CytoSorb® Guide

Practice Manual

CytoSorbents™

WORKING TO SAVE LIVES

Literature / Disclaimer

* Brouwer et al., Hemoadsorption with CytoSorb® shows a decreased observed versus expected 28-day all-cause mortality in ICU patients with septic shock: a propensity-score-weighted retrospective study. Crit Care 2019; 23(1):317
* Hawchar et al., Extracorporeal cytokine adsorption in septic shock: A proof of concept randomized, controlled pilot study. J Crit Care 2019; 49:172-178
* Friesecke et al., Extracorporeal cytokine elimination as rescue therapy in refractory septic shock: a prospective single-center study. J Artif Organs 2017; 20(3):252-259
* Kogelmann et al., Hemoadsorption by CytoSorb® in septic patients - a case series. Crit Care 2017; 21(1):74
* Garau et al., Hemadsorption during cardiopulmonary bypass reduces interleukin 8 and tumor necrosis factor α serum levels in cardiac surgery: an RCT. Min Anesth 2019; 85(7):715-723
* Calabro et al., Blood Purification With CytoSorb® in Critically Ill Patients: Single-Center Preliminary Experience. Artif Organs 2019; 43(2):289-294
* Traeger et al., Hemodasorption treatment of patients with acute infective endocarditis during surgery with cardiopulmonary bypass - a case series. Int J Art Organs 2017; 40(5):240-249
* Buttner et al., Application of Hemoadsorption in a Case of Liver Cirrhosis and Alcohol-Related Steatohepatitis with Preexisting Hepatitis C Infection. Blood Purif 2017; 44(1):30-31
* Friesecke et al., International registry on the use of the CytoSorb® adsorber in ICU patients: Study protocol and preliminary results. Med Klein Intens Not 2019; 114(8):699-707
* Kuehne et al., Comparison of intra-operative versus intra- plus postoperative hemoadsorption therapy in cardiac surgery patients with endocarditis. Int J Artif Organs 2019; 42(4):194-200
* Traeger et al., Hemoadsorption treatment with CytoSorb® in patients with extracorporeal life support therapy: A case series. Int J Artif Organs 2020; 43(8):422-429
* Hassan et al., CytoSorb® adsorption during emergency cardiac operations in patients at high risk of bleeding. The Annals Thorac Surgery 2019; 108(1):45-51
* Napp et al., Rationale of Hemoadsorption during Extracorporeal Membrane Oxygenation Support. Blood Purif 2019; 48(3):203-214

Visit
www.cyto.zone/literature
for an overview of all references.

Table of contents

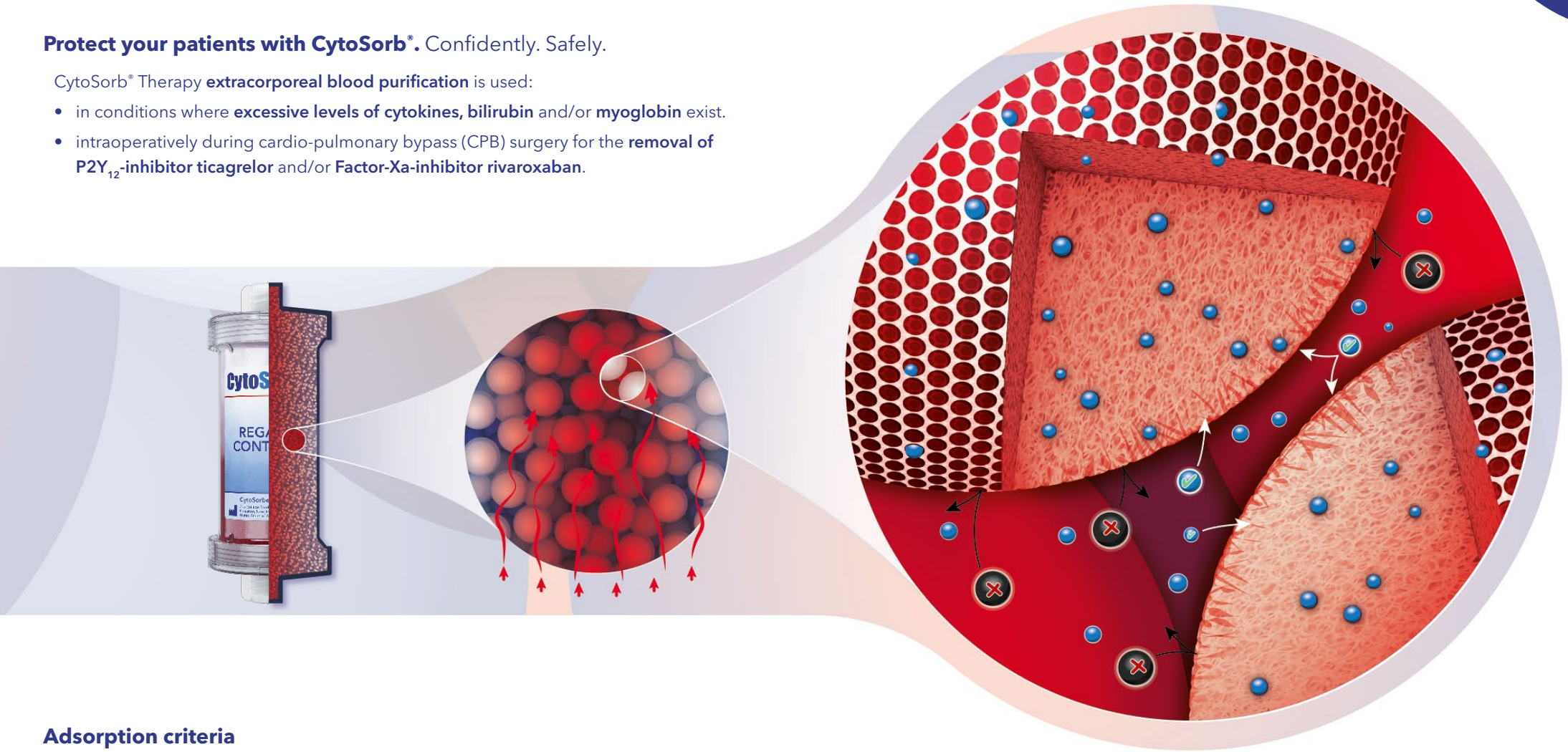
01

CytoSorb® 300

Protect your patients with CytoSorb®. Confidently. Safely.

CytoSorb® Therapy **extracorporeal blood purification** is used:

- in conditions where **excessive levels of cytokines, bilirubin** and/or **myoglobin** exist.
- intraoperatively during cardio-pulmonary bypass (CPB) surgery for the **removal of $P2Y_{12}$-inhibitor ticagrelor** and/or **Factor-Xa-inhibitor rivaroxaban**.



Adsorption criteria

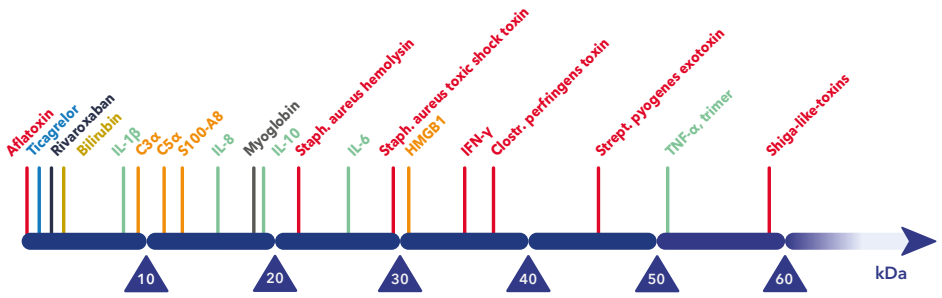
Hydrophobic attraction to surface

Concentration dependent

Size selection <60 kDa

How CytoSorb® works

CytoSorb® is a technology complementary to dialysis that removes a broad range of substances that conventional dialysis does not remove.



CytoSorb® specifically removes

- Cytokines
- Bilirubin
- Myoglobin
- Ticagrelor
- Rivaroxaban

Beads matter

CytoSorb® is a whole blood adsorber with high efficiency and rapid clearance thanks to:

- **proprietary porous polymer beads** preventing or reducing surface activation, blood clotting, cell adhesion, hemolysis, and complement activation
- **millions of optimally-sized pores and channels** in the beads providing a huge internal surface area and massive adsorption capacity (<60 kDa)
- **tightly packed beads** with high flow, low resistance matrix with uniform blood flow, optimizing blood and bead contact
- **safe and easy setup** with just saline flushing, no heparinization needed during priming

Proven Safety

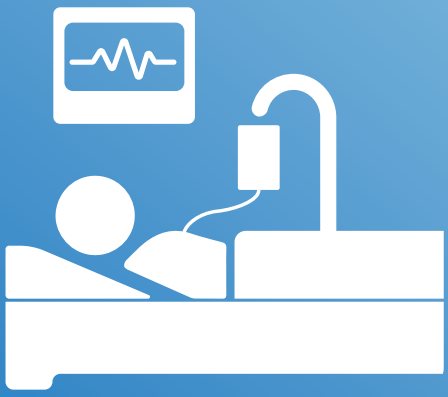
CytoSorb® has been shown in clinical studies to have:

- concentration dependent removal [1]
- no activation of the coagulation and complement systems [2, 3]

References:

1. Song et al., Blood Purif 2004; 22(5):428-434
2. Bernardi et al., Crit Care 2016; 20(1):96
3. Gleason et al., Sem Thorac Cardiovasc Surg 2019; 31(4):783-793

Critical Care



Decision support for initiating CytoSorb® Therapy: Timing, duration, criteria

The score can be taken 6 hours after diagnosis of septic shock/start of standard therapy to define severity and support decision making in regards to initiation of CytoSorb® Therapy.

