Select Considerations for Venous Access Options for **THERAKOS™ CELLEX™ Photopheresis System**

Actor Portrayal

Venous Access Information Brief

Indication:

The THERAKOS™ CELLEX™ Photopheresis System is indicated for use in the ultraviolet-A (UVA) irradiation, in the presence of the photoactive drug 8-methoxypsoralen (8-MOP), of extracorporeally circulating leukocyte-enriched blood, in the palliative treatment of the skin manifestations of cutaneous T-cell lymphoma (CTCL) and systemic sclerosis (SSc).

This piece is intended as background information for healthcare providers. It is not a comprehensive presentation, or intended as medical advice, and should not replace clinical judgment. You are advised to use your own medical judgment when diagnosing and treating patients. This disease awareness material is produced by Mallinckrodt for distribution by its marketing team.

Therakos™ PHOTOPHERESIS

Venous Access Considerations

- Peripheral venous access may minimize the risk of infection.[1,2]
- Data on infection risk have shown that if peripheral vein access is a safe and effective option, it may be preferred to central venous catheter.[3]
- Use qualified staff to conduct a vein assessment to identify patients with adequate veins for peripheral access.[4,5]
- Ultrasound guidance for peripheral access has been shown to reduce the need for central venous catheter placement by as much as 85%.[6]
- Careful planning to ensure the appropriate vascular access route and which devices are used will help prevent failed or shortened therapies due to access issues.[1,2]
- Overall treatment time is dependent upon the performance of the access selected.[1,2]

Actor Portrayals

Select Clinical Decision Factors

Important Guideing Principles for Venous Access Selection

Clinicians will determine the venous access option most suitable for the patient undergoing treatment.[1,2]

The ideal route should aim to minimize risks of infection or other complications; an have minimal interference with the patient's qualify of life.[8]

Factors to consider when deciding upon venous access include, but are not limited to:

- Type of procedure and desired flow rate.[9] ECP flow rates of 15mL/min or less can lead to increased centrifuge chamber temperature.[10]
- The patient's vascular anatomy, mobility and hygiene.[9]
- Acuity, frequency and anticipated duration of procedure (as determined by the underlying disease state and response to treatment).[9]
- Patient preference.[7]
- Effect of device on patient's quality of life.[8]

Venous Access Specifications

THERAKOS Venous Access Specifications

The target whole blood processed volume during the Therakos procedure is 1500ml; patients become approximately 350-450mL fluid positive at the end of the procedure. Therakos recommends nurses oversee only one ECP procedure at a time, working under the direction of a physician per the facility's protocol.

In Single Needle Mode, the access device must be capable of withstanding the negative pressure required to collect whole blood and the positive pressure used to return blood components. In Double Needle Mode, it may be possible to use a large gauge device for DRAWING and a smaller gauge device for RETURNING. Therakos strongly recommends that more than one type of device be available, so clinicians are able to select the one most suitable for the patient undergoing treatment. The following devices are suitable for venous access during a THERAKOS™ Photopheresis treatment:[1,2]

Peripheral Venipuncture[1,2]

Needle Size	DRAWING or RETURNING
16G, 17G Fistula Needles	DRAWING or RETURNING
17G, 18G IV Catheter (High durometer angiocatheter)	DRAWING or RETURNING
20G IV Catheter (High durometer angiocatheter)	RETURNING

- Due to their small size and flexibility, peripherally inserted central catheters (PICCs) limit the maximum flow rates that can be used.[11]

Please consult the THERAKOS™ Photopheresis™ System Operator's Manual, available by calling 1-877-566-9466. Please also consult the full product monograph for the appropriate 8-methoxypsoralen formulation for important information related to adverse reactions, drug interactions, and dosing.

Central Venous Access (CVC)

- When peripheral venipuncture is not possible, alternative devices such as long-term indwelling catheters, temporary catheters, or subcutaneous ports may be used providing they meet the requirements below.[1,2]
- Any catheter intended to be used with the THERAKOS™ CELLEX™ Photopheresis System must be able to withstand the negative pressure of the peristaltic pressure pumps without collapsing and they must provide a flow rate of at least 15mL/min.[1,2]

Overall requirements[1,2]:

- Minimal internal diameter 3.0 mm or 9FR for 5.1 software
- Maximum length 36 cm
- High durometer or stiffness of catheter (such as a hemodialysis or apheresis catheter) designed for high flow output.

