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ENZON PHARMACEUTICALS, INC. FOCUSED ON ONCOLOGY PATIENT CARE

Enzon Pharmaceuticals, Inc., (Bridgewater, New Jersey), is a biopharmaceutical company dedicated to the discovery, development, manufacture, and commercialization of pharmaceuticals, and is committed to advancing therapies in the hematology/oncology area.

ONCASPAR® (PEG-L-asparaginase) is an oncolytic agent indicated for patients with acute lymphoblastic leukemia who require L-asparaginase in their treatment regimen, but have developed hypersensitivity or allergy to the native forms of L-asparaginase. Monometh-oxypolyethylene glycol (PEG) modification of L-asparaginase allows for the extended therapeutic activity of ONCASPAR. When compared to native L-asparaginase formulations, ONCASPAR provides sustained asparagine depletion, and offers significantly increased half-life in blood (*1*), which allows for a convenient, 14-day dosing regimen. Native asparagine products require dosing as frequently as twice each week.

ONCASPAR also enables many previously hypersensitive patients to be rechallenged (*2,3*). The drug is associated with significantly reduced antibody formation and with prolonged activity in the presence of neutralizing antibodies, an important consideration in asparagine depletion therapy (*4*). The drug is contraindicated in patients with a history of pancreatitis, patients who have had significant hemorrhagic events associated with prior L-asparaginase therapy, or those who have had previous serious allergic reactions or other unacceptable adverse reactions to ONCASPAR (*5*). Generally prescribed in combination with other chemotherapeutic agents, ONCASPAR use as a single agent should only be undertaken when multi-agent chemotherapy is judged to be inappropriate for the patient.

DEPOCYT® (cytarabine liposome injection), also marketed by Enzon Pharmaceuticals, is a sustained release, injectable formulation of the chemotherapeutic agent cytarabine. DEPOCYT was approved in 1999 for the treatment of lymphomatous meningitis. Gradual, sustained release of cytarabine into the spinal fluid results in prolonged exposure to active therapy, more uniform distribution (*5*), and an extended dosing interval of once every two weeks followed by an additional dosing interval of once per month for five months (*6*), as opposed to twice weekly dosing with unmodified cytarabine. DEPOCYT can be administered by a simple spinal injection, which avoids the need for surgical insertion of a reservoir into the brain that is often necessary for frequent administration with standard cytarabine. This results in a better quality of life for patients, with fewer injections and hospital visits required for effective therapy, while minimizing the need for invasive and costly surgery. DEPOCYT (cytarabine liposome injection) is contraindicated in patients who are hypersensitive to cytarabine or any component of the formulation, and in patients with active meningeal infection.

ABELCET® (amphotericin B lipid complex injection) is an intravenous antifungal agent indicated for the treatment of severe invasive fungal infections in immunocompromised patients who are refractory to or intolerant of conventional amphotericin B therapy. ABELCET was developed to treat a broad range of systemic fungal infections, such as candidiasis, aspergillosis, and cryptococcal meningitis. These infections are associated with fatality rates of up to 90 percent.

The incidence of severe systemic fungal infections is on the rise. This phenomenon can be attributed to the increasing number of immunocompromised patients that has partly resulted from advancements in medical treatment, such as aggressive chemotherapy or transplantation procedures. These life-threatening fungal infections remain difficult to diagnose and to treat, and therefore carry a poor prognosis.

The unique ribbon-like structure of ABELCET allows high doses of amphotericin B to be delivered, maximizing efficacy in life-threatening fungal infections. The drug not only retains the

broad-spectrum antifungal activity of the conventional form of amphotericin B, but alleviates the renal toxicity associated with the native form.

ABELCET provides fast delivery of active drug, with release of approximately 60 to 75 percent of the amphotericin B from the lipid structure within the first 3 hours of administration (*7, 8**). It is rapidly and extensively cleared from the blood and distributed by macrophages throughout the reticuloendothelial system, accumulating in tissues that are common sites of fungal infection (*9-11*).

The fungicidal action of ABELCET begins at the site of infection, where fungal and mammalian cells release phospholipases. The phospholipases cleave lipids from ABELCET and release free amphotericin B, which binds to ergosterol in the fungal cells, altering the cytoplasmic membrane. As the fungal membrane permeability changes, it allows leakage of cytoplasmic components, resulting in the death of the fungal cell (*12-14*).

"ABELCET has significantly advanced the approach to antifungal therapy," says Hillard M. Lazarus, MD, FACP, Professor of Medicine, Case Western Reserve University (Cleveland, OH). "ABELCET has a rapid onset of action and is generally well-tolerated, especially if saline pre-hydration and post-hydration are used to prevent renal dysfunction and pre-meds are given for rigors or fever."

ABELCET provides a high level of tissue penetration to critical sites of fungal infection, with the highest concentrations accumulating in the lungs, liver, and spleen, without similar increases in renal tissue (*15*). The lung is the most common site of *Aspergillus* infection (*16*). According to Jayesh Mehta, MD, Professor, Medicine/Hematology-Oncology, Robert H. Lurie Comprehensive Cancer Center of Northwestern University (Chicago, IL), "ABELCET is an effective treatment with less kidney toxicity compared to conventional amphotericin and its unique structure allows it to concentrate in the lungs. It has proven efficacy in a wide variety of fungal infections at a reasonable cost, and its excellent safety profile has been proven in thousands of patients."

Aspergillus	Candida	Cryptococcus	Fusarium	Zygomycetes
65% (240/368)	76% (704/923)	85% (86/101)	58% (15/26)	72% (46/64)

Response data collected from thousands of patients treated with ABELCET in the CLEAR® program show favorable clinical response rates. In 2751 evaluable patients, infections were classified by fungal type. The clinical response rates are indicated in the table above (*17-20*†).

The adverse events most commonly reported with ABELCET are transient chills and/or fever during infusion of the drug. ABELCET is contraindicated in patients who have shown hypersensitivity to amphotericin B or any other component in the formulation.

* Results from in vitro data do not necessarily predict clinical outcome.
** Published data as of 4/05.
† Complete, partial, and stable responses.

For more information about ONCASPAR®, DEPOCYT®, or ABELCET®, or other products marketed by Enzon Pharmaceuticals, Inc., call 1-866-792-5172, or visit the company's Web site at www.enzon.com.

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