

## Regimen Monograph

[Regimen Name](#) | [Drug Regimen](#) | [Cycle Frequency](#) | [Premedication and Supportive Measures](#) | [Dose Modifications](#) | [Adverse Effects](#) | [Interactions](#) | [Drug Administration and Special Precautions](#) | [Recommended Clinical Monitoring](#) | [Administrative Information](#) | [References](#) | [Other Notes](#) | [Disclaimer](#)

## A - Regimen Name

## FU(CIV-RT) Regimen

Fluorouracil

**Disease Site**      Gastrointestinal  
Pancreas

**Intent**              Adjuvant  
Palliative

**Regimen Category**      **Evidence-Informed :**

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

[back to top](#)

## B - Drug Regimen

<a href="#">fluorouracil</a>	225 mg /m <sup>2</sup> /day	IV over 24 hours as continuous infusion	Concurrent with radiotherapy
------------------------------	-----------------------------	-----------------------------------------	------------------------------

[back to top](#)

## C - Cycle Frequency

During Entire Course of Radiotherapy

[back to top](#)

## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Minimal

[back to top](#)

## E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Patients should be tested for DPD deficiency before starting treatment with fluorouracil. Refer to the [DPD Deficiency Guidance for Clinicians](#) for more information.

In patients with unrecognized DPD deficiency, acute, life-threatening toxicity may occur; if acute grade 2-4 toxicity develops, treatment should be stopped immediately and permanent discontinuation considered based on clinical assessment of the toxicities.

### **Dosage with toxicity**

Toxicity or Counts (x10 <sup>9</sup> /L)	During Cycle	For Next cycle
Platelets < 80 or ANC < 1.5	Hold*	May consider ↓
Bleeding, febrile neutropenia	Hold*	↓ by 25%
≥ grade 3 GI	Hold*	↓ by 25%
CNS	Hold*	↓ by 25%
Cardiac	Hold*	Consider discontinuing
* Do not retreat until ANC ≥ 1.5 x 10 <sup>9</sup> /L , platelets ≥ 100 x 10 <sup>9</sup> /L and organ toxicity ≤ grade 2. With severe toxicity, consider testing for DPD deficiency prior to rechallenge.		

**Hepatic Impairment**

Suggested example:

Bilirubin		AST/ALT	Fluorouracil (% previous dose)
< 2 x ULN	and	3-5 x ULN	75 %
2-4 x ULN	or	5-10 x ULN	50-75%
≥ 4 x ULN	or	≥ 10 x ULN	Discontinue

**Renal Impairment**

No adjustment required, although reduction may be considered with severe renal insufficiency.

[back to top](#)**F - Adverse Effects**Refer to [fluorouracil](#) drug monograph(s) for additional details of adverse effects

Prolonged 5FU infusion regimens have more Hand-Foot Syndrome and less myelosuppression and GI effects, compared to bolus regimens.

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
<ul style="list-style-type: none"> <li>• Myelosuppression ± infection, bleeding</li> <li>• Hand-foot syndrome</li> <li>• Stomatitis</li> <li>• Diarrhea</li> <li>• Anorexia</li> <li>• Photosensitivity</li> <li>• Rash</li> </ul>	<ul style="list-style-type: none"> <li>• Cardiotoxicity</li> <li>• Arterial thromboembolism</li> <li>• Venous thromboembolism</li> <li>• Leukoencephalopathy</li> <li>• Optic neuritis</li> <li>• Hemolysis / hemolytic uremic syndrome</li> <li>• ↑ LFTs</li> </ul>

[back to top](#)

## G - Interactions

Refer to [fluorouracil](#) drug monograph(s) for additional details

Fluorouracil is a known radiation-sensitizer. Patients should be carefully monitored for gastrointestinal toxicity when they are receiving concurrent 5FU-Radiation therapy.

