



**D2000 Cartridge
Instructions for Use**

For use in the U.S. under FDA EUA200148: Authorization for Emergency Use in patients with COVID-19 admitted to the ICU with confirmed or imminent respiratory failure

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Explanation of Symbols in Labeling



Keep Dry



Manufacturer Contact Information



Lot Number



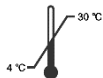
See instructions and warnings prior to use



Sterilized by Steam



Single Use Only



Indicates Temperature Limits for Storage



Indicates Expiration Date

Device Description

The Depuro D2000 Cartridge consists of a sterile, self-contained disposable Cartridge. The Cartridge is intended to assist in blood detoxification. It can be used in instances of drug overdose, hepatic encephalopathy, liver failure, in any condition which results in the release of endotoxin into the bloodstream, and in any condition which generates excess inflammatory response, such as sepsis, septic shock, or systemic inflammatory response syndrome (SIRS).

The Depuro D2000 Cartridge operates in conjunction with standard CRRT devices, or with any plasma separation device in the hospital. The Cartridge is integrated into the extracorporeal circuit, downstream from where the plasma is separated. After priming the D2000 Cartridge and assembling the inlet and outlet lines to the plasma separation extracorporeal circuit, plasma filtration should run for 4 hours, to be repeated as needed.

In bench testing, the Depuro D2000 Cartridge has been shown to remove statistically significant proportions of IL-3, IFN-gamma, IL-10, IL-1B, IL-6, IL-8, MCP-1, TNF-alpha, creatinine, bile acids, and bilirubin when compared to control. The adsorption materials used in the D2000 Cartridge have also been demonstrated to be efficacious in the treatment of drug overdose, including acetaminophen overdose, uremia, barbiturate poisoning, and in the removal of glutethimide.

Treatment duration and indication for exchange of the cartridge depend on the clinical course. The maximum treatment time per single cartridge is 4 hours.

The instructions herein must be carefully and fully observed to ensure the safe and effective use of the D2000 Cartridge. All related personnel must be completely familiar with these instructions before using the D2000 Cartridge.

The D2000 Cartridge must never be used for any purpose other than the indication described in these instructions. Depuro LLC will bear no responsibility whatsoever in relation to its use for any other purpose.

Indications

- The Depuro D2000 Cartridge is intended for adjunct use in the treatment of drug overdose and poisonings and in any condition that requires a reduction of metabolic waste products or inflammatory cytokines.
- The D2000 Cartridge filters plasma. It works with standard hospital equipment and blood lines and can be used when acute hemodialysis, apheresis, or therapeutic plasma exchange (TPE) is prescribed by a physician.

Contraindications

- The Depuro D2000 Cartridge should not be used in patients <18 years of age.
- The Depuro D2000 Cartridge should not be used in women who are pregnant or breastfeeding.
- The Depuro D2000 Cartridge should not be used in patients for whom treatment with an anticoagulant is inappropriate or are at increased risk for bleeding
- The Depuro D2000 Cartridge should not be used in patients with a known hypercoagulable condition manifesting in history of highly suspected deep venous thrombosis or pulmonary embolism.

Warnings

- Do not treat patients who are actively bleeding. If patients begin bleeding during a treatment, discontinue treatment.
- Due to the possibility of coagulation factor adsorption in the D2000 Cartridge, the use of this product in the treatment of patients who have a bleeding tendency must be approved by the responsible physician.
- Carefully read these Instructions for Use before performing filtration with the Depuro D2000 cartridge. Also consult and understand the plasma separator Instructions for Use.
- The D2000 Cartridge is for single use only. DO NOT REUSE due to risk of infection or contamination.
- The D2000 Cartridge is for use with plasma only and not for use with whole blood.
- Use proper aseptic technique during assembly and use to avoid contamination.
- The D2000 Cartridge must be fully primed before use by the procedure described in this manual.
- The D2000 Cartridge must be used only in accordance with the directions of a responsible physician who is familiar with the condition of the patient.
- During plasma purification, continuously monitor patient's condition and any possible reactions to the plasma purification process by observing physiologic parameters including body temperature, heart rate, respiratory rate, blood pressure, and coagulation time. In the event of any abnormality, suspend treatment in accordance with the directions of the responsible physician. D2000 Cartridge blood flow rate and anticoagulant flow rate must also be constantly monitored.

