Regimen Monograph

A - Regimen Name

CRBPDOCE Regimen

DOCEtaxel-CARBOplatin

Disease Site	Gynecologic - Ovary
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 advanced or recurrent epithelial ovarian, fallopian tube and primary peritoneal cancers

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B - Drug Regimen

DOCEtaxel	75 mg /m²	IV	Day 1
CARBOplatin	AUC 4 to 6	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 6 cycles unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

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

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

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

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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 days	↓ 1 AUC	75%
Grade 3 rash	Or	Grade 3 Neurotoxicity	↓ by 1 AUC at restart	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 ≥ 1.5 x 10^9/L, platelets ≥ 100 x 10^9/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 , but caution should be exercised in elderly patients with poor performance status who are receiving docetaxel.
- Caution should be exercised and dose reduction considered as elderly patients may have more severe myelosuppression and neuropathy with carboplatin.

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F - Adverse Effects

Refer to DOCEtaxel, CARBOplatin 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
• Alopecia • Fatigue • Myelosuppression +/- infection, bleeding (may be severe) • Nausea, vomiting	• Neuropathy (may be severe) • Rash (may be severe) • Fluid retention • Mucositis • Diarrhea • Abnormal electrolytes • Increased LFTs (may be severe) • Nail disorder • Nephrotoxicity (may be	• Hypersensitivity (may be severe) • Musculoskeletal pain • Ototoxicity	• Arrhythmia • Cardiotoxicity • Arterial thromboembolism • Venous thromboembolism • Cytoid macular edema • GI obstruction, perforation • DIC • Hemolytic uremic syndrome • Pneumonitis • Seizure

	severe)		

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G - Interactions

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

- Caution and monitor with nephrotoxic and ototoxic drugs (i.e. aminoglycosides)
- Caution and monitor INR for patients receiving warfarin
- Caution and monitor phenytoin levels for patients receiving phenytoin
- Docetaxel is a substrate of CYP3A4 and PgP. Caution and monitor with inducers and inhibitors of these isoenzymes.
- Consider docetaxel dose reduction when given with strong CYP3A4 inhibitors
- Avoid combining docetaxel with dronedarone (severe toxicity reported)

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H - Drug Administration and Special Precautions

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

Administration

Carboplatin:

- Mix in 100mL to 250mL bag (5% Dextrose or Normal Saline); infuse IV over 15 to 60 minutes.
- Incompatible with sets, needles or syringes containing aluminum – leads to precipitation and loss of potency.
- Protect from light.

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 185 mg, use a larger volume of the infusion vehicle so the maximum concentration is not exceeded.
- Infuse through main IV line over 1 hour.
- To minimize exposure to DEHP leaching from PVC infusion equipment, use non-PVC (polyolefin, polypropylene) bags and administer through polyethylene-lined infusion 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.

Contraindications:

- Patients who have a severe hypersensitivity to these drugs or other platinum containing compounds/other drugs formulated with polysorbate 80.
- Patients with neutrophil counts of <1.5 x 10^9/L
- Patients with severe hepatic or renal impairment, severe myelosuppression or bleeding tumours

Warnings/Precautions

- Avoid concomitant use of docetaxel and drugs that inhibit CYP3A4 (See Interactions section).
- Caution with carboplatin and patients with abnormal renal function or who are receiving concomitant nephrotoxic drugs
- Use docetaxel with caution in patients with preexisting effusions or ascites.
- Docetaxel contains ethanol (± 1g/m2; 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.
- Carboplatin and docetaxel are not recommended for use in pregnancy (**contraindicated** with docetaxel). Adequate contraception should be used by both sexes during treatment, and for at least 6 months after the last dose. Breastfeeding is contraindicated with docetaxel and not recommended with carboplatin.

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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 and electrolytes (including magnesium); Baseline and before each treatment
- Renal and liver function tests; Baseline and before each treatment
- Clinical toxicity assessment (including infection, bleeding, neurologic, ototoxiciy, musculoskeletal pain, hypersensitivity, lethargy, GI, fluid retention, cutaneous effects, ophthalmic, cardiac, respiratory, thromboembolism); at each visit

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- INR in patients receiving warfarin; baseline and regular

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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 and docetaxel drug monographs, Cancer Care Ontario.

Markman M, Kennedy A, Webster K, et al. Combination chemotherapy with carboplatin and docetaxel in the treatment of cancers of the ovary and fallopian tube and primary carcinoma of the peritoneum. J Clin Oncol 2001;19:1901-5.

Vorobiof DA, Rapoport BL, Chasen MR, et al. Phase II clinical trial of carboplatin and docetaxel in patients with metastatic ovarian cancer: active combination with low incidence of peripheral neuropathy. J Gynecol Cancer 2003;13:287-91.

Wang Y, Herrstedt J, Havsteen H, et al. A multicenter, non-randomized, phase II study of docetaxel and carboplatin administered every 3 weeks as second line chemotherapy in patients with first relapse of platinum sensitive epithelial ovarian, peritoneal or fallopian tube cancer. BMC Cancer 2014;14:937.

PEBC Advice Documents or Guidelines

- Systemic Therapy for Recurrent Epithelial Ovarian Cancer

June 2019 Updated emetic risk category

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L - Other Notes

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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