Regimen Monograph

A - Regimen Name

CRBPDOCE Regimen

DOCEtaxel-CARBOplatin

Disease Site	Lung - Non-Small Cell
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	Alternative to cisplatin-docetaxel for the treatment of locally advanced or metastatic non-small cell lung cancer

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B - Drug Regimen

DOCEtaxel	75 mg /m²	IV	Day 1
CARBOplatin	AUC 5	IV	Day 1

Adjust Carboplatin dose to AUC target (using Calvert formula) as outlined in the "Other Notes" section.

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

For a usual total of 4 to 6 cycles in responding patients, unless disease progression or unacceptable toxicity occurs.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate + NK1 antagonist (Carboplatin AUC ≥ 5)

Other Supportive Care:

Dexamethasone 8 mg bid po for 3 days starting 1 day before docetaxel (prevent anaphylaxis/fluid retention.)

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. The following recommendations have been adapted from clinical trials or product monographs and could be considered.

Dosage with toxicity

Toxicity Type / Counts x 10^9/L		Toxicity Type / Counts x 10^9/L	Carboplatin[1]	Docetaxel[1] (% previous dose)
Febrile Neutropenia	OR	Grade 4 ANC ≥ 7 d	↓ 1 AUC	75%
Grade 3 rash	Or	Grade 3 Neurotoxicity	Restart by ↓ 1 AUC	Restart at 75%. Discontinue if recurs
Any occurrence of cystoid macular edema			No change	Hold and investigate; refer patient promptly to an ophthalmic examination. Discontinue if confirmed.
Other Grade 3 major organ / non-hematologic			↓ 1 AUC	75%
Grade 4 major organ / non-hematologic			Discontinue	Discontinue

[1]Prior to retreatment, toxicity should have recovered to ≤grade 2, ANC to ≥1.5x10^9/L, platelets ≥100x10^9/L

Hepatic Impairment

	AST and/or ALT		Alk Phosp		Bilirubin	Docetaxel (% previous dose)	Dose of Carboplatin
Mild-moderate	> 1.5 X ULN	AND	> 2.5 x ULN			Do not treat	No dose adjustment required
Severe	> 3.5 x ULN	OR	> 6 x ULN	OR	> ULN	Do not treat. Discontinue if treatment already started.	

Renal Impairment

- As creatinine clearance changes, adjust dosage of carboplatin using the Calvert Formula. (See Section: Other Notes)
- Modification for docetaxel not required.

Dosage in the Elderly

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

For carboplatin, caution should be exercised and dose reduction considered as elderly patients may have more severe myelosuppression and neuropathy.

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F - Adverse Effects

Refer to DOCEtaxel, CARBOplatin 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 reactions (may be severe) • Musculoskeletal pain (may be severe) • Fluid retention (may be severe) • Neuropathy (including ototoxicity) • Cutaneous (skin and nails) • Fatigue • GI (nausea, stomatitis, diarrhea) • Alopecia • Nephrotoxicity • Electrolyte abnormalities • Lacrimation / lacrimal duct obstruction	• Secondary malignancies • Pneumonitis • Arterial Thromboembolism • Venous Thromboembolism • Hemolytic-uremic Syndrome • GI perforation / obstruction • Arrhythmia, heart failure • DIC • ↑ LFTs (may be severe) • Cystoid macular edema

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G - Interactions

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

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H - Drug Administration and Special Precautions

Refer to DOCEtaxel, CARBOplatin 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

- Baseline and regular CBC and electrolytes (including magnesium)
- Baseline and regular renal and liver function tests
- Clinical toxicity assessment (including infection, bleeding, neurologic, ototoxiciy, musculoskeletal pain, hypersensitivity, lethargy, GI, cutaneous effects, ophthalmic, cardiac, reespiratory, thromboembolism); 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 to 3 hours
Pharmacy Workload (average time per visit)	35.656 minutes
Nursing Workload (average time per visit)	59.167 minutes

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K - References

Carboplatin, docetaxel drug monograph, Cancer Care Ontario.

Fossella F, Pereira J, von Pawel J, et al. Randomized, multinational, phase III study of docetaxel plus platinum combinations versus vinorelbine plus cisplatin for advanced non-small-cell lung cancer: The TAX 326 study group. JCO 21(16): 3016-3024, 2003.

PEBC Advice Documents or Guidelines

- Systemic Treatment for Patients with Advanced Non-Small Cell Lung Cancer

August 2021 Modified Rationale and Uses section

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L - Other Notes

There is no convincing evidence that any new agent (gemcitabine, vinorelbine, docetaxel, paclitaxel, irinotecan, pemetrexed) in combination with platinum is superior to any other platinum plus new agent combination.

For patients receiving platinum-based doublet therapy, a recommendation in favour of cisplatin over carboplatin is made based on a probable modest improvement in survival and an improvement in response. Cisplatin regimens result in more frequent nausea/vomiting and nephropathy, while thrombocytopenia is worse with carboplatin. Given the poor prognosis in this population, the relative toxicities and QOL differences should be given strong consideration.

Calvert Formula

DOSE (mg) = target AUC X (GFR + 25)

- AUC = product of serum concentration (mg/mL) and time (min)
- GFR (glomerular filtration rate) expressed as measured Creatinine Clearance or estimated from Serum Creatinine (by Cockcroft and Gault method or Jelliffe method)

(Calvert AH, Newell DR, Gumbrell LA, et al, Carboplatin dosage: Prospective evaluation of a simple formula based on renal function. J Clin Oncol, 1989; 7: 1748-1756)

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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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