

Efferon® LPS Clinical Practice Guidance

Manufacturer's Recommendations for Safe and Effective Application of Efferon Hemoadsorption Therapy

The role of hemoadsorption therapy is steadily expanding, particularly in acute care settings for the management of sepsis and severe systemic inflammation. However, despite its growing use and supporting evidence, there are still no internationally recognized clinical guidelines that clearly define *when* and *how* this therapy should be applied in daily clinical practice. As a result, many physicians currently rely on personal experience or peer exchange between hospitals.

This document has been developed by Efferon OÜ, the manufacturer of the Efferon® LPS device, to provide practical, evidence-based recommendations drawn from published studies, ongoing research, and real-world clinical experience. Its purpose is to support physicians in using Efferon® Therapy safely, effectively, and with confidence in their intensive care settings.

This Clinical Practice Guidance is intended for healthcare professionals involved in the care of patients with sepsis, septic shock, or other severe inflammatory conditions. It is not a formal treatment protocol and does not replace clinical judgment. Rather, it serves as a practical, IFU-aligned reference summarizing current best practices and accumulated clinical experience.

The document provides structured recommendations to guide the prescription, preparation, and clinical application of Efferon® LPS therapy in adult ICU patients. Its goal is to promote the consistent and safe integration of hemoadsorption as an adjunctive treatment alongside established intensive care measures, including source control, antimicrobial therapy, and organ support.

Note: Clinicians should always refer to the most recent version of the Efferon® LPS IFU for detailed technical and safety information before starting therapy.

Each treatment decision should be based on the individual patient's condition and made by the responsible medical team.

1. Core Indications

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

Note: Hemoadsorption is most effective when initiated early—before irreversible organ damage occurs.

2. Identifying suitable patients

- Documented diagnosis of sepsis or septic shock confirmed according to SEPSIS-3 criteria.
- Persistent or escalating vasopressor requirement, defined as the need for at least one of the vasopressors listed below at or above the specified dose:
 - Norepinephrine > 0.05 µg/kg/min
 - Dopamine > 10 µg/kg/min
 - Phenylephrine > 0.4 µg/kg/min
 - Epinephrine > 0.05 µg/kg/min
 - Other vasopressors (any dose) in combination with the above agents
- Progressive organ dysfunction (reflected by increasing SOFA score and/or clinical signs of worsening ARDS or AKI).
- Continuous intravenous infusion therapy at a rate of at least 30 mL/kg administered within 24 hours after inclusion (performed under dynamic hemodynamic monitoring and bedside ultrasound control).
- Early postoperative period ($\leq$ 24 hours after surgery when performed as a required source-control or revision procedure).
- The patient’s condition allowed the use of the Efferon® LPS cartridge for at least 4 hours.

NOTE: Hemoadsorption therapy may be initiated if any of the above criteria are met, the patient’s condition allows the use of the Efferon® LPS cartridge for at least 4 hours, and the treating team considers the patient clinically suitable for Efferon® LPS therapy.

3. Key safety considerations

3.1 Use with caution/ contraindications

- Uncontrolled bleeding, uncorrected hypovolemia, pregnancy.
- Anaphylactic or nonspecific reaction to the components of the extracorporeal circuit.

3.2 General precautions

Efferon® LPS should be used only by qualified healthcare professionals experienced in extracorporeal blood purification therapies. As with any extracorporeal procedure, certain risks may occur, including hypovolemia, bleeding, catheter-related infection, air embolism, individual intolerance to components of the extracorporeal circuit, increased clearance of concomitant medications, hemolysis, thrombocytopenia, or premature circuit clotting, which may result in insufficient treatment dose or economic loss.

3.3 Antibiotic Management

Recent clinical data on Efferon® LPS therapy demonstrated that adsorption of commonly used antibiotics is minimal when hemoadsorption is initiated within 30 minutes after antibiotic infusion. The observed adsorbed fractions were approximately 5% for vancomycin, 12% for meropenem, and 20% for linezolid.

As a general recommendation, it is advisable to start Efferon® Therapy at least 30 minutes after completing antibiotic administration to minimize drug adsorption and ensure optimal antimicrobial exposure.

4. How to perform the treatment

4.1 General workflow

- Initiate early once criteria are met and contraindications are excluded.
- Standard course:
 - Perform one treatment session lasting 4 to 12 hours.
 - After completion of the first cartridge, the treating physician should reassess the patient's clinical condition to determine whether additional hemoadsorption sessions are required.

4.2 When to Stop or Replace the Device

- If circuit pressure increases (TMP or ΔP [inlet–outlet] > 150 mmHg; inlet pressure > 200 mmHg) or if the adsorber shows visible signs of clotting, the cartridge should be replaced, or the treatment session should be terminated.
- In cases where prolonged or repeated therapy is clinically indicated, a new Efferon® LPS cartridge may be connected. The decision to continue or repeat treatment should always be based on the patient's clinical condition and the professional judgment of the treating team.

4.3 Connection modes

Follow the *Instructions for Use (IFU)* and the circuit assembly guide when setting up the system. Efferon® LPS can be connected and operated in the following modes:

- Isolated hemoadsorption
- In combination with RRT, ECMO, or CPB systems

4.4 Priming

- Rinse with ≥ 1 L of saline and 10,000 IU of heparin.
- Maintain aseptic conditions and remove all air.

4.5 Blood flow rate (Qb)

- Isolated hemoadsorption: 100–150 mL/min.
- Maximum flow rate 700 mL/min for the combined therapy.

4.6 Pressure safety limits

- ΔP (inlet–outlet) ≤ 150 mmHg; inlet ≤ 200 mmHg.

4.7 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): as per local CRRT protocol; a hemodialyzer/hemofilter should be used downstream of Efferon® LPS to remove calcium citrate complexes.

4.8 Monitoring during treatment

Close observation throughout hemoadsorption therapy is essential to ensure that the procedure proceeds safely and effectively. Patients should be monitored in the same way as during any other extracorporeal treatment, with particular attention to hemodynamic stability, anticoagulation status, and the function of the extracorporeal circuit.

- Continuous: hemodynamics, vasopressors, circuit pressures, alarms.
- Intermittent: labs, oxygenation, coagulation, electrolytes.
- Response signals: $\downarrow$ vasopressors, improved MAP, $\text{PaO}_2/\text{FiO}_2$, organ function stabilization.

5. Clinical Benefits

Recent clinical data obtained using Efferon® LPS and other 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 resolution (reduction 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 in PaO₂/FiO₂ during 3 days (50 % proportion of responders).

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