Mallinckrodt Pharmaceuticals

Therakos™ ECP EDGE

Transforming service into solutions

Therakos™ ECP Immunomodulation

Important safety information for the THERAKOS™ Photopheresis procedure

INDICATION:
The THERAKOS™ CELLEX™ Photopheresis System is used for the palliative treatment of the skin manifestations of cutaneous T-cell lymphoma (CTCL) and systemic sclerosis (SSc). Only health care professionals with training in THERAKOS Photopheresis should administer this therapy.

CONTRAINDICATIONS:
Certain underlying medical conditions contraindicate THERAKOS Photopheresis, including:
- Patients who cannot tolerate extracorporeal volume loss during the leukocyte enrichment phase
- 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.
- Thromboembolic Events: Thromboembolic events, including pulmonary embolism and deep vein thrombosis, have been reported in the treatment of GvHD, an indication not approved in Canada. Special attention to adequate anticoagulation is advised when treating patients with Graft versus Host Disease (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, 37.7-38.9° C (100-102° 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.

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Important safety information for Methoxsalen used in conjunction with THERAKOS™ Photopheresis

CONTRAINDICATIONS:

Methoxsalen is contraindicated in patients exhibiting idiosyncratic reactions to psoralen compounds. Patients possessing a specific history of a light sensitive disease state should not initiate methoxsalen therapy.

Methoxsalen is contraindicated in patients with aphakia.

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. Patient exhibiting multiple basal cell carcinomas or have 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 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.

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1. Company Overview

Therakos™ ECP Immunomodulation

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ECP: extracorporeal photopheresis.

Therakos™ ECP Immunomodulation

1.1 About Mallinckrodt Pharmaceuticals

Mallinckrodt Pharmaceuticals

Therakos™ ECP Immunomodulation

About Mallinckrodt Pharmaceuticals

Patients are at
THE HEART
of everything we do

Mallinckrodt Pharmaceuticals

Therakos™
ECP Immunomodulation

About Mallinckrodt Pharmaceuticals

Global Footprint

3400+
employees across the globe

- Global HQ
- 11 Corporate / Commercial Offices
- 8 Manufacturing / Research & Development Facilities
- 5 Regional Service Centers

Mallinckrodt Pharmaceuticals

Therakos™ ECP Immunomodulation

About Mallinckrodt Pharmaceuticals

Our values are the foundation of our company

Patient–Centric

"We put our patients first"

- Patients and their families are at the heart of what we do.
- Our decisions and our actions are guided by our commitment to improve lives.

Integrity

"We do the right thing"

- We do what we say we are going to do
- We can be trusted to align our actions and our words with our mission and values

Innovative

"We innovate to thrive"

- By thinking differently, we solve complex challenges with innovative solutions.
- We are agile, always seeking new ways to continuously improve our performance.

Collaborative

"We own it, together"

- We hold ourselves and each other accountable for our shared success.
- We are inclusive and work together towards our common goals.

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Therakos™ ECP Immunomodulation

1.2 The Therakos™ brand

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Therakos™ ECP Immunomodulation

The Therakos™ brand

Therakos is a specialty brand of Mallinckrodt which focuses on the delivery of ECP Immunomodulation. We provide products and services aimed at advancing the science and clinical practice of the therapy and are committed to doing everything we can to help provide optimal delivery of ECP Immunomodulation for both HCPs and patients.

We have a **more than 30-year history in the field of ECP** and, as such, have solid expertise and experience, as well as a multidisciplinary personnel who cater to specific customer needs.

Mallinckrodt Pharmaceuticals

Therakos™ ECP Immunomodulation

ECP: extracorporeal photopheresis.

The evolution of our integrated ECP Immunomodulation platforms in Canada

1999

THERAKOS™ UVAR XTS™ Photopheresis System

2009

THERAKOS™ CELLEX™ Photopheresis System

2018

CELLEX™ 5.1 System Upgrade

By listening to the evolving needs of our customers, we've launched the new PLUS system upgrade designed to help provide an easier and smoother integrated ECP experience

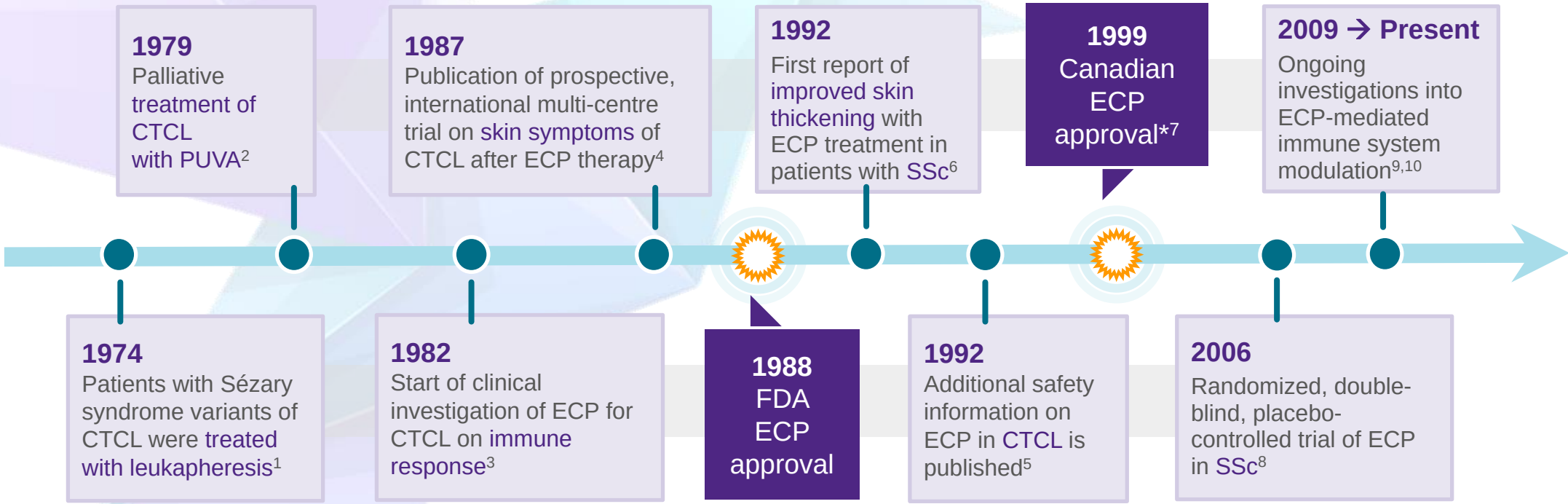
We are always working on ways to innovate and improve our delivery systems. Our development of future concepts will aim to focus on enhancing patient safety and intuitive user experience.

