

*The following is a message from the FDA's Office of Oncology Drug Products Director, Dr. Richard Pazdur:*

On September 6, 2007, the U.S. Food and Drug Administration approved dexrazoxane hydrochloride for injection (Totect™), equivalent to 500 mg dexrazoxane, for the treatment of extravasation resulting from intravenous anthracycline chemotherapy.

In two studies, patients who were receiving single-agent anthracycline intravenously (usually as part of combination chemotherapy) and who developed extravasation symptoms of pain, burning, swelling, and/or redness near the infusion site received Totect™ to reduce surgical interventions for tissue injury following anthracycline extravasation. The protocol required extravasation to be confirmed by the presence of fluorescence in tissue biopsies.

The first Totect™ dose was given as soon as possible and within 6 hours following extravasation. After the first dose, treatment was repeated 24 and 48 hours later for a total of 3 doses. Totect™ was administered as a 1-2 hour IV infusion through a different venous access location. The first and second doses were 1000 mg/m<sup>2</sup> and the third dose was 500 mg/m<sup>2</sup> up to a maximum daily dose of 2000 mg on days 1 and 2 and 1000 mg on day 3.

Extravasation was confirmed in 57 evaluable patients. The anthracyclines most commonly involved were epirubicin (56%) and doxorubicin (41%). Peripheral sites of extravasation included the forearm in 63%, the hand in 21%, and the antecubital area in 11%; four patients received the anthracycline via a central venous access device (CVAD). Most patients presented with swelling (83%), redness (78%), and pain (43%).

After Totect™ treatment, only one of the 57 evaluable patients required surgery. Thirteen patients had late sequelae at the event site such as pain, fibrosis, atrophy, and local sensory disturbance; all were judged as mild except in the one patient who required surgery. None of the 4 patients with CVADs required surgical intervention.

Totect™ is a cytotoxic drug. When administered to patients receiving anthracycline-containing cytotoxic therapy, additive cytotoxicity may occur. Treatment with Totect™ is associated with leukopenia, neutropenia, and thrombocytopenia. Reversible elevations of liver enzymes may occur. Renal excretion is the primary metabolic pathway. Dimethylsulfoxide (DMSO) should not be used in patients who are receiving dexrazoxane to treat anthracycline-induced extravasation.

Full prescribing information including clinical trial information, safety, dosing, drug-drug interactions and contraindications is available at <http://www.fda.gov/cder/foi/label/2007/022025lbl>.