage, required to maintain mean arterial pressure above 65 mm Hg, by ≥70 % during 3 days (50 % proportion of responders);
- oxygen metabolism function improvement expressed as 20 % increase of PaO2/FiO2 during 3 days (50 % proportion of responders).

Critical patients, intended to be treated with Efferon® LPS hemoperfusion, represent a highly heterogeneous population. Course and outcome of their treatment depends on the source control of the infection, adequacy of antibiotic therapy, fluid management, respiratory support, time window of the intervention, and many other variables. A certain subpopulation of patients does not always respond to hemoperfusion therapy with expected benefits. Hemoperfusion is an adjuvant treatment. It cannot be regarded as monotherapy with independent stand-alone benefits.

11. PERFORMANCE CHARACTERISTICS

Design	Efferon® LPS is a sealed polycarbonate cylinder filled with a suspension of adsorbent beads in an isotonic sodium chloride solution with two dialysis-type connectors at the edges
Dimensions	Diameter × length: 60 × 220 mm
Polymeric adsorbent	Hypercrosslinked styrene-divinylbenzene copolymer surface-modified with an LPS selective ligand
Weight	350 g
Inner Volume	210 mL
Appearance	Device is filled with 190 mL of adsorbent. Remaining free space between adsorbent beads is filled with 0,9 % sodium chloride solution
Sterilisation	Radiation sterilisation
Packaging	Efferon® LPS is packaged in non-toxic PE/PA bag, welded on both sides with at least 5 mm seam
Recommended blood flow rate	100-300 mL/min
Maximum blood flow rate	700 mL/min
Maximum circuit pressure	up to 700 mmHg

12. DEVICE CONNECTION TO THE EXTRACORPORAL CIRCUIT

Required equipment and consumables

Efferon® LPS is intended for use with standard, commercially available bloodlines compatible with the standard pump system. Female blood line DIN connectors are required to connect with Efferon® LPS blood ports. Efferon® LPS may be used with extracorporeal blood pumps, e.g. intermittent hemodialysis, continuous renal replacement therapy (CRRT), and extracorporeal membrane oxygenation (ECMO) equipment where hemofilters/dialyzers are used.

Minimal equipment and consumables consist of:

- perfusion pump with hemoperfusion mode and monitoring equipment (measurement of blood flow and pressure gradient) and an air trap,
- double lumen/two-way perfusion catheter,
- a set of bloodlines for extracorporeal blood purification,
- 0,9 % sodium chloride solution (1 liter),
- heparin or sodium citrate,
- bag for collecting the rinsing solution.

Preparation

Efferon® LPS is intended to be used with commercially available bloodlines connected to devices for renal replacement therapy (RRT), heart-lung machine (HLM) or extracorporeal membrane oxygenation (ECMO). Connecting elements – standard dialysis threaded connectors (DIN-lock). It is possible to carry out hemoperfusion both in stand-alone or in combination with RRT, ECMO and HLM. In combination with RRT, Efferon® LPS is connected in series before or after the dialyzer/hemofilter. In combination with ECMO/HLM, Efferon® LPS is con-

CE 2265

Efferon OÜ
Harju maakond, Tallinn,
Kristiine linnaosa, Mooni tn 18,
10613, Estonia
Email: mail@efferon.com
Phone: +37256310093

nected in bypass mode. Special bloodline adapters are required for such integration.

Device must be sterile and hermetically sealed and could be used only after a thorough visual inspection. Do not use Efferon® LPS if there's any damage of vacuum packaging, sterility of device itself or after the expiration date indicated on the packaging. In case of detection of defects in sterile packaging, resulting in a violation of sterility, you must contact the manufacturer. Unpacking and connection of bloodlines to ports should be performed under aseptic conditions. Device must be rinsed before hemoperfusion.

Gravity rinsing

1. Take a bag with one liter of sterile isotonic (0,9 %) sodium chloride solution and 10.000 IU of heparin and connect the rinsing bloodline to it. Prime the bloodline with saline to purge air.

2. Mount Efferon® LPS into the holder in a vertical position.

3. Remove the cap from the bottom port of Efferon® LPS and connect the pre-filled rinsing bloodline to it.

4. Remove the cap from the upper port of the Efferon® LPS, connect the rinsing bloodline to it, and apply a clamp to it.

5. Connect the outlet from the rinsing bloodline to the rinse solution collection bag.

6. Remove the clamps from the rinsing bloodlines and rinse Efferon® LPS with roughly one liter of rinsing solution. Tap the device gently to purge air.

7. Apply clamps to both rinsing bloodlines. Disconnect and discard the filled saline bag. The device is ready for use!

Perfusion pump rinsing

1. Mount Efferon® LPS into the holder in a vertical position.

2. Connect the red and blue bloodlines to the bottom and upper ports of the Efferon® LPS.

3. Fill the blood circuit with sterile isotonic (0,9 %) sodium chloride solution and 10.000 IU of heparin according to the user manual for the perfusion pump.

4. In recirculation mode, rinse the device with roughly one liter of rinsing solution at a rate of (100-200) mL/min. Tap the device gently to purge air. The device is ready for use!