Future Photopheresis System Concept

ECP: extracorporeal photopheresis.

1.3 Extracorporeal Photopheresis (ECP)

ECP Immunomodulation in CTCL & SSc



*The THERAKOS™ CELLEX™ Photopheresis System is used for the palliative treatment of the skin manifestations of cutaneous T-cell lymphoma (CTCL) and systemic sclerosis (SSc)

CTCL: cutaneous T-cell lymphoma; ECP: extracorporeal photopheresis; PUVA: psoralen plus ultraviolet A, SSc: systemic sclerosis

1. Edelson R, et al. N Engl J Med. 1974;291:293-294; 2. Gilchrest BA. Cancer Treat Rep. 1979;63:663-667; 3. Knobler R, et al. Med Clin North Am. 1986;70:109-138; 4. Edelson R, et al. N Engl J Med. 1987;316:297-303; 5. Heald P, et al. J Am Acad Dermatol. 1992;27:427-433. 6. Rook AH, et al. Yale J Biol Med. 1989;62:639-645; 7. Health Canada. Medical Device Archived License Listing Database. Accessed: 29 July 2020. 8. Knobler RM, et al. J Am Acad Dermatol. 2006;54:793-799; 9. Quaglino P, et al. Int J Immunopathol Pharmacol. 2009;22:353-362; 10. Papp G, et al. Clin Immunol. 2012;142:150-159.

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Therakos™ ECP Immunomodulation

International guideline recommendations for ECP

Disease	Society / Association	Strength / Grade	Region	Year
Skin Manifestations of CTCL	National Cancer Institute (NCI)	Not specified	US	2015
	European Dermatology Forum (EDF)	Not specified	EU	2014
	American Society for Apheresis (ASFA)	1B for erythodermic, 2C for non-erythrodermic	US	2016
	National Comprehensive Cancer Network (NCCN)	2A[4]	US	2014
	United States Cutaneous Lymphoma Consortium (USCLC)	II-2[5]	UK	2011
	United Kingdom Photopheresis Society (UKPS)	A	UK	2017
	European Organization for Research and Treatment of Cancer (EORTC)	Level 3	EU	2017
Systemic Sclerosis	American Society for Apheresis (ASFA)	2A	US	2016
	European Dermatology Forum (EDF)	Not specified	EU	2014

CTCL: cutaneous T-cell lymphoma; MF/SS: mycosis fungoides/Sézary syndrome; ECP: extracorporeal photopheresis; SSc: systemic sclerosis.

1. NCI 2015 – National Cancer Institute: Mycosis Fungoides and Sézary Syndrome Treatment (PDQ®) 2017 (available at https://www.cancer.gov/types/lymphoma/hp/mycosis-fungoides-treatment-pdq#section/_73). 2. EDF 2014 – Knobler R, et al. Guidelines on the use of extracorporeal photopheresis. J Eur Acad Dermatol Venereol. 2014;28 Suppl 1:1-37. 3. ASFA – Schwartz J, et al. – Guidelines on the Use of Therapeutic Apheresis in Clinical Practice-Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Seventh Special Issue. J Clin Apher. 2016;31(3):149-162. 4. NCCN 2014 – National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Available at: http://www.nccn.org/about/nhl.pdf. 5. USCLC 2011 – Olsen EA, et al. Sézary syndrome: immunopathogenesis, literature review of therapeutic options, and recommendations for therapy by the United States Cutaneous Lymphoma Consortium (USCLC). J Am Acad Dermatol. 2011;64(2):352-404. 6. UKPS 2014 – Das-Gupta E, et al. Extracorporeal photopheresis for treatment of adults and children with acute GVHD: UK consensus statement and review of published literature. Bone Marrow Transplant. 2014;49(10):1251-1258. 7. EORTC 2017 – Trautinger F, et al. European Organisation for Research and Treatment of Cancer consensus recommendations for the treatment of mycosis fungoides/Sézary syndrome – Update 2017. Eur J Cancer. 2017;77:57-74. 8. EDF 2014 – Knobler R, et al. Guidelines on the use of extracorporeal photopheresis. J Eur Acad Dermatol Venereol. 2014;28 Suppl 1:1-37. 9. Knobler et al. European Dermatology Forum S1-guideline on the diagnosis and treatment of sclerosing diseases of the skin, Part 1: localized scleroderma, systemic sclerosis and overlap syndromes. *JEADV*. 2017. 10. Knobler et al. European dermatology forum S1-guideline on the diagnosis and treatment of sclerosing diseases of the skin, Part 2: Scleromyxedema, scleredema and nephrogenic systemic fibrosis. *JEADV*. 2017. 11. ASFA – Schwartz J, et al. – Guidelines on the Use of Therapeutic Apheresis in Clinical Practice-Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Seventh Special Issue. J Clin Apher. 2016;31(3):149-162