[back to top](#)

## H - Drug Administration and Special Precautions

Refer to [fluorouracil](#) drug monograph(s) for additional details

### **Administration:**

#### IV CONTINUOUS INFUSION:

- Continuous infusion using CADD infusion pump, or similar device
- Infuse through central venous access device, if available
- Infusion volume and duration depend on protocol.
- Protect from light
- Incompatible with doxorubicin, epirubicin, diazepam, methotrexate and cytarabine; line must be flushed between administrations of fluorouracil and these agents

### **Contraindications:**

- patients with poor nutritional state
- patients with depressed bone marrow function (prior pelvic irradiation / marrow infiltration)
- patients with potentially serious infections
- patients with known hypersensitivity to the drug or any of its excipients
- patients with known complete absence of dihydropyrimidine dehydrogenase (DPD) activity. Refer to the [DPD Deficiency Guidance for Clinicians](#) for more information.

### **Precautions:**

- Use with extreme caution in patients who have undergone recent major surgery, with renal or hepatic impairment, widespread bone marrow involvement, or are suspected to have DPD deficiency. Refer to the [DPD Deficiency Guidance for Clinicians](#) for more information.

[back to top](#)

## I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

### Recommended Clinical Monitoring

- CBC; baseline and before each dose
- Liver function tests; baseline and as clinically indicated
- Clinical toxicity assessment and grading of stomatitis, diarrhea, bleeding, infection, local site toxicity, skin effects; at each visit
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

### Suggested Clinical Monitoring

- Renal function tests; baseline and as clinically indicated

[back to top](#)

## J - Administrative Information

Approximate Patient Visit	0.5 hour
Pharmacy Workload (average time per visit)	22.05 minutes
Nursing Workload (average time per visit)	45 minutes

[back to top](#)

## K - References

Fluorouracil drug monograph, Cancer Care Ontario.

Fisher BJ, Perera FE, Kocha W, et al. Analysis of the clinical benefit of Fluorouracil and radiation treatment in locally advanced pancreatic cancer. *International Journal of Radiation Oncology, Biology, Physics* 1999;45(2):291-5.

Regine WF, Winter KA, Abrams RA, et al. Fluorouracil vs gemcitabine chemotherapy before and after fluorouracil-based chemoradiation following resection of pancreatic adenocarcinoma: a randomized controlled trial. *JAMA* 2008;299(9):1019-26.

---

Thomas PR. Radiotherapy for carcinoma of the pancreas. *Seminars in Oncology* 1996;23(2):213-9.

**April 2023** Updated DPD deficiency information in the Dose Modifications and Special Precautions sections, and fluorouracil antidote information in the Other Notes section.

[back to top](#)

## L - Other Notes

Schedule pump teaching session BEFORE first day of infusion.

### Antidote for Fluorouracil Overdose:

**Uridine triacetate** is a prodrug of uridine and is a specific antidote for treating fluorouracil overdose or severe early onset toxicities. If available, consider administering as soon as possible (i.e. within 96 hours) for suspected overdose. If not available, treatment is symptomatic and supportive.

For usage approval and supply, contact Health Canada's [Special Access Program](#) (SAP) (Phone: 613-941-2108. On-call service is available for emergencies). Uridine triacetate (Vistogard®) is supplied by its manufacturer in the United States (Wellstat Therapeutics).

The recommended dosing and administration for **uridine triacetate** in patients  $\geq 18$  years is:

- 10 grams (1 packet of coated granules) orally every 6 hours for 20 doses in total, without regards to meals.
- Granules should not be chewed. They should be mixed with 3 to 4 ounces of soft foods such as applesauce, pudding or yogurt.
- The dose should be ingested within 30 minutes of preparation, followed by at least 4 ounces of water.
- Refer to the prescribing information on dose preparation for NG-tube or G-tube use.

Additional resources on the management of fluorouracil infusion overdose:

- [Management of Fluorouracil Infusion Overdose Guideline](#) (Alberta Health Services)
- [Management of Fluorouracil Infusion Overdose at the BCCA - Interim Guidance](#) (BC Cancer Agency)

[back to top](#)

---

**M - Disclaimer****Regimen Abstracts**

*A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.*

*Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.*

**Regimen Monographs**

*Refer to the [New Drug Funding Program](#) or [Ontario Public Drug Programs](#) websites for the most up-to-date public funding information.*

*The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.*

*The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.*

*Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.*

*While care has been taken in the preparation of the information contained in the Formulary, such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability.*

*CCO and the Formulary's content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person's use of the information in the Formulary.*

[back to top](#)