Regimen Monograph

A - Regimen Name

FUMTMC(RT) Regimen

Mitomycin-Fluorouracil

Disease Site	Gastrointestinal Anus
Intent	Adjuvant (Combined modality with radiation)
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.
Rationale and Uses	In combination with radiation for all stages of localized, unresected squamous cell cancer of the anal canal, to improve local control and reduce colostomy rates

back to top

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B - Drug Regimen

fluorouracil	1000 mg /m²/day	IV over 24 hours as continuous infusion	For 96 hours (on Days 1-4 and Days 29-32)
mitomycin	10* mg /m²	IV	on Days 1 and 29

*Maximum 20 mg per dose; alternative mitomycin schedule: 12 mg/m^2 IV on Day 1 ONLY

back to top

C - Cycle Frequency

CONCURRENT WITH RADIATION

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Low

Febrile Neutropenia Risk: Low

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.

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Dosage with toxicity

Hematologic Toxicities
See appendix 6 for general recommendations.

GI Toxicities

Toxicity	Action
If Mucositis or Diarrhea ≥ Grade 3 in previous course	**REDUCE** to 2/3 dose of 5-FU
If Hand-Foot Syndrome ≥ Grade 2	**REDUCE** to 2/3 dose of 5-FU

Hepatic Impairment

If Bilirubin > 4 x ULN, OMIT 5FU dose.

Renal Impairment

If serum creatinine > 150 µmol/L, OMIT dose of Mitomycin

back to top

F - Adverse Effects

Refer to fluorouracil, mitomycin drug monograph(s) for additional details of adverse effects

Prolonged fluorouracil regimens have more hand-foot syndrome, but less myelosuppression and GI effects compared to bolus infusions.

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Myelosuppression +/- infection, bleeding • Mucositis	• Nephrotoxicity • Increased LFTs • ARDS

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• Alopecia • Anorexia • Diarrhea • Fatigue • Photosensitivity • Rash • Hand-foot syndrome	• Arterial thromboembolism • Venous thromboembolism • Cardiotoxicity • Hemolysis • Hemolytic uremic syndrome • Radiation recall reaction

back to top

G - Interactions

Refer to fluorouracil, mitomycin drug monograph(s) for additional details

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

back to top

H - Drug Administration and Special Precautions

Refer to fluorouracil, mitomycin drug monograph(s) for additional details

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 cycle.
- Liver & renal function tests; baseline and before each cycle.
- Clinical toxicity assessment (including stomatitis, skin, local toxicity); At each visit

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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back to top

J - Administrative Information

Approximate Patient Visit	Day 1: 1 hour; 5FU only: 0.5 hour
Pharmacy Workload (average time per visit)	21.146 minutes
Nursing Workload (average time per visit)	58.333 minutes

back to top

K - References

Ajani JA, Winter KA, Gunderson LL, et al. Fluorouracil, mitomycin, and radiotherapy vs fluorouracil, cisplatin, and radiotherapy for carcinoma of the anal canal: a randomized trial. JAMA 2008;299:1914-21.

Bartelink H, Roelofsen F, Eschwege F, et al. Concomitant radiotherapy and chemotherapy is superior to radiotherapy alone in the treatment of locally advanced anal cancer: results of a phase III randomized trial of the European Organization for Research and Treatment of Cancer Radiotherapy and Gastrointestinal Cooperative Groups. J Clin Oncol 1997;15:2040-9.

Cummings B, Keane T, O Sullivan et al. Epidermoid anal cancer: treatment by radiation alone or radiation and FLUOROURACIL with or without mitomycin C. Int J Radiat Oncol Phys 1991. 21:1115-25

Flam M, John M, Pajak TF, et al. Role of mitomycin in combination with fluorouracil and radiotherapy, and of salvage chemoradiation in the definitive nonsurgical treatment of epidermoid carcinoma of the anal canal: results of a phase III randomized Intergroup study. J Clin Oncol 1996;14:2527-39.

Fluorouracil and mitomycin drug monograph, Cancer Care Ontario.

UKCCCR Anal Cancer Trial Working Party. Epidermoid anal cancer: results from the UKCCCR randomised trial of radiotherapy alone versus radiotherapy, 5-fluorouracil, and mitomycin. Lancet 1996;348:1049-54.

PEBC Advice Documents or Guidelines

- Management of Squamous Cell Cancer of the Anal Canal

April 2023 Updated DPD deficiency information in the Dose Modifications section and fluorouracil antidote information in the Other Notes section.

back to top

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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 ≥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

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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.

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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.

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back to top

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