A NEW TREATMENT OPTION FOR PEOPLE LIVING WITH CTCL

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For people living with cutaneous T-cell lymphoma (CTCL), treatment is often a journey. Many patients receive several different therapies over time as their disease changes or becomes less responsive to treatment. Having additional options is important, especially when CTCL returns after previous therapy or becomes more difficult to control.

Denileukin diftitox-cxdl (LYMPHIR™) is one of the newest FDA-approved systemic treatments for adults with relapsed or refractory stage I–III CTCL who have received at least one prior systemic therapy. Approved by the U.S. Food and Drug Administration (FDA) in 2024, denileukin diftitox-cxdl represented the first new FDA-approved systemic treatment for CTCL in more than seven years, offering an additional option for patients and their healthcare teams.

Unlike traditional chemotherapy, denileukin diftitox-cxdl is a targeted biologic therapy. It is designed to recognize the interleukin-2 (IL-2) receptor, which is found on many CTCL cells. After attaching to these cells, the medication delivers a toxin inside the cell, leading to lymphoma cell death. Researchers also believe it may help change the immune environment around the lymphoma in ways that make it less supportive of cancer growth. Together, these actions make denileukin diftitox-cxdl different from other currently available CTCL treatments.

Some members of the CTCL community may remember Ontak®, an earlier version of denileukin diftitox that was available years ago. Ontak was voluntarily withdrawn from the market in 2014 because of manufacturing issues, not because the treatment approach itself was found to be ineffective. Denileukin diftitox-cxdl is a reformulated, newly manufactured version with improved purity that underwent new clinical testing before receiving FDA approval. For patients familiar with Ontak, this history helps explain why denileukin diftitox-cxdl may sound familiar while representing a newly approved treatment.

Denileukin diftitox-cxdl is given by intravenous (IV) infusion. Treatment is administered once daily for five consecutive days (Days 1 through 5) of a 21-day treatment cycle. Each infusion takes about one hour, although additional time is usually needed for premedications, preparation, and observation before patients leave the infusion center. In the pivotal clinical trial, patients could receive up to eight treatment cycles,

with additional treatment allowed for those who continued to benefit. Because treatment requires five consecutive infusion visits every three weeks, patients may want to consider how the schedule fits with work, family responsibilities, travel, and other commitments.

The treatment was studied in a clinical trial known as Study 302. About one in three patients (36%) experienced an objective response, meaning their CTCL improved with treatment. Some patients achieved complete responses, while others experienced partial improvement. Responses often occurred relatively quickly, with a median time to response of about six weeks. Among patients who responded, more than half maintained their response for at least six months. For many people living with CTCL, improvement is measured not only by changes in skin lesions but also by relief from symptoms that affect daily life. In the study, about one-third of patients who had itching before treatment experienced a clinically meaningful reduction in pruritus that lasted at least four weeks.

Like all cancer treatments, denileukin diftitox-cxdl has potential risks and side effects. The medication carries the FDA's strongest safety warning (a Boxed Warning) for capillary leak syndrome (CLS), a potentially serious condition in which fluid leaks from blood vessels into surrounding tissues. Symptoms may include swelling, rapid weight gain, dizziness, low blood pressure, or shortness of breath. Most cases of CLS in the clinical trial occurred during the first two treatment cycles, making careful monitoring especially important early in treatment.

The risk is higher in patients with low blood albumin levels, so patients must have an albumin level greater than 3 g/dL before starting therapy, and albumin is monitored throughout treatment. Other possible side effects include infusion reactions, changes in liver tests, vision changes, fatigue, rash, nausea, swelling, chills, fever, constipation, muscle or joint pain, and changes in blood counts or other laboratory tests. Patients should promptly report new or worsening symptoms to their healthcare team.

A conversation about denileukin diftitox-cxdl may be appropriate when CTCL remains active despite one or more previous systemic treatments, particularly if skin tumors, plaques, or persistent itching continue to affect quality of life. It may be especially relevant for some patients with tumor-stage disease (i.e., Stage IIB), although treatment decisions are always individualized. A CTCL specialist can help determine whether it fits into a patient's overall treatment plan based on prior therapies, disease characteristics, other medical conditions, and personal goals.

For many people with CTCL, a successful treatment does not necessarily mean that every sign of disease disappears. Success may instead mean fewer or flatter skin lesions, less itching, fewer tumors or plaques, better sleep, improved comfort, less need for additional therapies, or simply feeling better day to day. Some patients may achieve a partial response that makes their disease easier to manage, while others may experience a deeper or more durable remission. The goals of treatment are different for every person, and those goals should guide conversations about whether denileukin diftitox-cxdl is an appropriate option.

As with any CTCL treatment, choosing denileukin diftitox-cxdl is a shared decision between patients and their healthcare team. Understanding how the treatment works, what benefits it may offer, the possible risks, and the commitment required for treatment and monitoring can help patients make informed decisions about where denileukin diftitox-cxdl fits into their CTCL journey.

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