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1.4 The THERAKOS ECP Immunomodulation™ Procedure

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The THERAKOS ECP Immunomodulation™ Procedure

1. The instrument collects blood from the patient
2. The blood is separated by centrifugation
3. Red blood cells and plasma are returned immediately to the patient
4. Methoxsalen* is added to the buffy coat and cells are photoactivated by UVA light
5. The photoactivated buffy coat is reinfused to the patient

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ECP: extracorporeal photopheresis; UVA: ultraviolet.

*Exact mechanism of methoxsalen is unknown.

Therakos™ ECP Immunomodulation

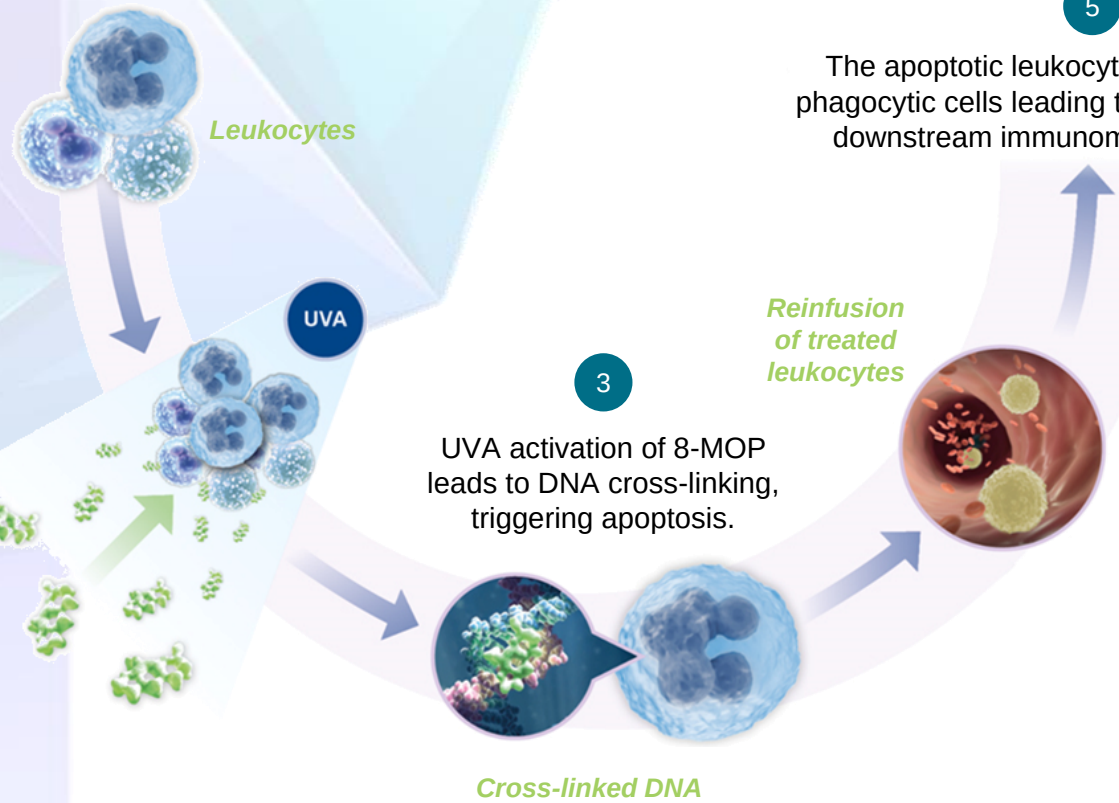
THERAKOS ECP Immunomodulation™ Procedure

Extracorporeal photopheresis (ECP) is an immunomodulatory therapeutic procedure with a number of different steps[1,2]

THERAKOS™ CELLEX™ Photopheresis System Instrument performs these steps in a single, closed and integrated system[3]

1

Blood is collected from the patient and fractionated via centrifugation. The 'buffy coat' (the fraction which contains the majority of leukocytes and platelets), is isolated, and the remaining blood returned to the patient.



2

The buffy coat is treated with 8-MOP and then exposed to UVA light.

3

UVA activation of 8-MOP leads to DNA cross-linking, triggering apoptosis.

4

The buffy coat, containing living, dead or dying cells/subcellular fragments, in addition to soluble factors, is released back into the patient's bloodstream.

5

The apoptotic leukocytes are engulfed by phagocytic cells leading to a range of indirect, downstream immunomodulatory effects.

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Therakos™ ECP Immunomodulation

8-MOP: 8-methoxypsoralen; ECP: extracorporeal photopheresis; UVA: ultraviolet-A.

1. Arora & Setia. Asian J Transfus Sci. 2017;11(2):81-86; **2.** Cho *et al.* Front Med (Lausanne) 2018; **3.** UVADEX™ Product Monograph 2014.