	0 Points	1 Point	2 Points
Lactate mmol/l	< 2.0		≥ 2.0
Lactate change / 6 hours	↓ decrease	↑ ≤ 50%	↑ > 50%
NE* µg/kg/min (MAP** ≥ 65)	< 0.1		≥ 0.1
NE* change / 6 hours	↓ decrease	↑ ≤ 50%	↑ > 50%
2nd catecholamine / 2nd vasopressor	No	Yes	
Hydrocortisone use	No	Yes	
Volume Bolus 30 ml/kgbw***	No	< 2 Boli	≥ 2 Boli

* Norepinephrine
** Mean Arterial Pressure
*** Kilogram Body Weight

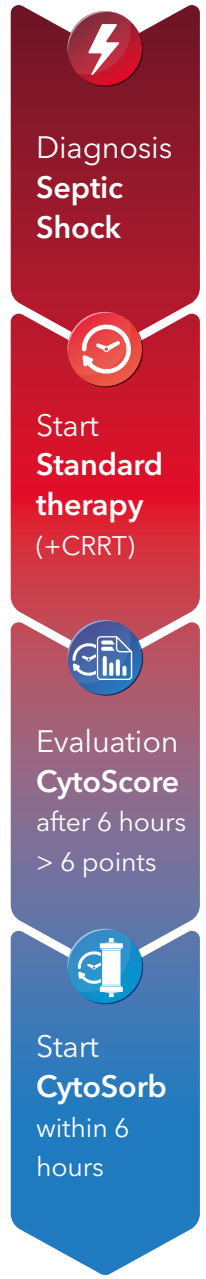
Visit
www.cyto.news/cytoscore
for the digital version of the CytoScore

Note

Final prospective validation of the score is still pending, however first retrospective evaluation of the score observed outcome benefits, when CytoSorb® Therapy was initiated in septic shock patients with the following criteria:

- **Indication for CRRT due to AKI**
- **CytoScore at hour 6 of > 6 points**
- **Initiation of CytoSorb® Therapy < 12 hrs. after diagnosis of septic shock/start of standard therapy**

Reference: Kogelmann et al., J Clin Med 2021; 10: 2939



Patient selection

- Refractory septic/vasoplegic shock
- High (and increasing) need for vasopressors
- Inadequate response to standard of care
- Biomarkers (if available):
  - IL-6 > 500 pg/ml,
  - PCT > 3 µg/L,
  - Ferritin > 1000 µg/L

Timing

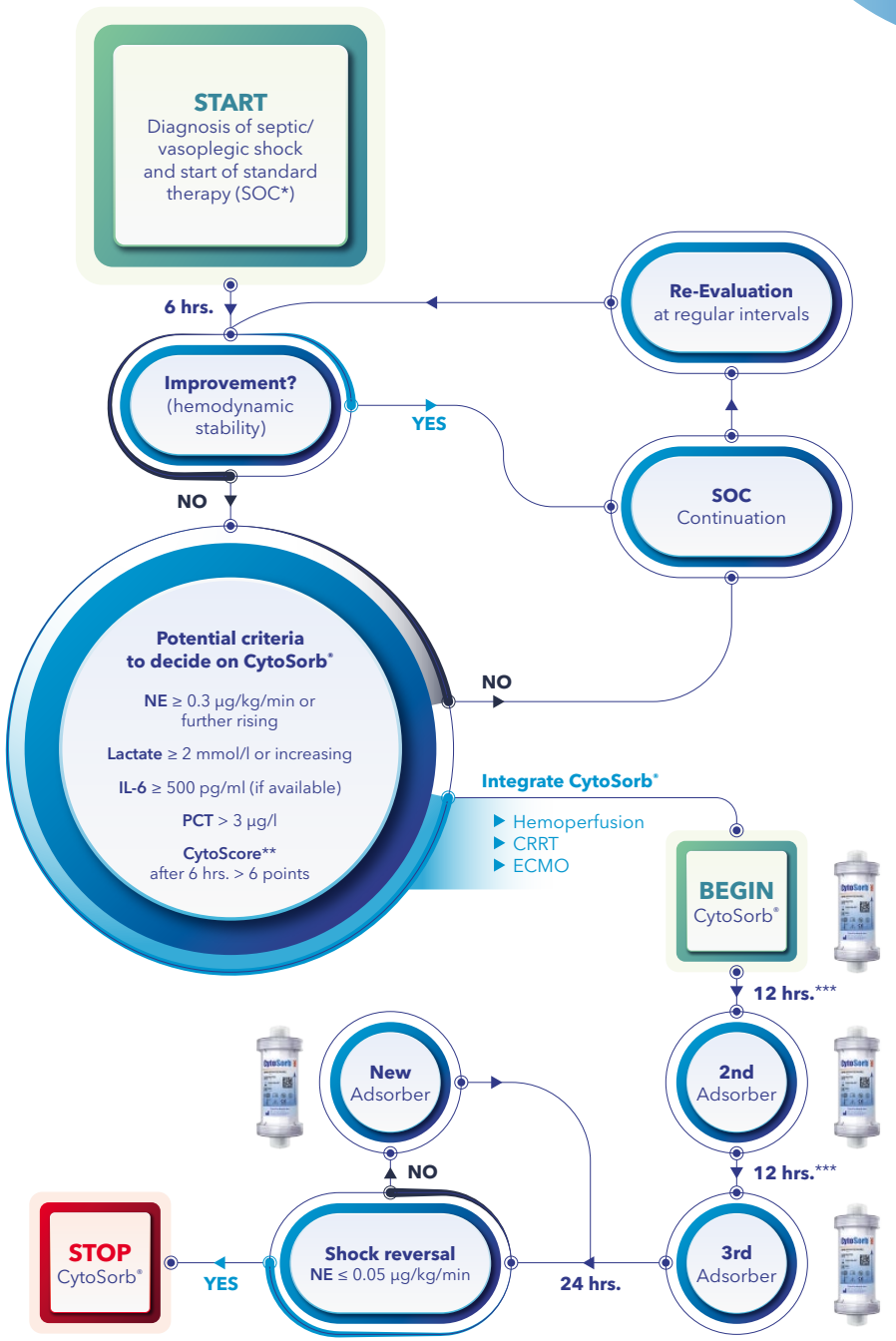
- Ideally < 12 hours after diagnosis/start of standard therapy
- Don't wait until lactate is > 6.5/7 mmol/L

Dosing

- Continue until sufficient hemodynamic stabilization is achieved
- Change after 12 hours if instability persists

Visit
www.cyto.zone/flow-sep/eng

for the digital version of the Flowchart septic/vasoplegic shock



* SOC: Standard of Care

** Reference: Kogelmann et al., J Clin Med 2021;10: 2939

*** Depending on the individual clinical course (e.g. persistent, pronounced reduction in the vasopressor dose under CytoSorb®), the indicated times can also be extended to longer intervals, or the therapy as a whole can also be terminated earlier. Sufficient control of the underlying cause is a prerequisite of therapeutic success.

