THERAKOS™ CELLEX™ Photopheresis System Receives CE Certificate Unde the European Union Medical Device Regulation (EU MDR)

September 3, 2024

– THERAKOS, the world's only fully integrated and validated Extracorporeal Photopheresis (ECP) system,[1] received this CE certificate under the EU's new and more rigorous certification process –

DUBLIN, Sept. 3, 2024 /PRNewswire/ -- Mallinckrodt plc, a global specialty pharmaceutical company, announced that the THERAKOS™ CELLEX™ Photopheresis System has obtained CE Certification under the updated European Union Medica Device Regulation (EU MDR) 2017/745.

The EU MDR 2017/745 is a rigorous regulatory certification program for medical devices intended to support innovation while maintaining safety. The process for THERAKOS to achieve this new CE certificate involved a quality management system audit of the Dublin site, a technical review, a microbiological review, and a thorough clinical assessment.

The EU MDR application for THERAKOS was submitted in September 2022. Along with addressing the new requirements for medical devices, this submission also included two important design enhancements:

- The addition of the anticoagulant ACD-A to the current labelling and relative Software changes to ensure optimal patient and operator experience
- Material changes to remove DEHP (phthalate) and ensure compliance to latest Restriction of Hazardous Substances in Electrical and Electronic Equipment (RoHS) standards

THERAKOS is approved for use in patients who require the administration of photopheresis. This includes patients older than 18 with Cutaneous T Cell Lymphoma or Solid Organ Transplant Rejection (heart, lung), and patients older than 3 with Acute and Chronic Graft versus Host Disease.

"We are pleased THERAKOS has received the CE Certificate under the new EU MDR requirements that have been put in place to ensure the highest quality and safety standards for medical devices in the EU," said **Christopher Hirt, MD, Vice President Hospital International**. "Importantly, THERAKOS was granted this certificate after meeting the increased safety and performance requirements, which may give healthcare providers even greater confidence when treating patients."

About THERAKOS™ CELLEX™ Photopheresis System
The THERAKOS CELLEX Photopheresis System is the world's only fully integrated and validated ECP system.[1] THERAKOS performs ECP using patented technology that collects, separates and treats a small amount of white blood cells (immune cells) while the patient is connected to the instrument. The treated cells are then returned to the patient where they help to modify the immune response in a process called immunomodulation. It is used to treat a range of immune-mediated diseases. THERAKOS Systems are used by over 300 treatment centres in over 30 countries worldwide.[2]

About Extracorporeal Photopheresis (ECP)
Extracorporeal photopheresis (ECP) is an immunomodulatory therapy that has demonstrated efficacy in various T-cell and immune-mediated diseases.[3] ECP is recommended by international and national guidelines for a spectrum of diseases, including cutaneous T-cell lymphoma (CTCL), acute and chronic graft-versus-host disease (aGvHD and cGvHD), chronic lung allograft dysfunction-bronchiolitis obliterans syndrome (CLAD-BOS) and after cardiac transplantation.[4,5,6,7,8,9,10,11,12,13,14,15]

IMPORTANT SAFETY INFORMATION FOR THE THERAKOS™ PHOTOPHERESIS PROCEDURE UNDER EU MDR

Indications under EU MDR
The THERAKOS™ CELLEX™ Photopheresis System is indicated for patients older than 18 years of age for the administration o photopheresis in the following:

- Cutaneous T Cell Lymphoma (CTCL)
- Solid Organ Transplant Rejection (SOT) (heart, lung)

The THERAKOS™ CELLEX™ Photopheresis System is indicated in patients older than 3 years of age for the management of

- Acute and Chronic Graft versus Host Disease (aGvHD, cGvHD)

Contraindications

THERAKOS ™ Photopheresis is contraindicated in:

- Patients possessing a specific history of a light sensitive disease
- Patients who cannot tolerate extracorporeal volume loss or who have white blood cell counts greater than 25,000 / mm^3
- Patients who have coagulation disorders or who have previously had a splenectomy

