

Regimen Monograph

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A - Regimen Name

CAPE(RT) Regimen

Capecitabine

Disease Site Gastrointestinal - Colorectal

Intent Neoadjuvant

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 For the neo-adjuvant treatment of rectal cancer.

Supplementary Public Funding [capecitabine](#)
ODB - General Benefit (capecitabine) ([ODB Formulary](#))

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B - Drug Regimen[capecitabine](#)825 mg /m²

PO

BID*

(Outpatient prescription in 150 mg and 500 mg tablets; *Total dose 1650 mg/m²/day)

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Either on days of radiation (5 days per week) OR continuously (7 days per week) during radiotherapy (single cycle).

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Antiemetic Regimen: Minimal

Febrile Neutropenia Risk: 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.

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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 $\geq 1.5 \times 10^9/L$ and/or platelet counts of $\geq 100 \times 10^9/L$. 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 (% 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	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 OR 50%
2nd appearance OR any occurrence of confirmed leukoencephalopathy	Discontinue permanently	—

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.

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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
<ul style="list-style-type: none"> • Hand-foot syndrome 	<ul style="list-style-type: none"> • Diarrhea (may be severe) • Nausea, vomiting 	<ul style="list-style-type: none"> • Mucositis • Increased LFTs (may be severe) • Fatigue • Abdominal pain 	<ul style="list-style-type: none"> • Cardiotoxicity • Venous thromboembolism • Arterial thromboembolism • Hypersensitivity • Myelosuppression +/- infection, bleeding • Leukoencephalopathy • GI perforation, obstruction • Idiopathic thrombocytopenic purpura • Eye disorders • Renal failure

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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.

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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 15°C to 30°C 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

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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 regular
- INR or PT; baseline and regular if on anticoagulants
- Clinical toxicity assessment for diarrhea, dehydration, infection, stomatitis, rash, hand-foot syndrome, cardiac, hepatic and neurotoxicity; 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)

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Outpatient prescription for home administration

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K - References

Capecitabine drug monograph, Cancer Care Ontario.

Clinical Practice Guidelines in Oncology (NCCN Guidelines). Colon Cancer. Version 3.2015. NCCN.org

De Paoli, A, et al. Capecitabine in combination with preoperative radiation therapy in locally advanced, resectable, rectal cancer: a multicentric phase II study. *Ann Oncol* 2006;17:246-51.

Dunst J, Debus J, Rudat V et al. Neoadjuvant Capecitabine Combined with Standard Radiotherapy in Patients with Locally Advanced Rectal Cancer: Mature Results of a Phase II Trial. *Strahlenther Onkol* 2008;184(9):450-6.

Dupuis O, Vie B, Lledo G et al. Preoperative treatment combining capecitabine with radiation therapy in rectal cancer: a GERCOR Phase II Study. *Oncology* 2007;73(3-4):169-76

Hofheinz R, Wenz F, Post S, et al: Capecitabine (Cape) versus 5-fluorouracil (5-FU)-based (neo)adjuvant chemoradiotherapy (CRT) for locally advanced rectal cancer (LARC): Long-term results of a randomized, phase III trial. 2011 ASCO Annual Meeting. [Abstract 3504](#). Presented June 4, 2011.

Roh MS, Yothers GA, O'Connell MJ, et al: The impact of capecitabine and oxaliplatin in the preoperative multimodality treatment in patients with carcinoma of the rectum: NSABP R-04. 2011 ASCO Annual Meeting. [Abstract 3503](#). Presented June 4, 2011.

April 2018 updated capecitabine funding to general benefit

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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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