Liver

Patient selection

- Bilirubin > 10 mg/dl (> 170 µmol/l)
- Hepatic encephalopathy grade ≥ 2
- Acute Liver Failure or Acute-on-Chronic Liver Failure grade 2-3
- Concomitant vasoplegic shock not responding to standard therapy (best to be used within first 24 hrs.)
- Onset of liver failure after surgery or transplantation
- Intractable pruritus

Timing

- Integrate CytoSorb® in hemoperfusion, CRRT or ECMO

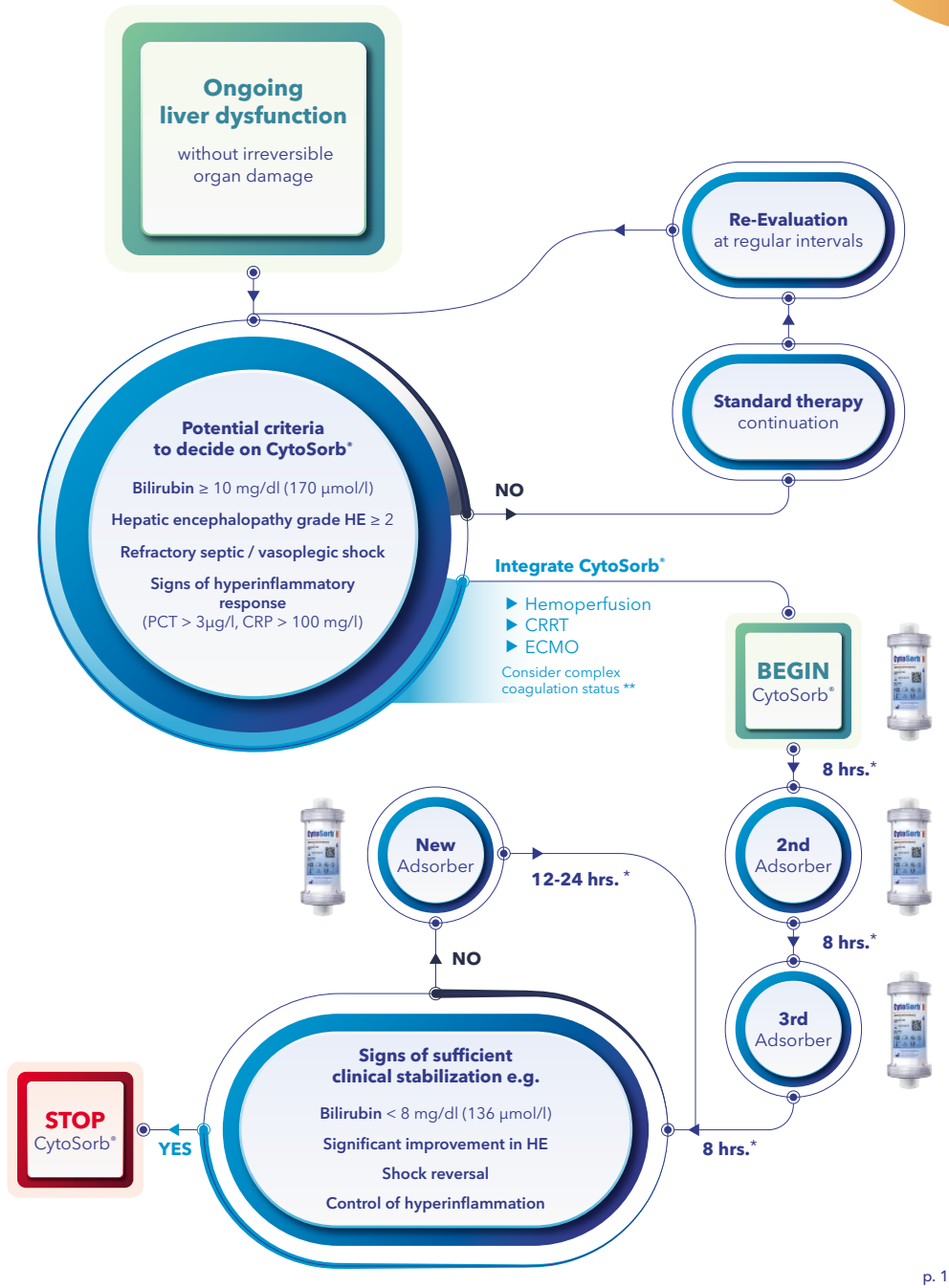
Dosing

- Consider changing the adsorber after 8 hours until sufficient stabilization/clinical improvement is seen

Visit

www.cyto.zone/flow-lvr/eng

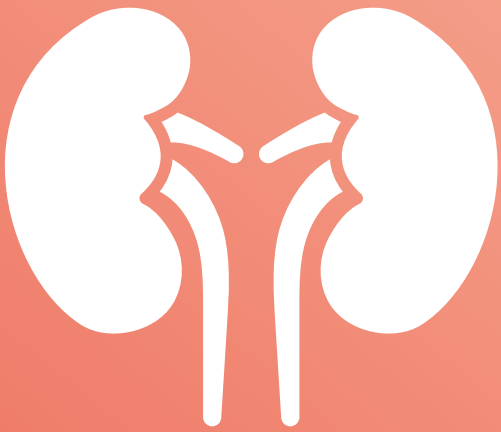
for the digital version of the Flowchart liver dysfunction



* Depending on the individual's clinical course (e.g. persistent pronounced reduction in bilirubin levels) it may be possible to deviate from the indicated times to longer intervals or even terminate the therapy earlier. If feasible, please consider consecutive pre-and post-adsorber blood sampling as aid for assessing saturation of the adsorber. Sufficient control of the underlying cause is a prerequisite for therapeutic success.

** Anticoagulation must be carefully implemented. Do not rely solely on PT or INR values.

Kidney



Patient selection

- Confirmed/ suspected rhabdomyolysis with impending/existing acute kidney injury (AKI)
- Myoglobin levels > 10,000 µg/l
- If myoglobin levels are unavailable, CK levels or myoglobinuria might provide clues as to the status or progression of the clinical condition (no direct removal of CK by the adsorber!)
- Contraindication for intensified fluid therapy

Timing

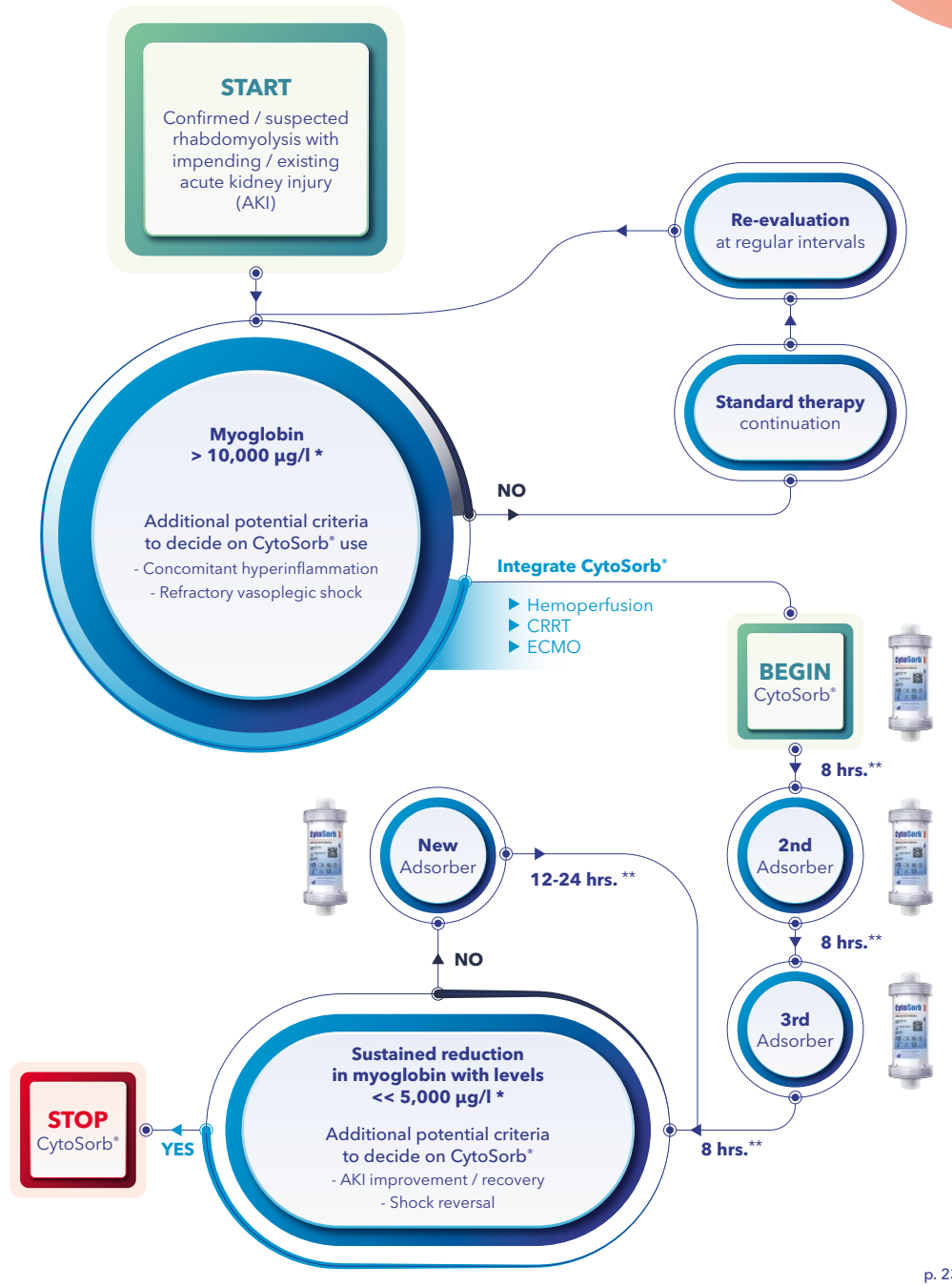
- Ideally start within the first 24 hrs. after diagnosis/onset of severe rhabdomyolysis
- In general start early before irreversible damage occurs

Dosing

- Consider changing adsorber after 8 hours until sufficient stabilization/clinical improvement has occurred or myoglobin levels well below 5000 µg/l have been reached.