Non-tunneled catheters for short term (<2 weeks) use[12]:

- Associated with high risk of infection

Tunneled cuffed catheters for long term (weeks to months or longer) use[12]:

- Indicated for access required greater than 3 weeks in duration.[12]
- Data has shown non-tunneled catheters have a greater rate of infection compared with tunneled cuffed catheters.[12]

Recirculation:

- According to Howell et al. (2015), recirculation is a particular problem when using dual-lumen CVCs with non-staggered ends for both access and return.[13]
- CVC placement and care may contribute to recirculation, with biofilm, thrombus and looping of the catheter in the vein causing increases in recirculation. Blood volume processed may be increased to compensate for recirculation.[13]

Venous Access Specifications

Some recirculation management considerations:

- Insertion of peripheral cannula for return when using a CVC with non-staggered ends for access has demonstrated a reduction in CVC related recirculation problems.[13]

Implanted Venous Access Devices

- Subcutaneous ports designed specifically for high-speed infusions will not provide adequate output for DRAWING. Implant only ports are designed for both high-speed input and output.[1,2]
- Most implanted access devices require the use of large bore (e.g., 16 gauge) noncoring needles. Because these needles penetrate the septum each time the port is accessed, the septum can deteriorate with repeated use leading to the need to replace the device.[11]
- The Vortex ports (AngioDynamics, Latham, NY) are commonly used.[11]

AV Fistula or Shunts

- The THERAKOS™ CELLEX™ Photopheresis System is capable of both DRAWING from, and RETURNING to an AV Fistula or shunt. Carefully follow all center-specific guidelines for accessing and maintaining the graft.[1,2]
- AV Fistula use in apheresis is uncommon.[14]
- Education on proper access, maintenance, and safety is needed when fistulas are being considered.[4,14]
- AV Fistulas require surgical creation and a waiting period of several weeks for wound healing and maturation, therefore may be preferred for patients in need of a longer course of apheresis.[7,14]

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Patient Education and Operator Considerations

Some Considerations for Patient Education Related to Vascular Access

For 2 Days before Treatment[18]	On the Day of Treatment[18]
☐ Drink plenty of fluids such as water or juice ☐ Avoid caffeine ☐ Avoid alcohol	☐ Visit the restroom right before the treatment.
Rationale: Having more fluid in the body helps blood flow better. Both caffeine and alcohol can cause the body to have less fluid.	Rationale: Patients will need to remain attached to the instrument during the procedure, so this action may help with patient comfort.

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Be sure to use educational resources that are understandable and actionable. These elements include consideration of health literacy levels, cultural congruence, primary language, and instructional methods. Avoid medical jargon, and use simple terminology.[15]

Patient Education and Operator Considerations (cont.)

Some Operator Considerations Related to Vascular Access

- The use of dry heat has been demonstrated to increase the likelihood of successful peripheral catheter insertion.[16]
- Use of visualization technologies has been demonstrated to aid in vein identification and selection in patients with difficult venous access.[16]
- Patients are often required to squeeze a ball to assist with the blood flow.[5]
- Generally, shorter wider needle/catheter/cannula lumens provide better flow, however, actual flow rates are affected by other factors e.g. patient tolerance of fluid shifts, vein size and turgor, catheter position or buildup of biofilm and fibrin sheath.[17]

Potential Alarms

Alarms Potentially Related to Poor Access

Performing ECP on a patient with inadequate vascular access may result in instrument alarms including, but not limited to:

Collect Pressure![1,2]

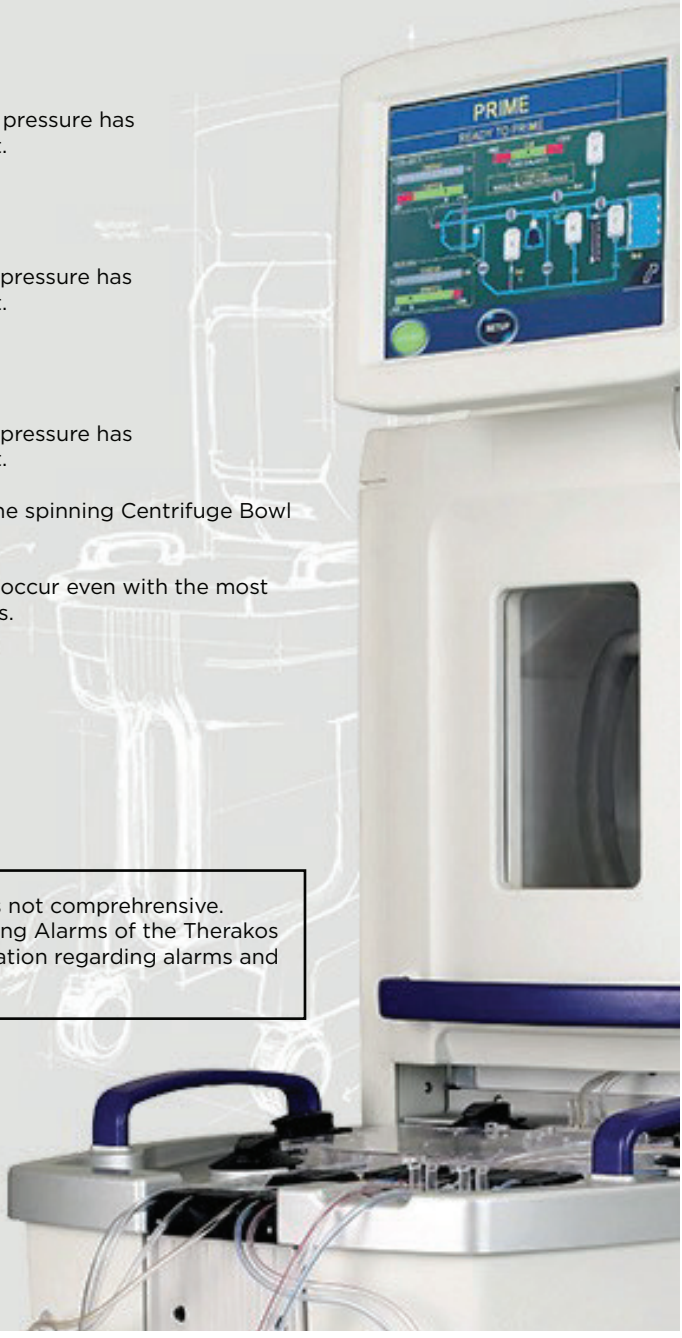
- Occurs when Collect line pressure has exceeded the preset limit.

