Regimen Monograph

A - Regimen Name

CAPEDOCE Regimen

Capecitabine-DOCEtaxel

Disease Site	Breast
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	Treatment of anthracycline resistant metastatic breast cancer. (Due to the toxicity level of the regimen, it should be used in younger patients with good performance status.)
Supplementary Public Funding	**capecitabine** ODB - General Benefit (capecitabine)

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B - Drug Regimen

DOCEtaxel	75 mg /m²	IV	Day 1
capecitabine	1000 mg /m²	PO	BID, Days 1 to 14

(Total capecitabine dose 2000 mg/m^2/day)

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until evidence of disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low
No routine prophylaxis for capecitabine

Other Supportive Care:

- Dexamethasone 8 mg bid po for 3 days starting 1 day prior to docetaxel (prevent anaphylaxis / fluid retention.)
- 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. Practitioner may elect not to reduce dose for toxicities unlikely to become serious or life-threatening.

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.

The beginning of a cycle should be delayed until neutrophil count is ≥ 1.5 x 10^9/L, platelets ≥100 x 10^9/L and patient has recovered from severe toxicity in the previous cycle. In general, doses reduced for toxicity should not be re-escalated. However, if docetaxel is permanently discontinued, and toxicity with capecitabine as a single agent is ≤ grade 1, consider escalation of the capecitabine dose to standard dosing by increments of 25%.

Dosage with toxicity

Table A: Hematologic Toxicity

Toxicity and Grade	Within a Cycle	Day 1 of subsequent cycle	
	Capecitabine	Capecitabine	Docetaxel Dose
Grade 3 or 4 neutropenia only	Monitor	No change[1]	No change[1]
Grade 3 or 4 neutropenia with ≥ grade 2 non-hematological toxicity	Hold until ≤ grade 1	No change[1]. Refer to table below for non-hematological toxicity.	No change[1]. Refer to table below for non-hematological toxicity.
Grade 4 neutropenia ≥ 7 days/ febrile neutropenia	Hold until neutrophils ≥1.5 x 10^9/L	No change[1], or consider dose modification	55mg/m^2 (1). If recurs, discontinue

[1]Do not retreat until platelets ≥100 x 10^9/L, neutrophil ≥1.5 x 10^9/L, and other toxicities ≤ grade 1.

Table B: Non-hematologic Toxicity

For first appearance of cystoid macular edema, hold **docetaxel** and investigate; refer patient promptly to an ophthalmic examination. Discontinue **docetaxe**l if confirmed.

<table>
<tr><th rowspan="2"></th><th colspan="2">Grade 2</th><th colspan="2">Grade 3</th><th>Grade 4</th></tr>
<tr><th>Docetaxel</th><th>Capecitabine</th><th>Docetaxel</th><th>Capecitabine</th><th></th></tr>
<tr><td>1st appearance</td><td>Hold until ≤ grade 1.</td><td>Hold until ≤ grade 1.</td><td>Hold until ≤ grade 1 then ↓ to 55mg/m2. Discontinue if > 2wk delay or grade 3 toxicities recur.</td><td>Hold until ≤ grade 1 then give 75% of original dose.</td><td rowspan="2">Discontinue docetaxel and capecitabine.

If deemed appropriate by the physician and no evidence of SJS/TEN^, may continue with single agent capecitabine at 50% of original dose.</td></tr>
<tr><td colspan="3">Discontinue if any evidence of SJS ^.</td></tr>
<tr><td>2nd appearance</td><td>Hold until ≤ grade 1, then ↓ to 55mg/m2</td><td>Hold until ≤ grade 1, then give 75% of original dose</td><td>Discontinue</td><td>Hold until ≤ grade 1, then give 50% of original dose</td><td>Discontinue</td></tr>
<tr><td>3rd appearance</td><td>Discontinue</td><td>Hold until ≤ grade 1, then give 50% of original dose</td><td colspan="2">Discontinue</td><td>Not applicable</td></tr>
<tr><td>4th appearance</td><td colspan="2">Discontinue</td><td colspan="2">Not applicable</td><td>Not applicable</td></tr>
</table>