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2. Therakos™ ECP EDGE Service Value Offering

Therakos™ ECP Immunomodulation

Because we believe our customers and their patients deserve more

Beyond **THERAKOS™ CELLEX™ Photopheresis System**, our integrated ECP immunomodulation technology, we offer THERAKOS ECP EDGE – a comprehensive range of support services to better help healthcare professionals (HCPs) to **deliver optimized ECP immunomodulation to patients**

- **Performance**
- **Validated Technology**
- **Patient & Customer Focus**

THERAKOS ECP EDGE

Transforming service into solutions

Mallinckrodt Pharmaceuticals

Therakos™ ECP Immunomodulation

Therakos™ ECP EDGE

Performance

Validated Technology

Patient & Customer Focus

THERAKOS ECP EDGE

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Therakos™ ECP Immunomodulation

CELLEX™ Photopheresis System – Our Foundation

The Therakos™ Photopheresis System is **the only ECP platform in Canada**

- The THERAKOS™ CELLEX™ Photopheresis System represents our latest advancement in integrated ECP immunomodulation technology
- CELLEX™ is a device that we're committed to improving, according to your evolving needs. It's why we make regular updates to the system, all designed to improve user experience and provide optimal delivery of ECP therapy

Flexibility and adaptability facilitate service provision

The CELLEX™ System offers operational advantages:

- A mobile, compact system that is easily moved / transported within the unit*
- Choice of single- or double-needle mode according to venous access conditions, and the ability to switch between the two at any time during the procedure[1]
- User self-sufficiency enabled via effective troubleshooting capabilities

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*Please inform your key account manager of device location changes within your unit.

1. Therakos, Inc. Operator's Manual. THERAKOS™ CELLEX™ Photopheresis System.

Therakos™ ECP Immunomodulation

Therakos™ ECP EDGE

Performance

Validated Technology

Patient & Customer Focus

THERAKOS ECP EDGE

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Therakos™ ECP Immunomodulation

Treat patients with validated technology

The CELLEX™ System is Canada's only fully integrated and validated platform for ECP.

With full integration comes the reassurance of a completely sterile and continuous process[1,2]

Because the patient remains connected to the CELLEX™ System throughout the procedure:

- Reinfusion errors or cross-contamination are minimized[1,2]
- There is minimal risk of microbial contamination

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Therakos™ ECP Immunomodulation

1. Knobler R, et al. 2014;28 Suppl 1:1-37. **2.** Perotti C, Sniecinski I. Transfus Apher Sci. 2015;52(3):360-368.

Therakos™ ECP EDGE

Performance

Validated Technology

Patient & Customer Focus

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Therakos™ ECP Immunomodulation

Focused on solutions for you with the patient's needs in mind

Our dedicated in-house support team (ONE team) will help ensure optimal delivery of ECP treatment to your patients.

- With all of our learning initiatives, we aim to provide the highest standards and contribute to the creation of a more informed medical community, which is better placed to deliver ECP Immunomodulation to patients.

Therakos™ ONE team solutions

- Operator training & troubleshooting
- Machine repair & servicing*
- Order taking & delivery
- Contract options & adaptations

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Therakos™ ECP Immunomodulation

*Applicable only for select service contracts

How we work toward our goal

Comprehensive training throughout

- Onsite initial training for nurses and other HCPs
- Periodic onsite training to help HCP teams become more confident
- Constant onsite procedural support, including training for specific patient needs
- Continuous improvement based on customer interaction