Visit
www.cyto.zone/flow-rhabdo/eng

for the digital version of the Flowchart rhabdomyolysis



* If myoglobin values are unavailable, CK levels or myoglobinuria may provide clues as to the status or progression in the clinical condition, but it should be noted that there is no direct removal of CK by the adsorber.

** Depending on the individual's clinical course (e.g. persistent pronounced reduction in myoglobin levels) it may be possible to deviate from the indicated times to longer intervals, or even to terminate the therapy earlier. Sufficient control of the underlying cause is a prerequisite of therapeutic success.

Cardiovascular

Patient selection

- Patients undergoing cardiac surgery who were pretreated with ticagrelor and/or rivaroxaban, with last dose of
  - Ticagrelor < 72 hrs.
  - Rivaroxaban < 48 hrs.

Timing

- Start therapy with the start of CPB. CytoSorb® is easily integrated into the CPB circuit (post-pump to venous reservoir)

Dosing

- Postoperative continuation (with a new adsorber integrated into an extracorporeal circuit) is normally NOT needed if CPB time > 60 min, but can be done if needed.

Visit
www.cyto.zone/flow-atr/eng
for the digital version of the Flowchart antithrombotic removal

* CytoSorb® integration into CPB

** CPB times should ideally be >60 minutes to allow enough time for sufficient substance removal by CytoSorb®

Patient selection

CytoSorb® Therapy may be considered during cardiac surgery for acute/active high-risk IE. Additional criteria for clinical use of CytoSorb® intraoperatively in IE patients may be the following:

- Fever
- Highly elevated inflammatory parameters
- Hemodynamic instability requiring high vasoactive support
- Staphylococcus aureus as pathogen

Timing

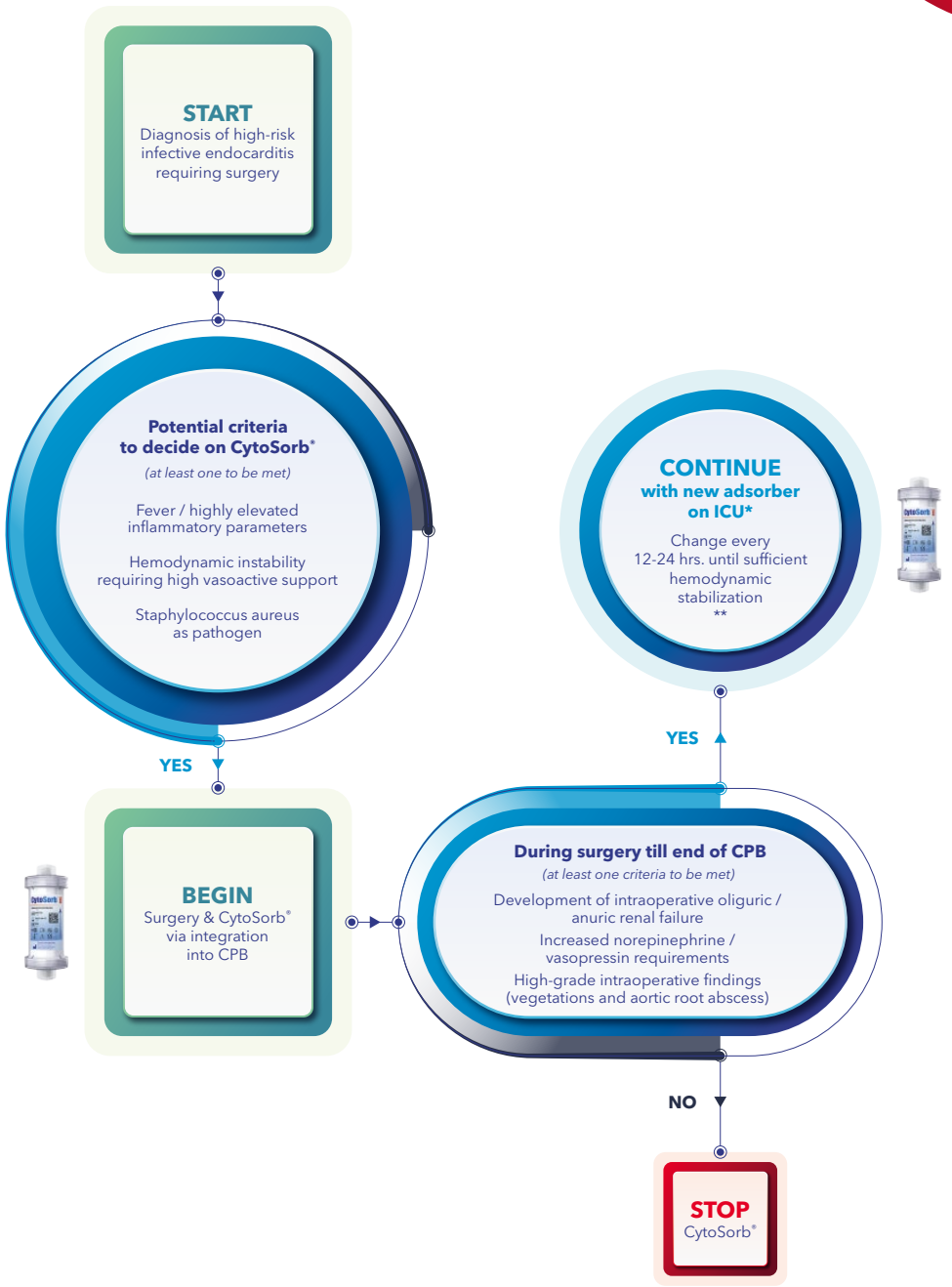
- Start therapy with the start of CPB. CytoSorb® is easily integrated into the CPB circuit (post-pump to venous reservoir)

Dosing

Consider postoperative continuation of CytoSorb® Therapy (with a new adsorber integrated into an extracorporeal circuit) in IE patients when the following signs are observed intraoperatively:

- Development of intraoperative oliguric/anuric renal failure
- Increased norepinephrine/vasopressin requirements
- High-grade intraoperative findings (vegetations and aortic root abscess)

Visit
www.cyto.zone/flow-ie/eng
for the digital version of the Flowchart infective endocarditis

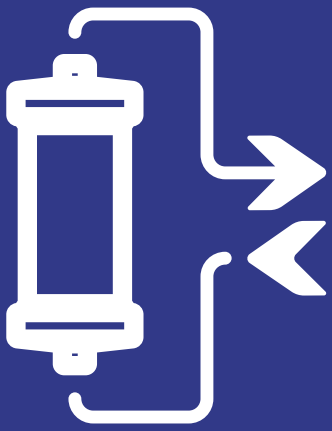


* Integration into CRRT, ECMO, Hemoperfusion

** For details please see CytoSorb® flowchart septic/vasoplegic shock

06

Quick Setup Guides



Visit
www.cyto.zone/setup

and learn more about
CytoSorb® integration options

Basic prerequisites

- CytoSorb® should be installed in a shunt off the main flow as is the current practice with hemoconcentrators
- Installation must never be into the main stream of a CPB or ECMO circuit
- Pressure or flow monitoring of the CytoSorb® bypass-line is recommended
- The recommended blood flow rate should be between 150 - 700 ml/min, with a minimum of 100 ml/min
- CytoSorb® is to be employed as an adjunctive, not as a causative therapy
- Treatment duration and indication for exchange of adsorber depends on the clinical course.
- The maximum treatment time per adsorber is 24 hours
- Continuous treatment is recommended rather than intermittent
- Contraindications for extracorporeal blood circuits apply

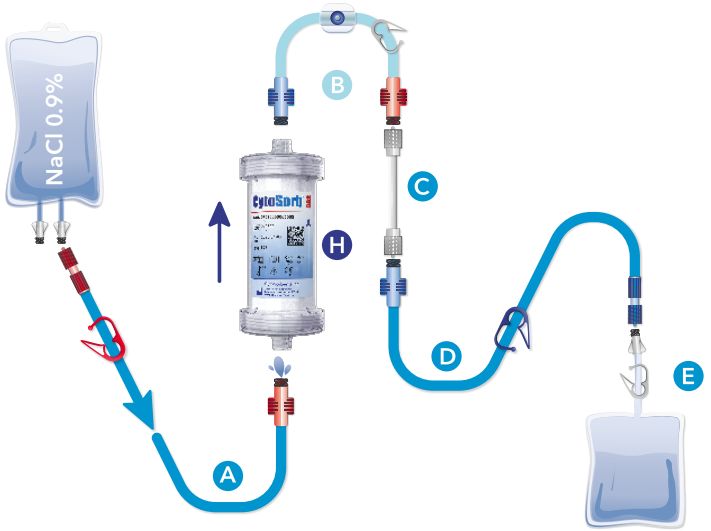
Consideration for anticoagulation

- Anticoagulation must be effective at the start of treatment.
- In general, no special adaptations of the standard of care protocols for CytoSorb® therapy are necessary. The specifications of the device manufacturer must be observed.
- Systemic heparinization
  - An aPTT of 60-80 sec or an ACT of 160-210 sec is usually sufficient for CytoSorb®. The aPTT or ACT should be checked regularly.
- Regional anticoagulation with citrate
  - Initial dose, blood flow rate, control and adjustment of calcium and citrate according to protocol used. Citrate and calcium additions are made at the usual sites of the CRRT.
  - The control of ionized calcium (CRRT circuit and patient) a few minutes after the start of treatment and at regular intervals of 2 to 4 hours is recommended.
  - If a hemofilter is not used to remove citrate-calcium complexes, only a time-limited treatment of 2 hours maximum is possible.
- The decision regarding dosage and target levels is the responsibility of the treating physician.
- In case of hemoadsorption (standalone application without hemofilter) use heparin anticoagulation only.

