

Regimen Monograph

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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

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B - Drug Regimen**CARBOplatin**

AUC 5

IV

Day 1

Adjust carboplatin dose to AUC target (using Calvert formula) as outline in "Other Notes" section.

etoposide100 mg /m²

IV

Days 1 to 3

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Until stable disease, disease progression, or unacceptable toxicity.

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

Other Supportive Care:

Also refer to [CCO Antiemetic Recommendations](#).

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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

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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
<ul style="list-style-type: none"> • Nausea, vomiting • Alopecia • Myelosuppression +/- infection, bleeding • Nephrotoxicity (may be severe) • Ototoxicity • Anorexia • Diarrhea • Mucositis • Abnormal electrolytes 	<ul style="list-style-type: none"> • Hypersensitivity • Arterial thromboembolism • Venous thromboembolism • Hemolytic uremic syndrome • Pneumonitis • Neurotoxicity, including optic nerve disorder • Radiation recall reaction, severe rash

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G - Interactions

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

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H - Drug Administration and Special Precautions

Refer to [CARBOplatin](#), [etoposide](#) 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; 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

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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.

PEBC Advice Documents or Guidelines

- [Systemic Therapy of Incurable Gastroenteropancreatic Neuroendocrine Tumours](#)

May 2019 Updated emetic risk category

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L - Other Notes

Calvert Formula:

$$\text{DOSE (mg)} = \text{target AUC} \times (\text{GFR} + 25)$$

- Target AUC of 4 to 6 mg/mL·min (previously treated patients) or 6 to 8 mg/mL·min (previously untreated patients)
- 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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