PlasFree	Document Title **Investigational ClearPlasma Device- Instruction for Use**		
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Approval				Controlled document
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1. Device Description

ClearPlasma™ is single-use, sterile, extracorporeal plasma absorber, intended for removal of Plasminogen from donor's plasma.
The body of the absorber is a plastic housing with three principal compartments – inlet, resin compartment and outlet. The compartments are divided by two membranes, which define the resin compartment's limits (Figure 1).
ClearPlasma™ is equipped with two extension tubes. These extension tubes are connected to ClearPlasma™ device by means of ISO 80369-7 Luer connectors. The distal ends of the extension tubes is also equipped with ISO 80369-7 connectors and caps, in order to allow connection with standard, commercially available, sterile bloodlines/infusion set/system and prevent tube lumen contamination (Fig.2).

ClearPlasma™ housing presents an impressed arrow and corresponding text "This side down" (refer to Figure 3) that indicate the correct connection orientation respect to the patient's vein access (in case of bed-side use) or collecting plasma bag (in case of Blood bank use). Moreover the company and device name are also impressed on the filter housing (Figure4).

ClearPlasma™ is provided sterile (gamma radiation sterilization) and pre-filled with 4% agarose beads resin and saline solution (refer to section §0 for details on device contact materials).

ClearPlasma™ medical device does not contain a medicinal product, is not produced by using animal tissue, does not incorporate human blood nor plasma derivative and is not manufactured utilizing non-viable tissues nor cells of human origin nor their derivatives.

Figure 1: ClearPlasma™ device (1) body, (2) cup, (3) membrane

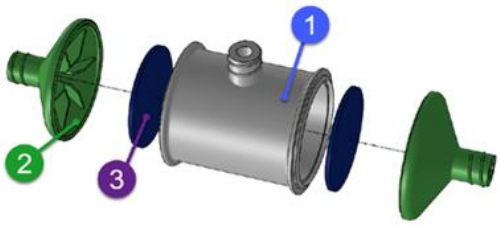


Figure 3: Flow direction marked on the device an arrow "This side down"

Figure 2: ClearPlasma™ device and its components – as provided to the user.

Figure 4: Company and Device name

2. Intended Use

The ClearPlasma™ is intended for removal of plasminogen from donor's plasma.

3. Intended Users

The ClearPlasma™ device is for professional use only.

ClearPlasma™ should only be used by personnel who have been properly trained in administration of extracorporeal therapies.

4. Use environments

ClearPlasma™ is intended to be used:

- in blood banks, when used connect to a collecting plasma bag, and
- in healthcare settings, when used connected to a patient's vein access in bed-side configuration.

5. Indications

ClearPlasma™ is indicated only for plasma, not to other blood components.

ClearPlasma™ is indicated for use in conditions where massive bleeding situations exist.

ClearPlasma™ is intended to be use on patient above 18 years old.

6. Contraindications

Do not use ClearPlasma™ if present one of the following situations:

- Risk of blood clotting
- Fluid accumulation in the brain
- Retinal thrombosis
- Experiencing a heart attack
- Maternity or breastfeeding– safety has not been established
- Patient younger than 18 years of age (safety has not been established)

- Patient with history of allergies to device components (refers to §15).

7. Warning

- Do not use ClearPlasma™ if it appears to be damaged.
- Do not use ClearPlasma™ if beads appear to be free-floating within the endcaps.
- Do not use ClearPlasma™ if the device does not seem to be full of liquid.
- Reuse of ClearPlasma™ may result in secondary infection, device clotting and/or a biohazardous situation.
- Do not use if package is damaged or opened.
- Keep away from sun or heat.
- Use ClearPlasma™ only with standard, commercially available, sterile bloodlines/infusion set/system equipped with Luer connectors compliant with ISO 80369-7.

8. Cautions

- The extracorporeal circuit should be monitored continuously during treatment for blood leaks. In the event of a blood leak during treatment, the health care provider should respond according to the facility's established protocols.
- Avoid the entry of air into ClearPlasma™. Air entering the extracorporeal circuit during treatment can result in serious injury or death. Check the integrity of all bloodlines and connections prior to the initiation of blood perfusion and periodically during the treatment. The venous return line or drip chamber should be continuously monitored with an air detector.
- ClearPlasma™ should only be used as directed by a physician.
- Pressure monitoring of the bloodline between the roller clamp and the ClearPlasma™ device is recommended.
- The fluid pathway in an intact device inside the protective pouch is sterile. Inspect the protective pouch for any sign of damage to the ClearPlasma™ device. Carefully remove ClearPlasma™ from the pouch and examine for defects.