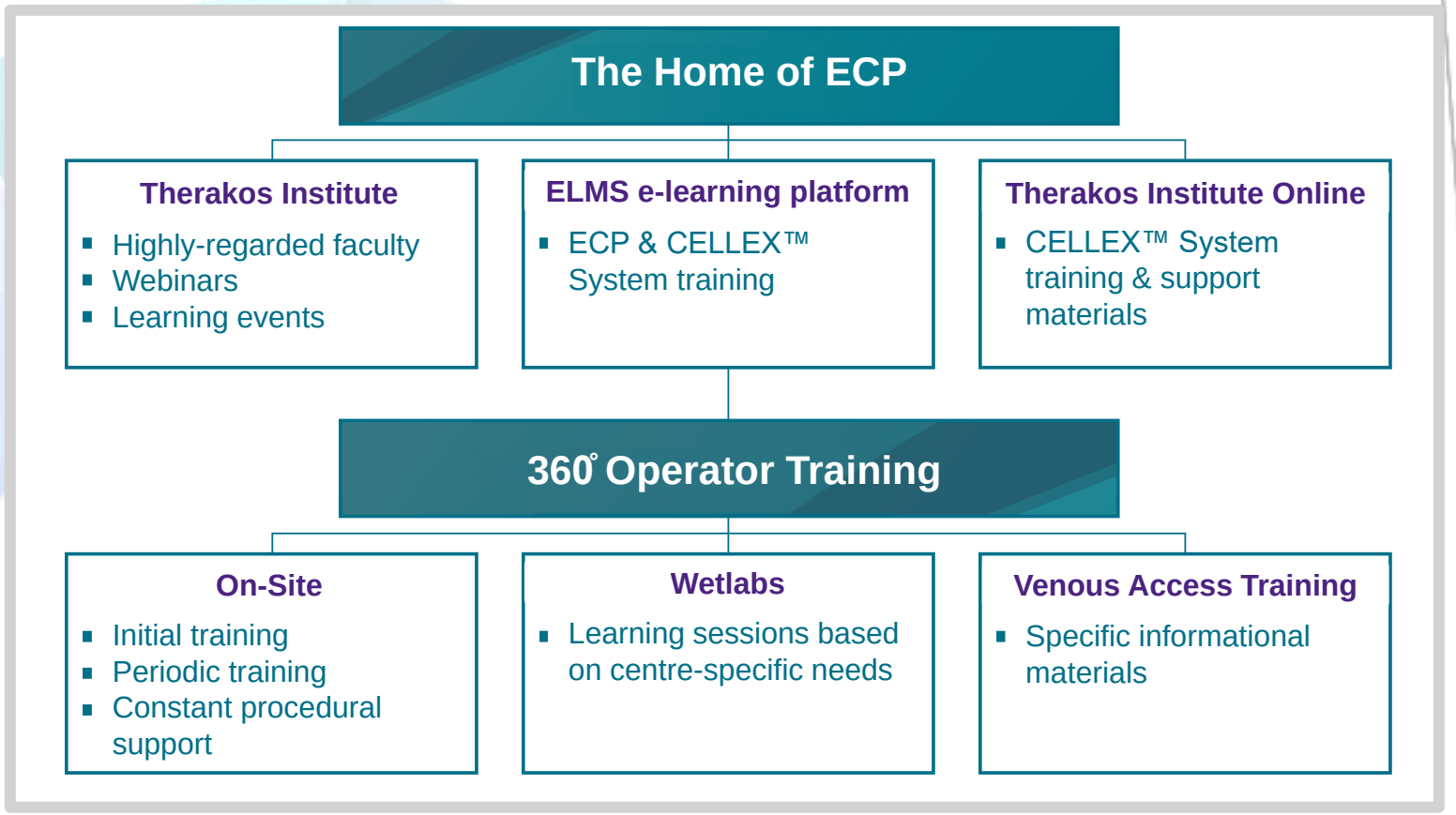
The Therakos ECP Institute Online

Offers a range of learning and self-study training opportunities available, including:

- Access to training sessions on ECP and immunomodulation
- Managing patient ECP procedures
- Access to all operator resources for optimal patient care

A direct connection to unique expertise

Our Medical Affairs team is always available to customers. One-to-one support means exclusive access to their specialist understanding of ECP



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Therakos™ ECP Immunomodulation

Support from the moment you join us

Remote and onsite support as and when you need it

- Our Customer Service team provides email and telephone support and information as soon as an order is made. They are there to enable a smooth delivery process and will support you should you have any aftersales queries.
- Our dedicated team of service engineers and support staff is on hand to help you get the most out of your system. As well as system installation, maintenance and upgrade support, the team will perform scheduled and preventative maintenance, as well as on-site repair when needed*.
- Our bilingual hotline provides rapid support and troubleshooting services from the same experts who visit you on-site

Single contact for procedural reporting

- Integrated ECP provides Mallinckrodt direct oversight and accountability for monitoring and maintaining a safety database for ECP

Hotline support is available 24/7/365 for:

- Customer service enquires
- Technical and clinical enquires

- Our Technical Service Field Specialists aim to provide fast turnaround times for repairs:

24 hours for critical repairs**

48 hours for non-critical repairs**

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Therakos™ ECP Immunomodulation

*applicable only for select service contracts
**for most locations in Canada

An ongoing commitment

We are committed to innovation and advancement in the scientific knowledge and clinical practice of ECP Immunomodulation. This is demonstrated, notably, by the investment we have made – and will continue to make – in supporting both research and clinical trials.

Mallinckrodt Pharmaceuticals

Therakos™ ECP Immunomodulation

How can we advance science?

Sharing scientific and clinical knowledge

Our expert Medical Affairs team helps us meet our goal to advance science and practice by continually building and supporting a network of HCPs, researchers and photopheresis experts.

So how exactly do we help?

Each member of our Medical Affairs team is an expert in the field of ECP and can help clinicians, researchers and societies on a range of subjects, including:

- Clinical guidelines and the latest scientific evidence
- The development of scientific articles, including data sourcing
- The continuous improvement of ECP immunomodulation therapy
- The development of scientific dossiers for reimbursement, stakeholders and processes

Because we believe our customers and their patients deserve more

- Performance
- Validated Technology
- Patient & Customer Focus

THERAKOS ECP EDGE

Transforming service into solutions

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For general enquiries please contact

CritCare-CanadianCustomerService@mnk.com or 1-877-566-9466

Therakos™ ECP Immunomodulation

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3. THERAKOS™ CELLEX™ Photopheresis System

Therakos™ ECP Immunomodulation

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Therakos™ ECP Immunomodulation

ECP: extracorporeal photopheresis.

3.1 Introduction to ECP with the THERAKOS™ CELLEX™ Photopheresis System

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Therakos™ ECP Immunomodulation

Designed for excellence in ECP

The CELLEX™ System is Canada's only fully integrated and validated ECP system, designed to help meet the needs of both you and your patients.[1]

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Therakos™ ECP Immunomodulation

1. Knobler R, et al. J Eur Acad Dermatol Venereol. 2014;28 Suppl 1:1-37.

THERAKOS™ CELLEX™ Photopheresis System – Canada's only fully integrated and validated ECP system[1]

Fully integrated and automated[1-3]

- Completely "closed" (in-line), sterile and continuous process[1]
- One mobile compact system

Designed to adjust to the patient

- Automated adaptation, customizable parameters, single- or double-needle mode[3]
- Versatility to treat all indicated disease states[5-6]

Integrated and validated specifically for ECP

- CE marked specifically for ECP[1]
- CELLEX™ System procedure time – as low as 75 minutes*[5]

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*With double-needle access.