- If any problem occurs during treatment with the D2000 Cartridge, immediately ensure the safety of the patient and take appropriate measures, such as discontinuation of the treatment or replacement of the D2000 Cartridge or one or more of its individual components, in accordance with the directions of the responsible physician.
- Because of the possibility that some types of medication may be removed by adsorption during treatment, the type of medication, dosage, method and timing of administration must follow the instructions of the responsible physician. Before, during, or after treatment with the D2000 Cartridge, any medication must be administered only in accordance with the directions of the responsible physician and the precautions and instructions relevant to the medication.
- Potential adverse events during use of the D2000 Cartridge include:
 - Thrombocytopenia
 - Bleeding
 - Leukocytosis
 - Removal of medications which were not intended for removal

Precautions

System Precautions: Before Use

- The D2000 Cartridge is not to be used after the expiration date has passed.
- The D2000 Cartridge must be stored in a clean, dry area, at 4-30°C (39-86°F).

- The D2000 Cartridge is comprised of plastic products and must not be exposed to excessive vibration or shock.
- The D2000 Cartridge is provided sterile and non-pyrogenic if its sterile barrier package and seal are intact.
- Do not re-sterilize.
- Examine each D2000 Cartridge paper peel pouch prior to use. Do not use any D2000 Cartridge device that appears to have been damaged or whose sterile-barrier seal has been broken.
- To avoid contamination, do not remove the D2000 Cartridge device from the sealed paper peel pouch until just before priming and assembly. Prime, assemble, and operate D2000 Cartridge using aseptic technique.
- Any D2000 Cartridge device showing signs of leakage or other abnormality during priming must be replaced, and the priming procedure restarted.
- The dosage of anticoagulant varies depending upon individual patients and should be determined by physician's instruction.

System Precautions: During Use

- Before and during treatment with the D2000 Cartridge, ensure there is no leakage in any extracorporeal circuit connection or component.
- The tolerance pressure of the D2000 Cartridge is 450 mmHg; however, inlet pressure must be maintained below 300 mmHg in order to prevent clogging and other abnormalities during operation. If pressure exceeds 300 mmHg at any time during operation, treatment is to be suspended and the cause of the high

pressure is to be resolved before continuing treatment. In the event that a cause cannot be resolved, the D2000 can be changed out or the treatment can be discontinued at the order of the treating physician.

- The appropriate method and dosage of anticoagulant administration related to the extracorporeal circulation will depend on the patient's condition, and must be determined in accordance with the directions of the responsible physician.
- Ensure that no air enters the patient's blood vessels during the procedure or during rinse-back.
- The D2000 cartridge may reduce antibiotic levels during treatment. A higher dose of antibiotics may need to be considered during treatment with the D2000 cartridge.
- The D2000 Cartridge may adsorb blood glucose. During and after treatment, closely monitor patient's blood glucose levels and adjust per hospital protocol.

System Precautions: Following Use

- Dispose of the used D2000 Cartridge device in accordance with official and institutional standards for biohazardous medical waste disposal.
- After treatment, monitor and adjust patient's blood anticoagulation levels per hospital protocol.

D2000 Cartridge Assembly and Preparation

The **Warnings** and **Precautions** sections must be fully and carefully read and understood before using the Depuro D2000 Cartridge.

NOTE: The Depuro D2000 Cartridge is designed for use with hospital plasma separation devices. Please refer to the Operator Manual for the proper use of the plasma separation machine.

NOTE: Perform all assembly and preparation procedures with aseptic technique.

NOTE: When indicated or ordered by the physician in charge, treatments may be interrupted or stopped by pressing the “Stop” button.