Step 1 Flush before integration

1. Completely prepare the device according to manufacturer's instructions (incl. flushing). If necessary during ongoing renal replacement therapy first interrupt the treatment (return blood and disconnect patient according to the manufacturer's instructions for each device).
2. Connect NaCl with Ⓐ **deaerate** and close **red clamp** on Ⓐ.
3. Connect Ⓐ bubble-free with CytoSorb® blood inlet Ⓗ (**bottom**).
   Observe flow direction!
4. Connect CytoSorb® blood outlet Ⓗ (**top**) with Ⓑ, Ⓒ, Ⓓ and Ⓔ.
5. Open **red clamp** on Ⓐ and rinse CytoSorb® Ⓗ by gravity with 2 liters NaCl and deaerate it by tapping.
6. Close **red clamp** on Ⓐ and **blue pinch clamp** on Ⓑ and Ⓓ.
7. Stop blood pump.

Caution: – Never remove both caps at the same time
– Use only plastic scissor clamps for 6.8 mm lines.

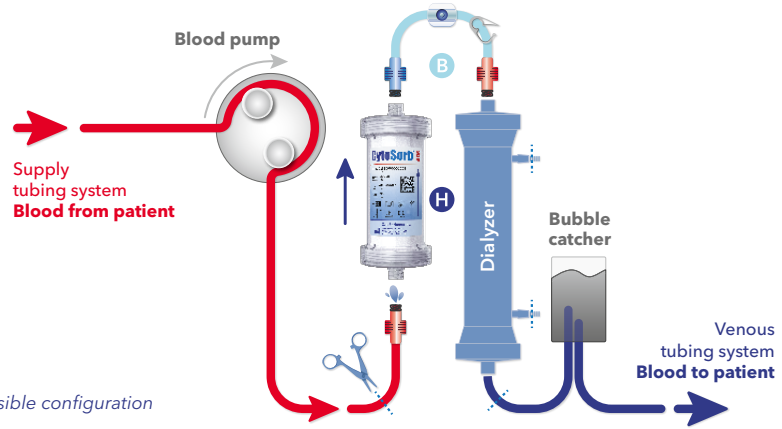


Step 2 Integration pre filter

1. Clamp all tubes at the dialyzer at ⋮ by use of **clamps**. Close **clamp** on Ⓑ.
2. Disconnect Ⓐ from CytoSorb® blood inlet Ⓗ (**bottom**) and discard it.
3. Disconnect **arterial blood tube** from dialyzer blood inlet and connect bubble-free with CytoSorb® blood inlet Ⓗ (**bottom**).
4. Disconnect Ⓒ from Ⓑ and discard Ⓒ, Ⓓ and Ⓔ.
5. Connect Ⓑ bubble-free with dialyzer blood inlet.
6. Remove all **clamps** at ⋮ and start blood pump.
7. Start patient treatment as prescribed.

Step 3 Change and remove a used adsorber

1. Stop current treatment and blood pump. Return blood and disconnect patient according to the manufacturer's instructions for the respective device.
2. Disconnect blood line to adsorber Ⓗ with **scissors clamp** at ⋮.
3. Close pinch clamp at Ⓑ on the hemofilter.
4. Discard used adsorber. (Inlet can be closed with used adapter Ⓑ).
5. To install fresh adsorber, go to **Step1**.
6. To continue operation without adsorber, connect blood line to hemofilter without bubbles and open all set clamps.

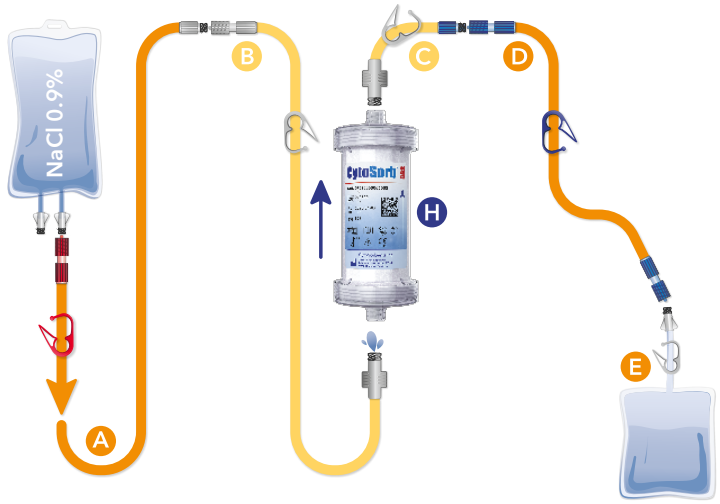


possible configuration

Step 1 Flush before integration

1. Completely prepare the device according to manufacturer's instructions (incl. flushing). If necessary during ongoing RRT (Renal Replacement Therapy) first interrupt the treatment (return blood and disconnect patient according to the manufacturer's instructions of each device).
2. Connect NaCl with A and B **deaerate** and close **red clamp** on A.
3. Connect B bubble-free with CytoSorb® blood inlet H (**bottom**).
   Observe flow direction!
4. Connect CytoSorb® blood outlet (**top**) with C, D and E.
5. Open **red clamp** on A and rinse CytoSorb® H by gravity with 2 liters NaCl and deaerate it by tapping.
6. Close **red clamp** on A and **blue clamp** on D. Close **clamps** on B and C.
7. Stop blood pump.

Cave: – Never remove both caps at the same time.
– Use only plastic scissor clamps for 6.8 mm lines.



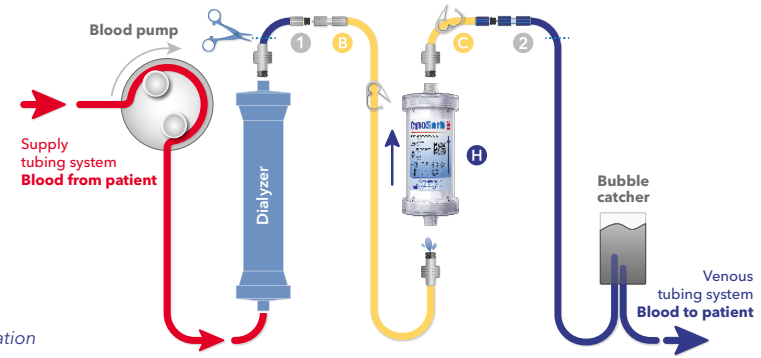
Step 2 Integration post filter

1. Clamp blood lines at the dialyzer blood outlet 1 and before the venous bubble catcher 2 at ¦ by use of **clamps**.
2. Disconnect saline solution and A from B and discard it.
3. Connect B with blood tube from dialyzer blood outlet 1.
4. Connect C from CytoSorb® blood outlet H (**top**) with line to venous bubble catcher 2.
5. Remove all **clamps** at ¦ and start blood pump.
6. Start patient treatment as prescribed.

Caution: CytoSorb® installed after the dialyzer, in post-dilution mode, in combination with a low blood flow rate may lead to blood clots. Please consider minimum blood flow according of citrate protocol. Pre-dilution is recommended with this set-up.

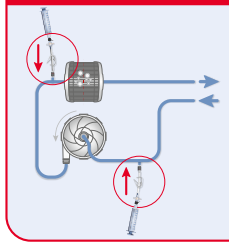
Step 3 Change and remove a used adsorber

1. Stop ongoing treatment. Perform blood return and patient disconnection according to the manufacturer's instructions for the respective device.
2. Clamp blood lines at the dialyzer blood outlet 1 and before the venous bubble catcher at 2 by use of **clamps**.
3. Close **clamps** on B and C.
4. Discard used adsorber. (Connect B and C before discarding).
5. To install a fresh adsorber, proceed with **Step 1**.
6. To continue operation without adsorber, connect 1 and 2 without bubbles and remove **clamps** at ¦ and restart CRRT procedure.



possible configuration

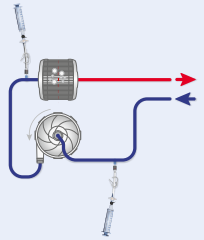
Setup: ECMO & ECMO-Connector



Prepare ECMO system.
The **CytoSorbents ECMO-Connector** allows the simple and safe addition of CytoSorb® when needed.