^SJS = Stevens-Johnson syndrome; TEN = toxic epidermal necrolysis

Hepatic Impairment

Bilirubin	AST or ALT		ALP	Capecitabine	Docetaxel % Starting Dose
≤ ULN	≤ 1.5 x ULN	AND	≤ 2.5 x ULN	Use with caution; no adjustment required	100%
≤ ULN	>1.5 – 3.5 X ULN	AND	>2.5 to 6 X ULN		Do not treat
≤ ULN	> 3.5 ULN	OR	> 6 X ULN (unless bone ONLY)	No information found; consider dose reduction or discontinue	Do not treat. Discontinue if treatment already started.
> ULN				Follow Table B	Do not treat. Discontinue if treatment already started.

Renal Impairment

Mild-moderate renal impairment results in increased exposure to capecitabine metabolites and an increase in severe toxicity.

CrCl (mL/min)	Capecitabine (% Starting Dose)	Docetaxel (% Starting Dose)
51-80	100%	100%
30-50	75% (use with caution)	100%
<30	Discontinue	100%

Dosage in the Elderly

For capecitabine, dose adjustment for the starting dose is not 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.

For docetaxel, no adjustment required, but caution should be exercised in elderly patients with poor performance status who are receiving docetaxel. Patients over the age of 60 years appear to have increased toxicity when docetaxel is used in combination with capecitabine.

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F - Adverse Effects

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

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Myelosuppression ± infection, bleeding (may be severe) • Hypersensitivity (may be severe) • Fluid retention (may be severe) • Cutaneous reactions (includes nails, hand-foot syndrome; may be severe) • Diarrhea, nausea/vomiting, stomatitis • Fatigue • ↑ LFTs (may be severe) • Alopecia • Neurotoxicity (may be severe) • Musculoskeletal pain (may be severe) • Lacrimation / lacrimal duct obstruction	• Arterial thromboembolism • Venous thromboembolism • Cardiotoxicity/arrhythmia • Pneumonitis • GI obstruction, perforation • DIC • Seizures • ITP • Secondary malignancies • Cystoid macular edema

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G - Interactions

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

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H - Drug Administration and Special Precautions

Refer to capecitabine, DOCEtaxel 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 at each visit
- INR and/or PT; Baseline and regular if on anticoagulants
- Liver function tests; Baseline and routine
- Renal function tests; Baseline and regular
- Regular toxicity assessment of infection, bleeding, fatigue, neurotoxicity, GI (e.g. diarrhea, stomatitis), dehyration, fluid retention, hypersensitivity, cutaneous reactions, hand-foot syndrome, thromboembolism, cardiovascular, musculoskeletal pain, ophthalmic, respiratory effects; 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	2 hours
Pharmacy Workload (average time per visit)	18.936 minutes
Nursing Workload (average time per visit)	54.167 minutes

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K - References

Capecitabine and docetaxel drug monographs, Cancer Care Ontario.

Chan S, Romieu G, Huober J.. Phase III study of gemcitabine plus docetaxel compared with capecitabine plus docetaxel for anthracycline-pretreated patients with metastatic breast cancer. J Clin Oncol 2009;27(11):1753-60.

Leonard R, O'Shaughnessy J, Vukelja S, et al. Detailed analysis of a randomized phase III trial: can the tolerability of capecitabine plus docetaxel be improved without compromising its survival advantage? Annals of Oncology 2006: 17; 1379–85.

O'Shaughnessy J, Miles D, Vukelja S, et al. Superior Survival With Capecitabine Plus Docetaxel Combination Therapy in Anthracycline-Pretreated Patients With Advanced Breast Cancer: Phase III Trial Results JCO, June 15, 2002 :2812-1823.

April 2023 Updated DPD deficiency information in the Dose Modifications section

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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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