

Uridine Triacetate (VISTOGARD®) Criteria for Emergency Use March 2017

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or <http://vaww.pbm.va.gov> for further information.

Exclusion Criteria *If the answer to the item below is met, then the patient should NOT receive uridine triacetate.*

- Time from end of fluorouracil infusion or last capecitabine dose is greater than 4 days (96 hours). Safety and efficacy of uridine triacetate initiated more than 4 days (96 hours) after end of infusion or last dose has not been established.

Inclusion Criteria *The answers to one of the following must be fulfilled in order to meet criteria.*

- Patient exhibits severe or life-threatening toxicity within 96 hours following the end of fluorouracil continuous IV infusion (CIVI) or capecitabine administration. See Issues for Consideration.

OR

- An overdose of fluorouracil continuous IV infusion or capecitabine is suspected, regardless of the presence of symptoms. See Issues for Consideration.

Procurement, Dosage and Administration

Procurement: Refer to Appendix A for [VA Ordering Information](#) to obtain antidote (uridine triacetate) from Cardinal Health Specialty

Premedication: Ondansetron 8 mg orally, should be given 20 minutes prior to each uridine dose

Dosage: 10 grams (1 packet) orally every 6 hours for 20 doses (full course), without regard to meals. Do not chew.

Administration (oral route)

- Mix each packet of granules with 3-4 ounces of soft foods (e.g. applesauce, pudding, yogurt) and ingest within 30 minutes
- Do not chew the granules. Drink at least 4 ounces of water.
- If patient vomits within 2 hours of a dose, initiate another complete dose as soon as possible after vomiting episode. Administer the next dose at the regularly scheduled time.
- If patient misses a dose, administer the dose as soon as possible. Give the next dose at the regularly scheduled time.

Administration [nasogastric (NG) or gastrostomy tube (G-Tube)]

- Prepare about 4 ounces (100 ml) of a food starch-based thickening product in water and stir briskly until thickener dissolved
- Crush contents of a 10 gram packet of granules to a fine powder
- Add crushed granules of antidote to prepared thickening product and mix thoroughly
- After administration of mixture through NG or G-Tube, flush tube with water

Management of Toxicity

- While awaiting arrival of antidote, consider admitting patient to inpatient unit and provide supportive care to reduce symptom severity (e.g. IV hydration, electrolyte replacement, treatment of diarrhea, mouth/skin care, granulocyte colony-stimulating factor administration, continuous cardiac monitoring)
- Avoid contraindicated medications that might interfere with clearance of fluorouracil or capecitabine (e.g. metronidazole, leucovorin, cimetidine, thiazide diuretics)
- Continue close monitoring post-hospitalization for possibly delayed adverse effects, particularly throughout the expected neutrophil nadir. Granulocyte colony-stimulating factors and antibiotics may need to be continued.
- Ensure patient/caregiver education about dosing preparation, premedication, schedule, taking a complete course of therapy (20 doses), missed doses and avoiding potential drug-drug interactions that may affect clearance of fluoropyrimidine.

Issues for Consideration

- **Uridine triacetate is NOT to be used to minimize non-emergent/non-life-threatening toxicity of fluorouracil or capecitabine, as use in this manner may diminish the efficacy of these drugs.**
- Examples of early onset fluoropyrimidine (i.e. fluorouracil or capecitabine) toxicities (not all inclusive)
Gastrointestinal: oral mucositis, diarrhea, anorexia **Cardiac:** arrhythmia, chest pain, cardiac arrest
Hematologic: neutropenia, thrombocytopenia **Dermatologic:** erythema, desquamation
Neurologic (CNS): altered mental status, seizures, confusion
- Definition of overdose. An overdose is when a patient receives 10% more than their intended dose (e.g. $\geq 110\%$ of planned dose), or if they received the full dose at an infusion rate that was 25% more than the intended rate.
 - Refer to Appendix B for data regarding observed and expected outcomes of fluorouracil overdose.
 - This chart contains data points from the Expanded Access Protocol, as well as historical data points related to treatment with supportive care only.
 - It can be used as a guide in conjunction with clinical assessment of the patient and their ability to manage supportive care issues. The Outcomes Chart does not incorporate patient clinical assessment.
 - Using the Outcomes Chart:
 - Calculate the amount of drug that patient received and the rate at which that amount was administered.
 - Plot Dose Rate (mg/hr) and fluorouracil total dose (mg) on chart, then refer to chart below

Plotted point resides in	Expected tolerated	Expected serious toxicity	Expected lethal
+ Clinical assessment	+ Clinical assessment	+ Clinical assessment	+ Clinical assessment
Strength of consideration	Weak	Moderate	Strong

VISTOGARD

(uridine triacetate)
Granules

Appendix A. VA Ordering Information

Restricted to Specialty Pharmacies or Distributors: Yes

Specialty Pharmacy or Distributor:

Cardinal Health Specialty (Cardinal Health 108) DUNS 786637033

To Set Up Account: Phone: 305-965-8005, Fax: 305-351-3001

Established Account Orders: Phone: 866-677-4844

Emergency Orders After Hours: Phone 866-677-4844, option 1

REMS Components: None

Ordering Details

Vistogard is only available to VA through Cardinal Health Specialty (Cardinal Health 108). Cardinal will accept wholesale orders for the product and no specialty pharmacy services are required.

