

Understanding THERAKOS™ Extracorporeal Photopheresis (ECP)



*Healthcare providers portrayed by clinical specialists employed by Mallinckrodt

**Intended for discussion between Health Care Professionals and
SSc Patients prescribed THERAKOS ECP**

What is photopheresis?

Photopheresis is also known as Extracorporeal Photopheresis, or ECP:

- “Extracorporeal” means outside the body.
- “Photopheresis” is the combination of two words. “Photo” which means light and “apheresis” which means separation.

So ECP involves collecting and separating a small fraction of your blood cells which then undergo light activated therapy outside the body before being returned.

What is ECP used for?

ECP is used to treat certain medical conditions caused by overreactions of the immune system.

Systemic sclerosis is an autoimmune rheumatic disease caused by excessive production and accumulation of collagen. Collagen is the main structural protein that makes up all of your tissues.

Accumulation of collagen may cause thickening, redness and irritation in the skin, inflammation and scarring that may impact internal organ function and injure small arteries.¹



How does ECP work?

In conditions such as systemic sclerosis, certain types of white blood cells can become overactive and start attacking your body. During ECP, a small amount of white blood cells are collected and treated with a photosensitizing agent, methoxsalen sterile solution, which is activated by exposure to ultraviolet-A (UVA) light.²



While the exact way in which ECP works in the body is unknown, the treated cells then can help to modify your immune response in a process called immunomodulation. ECP is “immunomodulatory” which means it changes the response of your immune system without suppressing it.²

This can help defend against infections caused by microorganisms that take advantage of weakened immune systems (opportunistic infections). Your immune system can also remember how to defend against toxins or foreign proteins (called antigens).²

Using ECP may allow the reduction of immunosuppressive drugs, which may be preferable when treating immune conditions.

What are the risks involved for ECP?

Ask your doctor or nurse if you have any other concerns about ECP. For complete safety information, please see the Consumer Information section of this brochure, or contact Mallinckrodt at 1-877-865-6850.

Side effects of ECP are most often related to a temporary drop in blood pressure due to changes in your blood volume during the treatment. Your doctor or nurse will monitor you during treatment for low blood pressure.

Venous access carries a small risk of infection and pain. The THERAKOS™ Photopheresis System is a “closed” system for ECP. This means that the blood that is collected and treated is never separated from you and the instrument to minimize the risk of infusion errors.

There are additional possible side effects, which include fever and skin redness. Please see the Consumer Information section of this brochure for complete safety information.

¹Scleroderma Canada. What is Scleroderma? Accessed: June 2020.

²Knobler, R. & Greinix, H.T. Extracorporeal Photopheresis: Cellular Photoimmunotherapy. © 2012 Walter de Gruyter & Co. KG, Berlin/Boston

What can I expect during my ECP treatment?

- 1** At the start of your treatment, you will be connected to the ECP instrument by a thin flexible tube (called a catheter), which will be inserted into a vein, usually in your arm. A small amount of blood will then start to be collected through this tube and into the ECP instrument.
- 2** During the collection, as your blood flows through the instrument, the different parts that make up your blood will be separated by centrifugation, in a process called apheresis. Your red blood cells and plasma are returned to you straight away, while your white blood cells remain in the ECP instrument for treatment.
- 3** Inside the ECP instrument, your white blood cells will be treated with the photosensitizing agent, which will then be exposed to UVA light to “activate” it.
- 4** The treated white blood cells are then returned to your bloodstream.

You will be connected to the ECP instrument for the entire process.

Treatment duration varies from patient to patient. Usually, it takes between 1 to 3 hours to complete.

The tubing is replaced for every patient and the ECP system is completely closed, so there is no chance that your blood will come into contact with that of any other patient.

How many treatments will I need?

The number of sessions will depend on the disease being treated, your symptoms and response to ECP. Your doctor will decide the number of treatments suited to your individual needs, and may prescribe a normal or accelerated treatment cycle.

The normal treatment cycle involves treatment on 2 successive days each month for 6 months. The accelerated treatment cycle involves a treatment schedule of 2 successive days every 2 weeks for 3 months. When maximum response is achieved, physicians can gradually decrease frequency of treatment. Your physician will determine the appropriate schedule based on your needs.

Your healthcare provider can review the THERAKOS™ CELLEX™ Photopheresis System procedural video with you.



When will I know it is working?

THERAKOS™ ECP has demonstrated positive effects in many people, but results vary, and it is difficult to predict the type and extent of response you will have.

The length of time it takes to respond to treatment will be different for every patient and will depend on the state of your immune system, the severity of your disease and how often you receive treatment.

Improvement may happen gradually. An “adequate response” is considered to be at least a 15% reduction in your skin severity score. Your physician will determine the appropriate schedule based on your needs.

Ask your doctor or nurse if you have any other concerns about ECP. For complete safety information, please see the Consumer Information section of this brochure, or contact Mallinckrodt at 1-877-865-6850.

