Regimen Monograph

A - Regimen Name

DOCE Regimen

DOCEtaxel

DOCE+TRAS Regimen

DOCEtaxel-Trastuzumab

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	For the treatment of metastatic breast cancer

Supplementary Public Funding

trastuzumab
New Drug Funding Program (Trastuzumab (Biosimilar) in combination with Chemotherapy - Metastatic Breast Cancer) (NDFP Website)

trastuzumab
New Drug Funding Program (Trastuzumab (Biosimilar) - Second Line - Metastatic Breast Cancer) (NDFP Website)

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B - Drug Regimen

Note: Different trastuzumab products are **NOT INTERCHANGEABLE.**

DOCEtaxel	100 mg /m²	IV	Day 1

For patients with HER2 positive tumours, trastuzumab may be given concurrently with docetaxel and then as a single agent.

trastuzumab	8 mg /kg	IV loading dose	Day 1, cycle 1 only

THEN,

trastuzumab	6 mg /kg	IV maintenance dose	Every 21 days

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

• Until disease progression or unacceptable toxicity occurs

• For patients with HER2 positive tumours, trastuzumab may be given concurrently and then as a single agent. Refer to TRAS (Breast - Advanced) regimen for details.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low

Other Supportive Care:

Also refer to CCO Antiemetic Summary

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Docetaxel Pre-medications (prophylaxis for infusion reaction):

- Dexamethasone* 8 mg PO BID for 3 days, starting 1-day pre-infusion†

* Do **not** discontinue dexamethasone, even in the absence of an IR, due to the benefits on other adverse effects (e.g. pain and edema).

† Dexamethasone 10-20 mg IV can be given if patient forgot to take oral doses.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Patients should not be treated until they have recovered from prior toxicity and have acceptable blood counts (ANC ≥ 1.5 x 10^9/L and platelets ≥ 100 x 10^9/L).

Dosage with toxicity

See TRAS (Breast - Advanced) regimen for details on **trastuzumab** dose modifications.

Toxicity (worst in previous cycle)	Docetaxel (% of previous dose)*
Febrile neutropenia / Grade 4 ANC ≥ 7 d	75%
Grade 3 skin/ neuro/ major organ/ non-hematologic toxicity	75%
Any occurrence of cystoid macular edema	Hold and investigate; refer patient promptly an ophthalmic examination. Discontinue if confirmed.
Grade 4 skin/ neuro/ major organ/ non-hematologic toxicity OR Recurrence of Grade 3 toxicity after prior dose reduction OR Any Severe Cutaneous Adverse Reactions (SCARs) (e.g. Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Acute generalized exanthematous pustulosis (AGEP))	Discontinue
* Do not retreat until ANC ≥ 1.5 x 10^9/L, platelets ≥ 100 x 10^9/L, and non-hematologic / organ toxicity ≤ grade 2.	

Management of Infusion-related reactions:

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Trastuzumab: Refer to the Trastuzumab drug monograph for details.

Docetaxel:

Grade	Management	Re-challenge
1 or 2	• Stop or slow the infusion rate. • Manage the symptoms. **Restart:** • After symptom resolution, restart with pre-medications ± reduced infusion rate.	• Consider re-challenge with pre-medications and at a reduced infusion rate. • After 2 subsequent IRs, replace with a different taxane. Give intensified pre-medications and reduce the infusion rate. • May consider adding oral montelukast ± oral acetylsalicylic acid.
3 or 4	• Stop treatment. • Aggressively manage symptoms.	• Re-challenge is discouraged, especially if vital symptoms have been affected. • Consider desensitization if therapy is necessary. • There is insufficient evidence to recommend substitution with another taxane at re-challenge. • High cross-reactivity rates have been reported.

Hepatic Impairment

Docetaxel: Patients with hepatic impairment have a higher risk of severe adverse effects, including fatal gastrointestinal hemorrhage, sepsis and myelosuppression.

Bilirubin		AST and/or ALT		Alkaline Phosphatase	Docetaxel dose
> ULN	AND	Any	AND	Any	Do not treat. Discontinue if treatment already started.
Any	AND	> 1.5 X ULN	AND	> 2.5 x ULN	

Trastuzumab: No adjustment required.

Renal Impairment

No adjustment required.

Dosage in the Elderly

For docetaxel, no adjustment required, but caution should be exercised in elderly patients with poor performance status.

For trastuzumab, no adjustment required; the risk of cardiac dysfunction and myelosuppression may be increased in elderly patients. The reported trials did not determine differences in efficacy between patients > 65 years versus younger patients.

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F - Adverse Effects

Refer to DOCEtaxel (± Trastuzumab) drug monograph(s) for additional details of adverse effects.

See TRAS (Breast - Advanced) regimen for details on trastuzumab adverse effects.