THERAKOS™ CELLEX™ Photopheresis System is not approved for use in paediatric populations[5].

1. Knobler R, et al. J Eur Acad Dermatol Venereol. 2014;28 Suppl 1:1-37. 2. Perotti C, Sniecinski I. Transfus Apher Sci. 2015;52(3):360-368. 3. Therakos, Inc. Operator's Manual. THERAKOS™ CELLEX™ Photopheresis System. 5. Bisaccia E, et al. Br J Dermatol. 2009;161(1):167-169. 6. Knobler RM, et al. J Am Acad Dermatol. 2006;54:793-799

Therakos™ ECP Immunomodulation

3.2 THERAKOS™ CELLEX™ Photopheresis System – experience and certification

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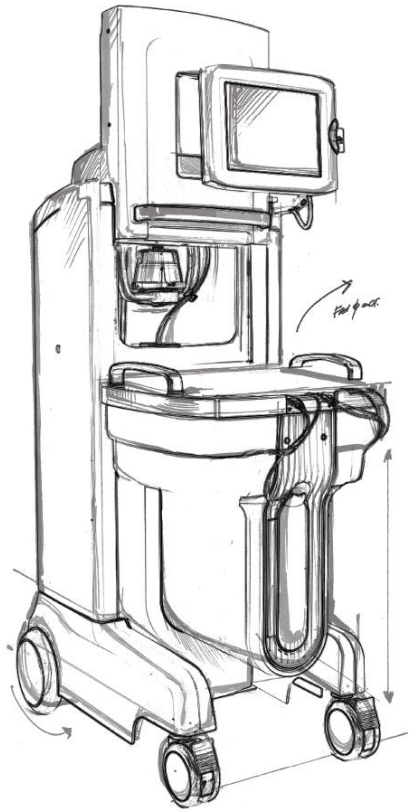
Therakos™ ECP Immunomodulation

Dedicated to the science and practice of ECP for over 30 years

We have been crafting ECP solutions (products, services and education) since 1987

THERAKOS™ CELLEX™ Photopheresis Systems have a worldwide reach

- Used by **>300 treatment centres** in **>30 countries**[1]
- ECP kits currently being provided for **>135,000 patient** treatments/year[1]
- **>1 million treatments** delivered in over **30 years**[1]



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Therakos™ ECP Immunomodulation

1. Therakos (UK) Ltd. Data on file. September 2020.

THERAKOS™ CELLEX™ Photopheresis System – Canada's only fully integrated and validated ECP system[1]

ISO 13485:2003 certified*[2]

Therakos Quality Management System certified for the design, manufacture, distribution and service of Photopheresis Systems

European Council Declaration of Conformity[3]

Medical Device Directive 93/42/EEC[4]

- Satisfies requirement that it can be used safely with the materials, substances and gases with which they enter into contact
- Satisfies requirement that performance is maintained in accordance with the intended use

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*Certified by a Notified Body (BSI Certificate of Registration number FM 72801)[2].

1. Knobler R, et al. J Eur Acad Dermatol Venereol. 2014;28 Suppl 1:1-37. 2. Therakos (UK) Ltd. Data on file. BSI. Certificate of Registration. Quality Management System – ISO 13485:2016. No. 72801. February 1, 2018. 3. Therakos (UK) Ltd. Data on file. BSI. EC Certificate – Full Quality Assurance System. No. CE00360. April 7, 2017. 4. European Council. Council Directive 93/42/EEC. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31993L0042&from=EN. Last accessed July 2019.

Therakos™ ECP Immunomodulation

3.3 Select Features of the THERAKOS™ CELLEX™ Photopheresis System

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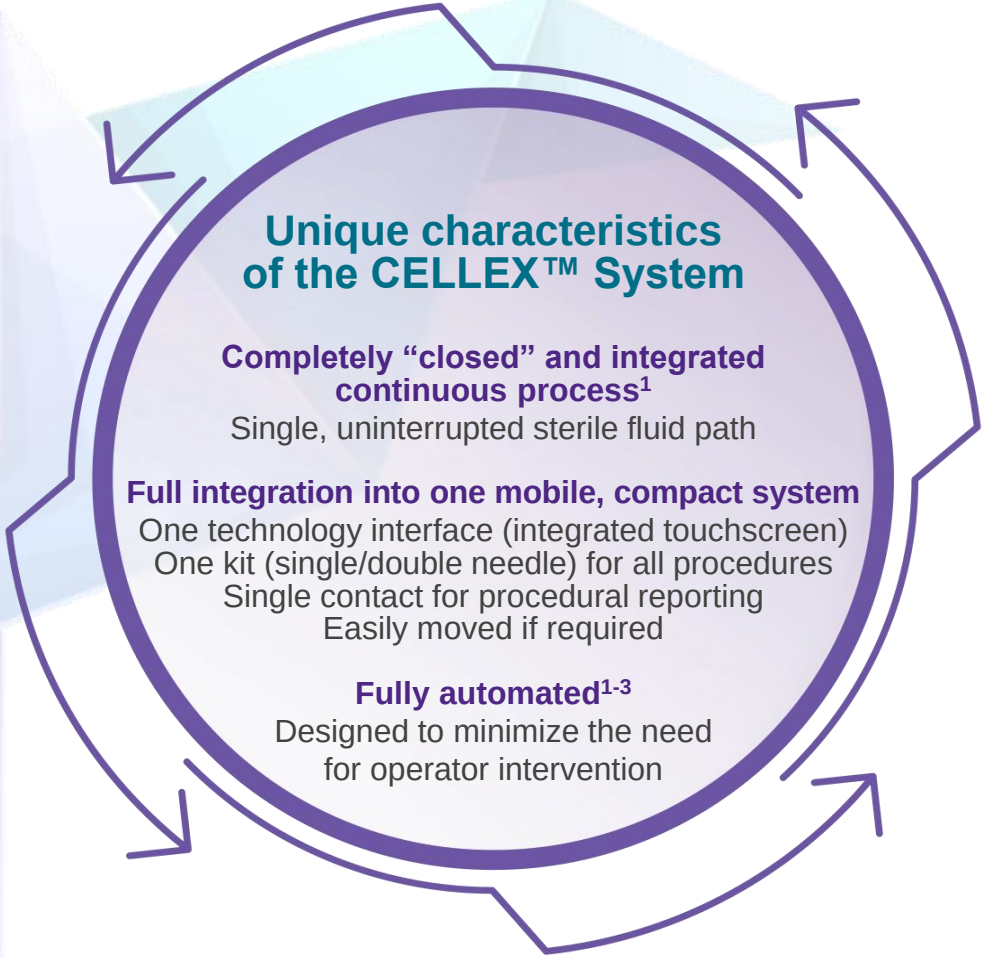
Therakos™ ECP Immunomodulation