How can I prepare for my ECP treatment?

There are several things you can do to help your ECP treatment session be as comfortable as possible. Your doctor or nurse will tell you the best way for you to prepare based on your individual health and medical condition.

Remember to tell your doctor or nurse about any other conditions (such as heart problems, or low blood volume/pressure) as well as any medications you may be taking before starting treatment.

Certain underlying medical conditions limit patient eligibility for ECP treatment*, including:

- Inability to tolerate loss of blood volume due to heart conditions or low blood volume or pressure
- Allergies or sensitivities to psoralen compounds
- Bleeding or clotting disorders
- Spleen removal
- Light sensitivity
- Eye lens removal
- Aphakia
- Pregnancy

The plan below has some useful tips that can help you get ready for treatment. Your care team can also provide you with the ECP patient calendar to help you track your treatment plan and any questions about the therapy.

	Two Days Before	The Evening Before	Day of Treatment
TIP	<ul style="list-style-type: none"> • Drink plenty of fluids • Avoid caffeine • Avoid alcohol 	<ul style="list-style-type: none"> • Eat a low-fat meal • Avoid food such as high-fat meat, cream, fried food, cheese, eggs, butter, and deserts 	<ul style="list-style-type: none"> • Eat a low-fat breakfast and lunch • Don't skip any meals • Visit the bathroom right before the treatment
WHY?	Having lots of fluid in your body helps your blood flow better during treatment. Both caffeine and alcohol can cause a reduction in your body fluids.	High levels of fat in the blood may make the cell-separation process more difficult and could result in the treatment being stopped before it's finished.	You will need to remain seated throughout the procedure. These tips can help you to stay comfortable during treatment.

*Please consult the full product monograph for the appropriate 8-methoxypsoralen formulation for important information related to adverse reactions, drug interactions, and dosing.

Will it be painful?

As with any needle puncture procedure, there may be some minor discomfort when the catheter is inserted into your vein.

During ECP you may sometimes feel different sensations that are not painful. These may include a slight pulsing from the ECP instrument's pump and a slight chill or cold sensation as blood is returned to your body.

You may feel weak or dizzy during, or immediately after your treatment. This sometimes Occurs because of a slight drop in blood pressure. Tell your doctor or nurse if this happens.



What should I do after my ECP treatment?

The photosensitizer used in ECP, can make you more sensitive to sunlight for about 24 hours after treatment. You should protect your eyes and skin by taking the following simple, but very important, precautions for 24 hours after every treatment:

- Avoid sunlight as much as possible, even indirect sunlight coming through a window
- Wear sunscreen SPF 15 or higher when exposed to sunlight (both outdoors and indoors)
- Wear UVA-protective, full-coverage sunglasses when exposed to direct or indirect sunlight

Ask your doctor or nurse if you have any other concerns about ECP. For complete safety information, please see the Consumer Information section of this brochure, or contact Mallinckrodt at 1-877-865-6850.

Important Safety Information for the THERAKOS™ Photopheresis Procedure

INDICATIONS:

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

CONTRAINDICATIONS:

Do not undergo THERAKOS Photopheresis Procedure if:

- You are unable to tolerate loss of blood volume
- You are allergic or hypersensitive to 8-methoxypsoralen/psoralen compounds
- You have a blood-clotting or bleeding disorder or have had your spleen removed

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:** Blood clots involving the lung and other parts of the body have been reported in patients being treated for Graft versus Host Disease (GvHD), an indication not approved in Canada.
- **Concomitant Therapy:** Tell your doctor if you are taking any other medications or are receiving other therapies to avoid increased disease activity caused by changes in your treatment plan.

ADVERSE REACTIONS:

Side effects of the Therakos Photopheresis Procedure include:

- Low blood pressure
- Fevers of 37.7-38.9°C (100-102°F) and redness of the skin 6 to 8 hours after treatment
- A decrease in red blood cells which may cause you to feel tired
- Infection and/or pain at the injection site

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

CONTRAINDICATIONS:

Do not use methoxsalen if:

- You are allergic or hypersensitive to 8-methoxypsoralen/psoralen compounds
- You have a history of a light-sensitive condition or disease
- You had an eye lens removed due to increased risk of retinal damage

WARNINGS AND PRECAUTIONS:

- Methoxsalen may increase your risk to sun sensitivity. Tell your doctor if you are taking other medications (either topically or systemically) with photosensitizing agents.
- Tell your doctor if you currently have skin cancer or if you had skin cancer in the past.
- Methoxsalen may cause harm to your unborn child. Tell your doctor if you are pregnant or plan to become pregnant.
- You must wear UVA light-absorbing, wrap-around sunglasses for 24 hours after treatment any time you are exposed to direct or indirect sunlight, and whether you are outdoors or exposed through a window.
- Safety in children has not been shown.

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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