Therakos PHOTOPHERESIS

PHOTOPHERESIS TREATMENT + ASSESSMENT SCHEDULE

STANDARD TREATMENT SCHEDULE

ACCELERATED TREATMENT SCHEDULE

When patients with skin manifestations of CTCL are unresponsive to skin-directed treatment, help tackle skin manifestations of CTCL with a strategic immune response.

THERAKOS Photopheresis offers 2 treatment schedules based on patient response.

INDICATIONS AND USAGE
UVADEX® (methoxsalen) Sterile Solution is indicated for extracorporeal administration with the THERAKOS® UVAR XTS® or THERAKOS CELLEX® Photopheresis System in the palliative treatment of the skin manifestations of Cutaneous T-Cell Lymphoma (CTCL) that is unresponsive to other forms of treatment.

SELECTED SAFETY INFORMATION
CAUTION: READ THE THERAKOS UVAR XTS or THERAKOS CELLEX PHOTOPHERESIS SYSTEMS' OPERATOR'S MANUAL PRIOR TO PRESCRIBING OR DISPENSING THIS MEDICATION.

UVADEX (methoxsalen) Sterile Solution should be used only by physicians who have special competence in the diagnosis and treatment of cutaneous T-cell lymphoma and who have special training and experience in the THERAKOS UVAR XTS or THERAKOS CELLEX Photopheresis System. Please consult the appropriate Operator's Manual before using this product.

Please see additional Important Safety Information on reverse side and Full Prescribing Information, including the BOXED WARNING for UVADEX, inside pocket, and see the appropriate THERAKOS Photopheresis System Operator's Manual.

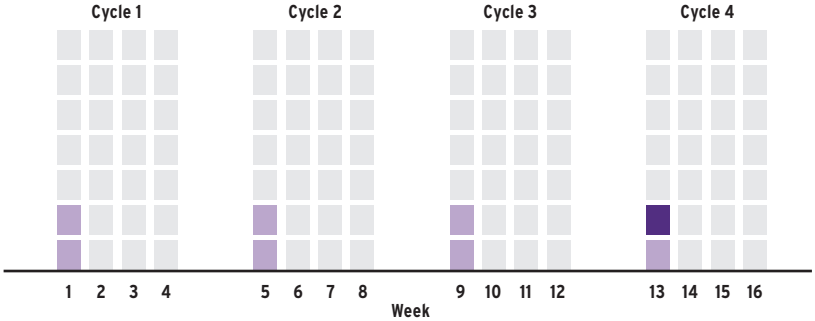
Standard Treatment Schedule

THERAKOS® Photopheresis for the treatment of skin manifestations of cutaneous T-cell lymphoma (CTCL) may follow a standard treatment schedule that encompasses a minimum of 6 months of continuous treatment before results can be fully assessed. Treatment is given on 2 consecutive days every 4 weeks with a patient assessment occurring during the 4th treatment cycle.

If skin score at patient assessment is the same or improved from baseline, patient may continue on the **standard treatment schedule**. If skin score at patient assessment has worsened, then patient may continue on the **accelerated treatment schedule**.

Treatment

Treatment/Assessment



2 Days

Patients should schedule **2 consecutive days** of THERAKOS Photopheresis treatments. This constitutes 1 treatment cycle.

4 Weeks

Every **4 weeks**, patients should return for their next treatment cycle (2 consecutive days). During the 4th treatment cycle, patients should be assessed.

6 Months

The standard treatment schedule should continue for a minimum of **6 months (7 treatment cycles)** before results can be fully assessed.

Accelerated Treatment Schedule

If an assessment of the patient during the 4th treatment cycle of the standard treatment schedule reveals an increased skin score from the baseline, the patient may begin the accelerated treatment schedule.

If a 25% improvement in the skin score is attained after 2 accelerated treatment cycles, the patient can be transferred back to the standard treatment schedule.

If the assessment does not reveal a 25% improvement, patients may maintain the accelerated treatment schedule. Patients maintained in the accelerated treatment schedule may receive a maximum of 20 cycles.

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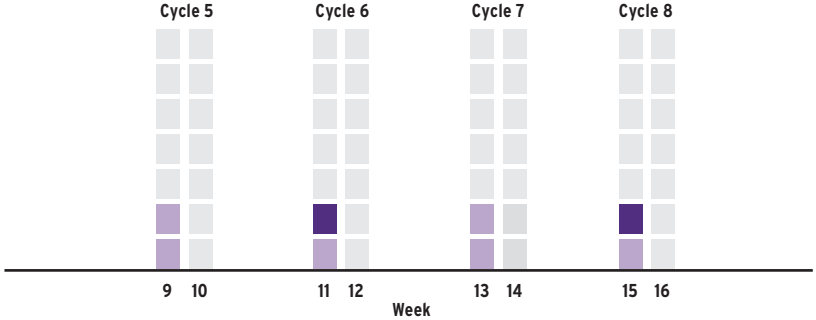

2 Days

The accelerated treatment schedule follows the same **2 consecutive days** of THERAKOS® Photopheresis treatments. One cycle equals 2 consecutive days.

2 Weeks

Every **2 weeks**, patients should return for their next treatment cycle. After every 2 treatment cycles, patients should be assessed.

12 Months*

Patients maintained at the accelerated treatment schedule may receive a maximum of **20 treatment cycles (12 months).*†**

*12 months is based on a total of 20 treatment cycles.

†There is no clinical evidence to show that treatment with UVADEX® beyond 6 months or using a different schedule provides additional benefit.

