

## What is ADVOS and what is ADVOS multi?

„ADVOS“ is an abbreviation for Advanced Organ Support.

„ADVOS multi“ is the designation for the machine that is used for organ support, whereby „multi“ means that several organs (lung, liver, kidneys) can be supported at the same time.

## Can the ADVOS device be used only for the lungs or can it be used for other individual organs?

Of course, the device can be used for just the lungs and also for other individual organs.

## What does „scalable support for multi-organ failure“ mean?

„Scalable Support“ means that, depending on the severity of the disease, for example one and the same machine can only support the lungs (CO<sub>2</sub> removal). If over the course of the disease, further organ support (e.g. kidney or liver) is needed then it can also be used to support these organs without the need for setting up the machine again or even changing the machine.

## What is innovative about the process?

The most innovative aspect is the method by which the advantages of albumin dialysis (high detoxification performance) are combined with other advantages (low albumin consumption, high dialysate flow, low blood flow). In addition, the scalability, which is the possibility of supporting the lungs, the liver, the kidney and the acid-base balance with a single machine, is a novelty which so far is only possible with the ADVOS multi.

## Can the procedure be reimbursed?

The method can be reimbursed for both kidney and liver dialysis. Reimbursement for CO<sub>2</sub> removal is under review.

## What does the treatment cost?

The cost of the treatment depends on several factors, such as whether the equipment is purchased, leased or provided by ADVITOS, either with or without a fixed consumption of consumables. For more details, please contact our sales representatives.

## How much is the equipment?

The cost of the equipment is dependent on several factors, such as whether the equipment is purchased, leased or provided by ADVITOS, either with or without a fixed consumption of consumables. For more details, please contact our sales representatives.

## Can the procedure be used in dialysis practices?

The equipment can also be used in dialysis practices.

## Can the machines also be loaned?

The machines are also loaned if a corresponding agreement is made with the hospital, the practice or the service provider. For more details, please contact us.

## What are the indications and contraindications for ADVOS?

The indications for ADVOS are listed in the following table.

Due to the variety of ADVOS, the method is applicable to a large number of pathologies.				
Importance of treatment	+ important	++ very important	+++ highest priority	
	Liver Support	Kidneys Support	Lungs Support	Stabilization acid-base balance
Multiple organ failure				
Post-surgical (e.g. after liver operations)	+++	+	+	++
Post-surgical (e.g. after a heart operation)	+	++	+++	+++
Cardiogenic shock	+	++	+++	+++
Septic shock	+	++	+++	+
Hypoxic liver failure	+++	+	+	+++
Liver failure				
Liver transplant (Waiting list & post-surgery)	+++	++	+	+
Acute liver failure	+++	++	+	+
Acute on chronic liver failure	+++	+	+	+
Lung failure				
Lung failure	+	++	+++	+++

The procedure is relatively contraindicated in children, pregnant women and nursing mothers, since there is no experience with these cases available so far. The procedure is contraindicated in patients with Creutzfeldt-Jakob infection due to the risk of cross-infection. In addition, the same contraindications apply as to common dialysis.

## Where can I see the ADVOS multi circuit?

The ADVOS multi circuit is installed inside the machine with 2 specially designed dialyzers.

## What is innovative about the procedure?

The most innovative aspect is the method by which the advantages of albumin dialysis (high detoxification performance) are combined with other advantages (low albumin consumption, high dialysate flow, low blood flow). In addition, the scalability, which is the possibility of supporting the lungs, the liver, the kidney and the acid-base balance with a single machine, is a novelty which so far is only possible with the ADVOS multi.

## For how long can the procedure be used?

The procedure can be used as long as the treating physician considers it necessary, whereby the machine must be disinfected every 24h. Thus, with 2 machines an uninterrupted treatment is possible.

## How long does the treatment last?

Treatment typically takes 8h or 24h, depending on the treatment goal. For example, a 24-hour, continuous treatment is useful for lung support; whereas, for liver or kidney dialysis, an 8-hour treatment can also be done. In general, the length of organ support depends on the attending physician. The method only requires disinfection of the machine every 24h. Thus, with 2 machines an uninterrupted treatment is possible.

## Will further options for organ support in the ADVOS be offered in the future?

Further options for organ support are in preparation, either in specially designed equipment or as a supplement within the ADVOS multi.

## For which patient groups is the procedure particularly suitable?

The method is particularly suitable for the following patients. (See also „What are Indications and Contraindications for ADVOS?“)

## Why are acidic and basic concentrates used?

Acidic and basic concentrates are used to reduce/elevate the pH in the two separate ADVOS regeneration circuits and to filter the toxins there.