Warnings and 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.
- Do not expose the device to a magnetic resonance (MR) environment. The device may present a risk of projectile injury, and thermal injury and burns may occur. The device may generate artifacts in the MR image, or may not function properly.
- Thromboembolic events, including pulmonary embolism and deep vein thrombosis, have been reported in the treatment of Graft versus Host Disease (GvHD). Special attention to adequate anticoagulation is advised when treating patients with GvHD.
- 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 Events

- Hypotension may occur during any treatment involving extracorporeal circulation. Closely monitor the patient during the entire treatment for hypotension.
- Transient pyretic reactions, 37.7–38.9°C (100–102°F), have been observed in some patients within six to eight hours of reinfusion of the photoactivated leukocyte-enriched blood. A temporary increase in erythroderma may accompany the pyretic reaction.
- Treatment frequency exceeding labelling recommendations may result in anaemia.
- Venous access carries a small risk of infection and pain.

Please refer to the THERAKOS ™ CELLEX ™ Photopheresis System Operator Manual for a complete list of warnings and precautions.

IMPORTANT SAFETY INFORMATION FOR METHOXSALEN USED IN CONJUNCTION WITH THERAKOS ™ PHOTOPHERESIS

Contraindications

Methoxsalen is contraindicated in:

- Patients exhibiting idiosyncratic or hypersensitivity reactions to methoxsalen, psoralen compounds, or any of the excipients
- Patients with co-existing melanoma, basal cell or squamous cell skin carcinoma
- Patients who are pregnant, and sexually active men and women of childbearing potential unless adequate contraception is used during treatment
- Patients with aphakia because of the significantly increased risk of retinal damage due to the absence of a lens

Warnings and Precautions

- Special care should be exercised in treating patients who are receiving concomitant therapy (either topically or systemically) with known photosensitizing agents.
- Oral administration of methoxsalen followed by cutaneous UVA exposure (PUVA therapy) is carcinogenic.
- Patients should be told emphatically to wear UVA absorbing, wrap-around sunglasses for twenty-four (24) hours after methoxsalen treatment. They should wear these glasses any time they are exposed to direct or indirect sunlight, whether they are outdoors or exposed through a window.
- Safety in children has not been established.

Refer to the package insert for methoxsalen sterile solution (20 micrograms / mL) or the oral 8-methoxypsoralen dosage formulation for a list of all warnings and precautions.

Please refer to the THERAKOS ™ CELLEX ™ Photopheresis System Operator Manual for a complete list of warnings and precautions and adverse events.

ABOUT MALLINCKRODT
Mallinckrodt is a global business consisting of multiple wholly owned subsidiaries that develop, manufacture, market and distribute specialty pharmaceutical products and therapies. The company's Specialty Brands reportable segment's areas of focus include autoimmune and rare diseases in specialty areas like neurology, rheumatology, hepatology, nephrology, pulmonology, ophthalmology, and oncology; immunotherapy and neonatal respiratory critical care therapies; analgesics; and gastrointestinal products. Its Specialty Generics reportable segment includes specialty generic drugs and active pharmaceutical ingredients. To learn more about Mallinckrodt, visit www.mallinckrodt.com.

CAUTIONARY STATEMENTS RELATED TO FORWARD-LOOKING STATEMENTS

This release contains forward-looking statements, including with regard to THERAKOS, its potential to improve health and treatment outcomes, and its potential impact on patients. The statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those in the forward-looking statements: the effects of Mallinckrodt's recent emergence from bankruptcy; satisfaction of, and compliance with, regulatory and other requirements; actions of regulatory bodies and other governmental authorities; changes in laws and regulations; issues with product quality, manufacturing or supply, or patient safety issues or adverse side effects or adverse reactions associated with THERAKOS; and other risks identified and described in more detail in the "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of Mallinckrodt's most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and other filings with the SEC, all of which are available on its website. The forward-looking statements made herein speak only as of the date hereof and Mallinckrodt does not assume any obligation to update or revise any forward-looking statement, whether as a result of new information, future events and developments or otherwise, except as required by law.

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