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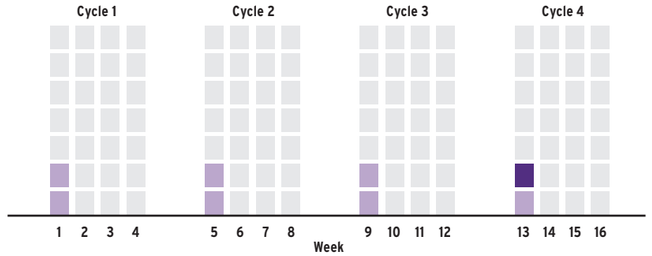

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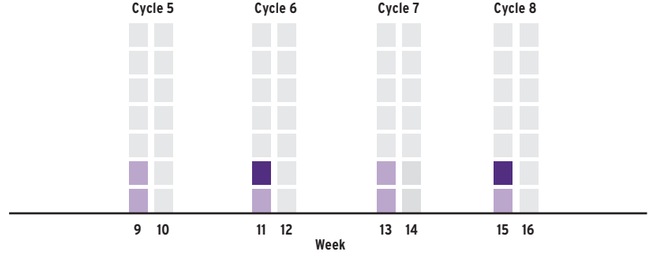

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CONTRAINDICATIONS

UVADEX is contraindicated in patients exhibiting idiosyncratic or hypersensitivity reactions to methoxsalen, other psoralen compounds, or any of the excipients. Patients possessing a specific history of a light-sensitive disease state should not initiate methoxsalen therapy.

Diseases associated with photosensitivity include lupus erythematosus, porphyria cutanea tarda, erythropoietic protoporphyria, variegate porphyria, xeroderma pigmentosum, and albinism.

UVADEX is contraindicated in patients with aphakia because of the significantly increased risk of retinal damage due to the absence of lenses.

Patients should not receive UVADEX if they have any contraindications to the photopheresis procedure.

WARNINGS AND PRECAUTIONS

- Patients who are receiving concomitant therapy (either topically or systemically) with known photosensitizing agents such as anthralin, coal tar or coal tar derivatives, griseofulvin, phenothiazines, nalidixic acid, halogenated salicylanilides (bacteriostatic soaps), sulfonamides, tetracyclines, thiazides, and certain organic staining dyes such as methylene blue, toluidine blue, rose bengal, and methyl orange may be at greater risk for photosensitivity reactions with UVADEX
- Oral administration of methoxsalen followed by cutaneous UVA exposure (PUVA therapy) is carcinogenic. Methoxsalen also causes DNA damage, interstrand cross-links and errors in DNA repair
- Methoxsalen may cause fetal harm when given to a pregnant woman. There are no adequate and well-controlled studies of methoxsalen in pregnant women. If UVADEX is used during pregnancy, or if the patient becomes pregnant while receiving UVADEX, the patient should be apprised of the potential hazard to the fetus. Women of childbearing potential should be advised to avoid becoming pregnant. It is not known whether this drug is excreted in human milk
- After methoxsalen administration, exposure to sunlight and/or ultraviolet radiation may result in "premature aging" of the skin
- Since oral psoralens may increase the risk of skin cancers, monitor closely those patients who exhibit multiple basal cell carcinomas or who have a history of basal cell carcinomas
- Serious burns from either UVA or sunlight (even through window glass) can result if the recommended dosage of methoxsalen is exceeded or precautions are not followed
- Patients should be advised to avoid all exposure to sunlight during the 24 hours following photopheresis treatment
- Exposure to large doses of UVA light causes cataracts in animals. Oral methoxsalen exacerbates this toxicity. Serum methoxsalen concentrations are substantially lower after extracorporeal UVADEX treatment than after oral methoxsalen treatment. Nevertheless, if the lens is exposed to UVA light while methoxsalen is present, photoactivation of the drug may cause adducts to bind to biomolecules within the lens
- Instruct patients emphatically to wear UVA-absorbing, wrap-around sunglasses for 24 hours after UVADEX treatment
- Safety in children has not been established
- Thromboembolic events, such as pulmonary embolism and deep vein thrombosis, have been reported with UVADEX administration through photopheresis systems for treatment of patients with graft-versus-host disease, a disease for which UVADEX is not approved.

ADVERSE REACTIONS

- Side effects of photopheresis (UVADEX used with the THERAKOS Photopheresis System) were primarily related to hypotension secondary to changes in extracorporeal volume (>1%)

For the THERAKOS® UVAR XTS®/CELLEX® Photopheresis Procedure:

INDICATIONS

The THERAKOS UVAR XTS Photopheresis System/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), in persons who have not been responsive to other forms of treatment.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

The THERAKOS UVAR XTS or THERAKOS CELLEX Photopheresis Systems are not designated, sold, or intended for use except as indicated.

Certain underlying medical conditions contraindicate THERAKOS Photopheresis, including patients:

- who cannot tolerate extracorporeal volume loss during the leukocyte-enrichment phase
- exhibiting idiosyncratic or hypersensitivity reactions to 8-methoxypsoralen/psoralen compounds
- with coagulation disorders
- who have had previous 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
- Patients who may not be able to tolerate the fluid changes associated with extracorporeal photopheresis should be monitored carefully
- Procedures, such as renal dialysis, which might cause significant fluid changes (and expose the patient to additional anticoagulation) should not be performed on the same day as extracorporeal photopheresis
- Individual patients may require a heparin dosage that varies from the recommended dose to prevent post-treatment bleeding or clotting during a treatment

ADVERSE REACTIONS

- 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 labeling recommendations may result in anemia
- Venous access carries a small risk of infection and pain

Please see accompanying Full Prescribing Information, including the BOXED WARNING for UVADEX, and see the appropriate THERAKOS Photopheresis System Operator's Manual.

Mallinckrodt Pharmaceuticals

www.therakos.com

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