Regimen Monograph

A - Regimen Name

CRBPETOP Regimen

CARBOplatin-Etoposide

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.
Rationale and Uses	Alternative to cisplatin-etoposide for the treatment of poorly-differentiated neuroendocrine carcinoma

back to top

B - Drug Regimen

CARBOplatin	AUC 5	IV	Day 1
Adjust carboplatin dose to AUC target (using Calvert formula) as outline in "Other Notes" section.			
etoposide	100 mg /m²	IV	Days 1 to 3

back to top

C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until stable disease, disease progression, or unacceptable toxicity.

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate + NK1 antagonist (Carboplatin AUC ≥ 5) (D1)
Low (D2,3)

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

back to top

E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations are in use at some centres.

Dosage with toxicity

See Appendix 6 for general recommendations.

Adjust dosage of Carboplatin in response to platelet counts using the Egorin Formula (see section,

"Other Notes")

Toxicity / Counts x 10^9/L		Toxicity / Counts x 10^9/L	Carboplatin (% previous dose)	Etoposide (% previous dose)
Febrile Neutropenia	or	Grade 4 ANC ≥ 5-7d Grade 4 platelets	75%#	75%
Grade 3 related organ			75%	75%
Grade 4 related organ			Discontinue	Discontinue

use Egorin formula if isolated thrombocytopenia

Hepatic Impairment

Bilirubin		AST/ALT	Carboplatin (% previous dose)	Etoposide* (% previous dose)
1-2 x ULN	and/ or	--	100%	50%
2-4 x ULN		2-5 x ULN	100%	25%
>4 x ULN		> 5 x ULN	100%	Discontinue

*Based on clinical judgment – less conservative adjustments can be considered if hepatic changes are secondary to metastases rather than hepatic cirrhosis or hepatitis.

Renal Impairment

Creatinine Clearance (mL/min)	Carboplatin (% previous dose)	Etoposide (% previous dose)
20 - 50	Use Calvert formula	75%
15 - < 20	Discontinue	
< 15		50% or omit

back to top

F - Adverse Effects

Refer to etoposide, CARBOplatin drug monograph(s) for additional details of adverse effects

More common adverse effects	Less common adverse effects, but may be severe or life-threatening
• Nausea, vomiting • Alopecia • Myelosuppression +/- infection, bleeding • Nephrotoxicity (may be severe) • Ototoxicity • Anorexia • Diarrhea • Mucositis • Abnormal electrolytes	• Hypersensitivity • Arterial thromboembolism • Venous thromboembolism • Hemolytic uremic syndrome • Pneumonitis • Neurotoxicity, including optic nerve disorder • Radiation recall reaction, severe rash

back to top

G - Interactions

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

back to top

H - Drug Administration and Special Precautions

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

back to top

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 before each cycle
- Baseline and regular liver function tests
- Baseline and regular renal function tests and urinalysis
- Blood pressure monitoring during infusion
- Clinical toxicity assessment (including stomatitis, neurotoxicity, ototoxicity, infection, bleeding, pneumonitis); at each visit

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

Suggested Clinical Monitoring

INR; Baseline and as clinically indicated
Liver function tests; Baseline and regular

back to top

K - References

Fjallskog, M-LH, et al. Treatment with cisplatin and etoposide in patients with neuroendocrine tumors. Cancer 2001; 92(5):1101-7.

Mitry E, et al. Treatment of poorly differentiated neuroendocrine tumours with etoposide and cisplatin. BJOC 1999; 81(8):1351-5.

Moertel CG, Kvols LK, O'Connell MJ, et al. Treatment of neuroendocrine carcinomas with combined etoposide and cisplatin: evidence of major therapeutic activity in the anaplastic variants of these neoplasms. Cancer 1991; 68: 22732.

Smith IE, Evans BD, Gore ME, et al. Carboplatin (Paraplatin; JM8) and etoposide (VP-16) as first-line combination therapy for small-cell lung cancer. J Clin Oncol. 1987 Feb; 5(2): 185-9.

June 2024 Removed PEBC guideline link

back to top

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)

back to top

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.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of

last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

While care has been taken in the preparation of the information contained in the Formulary, 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.

CCO and the Formulary's content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person's use of the information in the Formulary.

back to top