## What happens with the acids (HCl) and bases (NaOH) after they have passed through the ADVOS regeneration circuit?

Added acid and base are converted into water and saline in the ADVOS reservoir:  $\text{HCl} + \text{NaOH} \Rightarrow \text{H}_2\text{O} + \text{NaCl}$  and finally disposed of via the filtrate of the cleaning circuit.

## How are acids (HCl) and bases (NaOH) disposed of?

Added acids and bases are converted into water and saline in the ADVOS reservoir:  $\text{HCl} + \text{NaOH} \Rightarrow \text{H}_2\text{O} + \text{NaCl}$  and finally disposed of in the filtrate of the cleaning circuit. The filtrate itself is disposed of using the container system into the hospital/practice waste disposal outlet via ADVOS multi's liquid management system.

## Why are four dialyzers needed?

2 dialyzers are used in the purification circuit within the ADVOS multi-circuit (acid and base circulation), 2 additional dialyzers are used in blood circulation to ensure a high cleaning performance of the albumin dialysate.

## Which dialyzers can be used?

For regulatory reasons, only ADVOS dialyzers can be used. If dialyzers not approved by ADVITOS are used, any liability and responsibility for any complications or side effects for the treated patient are the sole responsibility of the attending clinician.

## What are the advantages over competitor's products?

ADVOS multi offers the following advantages over the competition:

- One single device for lung, liver and kidney support
- Simultaneous support for all 3 detoxification organs
- Focusing on a leading organ is possible
- Lung support without the need for large-scale vascular access and high flow rates
- Liver dialysis with highest detoxification performance
- Progressive treatment of renal failure by removing watery and additionally protein-bound nephrotoxins
- Bicarbonate-independent treatment of severe metabolic and respiratory acidosis
- Low consumption of albumin
- Continuous and intermittent treatment possible

## What clinical studies and publications are available?

Since the method is still very new, there are only a limited number of studies on animals and humans, which we would be pleased to send you. Further studies are underway or are being prepared, for example, our central patient register, in which almost every patient treated is compiled.

## What is the medical success?

Previous studies have shown good treatment successes, especially in the early onset of treatment. For details, please subscribe to our Literature-Service or contact experienced users.

## How often is the procedure used per patient?

The number of treatments depends on the pathology, typically patients are treated 5-10 times, but patients have already been treated up to 100 times.

## How does the CO<sub>2</sub> removal work in detail?

In contrast to all other combined dialysis equipment, ADVOS does not need a gas exchanger for CO<sub>2</sub> removal, rather it uses a chemical process: physiologically in the body CO<sub>2</sub> + H<sub>2</sub>O (carbon dioxide and water) is constantly in equilibrium with H<sup>+</sup> + HCO<sub>3</sub><sup>-</sup> (proton and bicarbonate), according to the so-called Henderson-Hasselbalch equation:



If on the right-hand side of the equation the proton (H<sup>+</sup>) and the bicarbonate (HCO<sub>3</sub><sup>-</sup>) are removed, the body recreates the latter two from carbon dioxide (CO<sub>2</sub>) and water (H<sub>2</sub>O), thus reducing the CO<sub>2</sub> on the left side of the equation.

If pH is increased in the ADVOS dialysate and the bicarbonate content is reduced at the same time, both protons (H<sup>+</sup>) and bicarbonate (HCO<sub>3</sub><sup>-</sup>) move from the blood into the dialysate and the CO<sub>2</sub> content in the blood is lowered.

## How long does setup take until the ADVOS is ready for use?

The setup of the device takes approx. 30-45 minutes, depending on user experience.

## What happens in the ADVOS multi circuit?

In the ADVOS multi circuit, the albumin dialysate is separated into 2 independent circuits and an acidic or basic concentrate is added. Increasing the pH in the acid circuit, positively charged substances (e.g. copper and CO<sub>2</sub>) are removed from the dialysate, while negatively charged substances (e.g. bilirubin and gall acids) are removed in the base cycle. Subsequently, the circuits merge and a reconstituted dialysate passes through the dialyzers.

## Which anticoagulants should be used?

All anticoagulants that are used for kidney dialysis can also be used in combination with ADVOS.

- Heparin
- Citrate - Calcium
- Epoprostenol (Flolan)
- Thrombin inhibitors (Argatroban)

For the recommended dosage, please refer to our ADVOS Quick-Guide or use hospital standards. The operation of the ADVOS multi without any anticoagulation cannot be recommended.

## How many treatments can be carried out?

The number of treatments is dependent on the pathology. Typically patients are treated 5-10 times, but patients have already been treated up to 100 times.

# Application

## Which disinfection method should be used in infectious patients?

We recommend a standard disinfection, which is always required after treatment. For patient changes, a subsequent Citrosterile disinfection is recommended.