Return Pressure![1,2]

- Occurs when Return line pressure has exceeded the preset limit.

System Pressure![1,2]

- Occurs when the system pressure has exceeded the preset limit.
- Allowing air to get into the spinning Centrifuge Bowl may form an air trap.
- Pressure alarms may still occur even with the most preferred access methods.



The information presented here is not comprehrensive. Please consult Section 6: Correcting Alarms of the Therakos Operations Manual for full information regarding alarms and device operation.

Important Safety Information for the THERAKOS™ Photopheresis Procedure

INDICATION:

The THERAKOS™ CELLEX™ Photopheresis System is indicated for use in the ultraviolet-A (UVA) irradiation, in the presence of the photoactive drug 8-methoxypsoralen (8-MOP), of extracorporeally circulating leukocyte-enriched blood, in the palliative treatment of the skin manifestations of cutaneous T-cell lymphoma (CTCL) and systemic sclerosis (SSc).

CONTRAINDICATIONS:

Certain underlying medical conditions contraindicate THERAKOS Photopheresis, including:

- Patients who cannot tolerate extracorporeal volume loss during the leukocyte enrichment phase
- Patients exhibiting idiosyncratic or hypersensitivity reactions to 8-methoxypsoralen/ psoralen compounds
- Patients with coagulation disorders or who have had previous splenectomy

WARNINGS & PRECAUTIONS:

THERAKOS Photopheresis treatments should always be performed in locations where standard medical emergency equipment is available. Volume replacement fluids and/or volume expanders should be readily available throughout the procedure.

- **MR-Unsafe:** Do not expose the device to a magnetic resonance (MR) environment. The device may present a risk of projective injury, and thermal injury and burns may occur. The device may generate artifacts in the MR image, or may not function properly.
- **Thromboembolic Events:** Thromboembolic events, including pulmonary embolism and deep vein thrombosis, have been reported in the treatment of Graft versus Host Disease (GvHD), an indication not approved in Canada. Special attention to adequate anticoagulation is advised when treating patients with GvHD.
- **Concomitant Therapy:** When prescribing and administering THERAKOS Photopheresis for patients receiving concomitant therapy, exercise caution when changing treatment schedules to avoid increased disease activity that may be caused by abrupt withdrawal of previous therapy.

ADVERSE REACTIONS:

Hypotension may occur during any treatment involving extracorporeal circulation. Monitor the patient closely during the entire treatment.

Transient pyretic reactions, 37.7-38.9o C (100-102o F), have been observed in some patients within 6-8 hours of reinfusion of the photoactivated leukocyte-enriched blood. A temporary increase in erythroderma may accompany the pyretic reaction.

Treatment frequency exceeding labeling recommendations may result in anemia.

Venous access carries a small risk of infection and pain.

Important Safety Information for Methoxsalen Sterile Solution Used in Conjunction with THERAKOS™ CELLEX Photopheresis System

CONTRAINDICATIONS

Methoxsalen Sterile Solution is contraindicated in:

- Patients exhibiting idiosyncratic reactions to psoralen compounds
- Patients with aphakia
- Patients possessing a specific history of a light-sensitive disease state

SERIOUS WARNINGS AND PRECAUTIONS

- **Concomitant Therapy:** Exercise care in treating patients who are receiving concomitant therapy (either topically or systemically) with known photosensitizing agents.
- **Carcinogenicity:** Oral administration of methoxsalen followed by cutaneous UVA exposure (PUVA therapy) is carcinogenic. Patients exhibiting multiple basal cell carcinomas or having a history of basal cell carcinoma should be diligently observed and treated.
- **Teratogenicity:** Methoxsalen may cause fetal harm when given to a pregnant woman. Women undergoing photopheresis should be advised to avoid becoming pregnant.
- **Cataractogenicity:** Patients should be told emphatically to wear UVA absorbing, wrap-around sunglasses for twenty-four (24) hours after methoxsalen treatment, any time they are exposed to direct or indirect sunlight and whether they are outdoors or exposed through a window.
- Safety in children has not been established.

FOR MORE INFORMATION

Please consult the full product monograph for methoxsalen sterile solution (if used in conjunction with the THERAKOS™ CELLEX™ Photopheresis System) and the Operator's Manual for the CELLEX system at https://www.mallinckrodt.ca/products/therakos/, or by calling us at 1-877-566-9466.

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