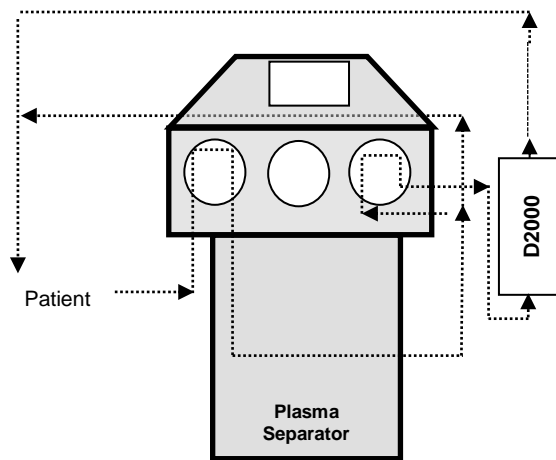


Figure 1 Diagram of D2000 in Plasma Separator Circuit

Frequently Asked Questions

- *What types of plasma separators are compatible with the Depuro D2000 Cartridge?*
 - The system should have:
 - Polysulfone or polyethersulfone membrane material
 - Contains bubble sensor
- *What plasma separator specifications have been tested with the Depuro D2000 Cartridge?*
 - Systems with:
 - $> 0.5 \text{ m}^2$ surface area
 - Nominal pore size ≥ 0.45 micron
- *What is a complete list of materials that I need to operate the Depuro D2000?*
 - You will need a plasma separator, a continuous renal replacement (CRRT) system with plasma adsorption function /capability or an apheresis machine with continuous plasma separation function, a tubing set that will accommodate the D2000 without any cutting or splicing to make it fit (example of not acceptable set: a cassette tubing set with bonded connections is not acceptable), an IV bag with human serum albumin and balanced electrolytes, a pressure cuff for the IV bag, a dialyzer blood tubing set, > 1.5 L waste bag and a syringe to deliver the HSA solution.

- *Should I run the CRRT or apheresis machine (plasma separator) self-checks and priming sequences?*
 - You should follow the manufacturer's Instructions for Use, including self-checks and priming sequences that are described.
- *How long should the patient cycle on the Depuro D2000 Cartridge?*
 - A patient can cycle on one D2000 Cartridge for up to 4 hours, at the discretion of the responsible physician.
- *What type of IV saline should I use?*
 - IV saline should be determined by the responsible physician. In the absence of special circumstance, we recommend adding 100 ml of 20% human serum albumin to 1 L of balanced electrolyte solution or bicarbonate based balanced electrolyte solution. Anti-coagulants such as heparin may be added to the priming solution at the discretion of the responsible physician.
- *What can the Depuro D2000 Cartridge filter from the patient's plasma?*
 - In benchtop studies, the D2000 has been shown to remove statistically significant proportions of the cytokines IL-3, IFN-gamma, IL-10, IL-1B, IL-6, IL-8, MCP-1, and TNF-alpha. It has also been shown to remove creatinine, bile acid, and bilirubin. This type of technology can also be used to treat drug overdose, such as in the case of acetaminophen overdose.

D2000 Cartridge Packaging

Within the D2000 Cartridge shelf box is a single D2000 Cartridge, contained within a foil pouch, and wrapped in bubble wrap. This foil pouch is a non-sterile outer barrier.



Figure 2 Non-Sterile Outer Foil Pouch

Within the foil pouch is a peel pouch which has been heat sealed and sterilized with moist heat (steam).

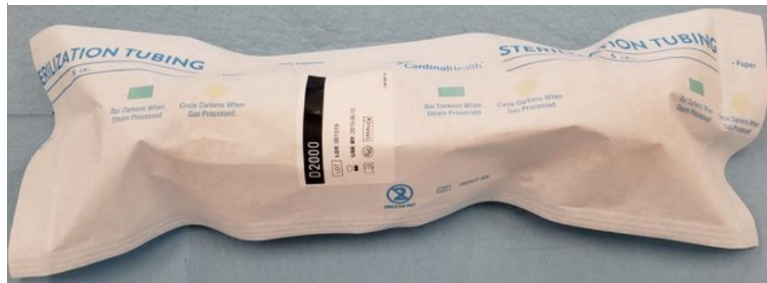
The front of the peel pouch consists of a clear film.

The back of the sealed peel pouch is made of medical grade paper.



Figure 3 Clear Front of Sterile-Barrier Peel Pouch within Foil Pouch

Figure 4 Back of Sterile-Barrier Paper Peel Pouch



The sterile D2000 Cartridge is within the peel pouch. Cartridge sterile barrier should be maintained until just before priming is initiated in order to avoid contamination.



Figure 5 D2000 Cartridge ('Adsorption Column')

Prime the D2000 Cartridge

Mount the D2000 vertically with the red (inlet) port facing upward.

Add 100 mL of 20% human serum albumin to a 1L saline bag.

Obtain a package of two dialysis blood line tubing sets (e.g. B. Braun SL-2010M2096), one for the D2000 inlet and one for the outlet (see Figure 7).

Place the bag of saline solution into a pressure cuff, spike the bag with the first dialysis blood line tubing set and prime the line.

Clamp line and hang bag from an upper hook.