## Why is a container used?

In the container, both the dialysate and the filtrate are stored and thus a treatment independent of osmosis water access is possible.

## Can the ADVOS multi be connected to a ring line?

The ADVOS multi cannot be connected directly to the ring line, but the water supply system for the ADVOS multi containers can be directly connected to the ring line.

## Can the ADVOS multi be operated on an outpatient similar to a conventional kidney dialysis?

Of course the ADVOS multi can also be used for outpatient kidney dialysis.

## What is the recommended anticoagulation method?

The recommended anticoagulation method is citrate anticoagulation. It is recommended to use the regular laboratory chemical monitoring procedures and to pay particular attention to citrate accumulation in patients with liver failure. So far, there have been no reported problems with the ADVOS multi associated with citrate anticoagulation.

## How much citrate and calcium must be given?

Citrate and calcium should be given according to the local clinical guidelines. You can find more information in the ADVOS Quick-Guide.

## What flow rates are used with the ADVOS multi?

The ADVOS multi works with blood flow rates of up to max. 400 ml / min and dialysate flow rates of up to 60 l / h. The flow rates can be varied depending on the detoxification performance and indication.

## What do I need next to the ADVOS consumables?

Albumin (2 x 100 ml 20%) cannot be supplied by ADVITOS and must be ordered separately from the respective hospital pharmacy. Similarly, the substances used for anticoagulation (e.g. citrate, heparin) should be provided by the hospital.

## Is the patient cooled?

No, the patient is not cooled, an integrated heating hose ensures a stable body temperature.

## How is the blood heated up again?

If the patient experiences heat loss, the blood is heated via a heating sheath on the tubing after the dialyzer.

## Is an additional heating blanket needed?

No, an extra heating blanket is not required.

## Can the ADVOS multi be used with citrate anticoagulation?

Yes, the ADVOS multi can be operated with citrate anticoagulation. In fact, citrate is the most commonly used method among users. It is recommended to use typical laboratory chemical control measures and to pay particular attention to citrate accumulation in patients with liver failure. So far, there have been no reported problems with the ADVOS multi associated with citrate anticoagulation.

# Application

## How does balancing work?

Balancing is done by the integrated scales in the suspended container.

## In which areas has the ADVOS multi been used so far? (Intensive care wards, peripheral dialysis?)

The ADVOS multi is currently used in intensive care units as well as in dialysis stations. On request, we will gladly provide you with corresponding reference addresses.

## To what extent are the ADVOS treatment fluids different from the dialysis fluids?

ADVOS treatment fluids differ from conventional dialysis fluids by the addition of albumin, which is significantly lower in comparison to competing systems. Bicarbonate can be added depending on the intended support target.

## How long does a treatment take?

Treatment typically takes 8h or 24h, depending on the treatment goal. For example, a 24-hour, continuous treatment is useful for lung support; for liver or kidney dialysis, an 8-hour treatment can be sufficient. In general, the length of organ support depends on the decision of the attending physician. The method only requires disinfection of the machine every 24h. Thus, with 2 machines an uninterrupted treatment is possible.

## How is training done?

New users are taken care of and trained by our experienced application specialists during initial on-site treatments. After that, we are available at any time via a 24/7 hotline. 0800 43 72 92 74.

## Who can I contact if I have problems?

Our 24/7 Hotline is at your disposal for any questions and any problems: 0800 43 72 92 74

## Current customers - Where is the procedure used?

The method is currently used in several (university) clinics. Contact addresses are available on request.

## What is the reimbursement situation?

The method can be reimbursed for both kidney and liver dialysis. Reimbursement for CO<sub>2</sub> removal is under review. Details are available from our sales representatives.

## How much does the equipment cost?

The cost of the equipment depends on several factors, such as whether the equipment is purchased, leased or provided by ADVITOS, either with or without a fixed consumption agreed number of consumables. For more details, please contact us.

## Where can I order equipment, consumables or spare parts?

Please use our service hotline 0800 43 72 92 74 or contact us at:

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## What is the company's history?

Since the company's foundation in 2005, ADVITOS has devoted itself to developing effective multi-organ support. After numerous in-vitro, preclinical and clinical trials, the procedure was approved in Europe in 2011 and has met with a strong positive response from clinical users.

## Is the company Quality and CE-certified?

The company is ISO 13485:2016 & MDD 93/42 EEG Annex 11.3 certified and covers, as a full provider, complete development as well as the production and qualification assurance for medical devices and the necessary treatment concentrates internally.

## Where can I apply for a job?

We gladly accept targeted applications for vacancies or initiative applications via our website.