Uridine Triacetate (Vistogard) for Fluourouracil Overdose

The FDA has approved the pyrimidine analog uridine triacetate (Vistogard – Wellstat Therapeutics) for emergency treatment of a fluorouracil (5-FU) or capecitabine (Xeloda, and generics) overdose or severe toxicity that occurs within 96 hours following administration of one of these drugs. Fluourouracil is a cytotoxic antimetabolite used to treat breast, colorectal, and other cancers; capecitabine is an oral prodrug of fluorouracil.

Uridine triacetate, a produg, is deacetylated to uridine after oral administration. Excess circulating uridine is converted into uridine triphosphate, which inhibits the cytotoxic activity of 5-fluorouridine triphosphate, a fluorouracil metabolite, by competing with it for incorporation into RNA.

FDA approval was based on two unpublished open-label studies (summarized in the package insert) in a total of 135 adults and children with overdoses of fluorouracil or capecitabine (n=117) or severe or life-threatening toxicities within 96 hours after their administration (n=18). The overall survival rate at 30 days was 96%.

In retrospective case reports that included 25 patients who received only supportive care after a fluorouracil overdose, the survival rate was 16%.

Vistogard is supplied as orange-flavored oral granules in single-dose packets containing 10 grams of uridine triacetate. The granules should be mixed with 3-4 ounces of soft food and taken every 6 hours for 20 doses. The recommended dose is 10 grams for adults and 6.2 grams/m² (10 grams maximum) for children. Mild to moderate nausea, vomiting, and diarrhea have been reported. The cost for one course of treatment is $75,000.1