Pharmacies that do not have an existing account with Cardinal Health Specialty must complete the “*Cardinal Health VA Ordering Authorization Form*” and call (305) 965-8005. No patient or provider information is provided.

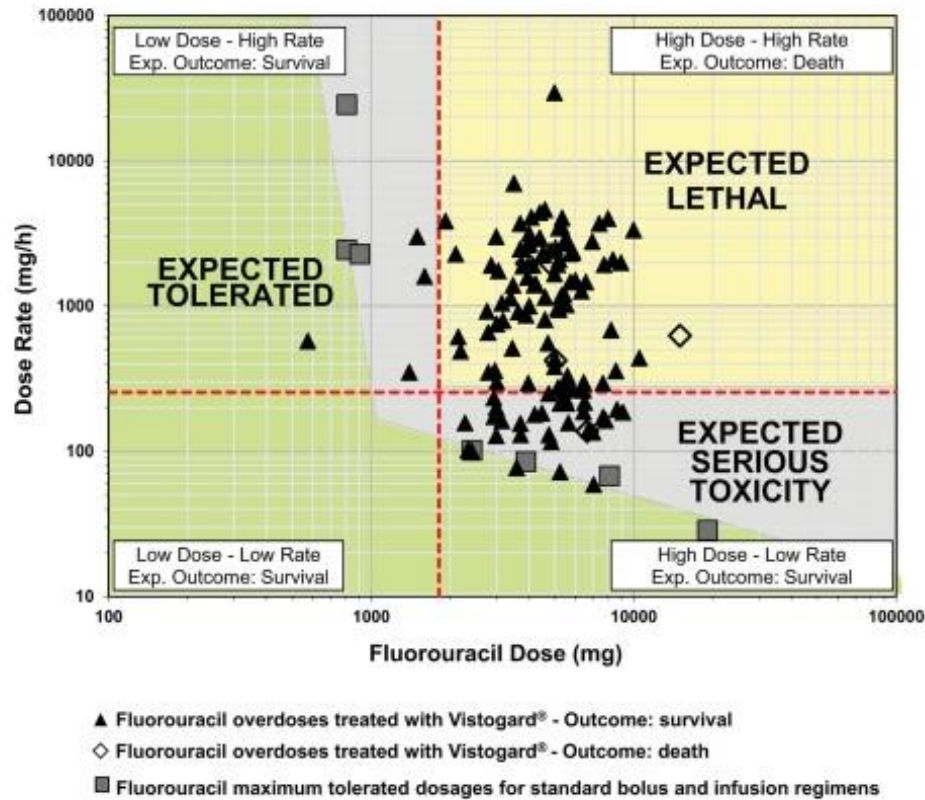
Once an account is established, the pharmacy should call (866) 677-4844 to place an order during standard business hours. Orders placed by 5:00 pm ET will arrive the next day. Orders placed after hours or on the weekend will arrive on Monday.

Pharmacies that need to place an emergency order during standard business hours and already have an account established, should call (866) 677-4844 and the order will be expedited. The estimated time of arrival depends on where the customer is located and the flights available will dictate the ETA. The customer service representative will provide more details.

Pharmacies that need to place an emergency order after hours for the next day on a weekend should call (866) 677-4844, option #1.

Updated 6/2016

Appendix B. 5-Fluorouracil Overdose Case Observed and Expected Outcomes.



5-Fluorouracil overdose case outcomes as a function of the infusion rate and dose. The expected tolerated zone is defined by the maximum tolerated doses of a variety of 5-Fluorouracil regimens. Patients in the expected lethal zone would be expected to die on the basis of the infusion rate and dose; patients in the expected tolerated zone as well as those in the expected serious toxicity zone would be expected to survive.

Ma WW, Saif MW, El-Rayes BF, et al. Emergency Use of Uridine Triacetate for the Prevention and Treatment of Life-Threatening 5-fluorouracil and capecitabine Toxicity. *Cancer*. 2017 Jan 1;123(2):345-356. doi: 10.1002/cncr.30321.