Regimen Monograph

A - Regimen Name

CAPECISP Regimen

CISplatin-Capecitabine

Disease Site	Gastrointestinal - Esophagus Gastrointestinal - Gastric / Stomach
Intent	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.
Rationale and Uses	An option to ECF, for the palliative treatment of inoperable advanced, metastatic or recurrent adenocarcinoma of the stomach or the gastroesophageal junction
Supplementary Public Funding	**capecitabine** ODB - General Benefit (capecitabine)

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B - Drug Regimen

CISplatin	80 mg /m²	IV over 2 hours	Day 1
capecitabine	1000 mg /m²	PO	BID* Days 1 to 14

(*Total dose 2000 mg/m^2/day)
(Outpatient prescription in 150mg and 500mg tablets)

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until disease progression or unacceptable toxicity occurs; usually given up to 6 cycles due to cumulative cisplatin toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: High
No routine prophylaxis for capecitabine

Febrile Neutropenia Risk: Moderate

Other Supportive Care:

• Standard regimens for Cisplatin premedication and hydration should be followed. Refer to local guidelines.

- Topical emollients (e.g. hand creams, udder balm) may ameliorate the manifestations of hand-foot syndrome in patients receiving capecitabine.
- Supportive care should be provided, including loperamide for diarrhea.

Also refer to CCO Antiemetic Recommendations.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations have been adapted from clinical trials or product monographs and could be considered.

Use capecitabine with extreme caution in patients with partial DPD deficiency; reduce the initial dose substantially, monitor frequently and adjust the dose for toxicity as recommended in the dosage with toxicity section. In patients with unrecognized DPD deficiency, acute, life-threatening toxicity may occur; discontinue if acute grade 2-4 toxicity develops.

Dosage with toxicity

Cisplatin:

Worst Toxicity in Previous Cycle	**Dose for this cycle (% previous dose)***
Grade 4 platelets, grade 4 ANC ≥ 5 days, thrombocytopenic bleeding or febrile neutropenia	75%
Grade 2 neurotoxicity /ototoxicity	75%
Grade 3 or 4 neurotoxicity/ototoxicity	Discontinue
Other grade 3 non-hematologic/organ	75%
Worst Toxicity in Previous Cycle (Continued)	**Dose for this cycle (% previous dose)***
Other grade 4 non-hematologic/organ	Discontinue
Hemolysis, optic neuritis, arterial thromboembolism, severe hypersensitivity reactions	Discontinue
* Do not retreat until platelets ≥100 x 10^9/L, ANC ≥ 1.5 x 10^9/L, toxicity has recovered to ≤ grade 2 (grade 1 for neurotoxicity) and creatinine ≤ grade 1.	

Dose Modifications: Capecitabine

Toxicity	Action During a Course of Therapy	Dose Adjustment for Next Cycle (% of starting dose)
Grade 1	Maintain dose level	Maintain dose level
Grade 2 1st appearance 2nd appearance 3rd appearance 4th appearance	 Interrupt until resolved to grade 0-1 Interrupt until resolved to grade 0-1 Interrupt until resolved to grade 0-1 Discontinue treatment permanently	 100% 75% 50% --
Grade 3 1st appearance 2nd appearance 3rd appearance OR any evidence of Stevens-Johnson syndrome or Toxic Epidermal Necrolysis	 Interrupt until resolved to grade 0-1 Interrupt until resolved to grade 0-1 Discontinue treatment permanently	 75% 50% --
Grade 4 1st appearance, including SJS, TENS, OR cardiotoxicity OR acute renal failure 2nd appearance	 Discontinue permanently or If physician deems it to be in the patient's best interest to continue and no evidence of Stevens-Johnson syndrome or toxic epidermal necrolysis, interrupt until resolved to grade 0-1. Discontinue permanently	 Discontinue or 50% --

Hepatic Impairment

No adjustment required for cisplatin.

Capecitabine:

- Use dose modification table above for increases in bilirubin.
- In patients with mild to moderate hepatic impairment due to liver metastases exposure is increased, but no dose adjustment is necessary, although caution should be exercised.
- The use of capecitabine in patients with severe hepatic impairment has not been studied.

Renal Impairment

Creatinine Clearance (mL/min)	Cisplatin (% previous dose)	Capecitabine (% previous dose)
61-80	100%	100% with close monitoring
51-60	75%	100% with close monitoring
46-50	75%	75%; use with caution
30-45	50%	75%; use with caution
<30	Discontinue	CONTRAINDICATED

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F - Adverse Effects

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

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Hand-foot syndrome (may be severe) • Diarrhea (may be severe) • Nausea, vomiting • Mucositis • ↑ LFTs (may be severe) • Fatigue • Abdominal pain • Nephrotoxicity (may be severe) • Electrolyte abnormalities • Neurotoxicity and ototoxicity (may be severe) • Myelosuppression ± infection / bleeding (may be severe)	• Venous Thromboembolism • Arterial Thromboembolism • GI obstruction • GI perforation • Cardiotoxicity, arrhythmia • Idiopathic thrombocytopenic purpura • Hypersensitivity • Hemolytic uremic syndrome, vasculitis • Secondary malignancies • Raynaud's • Hemolysis • Leucoencephalopathy • Rash

• Anorexia • Hyperuricemia	

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G - Interactions

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

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H - Drug Administration and Special Precautions

Refer to CISplatin, capecitabine 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

- Audiogram; as clinically indicated
- CBC; baseline and regular
- Electrolytes, including magnesium, sodium, potassium, phosphate and calcium; baseline and regular
- Baseline and regular liver & renal function tests
- INR or PT; baseline and regular if on anticoagulants
- Clinical toxicity assessment for diarrhea, dehydration infection, bleeding, stomatitis, rash, hand-foot syndrome, nausea/vomiting, neurotoxicity, ototoxicity, cardiac, thromboembolism and other GI toxicity; 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	3 hours
Pharmacy Workload (average time per visit)	36.087 minutes
Nursing Workload (average time per visit)	41.667 minutes

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K - References

Bang YJ, Van Cutsem E, Feyereislova A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet 2010; 376(9742): 687-97.

Capecitabine and cisplatin drug monographs, Cancer Care Ontario.

Kang YK, Kang WK, Shin D, et al. Capecitabine/cisplatin versus 5-fluorouracil/cisplatin as first-line therapy in patients with advanced gastric cancer: a randomised phase III noninferiority trial. Ann Oncol 2009;20(4):666-73.

PEBC Advice Documents or Guidelines

- Systemic Therapy for Advanced Gastric Cancer

May 2019 Updated emetic risk category

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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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