Therakos®
ECP Immunomodulation

Clinical Summary in CTCL

	Trial 1 Oral methoxsalen (N=40)*	Trial 2 Oral methoxsalen (N=57)*	Trial 3 UVADEX® (methoxsalen) (N=51)*
Mean age (years)	57	63.2	63
Mean number of prior CTCL therapies	3.7	3.3	4.3
Concomitant medications	Prednisone (<10 mg/day) and topical steroids permitted†	No restrictions†	Topical steroids (only to treat fissures on the soles of the feet/palms of the hands) permitted
Mean number of ECP treatments	64	31	20
Successful response rate within 6 months of beginning therapy‡ (≥25% reduction from baseline in skin score maintained for 4 consecutive weeks)	**54%** (21/39)	**28%** (16/57)	**33%** (17/51)
Median time to response (95% CI)	**103 days** (76-126)	**71 days** (68-153)	**84 days** (35-116)
Median duration of response (95% CI)	**419 days** (159-896)	**104 days** (35-318)	**140 days** (56-245)

All trials enrolled CTCL patients with tough-to-treat patch plaques, extensive plaques, and erythrodermic disease. No patients with disease in the tumour phase were treated, and there are no efficacy data available for UVADEX in these patients.

The higher response rate with oral methoxsalen in Trial 1 may be partly due to the administration of systemic steroids and patients receiving more ECP treatments in this trial.

Although the response rates in Trial 2 and Trial 3 were similar, the possibility that UVADEX is inferior to oral methoxsalen cannot be excluded due to the design and size of the trials.

There is no clinical evidence to show that treatment with UVADEX beyond 6 months provides additional benefit if the patient has not responded within this timeframe.

CTCL=cutaneous T-cell lymphoma; ECP=extracorporeal photopheresis.

* Three multicenter, single-arm, open-label clinical trials were performed to evaluate the efficacy and safety of photopheresis in the treatment of skin manifestations of CTCL. In Trial 1 (N=39), patients were treated with oral methoxsalen in conjunction with the UVAR XTS™ Photopheresis System. In Trial 2 (N=57), a 5-year post-approval follow-up, patients were treated with oral methoxsalen. In Trial 3 (N=51), patients were treated with UVADEX in conjunction with the UVAR XTS Photopheresis System. Patients across all 3 trials were initially treated on 2 consecutive days, every 4-5 weeks. Overall skin scores were used to assess the patient's response to treatment. The predefined successful response was a 25% reduction in skin score from baseline maintained for four consecutive weeks.

† Patients were permitted to receive topical and/or systemic agents in combination with THERAKOS® Photopheresis.

‡ Individual results may vary. These pivotal trials were conducted with oral methoxsalen or UVADEX in conjunction with the UVAR Photopheresis System, not the CELLEX Photopheresis System.

See Indication and Important Safety Information on back page.

INDICATION

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

- There is no clinical evidence to show that treatment with UVADEX beyond six months provides additional benefit if the patient has not responded within this timeframe.
- Not authorized for pediatric or geriatric use.

Read the THERAKOS CELLEX Photopheresis Systems Operator's Manual before administering the treatment.

CONTRAINDICATIONS

UVADEX is contraindicated in patients:

- Hypersensitive to this drug or any ingredient in the formulation
- Possessing a specific history of a light-sensitive disease state, such as lupus erythematosus, porphyria cutanea tarda, erythropoietic protoporphyria, variegate porphyria, xeroderma pigmentosum, and albinism
- With aphakia, because of the significantly increased risk of retinal damage due to the absence of lenses
- With severe cardiac disease, severe anemia, white blood cell count greater than 25,000/mm^3, previous splenectomy, and coagulation disorders
- With coexisting melanoma, basal cell, or squamous cell skin carcinoma

SERIOUS WARNINGS AND PRECAUTIONS

Carcinogenicity: Oral administration of methoxsalen followed by cutaneous UVA exposure (PUVA therapy) is carcinogenic. Because the dose of methoxsalen with UVADEX therapy is about 200 times less than with PUVA and the skin is not exposed to high cumulative doses of UVA light, the risk of developing skin cancer following UVADEX therapy may be lower

Mutagenicity: Methoxsalen causes DNA damage, interstrand cross-links, and errors in DNA repair

Teratogenicity: Methoxsalen may cause fetal harm when given to a pregnant woman. Both men and women who are being treated with UVADEX should take adequate contraceptive precautions both during and after completion of photopheresis therapy

Cataractogenicity: Patients should be told emphatically to wear UVA-absorbing, wraparound sunglasses for 24 hours after UVADEX 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

Skin Burning: 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 cover exposed skin or use sunblock (SPF 15 or higher) for 24 hours following treatment with methoxsalen, whether exposed to direct or indirect sunlight outdoors or through a window.

FOR MORE INFORMATION

See product monograph for UVADEX at health-products.canada.ca/dpd-bdpp/ for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece, and the appropriate THERAKOS Photopheresis System Operator's Manual. The product monograph is also available by calling us at 1-833-223-4ECP (1-833-223-4327).

Important Safety Information for THERAKOS® CELLEX® Photopheresis Procedure

INDICATION

The 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).

CONTRAINDICATIONS

Certain underlying medical conditions contraindicate THERAKOS CELLEX Photopheresis, including:

- Patients who cannot tolerate extracorporeal volume loss during the leukocyte enrichment phase
- Patients exhibiting idiosyncratic or hypersensitivity reactions to 8-methoxypsoralen/psoralen compounds
- Patients with coagulation disorders or who have had previous splenectomy

WARNINGS & PRECAUTIONS

THERAKOS CELLEX 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.

- **MR-Unsafe:** Do not expose the device to a magnetic resonance (MR) environment. The device may present a risk of projective injury, and thermal injury and burns may occur. The device may generate artifacts in the MR image, or may not function properly.
- **Thromboembolic Events:** Thromboembolic events, including pulmonary embolism and deep vein thrombosis, have been reported in the treatment of Graft versus Host Disease (GvHD, an indication not approved in Canada). Special attention to adequate anticoagulation is advised when treating patients with GvHD.
- **Concomitant Therapy:** When prescribing and administering THERAKOS CELLEX 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, 37.7–38.9ºC (100–102ºF), 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.

References: 1. UVADEX (methoxsalen) Product Monograph. **2.** Data on File - Ref-05182 Therakos (Canada) Company.

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