Regimen Monograph

A - Regimen Name

CAV Regimen

Cyclophosphamide-ADRIAMYCIN ® (DOXOrubicin)-VinCRIStine

Disease Site	Gastrointestinal - Neuroendocrine (GI)
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.

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B - Drug Regimen

cyclophosphamide	1000 mg /m²	IV	Day 1
DOXOrubicin	50 mg /m²	IV	Day 1
vinCRIStine	1.4 mg /m²	IV (maximum 2 mg)	Day 1

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

For a usual total of 6 cycles, unless disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: High

Other Supportive Care:

Also refer to CCO Antiemetic Summary

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E - Dose Modifications

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

Dosage with toxicity

Hematologic Toxicities: See general recommendations.

Neurotoxicity

Symptom	% usual Vincristine dose
Areflexia only	100 %
Abnormal buttoning, writing	67 %
Moderate motor neuropathy (± cranial)	Hold until recovery then reduce dose by 50%
Severe motor neuropathy	Omit

Hepatic Impairment

Bilirubin	Action
1. If Bilirubin 1-2 x ULN	**REDUCE** Vincristine and Doxorubicin to **50%** dose
2. If Bilirubin 2-4x ULN	**REDUCE** Vincristine and Doxorubicin to **25%** dose
3. If Bilirubin > 4 x ULN	**STOP** treatment with Doxorubicin

Doxorubicin is contraindicated in patients with severe hepatic impairment, especially with elevated bilirubin. Consideration should be given to dose modification for patients with severe increases in transaminases; limited data exists on the use of doxorubicin in this setting as these patients are routinely excluded from clinical trials.

Renal Impairment

Cyclophosphamide: Dosage may be halved or interval increased by 50-100% if CrCl<0.3 mL/second.

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F - Adverse Effects

Refer to cyclophosphamide, DOXOrubicin, vinCRIStine drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Nausea, vomiting • Increased LFTs • Alopecia • Anorexia, weight loss • Constipation • Diarrhea • Myelosuppression +/- infection, bleeding • Peripheral neuropathy (may be severe) • Rash	• Arterial thromboembolism • Venous thromboembolism • Cardiotoxicity • GI perforation • Hypersensitivity • Pancreatitis • Pneumonitis • SIADH • Prolonged QTc • Tumour lysis syndrome

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G - Interactions

Refer to cyclophosphamide, DOXOrubicin, vinCRIStine drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to cyclophosphamide, DOXOrubicin, vinCRIStine 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 before each cycle
- Baseline and regular liver function tests
- Baseline and regular renal function tests and urinalysis
- Cardiac examination especially with risk factors (including prior therapy with Epirubicin, Mitoxantrone, or other cardiotoxic drug), or a cumulative Doxorubicin dose of > 450 mg/ m^2
- Clinical toxicity assessment (including stomatitis, neurotoxicity, cardiotoxicity, local toxicity, cystitis)
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

Liver function tests; Baseline and regular

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J - Administrative Information

Approximate Patient Visit	1.5 hours
Pharmacy Workload (average time per visit)	36.054 minutes

Nursing Workload (average time per visit) 51.667 minutes

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K - References

Greco FA, et al. Treatment of oat cell carcinoma of the lung: Complete remissions, acceptable complications and improved survival. Brit Med J, 1978; 2: 10-11.

von Pawel J, Schiller JH, Shepherd FA et al. Topotecan versus cyclophosphamide, doxorubicin, and vincristine for the treatment of recurrent small-cell lung cancer. J Clin Oncol. 1999;17(2):658-67.

July 2019 Updated hyperlink to vincristine drug monograph

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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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