9. Side Effects

- Allergic Reactions:

  Some people have allergic reactions to blood received during a transfusion, even when given the right blood type. In these cases, symptoms include hives and itching. Like most allergic reactions, this can be treated with antihistamines. However, if the reaction becomes serious, a doctor should be consulted. A fever can be another side effect happening after a transfusion and should be with conventional treatment.

10. Limitations

ClearPlasma™ is not to be used for more than one treatment(one plasma bag).

ClearPlasma™ should be stored within the temperature range of 2-8ºC and used within temperature range of 2 to 30ºC.

10.1 Storing condition of Plasminogen Depleted Plasma (PDP) generated by ClearPlasma

1. If the Plasminogen Depleted Plasma (PDP) was filtered directly from fresh donor plasma, the PDP can be frozen and stored at -25°C, according to standard blood bank protocol, for up to 2 years before use.
2. If the Plasminogen Depleted Plasma (PDP) was filtered from thawed plasma, the PDP can be stored at 2-8 °C up to a week before use.

11. Foreseeable adverse events

- Wrong device connection orientation: user do not connect properly ClearPlasma and filtration of plasminogen is affected.
- Non-sterile connections: user do not connect properly the bloodline tubes to ClearPlasma, causing introduction of bacteria and/or virus into the blood lines and therefore patient inflammation.
- Plasma leakage during filtration: user do not connect properly the bloodline tubes to ClearPlasma, causing introduction of bacteria and/or virus into the blood lines and therefore patient inflammation.
- Device improper handling: user damage the device while opening the packaging.
- Reuse or re-sterilization of the device: user re-use or re-process the device causing patient injury.
- Use of non-conventional flow regulators/tubes or damaged tubes: inappropriate flow causing reduced device efficacy.
- Use of not standard, commercially available, sterile bloodlines/infusion set/system equipped with Luer connectors compliant with ISO 80369-7: the device cannot be connect causing ineffective treatment
- Misconnection to IV line: the device cannot be connected properly and may cause plasma leakage during filtration, ineffective treatment.
- Improper use of ClearPlamsa: user attempts to use the device below 5 ml/min or above 12 ml/min causing low transfusion (delay plasma effect in bleeding patients) or reduction of Clear Plasma efficiency to absorbed plasminogen levels.
- Ineffective treatment due to the use of a device that has leaked.

12.Instruction for use

ClearPlasma™ device should be placed at room temperature before use (refer to §10.1 for details).

According to the correct orientation positioning of the ClearPlasma™ defined by the impressed arrow (refer to §1, §0 and Figure 3), ClearPlasma™ needs to be connected to:

- **Upper-side bloodline:**
  A Primary Plasma Bag joined to sterile commercially available bloodlines / infusion set/system equipped with flow regulator or drip chamber or roller clamp and ISO 80369-7 connectors.
- **Lower-side bloodline:**
  Commercially available bloodlines / infusion set/system equipped with flow regulator or drip chamber or roller clamp and ISO 80369-7 connectors.
  - In case of bed-side configuration, the bloodlines could be connected with patient vein access.
  - In case of blood-bank configuration, a collecting plasma bag shall be connected to the bloodlines.

Please note: Each of the above related devices and tubes are not included with ClearPlasma™. Based on patient needs and characteristics (in case of bed-side use configuration), the physician shall evaluate the best sterile commercially available bloodlines / infusion set/ system device configuration.
For connection instruction regarding plasma bags/bloodline and bloodline/patient vein access, refer to the instruction for use related to these devices.

The connection between ClearPlasma™ and the other devices must be done under strict guideline and by certified employees.

12.1 Device Setting

1. Hang to an IV pole the **Upper-side bloodline**. Make sure that clamp available on the bloodline is in the closed configuration.
2. Set the flow regulator available on the bloodline for a flow X≤5ml/min and not exceeding 60 min of filtration
3. Carefully remove ClearPlasma™ from the pouch and examine for defects.
4. Connect ClearPlasma™ to the **Upper-side bloodline** by screwing the ISO 80369-7 connectors: the correct direction of connection is from the opposite side of the arrow imprinted on ClearPlasma™ (see Figure 3).
5. Connect ClearPlasma™ to the **Lower-side bloodline** by screwing the ISO 80369-7 connectors: the correct direction of connection is indicated by the arrow imprinted on ClearPlasma™ (see Figure 3). When connecting the **Lower-side bloodline** make sure that available clamp is in the close configuration
6. Open all available clamps and perform priming by allowing the plasma flow through the device and drizzle outside the lower tube for few seconds into an appropriate container, as per current procedures in the hospital/blood bank setting, avoiding user/patient/devices contamination. Ensure that all air has been removed.
7. Once the priming is completed, close the clamp available on the **Lower-side bloodline**.
8. Check if the all connections by screwing are conform in order to avoid fluid leak or air entrance.

