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	Breast
Intent	Adjuvant
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 use as adjuvant therapy in patients with residual disease after neoadjuvant chemotherapy. The Breast Drug Advisory Committee notes that a greater magnitude of benefit was seen in patients with triple-negative disease based on the subset analysis from the CREATE-X trial, and that consideration be given towards an upfront dose adjustment to facilitate tolerability and completion of the planned number of treatment cycles.
Supplementary Public Funding	**capecitabine** ODB - General Benefit (capecitabine) (ODB Formulary)

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B - Drug Regimen

capecitabine	1250 mg /m²	PO	BID Days 1 to 14

(Total dose 2500 mg/m^2/day)

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

For 6 to 8 cycles unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low – No routine prophylaxis; PRN recommended

Febrile Neutropenia Risk: Low

Other Supportive Care:

- Also refer to CCO Antiemetic Recommendations.
- **Screen for hepatitis B virus in all cancer patients starting systemic treatment.** Refer to the hepatitis B virus screening and management guideline.
- Topical emollients (e.g. hand creams, udder balm) may ameliorate the manifestations of hand-foot syndrome in patients receiving capecitabine.
- Standard antidiarrheal agents (e.g. loperamide) should be initiated, as medically appropriate, as early as possible.

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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 capecitabine. 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.

Dosage with toxicity

Patients with baseline neutrophil counts of <1.5 x 10^9/L and/or thrombocyte counts of <100 x 10^9/L should not receive capecitabine therapy.

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, neurotoxicity and hyperbilirubinemia. Practitioner may elect not to reduce dose for other toxicities unlikely to become serious or life-threatening.

Non-hematologic Toxicity:

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	Hold until resolved to ≤ grade 1	100%
2nd appearance	Hold until resolved to ≤ grade 1	75%
3rd appearance	Hold until resolved to ≤ grade 1	50%
4th appearance	Discontinue treatment permanently	Not applicable

Grade 3 1st appearance 2nd appearance 3rd appearance, OR any evidence of Stevens-Johnson syndrome or Toxic epidermal necrolysis	 Hold until resolved to ≤ grade 1 Hold until resolved to ≤ grade 1 Discontinue treatment permanently	 75% 50% Not applicable
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 1. Discontinue permanently	 Discontinue OR 50% Not applicable

Hematologic Toxicity:

Hold capecitabine during a treatment cycle in the presence of grade 3 or 4 hematologic toxicity.

Hepatic Impairment

Hepatic Impairment	Capecitabine Dose
Mild to moderate	No starting dose adjustment necessary; monitor closely
Severe	No data, has not been studied

Renal Impairment

Moderate renal impairment results in an increase in severe toxicity.

Creatinine Clearance (mL/min)	Capecitabine Dose
51 - 80	No adjustment required (with close monitoring)
30 - 50	75 % of recommended dose (use with caution and close monitoring)
<30	Do not use (Contraindicated)

Dosage in the Elderly

No dose adjustment for the starting dose is required but patients should be closely monitored. Older patients (≥ 65 years) 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
• Palmar-plantar erythrodysesthesia syndrome (PPES) (may be severe)	• Diarrhea (may be severe) • Nausea, vomiting	• Mucositis • ↑ Bilirubin (may be severe) • Fatigue • Abdominal pain	• Cardiotoxicity • Arterial / Venous thromboembolism • Hypersensitivity • Myelosuppression +/- infection, bleeding • Leukoencephalopathy • GI perforation / obstruction • Nephrotoxicity • Hepatic failure • Idiopathic thrombocytopenic purpura • Eye disorders • Dehydration • Rash

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G - Interactions

Refer to capecitabine drug monograph(s) for additional details.

- Concomitant use with sorivudine or analogues is contraindicated, given the increased risk of capecitabine toxicity (may be fatal). Wait at least 4 weeks after sorivudine (or chemically related analogues) treatment before starting capecitabine.
- Avoid concomitant administration with phenytoin as capecitabine may increase phenytoin levels.
- Caution and monitor with the coadministration of leucovorin as this may increase capecitabine toxicity.
- Caution and monitor PT/INR when administered with warfarin; capecitabine increases warfarin exposure.
- Caution with the use of proton pump inhibitors and monitor for reduced effectiveness of capecitabine; consider switching to a magnesium and aluminum hydroxide-containing antacid.

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H - Drug Administration and Special Precautions

Refer to capecitabine drug monograph(s) for additional details.

Administration:

- Oral self-administration; drug available by outpatient prescription.
- Doses are given orally approximately 12 hours apart, within 30 minutes after the end of a meal.
- Swallow tablets whole; do not crush or cut tablets.
- 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, 5-fluorouracil or any ingredient in the formulation or component of the container.
- Patients with severe renal impairment (CrCl <30 mL/min).
- Patients with known near or complete absence of DPD (dihydropyrimidine dehydrogenase) activity. Refer to the DPD Deficiency Guidance for Clinicians for more information.
- Concomitant use with sorivudine or related analogues (i.e. brivudine), given potential fatal drug interaction.

Other Warnings/Precautions:

- Contains lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption
- Use with caution in patients with risk factors for dehydration, pre-existing renal dysfunction or on nephrotoxic agents.
- Use with caution in patients with a history of cardiovascular disease as well as patients taking anticoagulants such as warfarin.
- Patients with partial DPD deficiency - use with extreme caution. Refer to the DPD Deficiency Guidance for Clinicians for more information.

Pregnancy/Lactation:

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Probable
  Documented in animal studies

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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.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- CBC; Baseline and at each visit
- Renal function tests; Baseline, at each visit and as clinically indicated
- Liver function tests; Baseline and as clinically indicated
- INR and/or PT; Baseline and as clinically indicated if patient is on anticoagulants
- Clinical toxicity assessment for diarrhea, dehydration, infection, stomatitis, rash or hand-foot syndrome, cardiac, hepatic and neurotoxicity; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Capecitabine drug monograph, Ontario Health (Cancer Care Ontario).

Masuda N, Lee SJ, Ohtani S, et al. Adjuvant Capecitabine for Breast Cancer after Preoperative Chemotherapy. N Engl J Med. 2017 Jun 1;376(22):2147-59.

July 2024 Updated Dose Modifications, Pregnancy/Lactation, Monitoring, and Other Notes sections

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L - Other Notes

Antidote for Capecitabine Overdose:

Uridine triacetate is a prodrug of uridine and is a specific antidote for treating capecitabine 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).

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.

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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.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

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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