Docetaxel:

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Alopecia (rarely permanent) • Myelosuppression +/- bleeding (may be severe) • Fatigue	• Neuropathy (may be severe) • Rash (may be severe) • Edema (may be severe) • Mucositis (may be severe) • Diarrhea (may be severe, especially with neutropenia) • Nausea/vomiting • Nail disorder	• Hypersensitivity (may be severe) • Musculoskeletal pain	• Arrhythmia • Cardiotoxicity • Arterial thromboembolism • Venous thromboembolism • GI obstruction / perforation • Injection site reaction • Radiation and injection site recall reaction • ↑ LFTs • Seizure • Cystoid macular edema • Tear duct obstruction • Pneumonitis/Adult Respiratory Distress Syndrome (ARDS) • Disseminated intravascular coagulation (DIC) • Secondary malignancies • Stevens-Johnson

			syndrome • Toxic epidermal syndrome • Acute generalized exanthematous pustulosis

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G - Interactions

Refer to DOCEtaxel (± Trastuzumab) drug monograph(s) for additional details.

- Avoid concomitant use of docetaxel with CYP3A4 inhibitors. If must use together, consider decreasing docetaxel dose (50% for strong inhibitors).
- Avoid concurrent use of docetaxel with dronedarone.
- Avoid concomitant use of trastuzumab with anthracyclines and other cardiotoxic drugs. Use with extreme caution with anthracyclines for up to 28 weeks after stopping trastuzumab.

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H - Drug Administration and Special Precautions

Refer to DOCEtaxel (± Trastuzumab) drug monograph(s) for additional details.

See TRAS (Breast - Advanced) regimen for details on trastuzumab Drug Administration and Special Precautions.

Administration - Docetaxel:

- Refer to the respective product monographs for preparation instructions. Mix in 250mL D5W or NS to a maximum concentration of 0.3-0.74 mg/mL. For doses over 200mg, use a larger volume of the infusion vehicle so the maximum concentration is not exceeded.
- Infuse through main IV line over 1 hour.
- In order to minimize patients' exposure to DEHP leaching from PVC bags or sets, use polyolefin or polypropylene infusion bags and polyethylene-lined administration sets.
- To minimize hypersensitivity reactions, docetaxel infusion should be started at a slow rate, then increased incrementally to planned rate.
- Monitor patient for signs of alcohol intoxication (due to alcohol content in formulation) during and after the infusion. Slowing the infusion rate during administration may help resolve symptoms.
- Injection site recall reactions (recurrence of skin reaction at a previous extravasation site after docetaxel is administered at a different site) have been observed.

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Contraindications - Docetaxel:

- Patients who have a history of hypersensitivity reactions to docetaxel, to other drugs formulated with polysorbate 80 or polyethylene glycol 300, or to any components of the formulation
- Patients with baseline neutrophil counts of $<1.5 \times 10^9$/L
- Patients with severe liver impairment

Other Warnings/Precautions - Docetaxel:

- Use with caution in patients with pre-existing effusions or ascites.
- Use with caution in patients who have hypersensitivity to paclitaxel. Patients who have previously experienced a hypersensitivity reaction to paclitaxel may develop a potentially fatal hypersensitivity reaction to docetaxel.
- Docetaxel contains ethanol (refer to respective product monographs) and may cause drowsiness. Patients should be cautioned regarding driving and the use of machinery immediately after receiving the infusion. Ethanol may be harmful to patients at risk of adverse

effects such as those with alcoholism, liver disease, epilepsy and children. Cases of alcohol intoxication have been reported.

Pregnancy/Lactation:

- DOCE and DOCE+TRAS regimens are **contraindicated** 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 **contraindicated** during treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects:
  - Docetaxel: Fertility may be affected, especially in males.
  - Trastuzumab: Unknown

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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.

Also refer to TRAS (Breast - Advanced) regimen for details on monitoring.

Recommended Clinical Monitoring

- CBC, including nadir counts; baseline and before each cycle
- Liver function tests; baseline and before each cycle
- Clinical toxicity assessment of infection, bleeding, neurotoxicity, fluid retention, hypersensitivity, lethargy, cutaneous reactions, thromboembolism, musculoskeletal pain, secondary malignancies, cardiovascular, ophthalmic, GI or 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

DOCE	2 hours
DOCE+TRAS	First cycle: 3 hours; Subsequent cycles: 2 hours

Pharmacy Workload **(average time per visit)**

DOCE	23.936 minutes
DOCE+TRAS	33.025 minutes

Nursing Workload **(average time per visit)**

DOCE	54.167 minutes
DOCE+TRAS	71.667 minutes

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K - References

Chan S, Friedrichs K, Noel D, et al. Prospective randomized trial of docetaxel versus doxorubicin in patients with metastatic breast cancer. J Clin Oncol 1999; 17: 2341-54.

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

Jones SE, Erban J, Overmoyer B, et al. Randomized phase III study of docetaxel compared with paclitaxel in metastatic breast cancer. J Clin Oncol. 2005 Aug 20;23(24):5542-51.

Nabholtz JM, Senn HJ, Bezwoda WR, et al. Prospective randomized trial of docetaxel versus mitomycin plus vinblastine in patients with metastatic breast cancer progressing despite previous anthracycline-containing chemotherapy. J Clin Oncol 1999;17:1413-24.

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

May 2024 Modified Pre-medications, Dose modifications, Adverse effects, Interactions, Drug Administration/Special Precautions, and Monitoring sections

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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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