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

CAPE Regimen

Capecitabine

Disease Site	Gastrointestinal - Pancreas
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.
Supplementary Public Funding	**capecitabine** ODB - General Benefit (capecitabine) (ODB Formulary)

back to top

B - Drug Regimen

capecitabine	1000-1250 mg /m² PO	BID* Days 1 to 14

(*Total dose 2000-2500 mg/m^2/day)

(Available as 150 mg or 500 mg tablets)

back to top

C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until disease progression or unacceptable toxicity

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Low

Other Supportive Care:

- 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.

back to top

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

Do not start treatment with capecitabine unless baseline neutrophil counts are ≥ 1.5 x 10^9/L and/or platelet counts of ≥ 100 x 10^9/L. Patients should be informed of the need to interrupt treatment immediately if moderate or severe toxicity occurs. Supportive care should be provided, including loperamide for diarrhea.

Doses should not be re-escalated if reduced for toxicity. Missed or omitted doses of capecitabine

should not be replaced.

Dose modifications are mandatory for gastrointestinal, dermatological toxicity and hyperbilirubinemia. Practitioner may elect not to reduce dose for other toxicities unlikely to become serious or life-threatening.

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 or TEN, OR cardiotoxicity OR acute renal failure 2nd appearance OR any occurrence of confirmed leukoencephalopathy	 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% --

Hematological Toxicities:

Modify according to protocol by which patient is being treated; if no guidelines available, refer to Appendix 6 for general recommendations. Hold capecitabine during a treatment cycle in the presence of grade 3 or 4 hematologic toxicity.

Hepatic Impairment

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

Renal Impairment

Moderate renal impairment results in an increase in severe toxicity.

Creatinine Clearance (mL/min)	% of starting dose
51-80	100 % with close monitoring
30-50	75 % (use with caution)
<30	CONTRAINDICATED

Dosage in the Elderly

No dose adjustment for the starting dose is required, but patients should be closely monitored and dose modification should be performed as described above. Older patients are more susceptible to the effects of fluoropyrimidine-based therapies with increased grade 3 / 4 adverse effects, especially when used in combination.

back to top

F - Adverse Effects

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

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Hand-foot syndrome	• Diarrhea (may be severe) • Nausea, vomiting	• Mucositis • Increased LFTs (may be severe) • Fatigue • Abdominal pain	• Cardiotoxicity • Venous thromboembolism • Arterial thromboembolism • Hypersensitivity • Myelosuppression +/- infection, bleeding • Leukoencephalopathy • GI perforation, obstruction • Idiopathic thrombocytopenic purpura • Eye disorders • Renal failure

back to top

G - Interactions

Refer to capecitabine drug monograph(s) for additional details

- Avoid concomitant administration with sorivudine or analogues given increased risk of capecitabine toxicity (may be fatal). Wait 4 weeks after sorivudine treatment before starting capecitabine.
- Avoid concomitant administration with phenytoin as capecitabine may increase phenytoin levels.
- Avoid leucovorin as this may increase capecitabine toxicity.
- Caution and monitor PT/INR when administered with warfarin; capecitabine increases warfarin exposure.

- Avoid concomitant administration of antacids; these may increase capecitabine exposure.
- Caution and monitor when administered with docetaxel; increased toxicity in elderly observed.

back to top

H - Drug Administration and Special Precautions

Refer to capecitabine drug monograph(s) for additional details

Administration:

- Doses are given orally approximately 12 hours apart, within 30 minutes after the end of a meal.
- If a capecitabine dose is missed, skip this and give the next dose at the usual time. Missed or omitted doses should not be replaced.
- Store tablets at 15ºC to 30ºC in the original package.

Contraindications:

- Patients who have a known hypersensitivity to capecitabine, its excipients, or 5-fluorouracil
- Patients with severe renal impairment (CrCl <30 mL/min)
- Patients with known near or complete absence of DPD (dihydropyrimidine dehydrogenase) deficiency
- Concomitant use with sorivudine or related analogues (i.e. brivudine) (see Interactions)
- Contains lactose and should not be used in patients with hereditary galactose/glucose/lactase disorders.

Other Warnings/Precautions:

- Use with caution in patients with risk factors for dehydration, pre-existing renal dysfunction, and on nephrotoxic agents
- Use with caution in patients with a history of cardiovascular disease as well as patients taking anticoagulants
- Use with extreme caution in patients with partial DPD deficiency

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 at each visit
- Renal function tests; baseline and at each visit
- INR or PT; baseline and regular if on anticoagulants
- Clinical toxicity assessment for diarrhea, dehydration, infection, stomatitis, rash, hand-foot syndrome, cardiac, hepatic and other GI toxicity; at each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Liver function tests; baseline and regular (if severe organ failure suspected)

back to top

J - Administrative Information

Outpatient prescription for home administration

back to top

K - References

Capecitabine drug monograph, Cancer Care Ontario.

Boeck S, Wilkowski R, Bruns CJ, et al. Oral capecitabine in gemcitabine-pretreated patients with advanced pancreatic cancer. Oncology 2007;73(3-4):221-7.

Cartwright TH, Cohn A, Varkey JA, et al. Phase II study of oral capecitabine in patients with advanced or metastatic pancreatic cancer. J Clin Oncol 2002;20(1):160-4.

April 2018 updated capecitabine funding to general benefit

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.

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back to top