⚠ **Caution!** After priming of adsorber with one liter heparinized rinsing solution, a fraction of heparin (2.000-2.500 IU) remains in the system (inside the adsorber and the bloodlines) and can be subjected to reinfusion when the treatment starts. For the **patients with intolerances to heparin**, lower body weights and higher risks of hemorrhagic complications this can yield additional hazards. In these cases, on discretion of physician, **another mode of rinsing (i.e. without heparin) should be considered.**

Initiation of treatment

1. Assemble and fill the circuit on the perfusion machine according to its user manual.

2. Stop the blood pump and close both bloodlines with clamps (red one (arterial) must be pre-filled).

3. Disconnect the rinsing bloodlines from Efferon® LPS and connect the blood lines of the extracorporeal circuit to it, ensuring that no air enters into the circuit.

4. Remove both clamps and turn on the blood pump.

Anticoagulation

Systemic (heparin): Before and during extracorporeal therapy maintain an anticoagulation level of (160-210) seconds ACT or (60-80) seconds aPTT.

Regional (sodium citrate): a hemodialyzer/hemofilter should be used downstream of Efferon® LPS to remove calcium citrate complexes.

Hemoperfusion

Set the necessary parameters of the procedure depending on the indications for extracorporeal therapy.

Therapy protocol:

- First treatment for 6-12 hours;
- Second treatment for another 6-12 hours.

Clinical assessment to be made after second treatment to determine if patient receives clinical benefit for continuation of therapy.

Adsorption clearances are decreasing over time due to deposition of plasma proteins (similar to "membrane clogging") so initial hours of hemoperfusion would yield more efficient removal than subsequent hours. Exact duration of treatment is always reliant on a clinical context. The permissible duration in the circuit is 24 hours.

Recommended blood flow rate through the device:

- 100-150 mL/min for isolated hemoperfusion;
- 150-300 mL/min for combination with RRT.

Termination of treatment

Displace blood from the circuit using isotonic (0,9 %) sodium chloride solution. This requires the following steps.

1. Disconnect the red line from the perfusion catheter and connect it to the bag with sterile isotonic sodium chloride solution.

2. Turn on the infusion pump and replace the blood out from the extracorporeal circuit.

3. Disconnect the blue bloodline from the catheter.

13. MEDICAL DEVICE MATERIALS

Device part	Material
Cylindrical casing	Polycarbonate
Cover	Polycarbonate
Filter	MABS (Terlux), PES
Silicone ring	Silicone
Small silicone rings	Silicone
Blood-conducting cavity plug	Polypropylene
Polymeric adsorbent "Efferon LPS"	Hypercrosslinked styrene-divinylbenzene copolymer surface-modified with LPS-selective ligand
Infusion solution	0,9 % sodium chloride solution
Self-adhesive indicator of the radiation sterilization process	Cellulose paper (wood-free paper)
Self-adhesive label	Cellulose paper
Individual packing	PE/PA bag: Multilayer bag from PE/PA (Polyethylene/ Polyamide)

14. TRANSPORTATION AND STORAGE

Transportation of the device and components in transport packaging must be carried out by any type of ground and air transport in accordance with the rules for the carriage of goods in force for this type of transport.

Transportation is carried out within the temperature range of 5 – 25 ºC and relative humidity from 20 % to 80 %.

Storage is carried out within the temperature range of 5 – 25 ºC and relative air humidity from 20 % to 80 %.

The application of medical device is carried out within the temperature range of 5 – 25 ºC and relative air humidity from 20 % to 80 %.

Devices should be stored indoors in consumer packaging and should be protected from direct sunlight.

It is not allowed to store products near sources of bright light and ultraviolet radiation, open containers with alkalis, acids, oils, gasoline and other organic solvents.

15. CONDITIONS OF DISPOSAL

If the medical device has been used, dispose of in accordance with local regulations in force.

Unused medical device is solid household waste.

⚠ **Attention!** A used medical device is a potentially biohazardous waste.

16. MANUFACTURER'S WARRANTY

The manufacturer guarantees compliance of products with the requirements of the technical documentation within the warranty period, provided that the consumer observes the rules of transportation and storage.

The guaranteed shelf life of the devices is 3 years from the date of sterilization within the temperature range of 5 – 25 ºC.

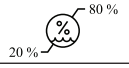
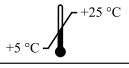
In the event of defects in device and packaging or missing labels, the supplier of the product should be notified. During the warranty period, the manufacturer replaces defective devices free of charge, unless the damage is the result of improper operation, transportation, storage or mechanical damage.

17. COMPLAINTS

For all questions related to the operation of the product, contact the manufacturer.

Please kindly be informed that any serious incident that has occurs in relation to the device should be reported to the manufacturer using the contact details provided on the cover page of this document and the competent authority of the Member State in which the user and/or patient is established.

18. EXPLANATION OF SYMBOLS

	Keep dry
	Fragile; handle with care
	Keep away from sunlight
	Manufacturer
	Sterilized using irradiation
	Single sterile barrier system
	Single sterile barrier system with protective packaging outside
	Do not re-use
	Do not use if package is damaged and consult instructions for use
	Consult instructions for use
	Caution
	Serial number
	Catalogue number
	Batch code
	Use by date
	Date of manufacture Country of manufacture
	Do not resterilize
	Humidity limitation
	Temperature limit
	Non-pyrogenic
	Medical device
	Unique device identifier
	European conformity