Step 2

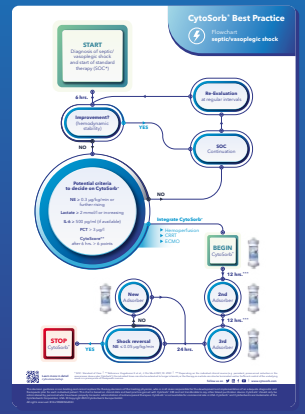
Start ECMO-Therapy



Evaluation of patient status / condition

Vasoplegic shock?

Ongoing hemodynamic instability despite ECMO therapy?



Flowchart septic/vasoplegic shock
cyto.zone/flow-sep/eng

NO

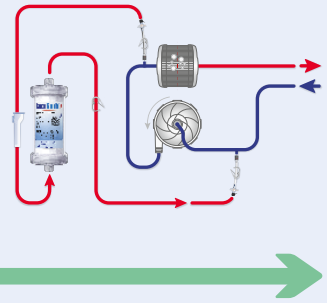
YES

Decision
Start CytoSorb® Therapy?

YES

NO

Application CytoSorb® Therapy



Continue CytoSorb® Therapy?

NO

YES

Remove used adsorber latest after 24h

Step 5

Preparation & Integration

Flushing of adsorber

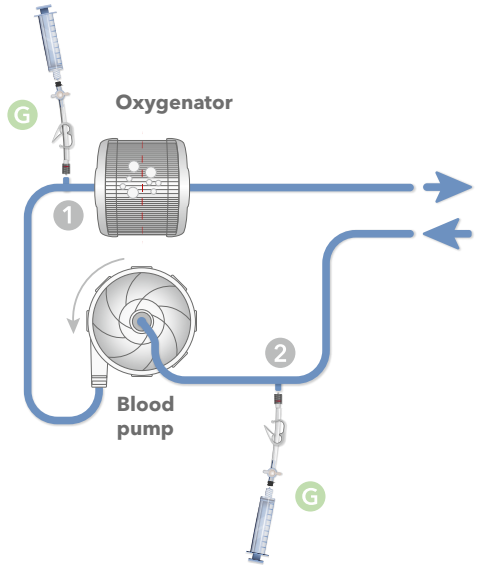
Step 2

Installation of adsorber

Step 3, Step 4

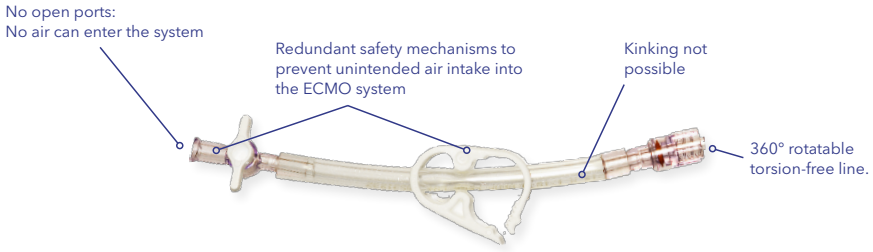
Step 1 preparation of the ECMO system

1. Set up the ECMO system dry, according to manufacturer's instructions.
2. Connect the first ECMO connector G with Luer-Lock of ECMO mainstream 1 in front of oxygenator membrane. **Note:** Adapter E can be used to connect ECMO connector G alternatively to DIN-Lock port on the oxygenator.
3. Connect second ECMO connector G with blood return port (Luer-Lock connector) to ECMO mainstream 2 in front of the pump.
4. Prime the ECMO system according to the manufacturer's instructions. Flush and deaerate G at 1 and 2 and close their clamps and stopcocks. Place a sterile, saline-filled 10 mL Luer-Lock syringe on the Luer-Lock connections of G at 1 and 2.



5. Connect the ECMO system to the patient according to the instructions of the attending physician if indicated.
6. According to the doctor's prescription, CytoSorb® H can be installed into the ECMO system. Please follow Step 2 and Step 3.
Note: Never use a connection on the ECMO mainline after the oxygenator for CytoSorb® blood return.

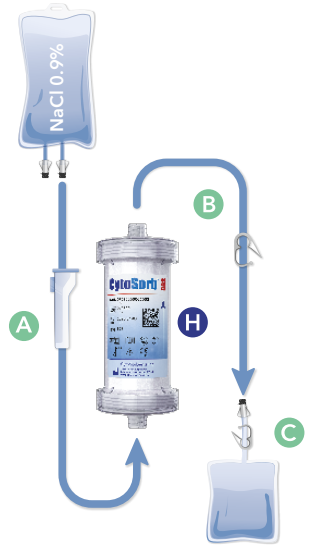
***CytoSorb® ECMO-Connector** Simple and safe connection



Step 2 CytoSorb® rinsing procedure

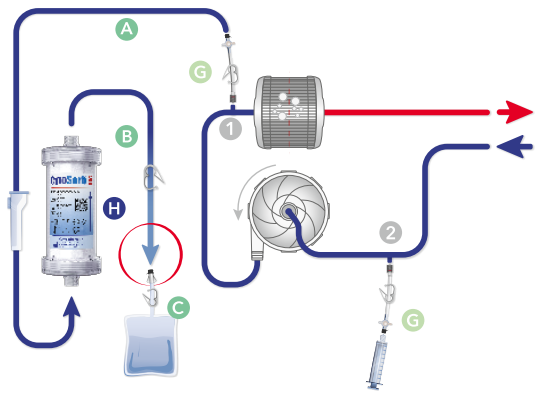
1. Connect line A with saline solution, deaerate it and disconnect it with the **clamp**.
Note: Use spike adapter D if necessary.
2. Remove the port plug only at the bottom of the CytoSorb® blood inlet H and connect the bubble-free, vented line A.
Observe flow direction (indicated by the arrow on the label).
3. Remove the port plug from the top of the CytoSorb® blood outlet H. Connect tube B and irrigation bag C.
Note: If CytoSorb® is used in series with a hemoconcentrator (HC), use adapter F, connect the HC to the blood outlet of H.
4. Open the **clamp** on line A and rinse CytoSorb® with gravity and vent it by tapping with the palm of your hand. In total 2 liters of isotonic saline solution are required for filling the lines and flushing CytoSorb®.
5. Close the **clamps** on lines A and B to prevent CytoSorb® H, A and B from running empty.
6. Close the **clamp** on the rinsing bag C.

Cave: – Never remove both caps at the same time.
– Use only plastic scissor clamps for 6.8 mm lines.



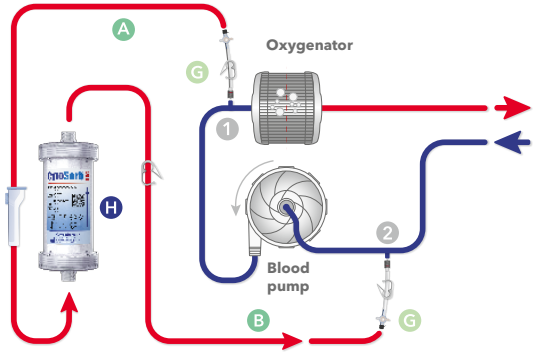
Step 3 Fill rinsed CytoSorb® with blood

1. Attach the CytoSorb® adsorber H, prepared according to Step 2, vertically to the ECMO device using the holder.
2. Detach line A from the saline bag and connect it bubble-free to the ECMO connector at G on 1 before Oxygenator membrane.
3. Open **clamp** and **stopcock** from G at 1. Open **clamp** at A, B and C.
4. Fill CytoSorb® bypass with blood and let saline solution flow into the rinsebag bag C.
5. As soon as blood becomes visible in tube B after CytoSorb®, close the clamp on B.



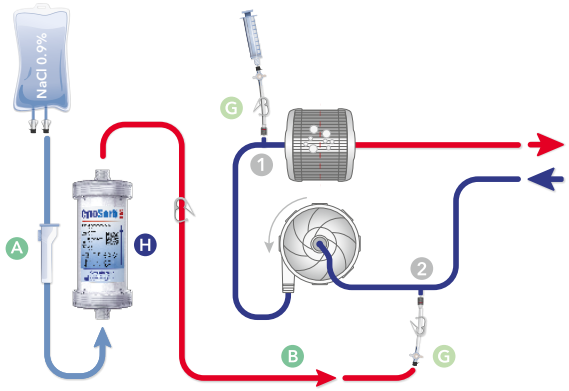
Step 4 Complete CytoSorb® Bypass

1. Connect the completely vented line B (from CytoSorb®) with the completely vented ECMO-Connector G to 2.
   Under no circumstances should air enter the system.
2. Open **clamp** on line B. Open **clamp** and **stopcock** from G at 2 (upstream of pump).
3. The blood flow through CytoSorb® can be monitored with the aid of an ultrasound Doppler probe (on line A or B) if necessary.
4. If necessary, the blood flow can be regulated by the **roll clamp** on line A. The recommended blood flow rate should be between 150 - 700 mL/min, with a minimum rate of at least 100 mL/min.