*Figure 6 Mounted D2000 and Saline Bag with HSA
Figure 7 Dialysis Blood Line Tubing Set*



Connect the other end of this dialysis blood line tubing set to the blue (bottom/outlet) port of the D2000, connecting the saline bag to the blue outlet port of the D2000 (see Figure 8).

Connect the second dialysis blood line tubing set to the red (inlet) port of the D2000 and the Luer connection end of the dialysis blood line tubing set to a waste bag with >1.5 L fluid capacity.

Pressurize the saline bag cuff to ~300 mmHg, open the IV line clamp and prime the D2000. The D2000 primes from outlet to inlet.

When the D2000 is full of fluid (approximately 200 ml), close clamps on both the IV lines and remove the D2000 from holder. Gently agitate the adsorbents by holding the D2000 and rocking it up and down to distribute adsorbents evenly.

Reinsert D2000 into holder (blue port down), open both IV lines clamp and continue to rinse with the 1L saline bag.

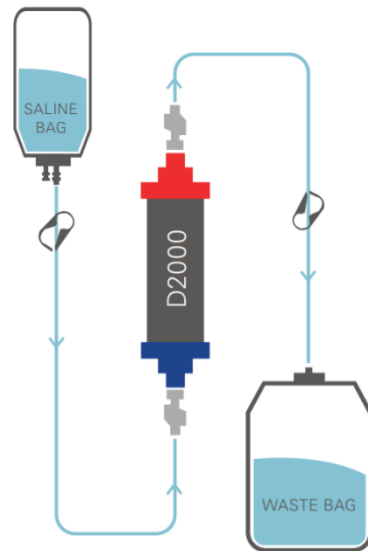


Figure 8 D2000 Priming Circuit

Prime the Plasma Separator

Prime the plasma separator per manufacturer's instructions.



Connect D2000 to the Plasma Separator

When the D2000 has finished priming, clamp both the inlet and outlet dialysis tubing lines. Remove the saline bag and the waste bag from the ends of the dialysis tubing sets.

If luer caps are available, remove the other end of the tubing sets from each port of the D2000 and cap both of the ends of the D2000. If luer cap are not available, leave the clamped tubing sets attached to the two ends of the D2000.

To aseptically insert the D2000 into the plasma circuit, first clamp the plasma and plasma reinfusion lines.

Next, remove the by-pass adapter one line at a time. The plasma reinfusion line connects to the blue (outlet) endcap of the D2000 and the plasma line connects to red (inlet) endcap of the D2000 (see Fluid Schematic in Figure 9).

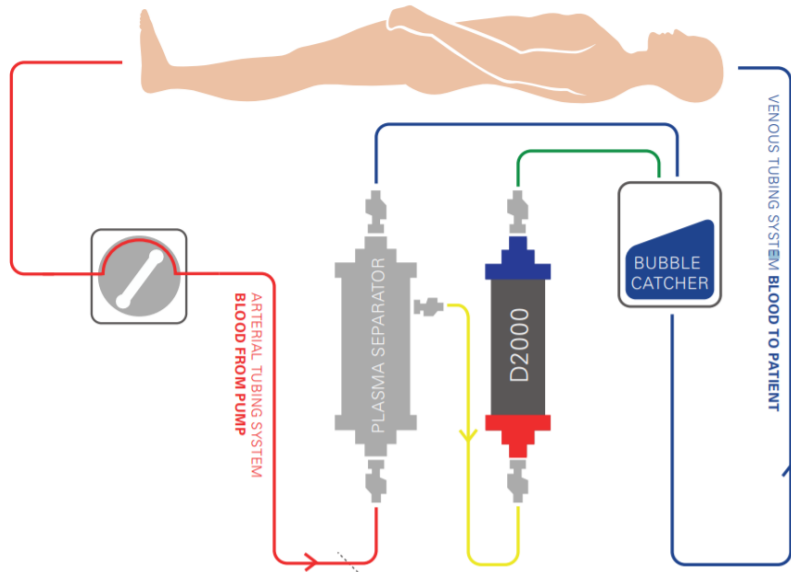


Figure 9 Fluid Schematic for Treatment with the D2000 Cartridge

When connecting each line, ensure the D2000 is held vertically before the tubing set or the cap is removed to avoid draining the priming solution. After the first line is secured, flip the D2000 180 degrees so that it is vertical when the second tubing set or cap is removed.

With minimum agitation, rotate D2000 so red port (inlet) is on the bottom and blue port (outlet) is on the top (see Figure 10). Open the clamps on the plasma line and the plasma reinfusion line.

