Understanding THERAKOS™ Extracorporeal Photopheresis (ECP)

Intended for discussion between Health Care Professional and Patient
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 was first used to treat skin symptoms associated with a type of blood cancer but it is now also used to treat a range of diseases caused by overreactions of the immune system. Examples include a condition called graft-versus-host disease (GvHD) that can occur after stem cell or bone marrow transplantation.

ECP is also used for organ transplant-related rejection (such as heart or lung transplants) and to treat other autoimmune disorders, such as systemic sclerosis and atopic dermatitis.

How does ECP work?

In conditions such as GvHD or autoimmune disorders, certain types of white blood cell can become overactive and start attacking your body. During ECP, a small amount of white blood cells are collected and treated with a photosensitizer, which is activated by exposure to ultraviolet-A (UVA) light. The treated cells then 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.

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).

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

What are the risks involved for ECP?

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. Other possible side effects such as fever or skin redness usually go away within a day. Venous access carries a small risk of infection and pain.

The THERAKOS™ Photopheresis System is the only approved “closed” system for ECP. This means that the blood that is collected and treated is never separated from you and the instrument so minimizing the risk of infusion errors when it is returned to the body.

Ask your doctor or nurse if you have any other concerns about ECP.

For complete safety information, including adverse events, please also see Full Prescribing Information for the appropriate Methoxsalen product.
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 photosensitizer, 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 anybody else’s.

How many treatments will I need?

Your treatment sessions will be repeated over time. 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.

When will I know it is working?

THERAKOS™ ECP has demonstrated positive effects in many people but 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 and it is important that you don’t give up or feel discouraged if you don’t see results straight away.

Watch the THERAKOS™ CELLEX™ Photopheresis System Video at www.therakos.co.uk
Will it be painful?

Most people report little or no discomfort during treatment. However, 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.

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.

The plan below has some useful tips that can help you get ready for treatment:

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<th>2 days before</th>
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<tr>
<td><strong>TIP</strong></td>
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<td>• Drink plenty of fluids</td>
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<td>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.</td>
<td>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.</td>
<td>You will need to remain seated throughout the procedure. These tips can help you to stay comfortable during treatment.</td>
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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.

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
Important Safety Information for the THERAKOS™ Photopheresis Procedure

INDICATIONS
The THERAKOS™ UVAR XTS™ and THERAKOS™ CELLEX™ Photopheresis Systems are indicated for the administration of photopheresis. Please refer to the appropriate product labelling for a complete list of warnings and precautions.

CONTRAINDICATIONS
THERAKOS™ Photopheresis is contraindicated in patients possessing a specific history of a light sensitive disease. THERAKOS™ Photopheresis is contraindicated in patients who cannot tolerate extracorporeal volume loss or who have white blood cell counts greater than 25,000 mm³. THERAKOS™ Photopheresis is contraindicated in 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. Safety in children has not been established.

Both men and women should take adequate contraceptive precautions both during and after completion of photopheresis 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.

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. Please refer to the appropriate product labelling 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. Methoxsalen is contraindicated in patients with co-existing melanoma, basal cell or squamous cell skin carcinoma. Methoxsalen is contraindicated in sexually active men and women of childbearing potential unless adequate contraception is used during treatment, and during pregnancy and lactation. Methoxsalen is contraindicated in 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. Because the dose with liquid methoxsalen is about 200 times less than with PUVA therapy and the skin is not exposed to high cumulative doses of UVA light, the risk of developing skin cancer following this therapy may be lower.

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 Methoxsalen (20 micrograms / mL) labelling or the oral 8-methoxypsoralen dosage formulation package insert for more information on protecting the patient from light and a list of all warnings and precautions.

For complete safety information, including adverse events, please see Full Prescribing Information for the appropriate Methoxsalen product.

THERAKOS is part of Mallinckrodt. For more information about THERAKOS™ ECP please visit: www.therakos.co.uk. www.mallinckrodt.com. Therakos (UK) Limited, 3 Lotus Park, The Causeway, Staines-upon-Thames, Surrey, TW18 3AG, UK. Tel: +44 (0) 1784 636 700. Email: CritCareTKS-TKSInfo@mnk.com. Mallinckrodt, the “M” brand mark and the Mallinckrodt Pharmaceuticals logo are trademarks of a Mallinckrodt company. Other brands are trademarks of a Mallinckrodt company or their respective owners. © 2019 Mallinckrodt.

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