Step 5 Removal of used adsorbers before installation of fresh adsorbers / Termination of CytoSorb® Therapy

1. Prepare a fresh bag of saline solution (2 liters, sterile, no bottle to reduce the risk of air aspiration into the system). Fill 2x10 mL Luer-Lock syringes with saline solution (air-free). Close **clamp** and **stopcock** from G on 1 and 2 and **clamp** on line A.
2. Release line A from G on 1 and connect it bubble-free to the fresh saline bag.
3. Place 10 mL Luer-Lock syringe filled with saline bubble-free on G on 1. Open **clamp** and **stopcock** and rinse G on 1. Then close **clamp** and **stopcock** G on 1.
   Under no circumstances should air enter the system.
   Leave Luer-Lock syringe on ECMO connector G (on 1).
4. Open **clamp** and **stopcock** from G on 2. Blood is returned from the CytoSorb® H into the ECMO system by flushing with saline solution. As soon as saline solution is visible in tube B, close **clamp** and **stopcock** from G on 2.
5. Disconnect line B. Place 10 mL Luer-Lock syringe filled with saline solution bubble-free on G on 2. Open **clamp** and **stopcock** and rinse G on 2.
6. Close **clamp** and **stopcock** from G on 2 again. **Under no circumstances should air enter the system.** Leave the Luer-Lock syringe on G on 2.
7. Discard used CytoSorb® H, lines A and B.



▶▶▶

To continue the CytoSorb® Therapy, please follow steps Step 3 & Step 4 to insert a new CytoSorb® adsorber into the ECMO system.

■

If it is decided that CytoSorb® Therapy is no longer required, the ECMO connectors G together with 1 and 2 should be removed from the ECMO system.

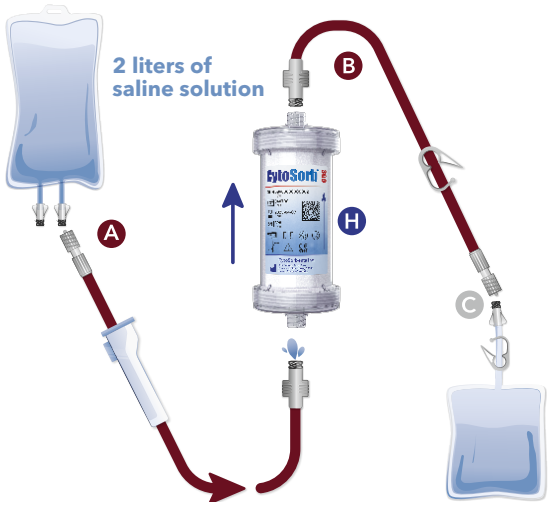
Step 1 – Preparation CPB

1. Setup the cardiopulmonary bypass machine completely according to the operating instructions of the device manufacturer (including priming).

Step 2 Preparation CytoSorb® Adsorber

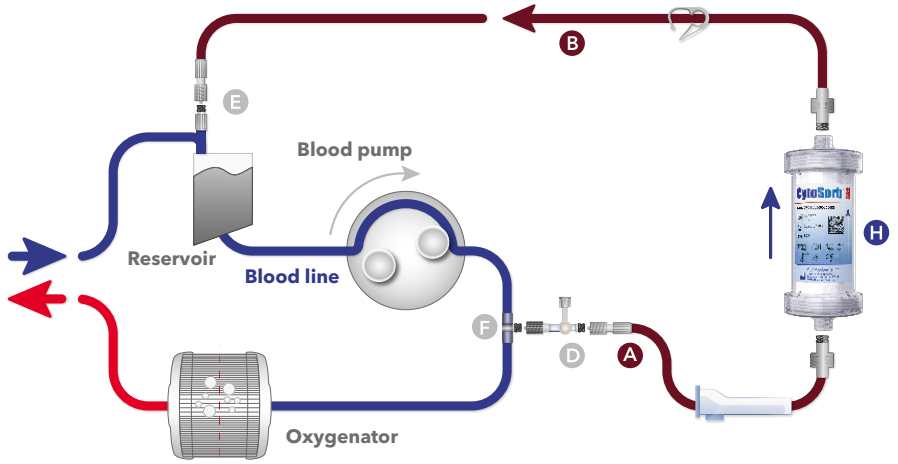
1. Connect Ⓐ with saline solution and deaerate. Close **clamp** on Ⓐ.
2. Connect Ⓐ bubble-free to CytoSorb® blood inlet Ⓗ (**bottom**).
   Observe the flow direction indicated on the label.
3. Connect CytoSorb® blood outlet Ⓗ (**top**) with Ⓑ and Ⓒ.
4. Open **clamp** at Ⓐ and flush CytoSorb® by gravity with 2 liters normal saline.
   Rinse saline solution and vent by tapping with the palm of the hand.
5. Close **clamps** on Ⓐ, Ⓑ and Ⓒ.

Cave: – Never remove both caps at the same time.
– Use only plastic scissor clamps for 6.8 mm lines.



Step 3 Integration of CytoSorb® in CPB

1. Mount CytoSorb® Ⓗ vertically on the heart-lung machine using the mounting device.
2. Separate Ⓐ from the saline bag and connect it bubble-free via a high-flow three-way valve to Ⓓ at Luer-Lock on the main line after the blood pump.
3. Connect Ⓑ to reservoir Ⓔ via a high-flow Luer-Lock connection.
4. If necessary, regulate the blood flow in the bypass by use of the **roller clamp** on Ⓐ.

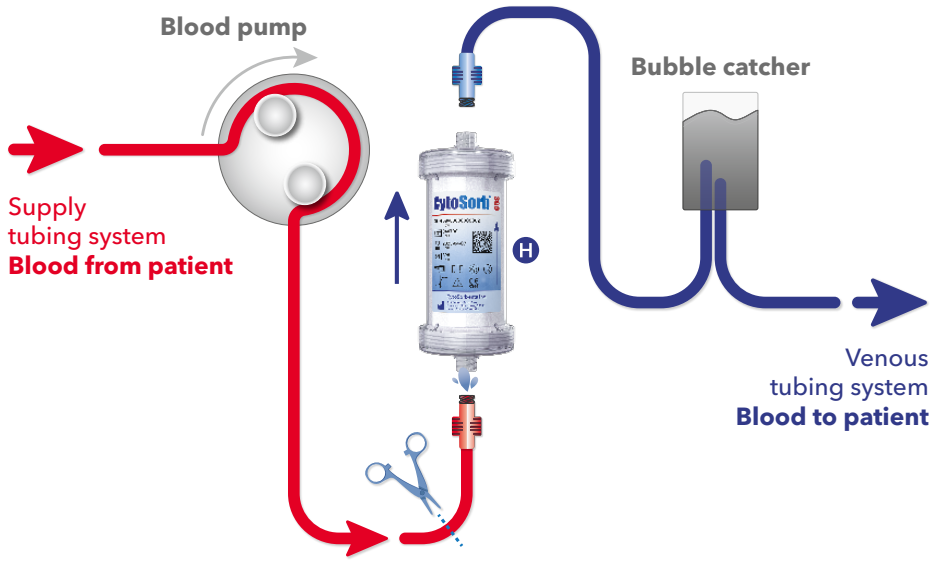


Step 1 Set-up

1. Set-up the device according to the manufacturer's instructions (dry).
2. Mount CytoSorb® (H) vertically into holder.
3. Start blood pump and deaerate **arterial tubing system** (Inbound line to adsorber must be refilled and air-free).
4. Stop blood pump and clamp **arterial tubing system** at ⋮ by using **scissor clamp**.
5. Only remove the port plug on the CytoSorb® inlet (H) (bottom).
6. Connect CytoSorb® (H) bubble-free with **arterial tubing system**. Observe flow direction!

Cave: – Never remove both caps at the same time.
– Use only plastic scissor clamps for 6.8 mm lines.

7. Now remove the blood outlet port plug (top) and connect CytoSorb® (H) with **venous tubing system**.
8. Remove **scissor clamp** from **arterial tubing system**.
9. Start blood pump (approx. 100 mL/min) and rinse system with 2 liters of saline solution.
10. Remove CytoSorb® (H) from the holder and deaerate it by tapping.
11. Start patient treatment as prescribed.



