Regimen Monograph

A - Regimen Name

CISPFU(RT) Regimen

CISplatin-Fluorouracil

Disease Site	Gastrointestinal - Esophagus Gastrointestinal - Gastric / Stomach
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.

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B - Drug Regimen

Weeks 1 and 5 concurrent with radiation:

CISplatin	75 mg /m²	IV	Day 1
fluorouracil	1000 mg /m²/day	IV over 24 hours as continuous infusion	Days 1 to 4

(Maximum 2000 mg/day)

Alternative Cisplatin Schedule:

CISplatin	25 mg /m²	IV	Days 1 to 3 OR Days 2 to 4

OR

CISplatin	15 mg /m²	IV	Days 1 to 5

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C - Cycle Frequency

Concurrent with radiation on Weeks 1 and 5

THEN post-radiation q 21 days for 4 cycles total

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D - Premedication and Supportive Measures

Antiemetic Regimen: High (≥ 70mg/m²)
Moderate (< 70mg/m²)

Febrile Neutropenia Risk: Moderate

Other Supportive Care:

Also refer to CCO Antiemetic Summary

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E - Dose Modifications

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

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

Toxicity	Action
If renal function has not returned to normal (CrCl < 1 mL/sec or Serum Creatinine > 136 µmol/L) by Day 1 of cycle	**OMIT** Cisplatin (Recommended action)

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F - Adverse Effects

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

Prolonged 5FU 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
• Nausea, vomiting • Nephrotoxicity (may be severe) • Hearing impairment • Myelosuppression +/- infection, bleeding • Abnormal electrolyte(s) • Anorexia • Diarrhea • Mucositis • Neurotoxicity • Photosensitivity • Rash	• Increased LFTs • Arterial thromboembolism • Venous thromboembolism • Cardiotoxicity • Hemolysis • Hypersensitivity • Radiation recall reaction • Seizure • Vasculitis

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G - Interactions

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

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

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H - Drug Administration and Special Precautions

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

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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. Interim counts should be done in first cycle and repeated if dose modifications necessary.
- Baseline and regular liver and renal function tests (including electrolytes and magnesium).
- Clinical toxicity assessment (including stomatitis, neurotoxicity, ototoxicity); at each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Approximate Patient Visit	Day 1-4: 3 to 4 hours
Pharmacy Workload (average time per visit)	19.124 minutes
Nursing Workload (average time per visit)	52.917 minutes

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K - References

Cisplatin and fluorouracil drug monographs, Cancer Care Ontario.

Bedenne L, Michel P, Bouché O, et al. Chemoradiation followed by surgery compared with chemoradiation alone in squamous cancer of the esophagus: FFCD 9102. J Clin Oncol 2007 Apr 1;25(10):1160-8.

Conroy T, Galais MP, Raoul JL, et al. Definitive chemoradiotherapy with FOLFOX versus fluorouracil and cisplatin in patients with oesophageal cancer (PRODIGE5/ACCORD17): final results of a randomised, phase 2/3 trial. Lancet Oncol.2014 Mar;15(3):305-14.

Herskovic A, Martz K, Muhyi A et al. Combined chemotherapy and radiotherapy compared with radiotherapy alone in patients with cancer of the esophagus. N Engl J Med 1992. 326:1593-8.

Minsky BD, Pajak TF, Ginsberg RJ, et al. INT 0123 (Radiation Therapy Oncology Group 94-05) phase III trial of combined-modality therapy for esophageal cancer: high-dose versus standard-dose radiation therapy. J Clin Oncol 2002 Mar 1;20(5):1167-74.

Tepper J, Krasna MJ, Niedzwiecki D, et al. Phase III trial of trimodality therapy with cisplatin, fluorouracil, radiotherapy, and surgery compared with surgery alone for esophageal cancer: CALGB 9781. J Clin Oncol. 2008 Mar 1;26(7):1086-92.

PEBC Advice Documents or Guidelines

- Preoperative or Postoperative Therapy for Resectable Esophageal Cancer
- Neoadjuvant or Adjuvant Therapy for Resectable Gastric Cancer
- Systemic Therapy for Advanced Gastric Cancer

August 2017 aligned intent, dosing and cycle frequency info with QBP

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L - Other Notes

Schedule pump teaching session BEFORE first day of infusion.

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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.

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