Regimen Monograph

A - Regimen Name

CRBPGEMC Regimen

Gemcitabine-CARBOplatin

Disease Site
Gastrointestinal
Hepatobiliary / Liver / Bile Duct

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 biliary tract carcinomas

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B - Drug Regimen

gemcitabine	1000 mg /m²	IV	Days 1 & 8
CARBOplatin	AUC 5	IV	Day 1

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

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until disease progression or unacceptable toxicity.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate + NK1 antagonist (Carboplatin AUC ≥ 5) (D1)
Low (D8)

Other Supportive Care:

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

Dose on Day 1 of Cycle:

Worst Toxicity in Previous Cycle			Gemcitabine	Carboplatin
Non-Hematologic (related organ)		**Hematologic**	**% Full Dose***	**% Full Dose***
Grade 3	or	Febrile neutropenia, thrombocytopenic bleeding	75%	75%#
Grade 4			Consider discontinuing, or ↓ to 75%	Consider discontinuing, or ↓ to 75%
Day 8 holds in > 1 cycle			75%	100%

Worst Toxicity in Previous Cycle (Continued)				
Non-Hematologic (related organ)		**Hematologic**	**Gemcitabine % Full Dose***	**Carboplatin % Full Dose***
Pneumonitis, Hemolytic Uremic Syndrome (HUS), Capillary Leak Syndrome (CLS)			Discontinue	Discontinue
Stevens-Johnson syndrome (SJS), Toxic epidermal necrolysis (TEN)			Discontinue	Discontinue
* Do not retreat until AGC ≥ 1.5 x 10^9/L, platelets ≥ 100 x 10^9/L and toxicity ≤ grade 2. # use Egorin formula if isolated thrombocytopenia				

Dose on Day 8 of Cycle:

Toxicity on Day 8 of cycle					
Non-hematologic (related organ)		**Hematologic**			**Gemcitabine (% Full Dose)**
		AGC (x 10^6/L)		**Platelets (x 10^6/L)**	
≤ grade 2	and	> 1000	and	> 100,000	100%
≤ grade 2	and	500-1000	or	50,000-100,000	Consider Omit, or ↓ to 75%
Grade 3 or 4	or	< 500	or	< 50,000	Omit, ↓ to 75% at restart (if applicable) for non-hematologic toxicity
Pneumonitis HUS SJS TEN CLS		-		-	Discontinue

Hepatic Impairment

Bilirubin		AST/ALT	Gemcitabine (% previous dose)	Carboplatin (% previous dose)
1-2 x ULN	And/or	<2 x ULN	100%	100%
2-4 x ULN		2-5 x ULN	Caution	100%
> 4 x ULN		> 5 x ULN	Caution, consider ↓	Caution, consider ↓

Renal Impairment

CrCl (mL/min)	Gemcitabine (% previous dose)	Carboplatin (% previous dose)
> 60	100%	Use Calvert formula
40-60	100%	
20-40	Caution	
< 20	Consider discontinuing or ↓	Discontinue

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F - Adverse Effects

Refer to gemcitabine, 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) • Fatigue, flu-like symptoms • Musculoskeletal pain • Rash (may be severe) • Edema • Nausea or vomiting • Diarrhea • Elevated LFTs (may be severe) • Neurotoxicity (ototoxicity) • Nephrotoxicity, proteinuria • Abnormal electrolytes	• Pneumonitis • Hemolytic-uremic syndrome • Secondary malignancies • Capillary leak syndrome • Arterial/venous thromboembolism • Arrhythmia • Cardiotoxicity • Hypersensitivity • Vasculitis • PRES

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G - Interactions

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

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H - Drug Administration and Special Precautions

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

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I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- Clinical toxicity assessment (including flu-like symptoms, fatigue, rash, edema, GI, pulmonary, neurotoxicity, infection, bleeding, ototoxicity); regular
- CBC; before each cycle and on day 8
- Baseline and regular liver function tests
- Baseline and regular renal function tests and electrolytes (including magnesium)
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Approximate Patient Visit	Day 1: 2 hours; Day 8: 45 minutes
Pharmacy Workload (average time per visit)	28.715 minutes
Nursing Workload (average time per visit)	42.917 minutes

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K - References

Carboplatin drug monograph, Cancer Care Ontario.

Gemcitabine drug monograph, Cancer Care Ontario.

Julka PK, Puri T, Rath GK, et al. A phase II study of gemcitabine and carboplatin combination chemotherapy in gallbladder carcinoma. Hepatobiliary Pancreat Dis Int 2006;5(1):110-4.

Williams KJ, Picus J, Trinkhaus, et al. Gemcitabine with carboplatin for advanced biliary tract cancers: a phase II single institution study. HPB (Oxford) 2010;12(6):418-26.

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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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