CE Certified / notified body / QM-System

YES / 0344 – DEKRA/ISO 13485

Intended use

The CytoSorb Device (CytoSorb®) is a non-pyrogenic, sterile, single-use device containing adsorbent polymer beads designed to remove cytokines, and/or bilirubin, and/or myoglobin and/or $P2Y_{12}$ inhibitor ticagrelor and/or rivaroxaban as blood passes through the device. CytoSorb is placed in a blood pump circuit.

Extracorporeal blood volume

150 ml

Adsorbent / surface

Proprietary and patented cross-linked divinylbenzene polymere, exclusively produced by CytoSorbents in the USA / 45,000m^2.

Adsorption spectrum / biocompatibility

Midsize hydrophobic molecules up to a size of approximately 60kDa / Biocompatibility tested as required in ISO10993

Mode of operation covered by IFU

Any extracorporeal blood ciruit (Hemoperfusion (HP)), intermittend hemodialysis (HD), continuous renal replacement therapy (CRRT), cardiopulmonary bypass (CPB), extracorporeal membrane oxygenation/extracorporeal life support (ECMO/ECLS).

Blood flow rates min-max

100 - 700 ml/min

Pressure drop ΔP (Hct 32% ± 3% bei 37°C ± 1°C)

Qb ≤ 700 ml/min	140 mmHg
Qb ≤ 500 ml/min	90 mmHg
Qb ≤ 200 ml/min	30 mmHg

Qb = blood flow

Priming fluid, procedure and duration

Flushing with 2 liters of sterile isotonic saline (NaCl 0,9%) / Priming takes approximately 5 minutes. CytoSorb® contains pre-loaded physiological saline with a pH level of 6.8 pre-flush. Heparin priming is NOT required to coat the bead surface prior to use.

Use on HIT patients if anticoagulated with citrate.

Max. pressure limit

760 mmHg

Max. treatment time per device

Change CytoSorb® after 24 hours maximum. Change CytoSorb every 12 hours for the first 24 hours if indicated by ongoing hemodynamic instability.

Anticoagulation

Heparin or citrate

Sterilization / shelf life / storage conditions

Gamma sterilization / 3 years / 1°C to 40°C

Multiple box size and weight

6 adsorber box: 33x24x36 cm, 3.5 kg

12 adsorber box: 41x33x26 cm, 7.0 kgt

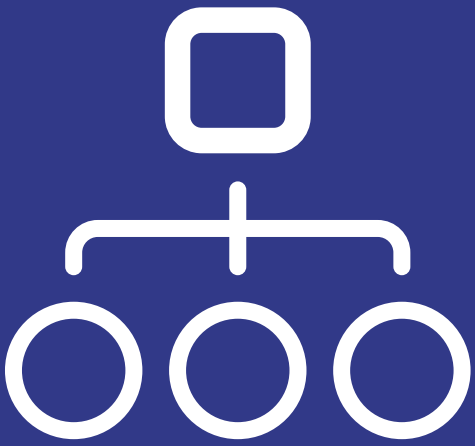
Further details

Latex- and PHT free product

GMDN-Code

34422 - Hemoperfusion system adsorption column

Classification of drugs



Insignificant in-vivo removal	**Low** in-vitro removal
Negligible clearance increase (<25%) or low percentage removal (<30%)	**<30% percentage removal, but no in-vivo data available**
Dose adjustment seems unnecessary*	Dose adjustment seems rather unnecessary*
Anidulafungin	Amikacin
Cefepime	Paracetamol (Acetaminophen)
Ceftriaxone	Theophylline
Ciprofloxacine	
Clarithromycin	
Clindamycin	
Flucloxacillin	
Ganciclovir	
Meropenem	
Metronidazole	
Piperacillin	

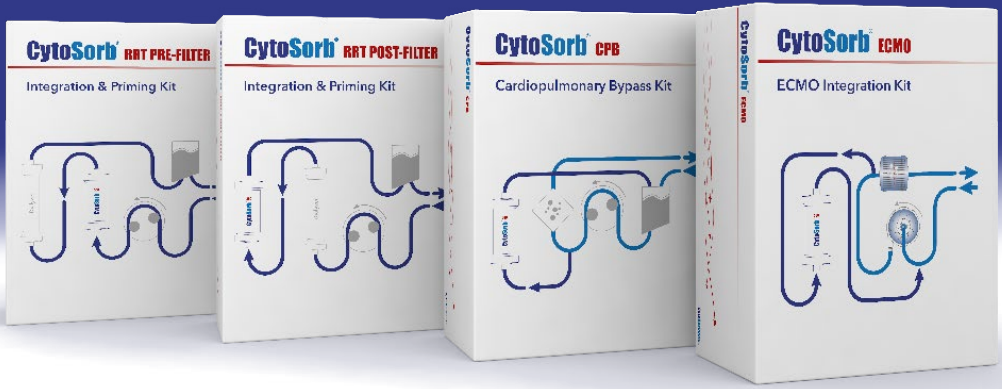
Moderate or high in-vitro removal	**Significant** in-vivo removal
>30% percentage removal, but no in-vivo data available	**>25% clearance increase, or >30% percentage removal**
Dose adjustment seems rather necessary*	Dose adjustment seems necessary*
Amiodarone	*Amphotericin B*
Amitryptiline	Apixaban
Amlodipine	Bivalirudin
Carbamazepine	Digitoxin
Cyclosporine	Flecainide
Dabigatran	*Fluconazole*
Diazepam	Linezolid
Digoxin	*Posaconazole*
Edoxaban	Teicoplanin
Gentamycin	*Tobramycin**
Iodixanol	Vancomycin
Ibuprofen	
Phenobarbital	
Phenytoin	
Quetiapine	
Remdesivir / GS-441524	
Rivaroxaban	
Tacrolimus	
Ticagrelor	
Valproic acid	
Verapamil	
Voriconazole	

Antiinfectives *Medication in italics:* animal data

* General view on clinically expected drug removal per category, based on available data. Therapeutic Drug Monitoring (TDM) is always recommended in principle, if available, to control dosing.

Modified from: Scheier et al. Mechanistic Considerations and Pharmacokinetic Implications on Concomitant Drug Administration During CytoSorb® Therapy. Critical Care Explorations 2022;4(5):e0688; More data might be available in the meantime. References available on request.

CytoSorb® Kits



The complete package for CytoSorb® integration into all renal replacement therapies, CPB and ECMO circuits

CytoSorb® 300 Adsorber

+ Priming Set
+ Integration Set
+ Quick Setup Guide

Simplifies CytoSorb® preparation and integration according to IFU

- ✔ Customized integration into all standard extracorporeal circuits*
- ✔ Time saving in preparation

Always at your fingertips: Faster processes from order to use

- ✔ Simplified logistics and warehousing
- ✔ Reduces individual orders of accessories
- ✔ Optimised outer packaging improves CO_2 footprint

A CytoSorb® Kit and a bag of saline solution and you're ready to go!

The customized kits include the CytoSorb® adsorber and all accessories for integration in hemodialysis, hemofiltration, CPB or ECMO according to manufacturer specifications. This gives you all the well-proven and documented benefits of CytoSorb® Therapy in one easy-to-use kit.

Kits	Order number	Packaging unit	RRT Pre-Filter	RRT Post-Filter	CPB	ECMO
CytoSorb® Pre-Filter Kit	**50-0110-01**	**10 Kits**				
CytoSorb® 300 Adsorber	1x 30-0031		✔			
CytoSorb® Pre-Filter Integration Adapter (1a)	1x 40-001a-01		✔			
CytoSorb® Pre-Filter Priming Set (1b)	1x 40-001b-01		✔			
CytoSorb® Post-Filter Kit	**50-0210-01**	**10 Kits**				
CytoSorb® 300 Adsorber	1x 30-0031			✔		
CytoSorb® Post-Filter Integration Adapter (2a)	1x 40-002a-01			✔		
CytoSorb® Post-Filter Priming Set (2b)	1x 40-002b-01			✔		
CytoSorb® CPB Kit	**51-0110-01**	**10 Kits**				
CytoSorb® 300 Adsorber	1x 30-0031				✔	
CytoSorb® CPB/ECMO Priming Set	1x 42-0002-01				✔	
CytoSorb® ECMO Kit	**42-0001-01**	**10 Kits**				
CytoSorb® 300 Adsorber	1x 30-0031					✔
CytoSorb® CPB/ECMO Priming Set	1x 42-0002-01					✔
CytoSorb® ECMO Connector*	**42-0001-01**	**6 Adapter**				
CytoSorb® EC Connector Set	6x 42-0001-01					✔

* The separate ECMO connectors are used on ECMO systems during priming to create an interface for accessories. This allows for quick and easy CytoSorb® adsorber integration and replacement at any time.

CytoSorbents ACADEMY

For all who want to know more

Take the opportunity and benefit from our bank of knowledge about

CytoSorb® application and
CytoSorb® therapy options.

Know more every time!

Register now at
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