Canada’s only fully integrated ECP system



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Therakos™ ECP Immunomodulation

1. Knobler R, et al. J Eur Acad Dermatol Venereol. 2014;28 Suppl 1:1-37. 2. Perotti C, Sniecinski I. Transfus Apher Sci. 2015;52(3):360-368. 3. Therakos, Inc. Operator’s Manual. THERAKOS™ CELLEX™ Photopheresis System.

Designed to adjust to the patient

CELLEX™ System automatically controls collection

Bowl optic sensor[1]

- Automatically identifies the red cell layer
  - Allows automated adaptation to the patient's plasma conditions
  - Delivers a consistent buffy coat

Haematocrit sensor[1]

- Automated detection of haematocrit
  - Automatically determines when buffy coat collection should end
  - Final data automatically informs photoactivation time

Automated flow rate controls[1]

- Helps reduce the need for operator interventions

*Healthcare provider portrayed by clinical specialist employed by Mallinckrodt

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Therakos™ ECP Immunomodulation

1. Therakos, Inc. Operator's Manual. THERAKOS™ CELLEX™ Photopheresis System.

Automation with the CELLEX™ System designed to help operators manage their patients

CELLEX™ System automation helps to streamline treatment management

Automated 8-MOP dosage calculation[1]

- Designed to help minimize dosage errors
  - Allows automated adaptation to the patient's plasma conditions
  - Delivers a consistent buffy coat

Specific algorithm for consistent UVA irradiation[1]

- Photoactivation time automatically calculated and set according to lamp life, % haematocrit and treatment volume
  - Helps minimize "burning" cells

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Therakos™ ECP Immunomodulation

1. Therakos, Inc. Operator's Manual. THERAKOS™ CELLEX™ Photopheresis System.

The versatility to treat patients with varying needs (1/2)

The CELLEX™ System technology enables the application of ECP to patients with various needs

Vascular access

Choice of single- or double-needle mode and ability to switch between the two according to venous access conditions

No lower limit for leukocyte levels

Continuous collection and separation enables treatment even with low leukocyte levels

Applicable for all indicated disease states

Full spectrum of white blood cells is collected, making treatment applicable to all indicated disease states

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Therakos™ ECP Immunomodulation

The versatility to treat patients with varying needs (2/2)

The CELLEX™ System technology enables the application of ECP to patients with various needs

Haemodynamic instability and low body weight

Blood priming and minimized extracorporeal volume enable treatment[1]

Abnormal lipid and bilirubin in plasma

Bowl Optic Sensor allows customization of the system to the needs of abnormal plasma conditions

Adjustable to cardiac, pulmonary or renal function

Double-needle mode minimizes fluid shifts

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Therakos™ ECP Immunomodulation

1. Bisaccia E, et al. Br J Dermatol. 2009;161(1):167-169.

The technology to deliver double-needle efficiency and delivery reassurance in one

The CELLEX™ System average treatment time[1]

- Single-needle mode: **103.0 mins**
- Double-needle mode: **74.4 mins**

Reassurance for you and the patient

Flexibility of switching between single- and double-needle modes at any time during the procedure:

- Enables adapting to patients' venous access conditions[1]

Because your patient remains connected throughout the procedure

- No re-infusion errors or cross-contamination[2,3]
- Minimal risk of microbial contamination[2,3]

Peristaltic pumps provide smooth vein pressure[4]:

- Gives confidence to you and comfort to your patients

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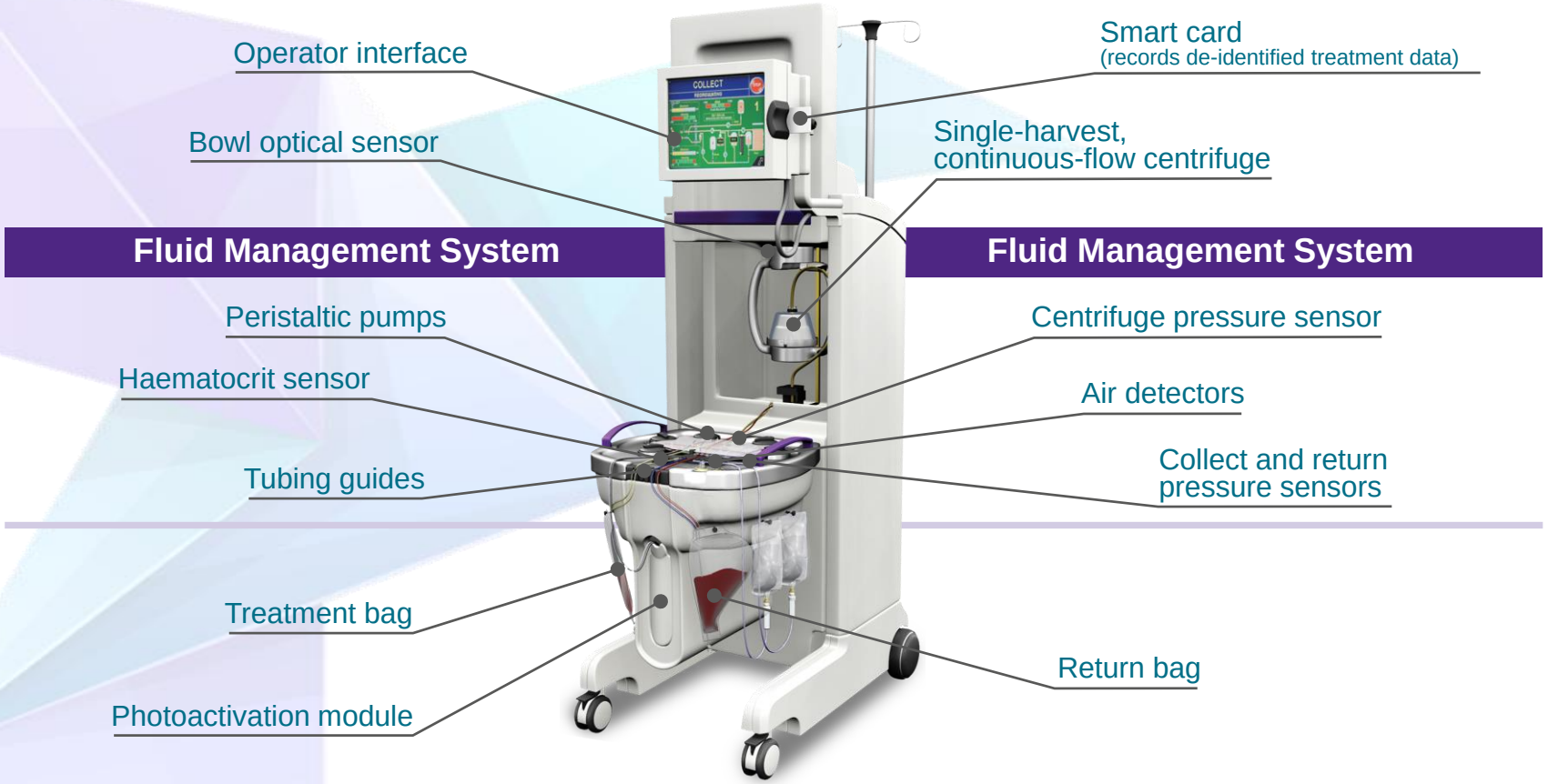
Therakos™ ECP Immunomodulation

1. Bisaccia E, et al. Br J Dermatol. 2009;161(1):167-169. 2. Knobler R, et al. J Eur Acad Dermatol Venereol. 2014;28 Suppl 1:1-37. 3. Perotti C, Sniecinski I. Transfus Apher Sci. 2015;52(3):360-368. 4. Therakos, Inc. Operator's Manual. THERAKOS™ CELLEX™ Photopheresis System.

THERAKOS™ CELLEX™ Photopheresis System – our latest, integrated ECP module



Continuous flow and fluid management help to minimize collection time and extracorporeal volume[1]

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1. Bisaccia E, et al. Br J Dermatol. 2009;161(1):167-169.

Important Safety Information for the THERAKOS™ Photopheresis Procedure

INDICATION:
The THERAKOS™ CELLEX™ Photopheresis System is used for the palliative treatment of the skin manifestations of cutaneous T-cell lymphoma (CTCL) and systemic sclerosis (SSc). Only health care professionals with training in THERAKOS Photopheresis should administer this therapy.

CONTRAINDICATIONS:
Certain underlying medical conditions contraindicate THERAKOS Photopheresis, including:

- Patients who cannot tolerate extracorporeal volume loss during the leukocyte enrichment phase
- 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.

- **Thromboembolic Events**: Thromboembolic events, including pulmonary embolism and deep vein thrombosis, have been reported in the treatment of GvHD, an indication not approved in Canada. Special attention to adequate anticoagulation is advised when treating patients with Graft versus Host Disease (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, 37.7-38.9° C (100-102° 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.

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Important Safety Information for Methoxsalen Used in Conjunction With THERAKOS™ Photopheresis

CONTRAINDICATIONS:

Methoxsalen is contraindicated in patients exhibiting idiosyncratic reactions to psoralen compounds. Patients possessing a specific history of a light sensitive disease state should not initiate methoxsalen therapy.

Methoxsalen is contraindicated in patients with aphakia.

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. Patient exhibiting multiple basal cell carcinomas or have 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 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.

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