9. Connect the **Lower-side bloodline** to the collecting plasma bag (in case of blood-bank configuration) or patient vein-access (in case of bed-side configuration).
10. Open the clamp available in the **Lower-side bloodline** and proceed with plasma filtration
11. When the filtration process ends, follow the instruction for use of the **Lower-side bloodline** for disconnection tasks from collection bag/patient vein access. Do not disconnect ClearPlasma form both the bloodlines. Discard ClearPlasma together with the bloodlines. Discard the ClearPlasma™ in an appropriate biohazard waste receptacle and according to current regulations.

13. Instruction for use during treatment

1. Check that the arrow impressed on ClearPlasma™ is pointing toward the floor during the whole filtration procedure.
2. Monitor the pressure in the extracorporeal circuit, including the line between the Plasma bag and ClearPlasma™. Investigate any indication of abnormal pressure.
3. Visually inspect the ClearPlasma™ for any signs of clotting or plasma leaks from the circuit. Report presence of clotting or blood leaks to the responsible medical professional.
4. Periodically monitor the extracorporeal circuit for evidence of obstruction, security of fittings, and air within the circuit.

14. Performance Characteristics

- The plasma flow is operating by gravity feed only
- Plasma filtering capacity volume: 250 mL
- Flow resistance (Qb < 500 mL/min): 300 mmHg
- Storage fluid: Saline solution
- Sterilization: Gamma Radiation
- Acceptable plasma flow rate: X≤5 mL/min and up to 60min of filtration.
- Pressure resistance of final device: the device is capable sustain up to 330 kPa positive air pressure.

15. Device Contact Materials

Device Part	Raw Materials
Resin	TXA conjugated 4% Agarose beads
Saline	Sodium Chloride 0.9% W/V
Filter housing	**BODY** and **CAP**: • Polycarbonate , PC- Makrolon® 2458 (Covestro) **PLUG**: • Silicone 80 Shore A
Membrane	Hydrophilic Polyethersulfone (PES)
50cm Extension Line	**LUER LOCK CAP:** • Polyethylene (PE) **LUER LOCK INTERNAL CONNECTOR:** • Polyvinylchloride (PVC) **TUBE:** • Polyvinyl chloride (PVC) **LUER LOCK EXTERNAL CONNECTOR:** • Acrylonitrile butadiene styrene (ABS) **PROTECTIVE SLEEVE:** • Polypropylene (PP)

16. Serious incident reporting

Any serious incident that has occurred in relation to the device should be reported to the PLAS-FREE responsible person and the competent authority of the Member State in which the user and/or patient is established.

17. Authorized Representative

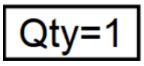
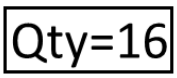
MedNet EC-REP IIb GmbH
Borkstrasse 10
48163Münster, Germany

18. Legal Manufacturer

Manufacturer: PLAS-FREE Ltd
Company# 515684009
Wadi El Haj 13,
Nazareth, Israel
ZIP 17111; PO box 1252
Ph: +972-46098615 Fax: +972-46564129
Email: info@plas-free.com

19. List of symbols on the ClearPlasma™ labeling

Symbol	Description
	Medical device
	Catalogue number
	Batch code
	Serial number
	Country of manufacture (Note: with a date of manufacture)
	Use-by date
	Do not re-use
	Non-pyrogenic
	Sterilized using irradiation (Note: By Gamma radiation)
	Consult instructions for use or consult electronic instructions for use IFU will be published on manufacturer website after granting of the CE mark.
	Temperature limitation
	Manufacturer: PLAS-FREE Ltd Company# 515684009 Wadi El Haj 13, Nazareth, Israel ZIP 17111; PO box 1252 Ph: +972-46098615, Fax: +972-46564129, Email: info@plas-free.com
	Authorized representative in the European community/European Union: MedNet, EC-REP IIb GmbH, Borkstrasse 10, 48163Münster, Germany
	Keep away from sunlight and heat

Symbol	Description
	Keep package dry and keep away from rain
	Do not use if package is damaged (or opened) and consult instructions for use
	Single sterile barrier system with protective packaging outside
	Product quantity: one unit (For Tyvek Label and Single Kit Carton Label)
Intended purpose	Sterile absorber for removal of Plasminogen from plasma units
Exclusively for clinical investigation	The device will be only used for clinical trials
	Product quantity: 16 units (For Cardboard box label)
	This Way up
	Fragile, Handle with care