Caution! Anticoagulation must be effective at the beginning of the treatment. Anticoagulation regimen should be chosen at the discretion of the responsible physician.



Figure 10 Image of D2000 in Fluid Circuit

Initiate Treatment

Adjust the “plasma flow rate” on plasma separation device to 25 ml/min and the “volume of plasma” to process 6000 ml. This may be managed by the physician to operate between 15 and 50 ml/min.

When authorized by physician, initiate the plasma separator’s plasma separation mode "THERAPY" sequence to initiate treatment.

In the absence of alarms and when it is otherwise safe to do so, slowly increase pump speed (blood flow rate) up to 125 ml/min (± 50 ml/min) over approximately 1 minute.

Warning! Monitor and adjust blood anticoagulation levels per hospital protocol.

Caution! The aPTT and ACT should be checked at regular intervals and closely monitored during the course of treatment to inform adequate anticoagulation.

NOTE: Check the circuit regularly to confirm there are no signs of blood clots, no air in the circuit, and the tubing lines are secure.

Conclusion of Treatment

Initiate CRRT or Apheresis machine chase-back sequence 10 min prior to conclusion of procedure.
Spike a 1L bag of a balanced electrolyte solution, prime the drip chamber and IV line, and close IV line clamp.

Aseptically connect the other end of the IV line to the blood line sample port located between the patient and the blood pump (see fluid schematic in Figure 11).

Reduce the blood flow rate to approximately 60 ml/min or as otherwise ordered by the responsible physician.

Open the IV clamp and the blood line sample clamp.

Under the direction or orders of the responsible physician, flush the line to the patient catheter and clamp the line between the sample port and the patient while assessing the patient's volume status.

Allow the plasma separator to draw solution from the IV bag and "chase" autologous blood and plasma back to the patient. (see Figure 11)

Under the supervision of the physician, stop the "chase" before the 1L IV bag is empty or the patient's condition warrants, whichever comes first.

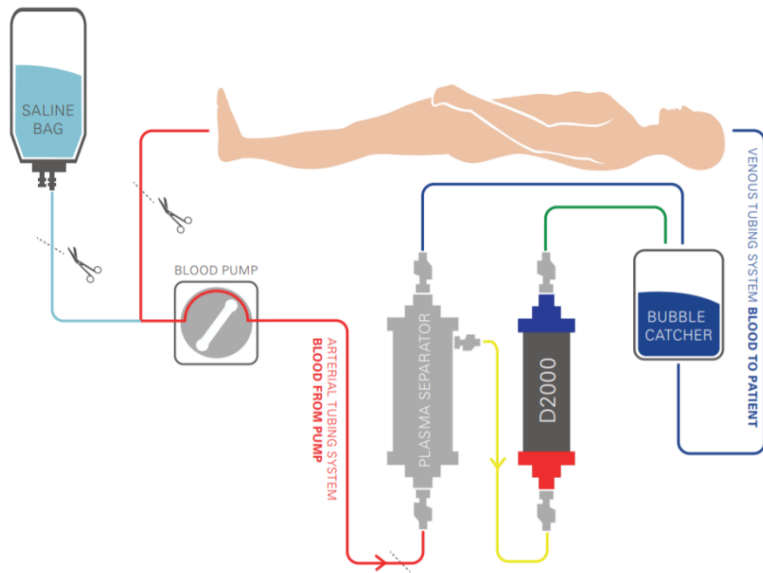


Figure 11 Schematic for Chase Back Procedure

If the physician in charge terminates the chase-back procedure prior to the re-transfusion of all autologous blood products from the circuit, aseptically drain remaining autologous blood products into a suitable transfer (transfusion) bag for later administration at the physician's discretion.

After the "Stop" button is pressed, and under the supervision of the responsible physician, clamp the inlet and outlet of the blood lines leading to the patient catheter.

Using aseptic and catheter-appropriate techniques, separate the lines from the catheter.

Treat and secure the catheter ports per the manufacturer's instructions and/or hospital standard operating procedure.

Dispose of used D2000 Cartridge according to your facility's procedure for biohazardous waste disposal.

Operation of the Plasma Separator

Refer to the Operator's Manual for all instructions related to the operation of the plasma separation device (e.g., CRRT system in plasma separation mode or Apheresis system with continuous plasma separation capabilities).



Notes:

Notes:

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Manufactured by:
Depuro LLC
21550 Oxnard Street
3rd Floor
Woodland Hills, CA 91367

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