

Regimen Monograph

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A - Regimen Name

CAPEGEMC Regimen

Gemcitabine-Capecitabine

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 Treatment of cholangiocarcinoma in patients who are not considered candidates for surgery with curative intent, but who are willing and able to tolerate treatment with chemotherapy. Phase III trials have not been conducted.

Supplementary Public Funding [capecitabine](#)
 ODB - General Benefit (capecitabine)

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B - Drug Regimen

gemcitabine	1000 mg /m ²	IV	Days 1 and 8
capecitabine	650 mg /m ²	PO	BID* Days 1 to 14

(*Total daily dose 1300mg/m²/day; Outpatient prescription in 150mg and 500mg tablets)

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until evidence of disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low
No routine prophylaxis for capecitabine

Other Supportive Care:

- Topical emollients (e.g. hand creams, udder balm) may ameliorate the manifestations of hand-foot syndrome in patients receiving capecitabine.
- Supportive care should be provided, including loperamide for diarrhea.

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.

Patients should be tested for DPD deficiency before starting treatment with capecitabine. Refer to the [DPD Deficiency Guidance for Clinicians](#) for more information.

In patients with unrecognized DPD deficiency, acute, life-threatening toxicity may occur; if acute grade 2-4 toxicity develops, treatment should be stopped immediately and permanent discontinuation considered based on clinical assessment of the toxicities.

Dosage with toxicity

Gemcitabine - Dose on Day 1 of Cycle:

Worst Toxicity in Previous Cycle			Dose for next cycle*
Non-hematologic (related organ)		Hematologic	% Full Dose
Grade 3	or	Febrile neutropenia, thrombocytopenic bleeding	75%*
Grade 4			Consider discontinuing, or ↓ to 75%*
Day 8/15 holds in > 1 cycle			75%*
<ul style="list-style-type: none"> • Pneumonitis • Hemolytic Uremic Syndrome (HUS) • Stevens-Johnson syndrome (SJS) • Toxic epidermal necrolysis (TEN) • Capillary Leak Syndrome (CLS) 			Discontinue

* Do not start new cycle until ANC ≥ 1500x 10⁶/L, platelets ≥ 100,000 x 10⁶/L and non-hematologic toxicity ≤ grade 2.

Gemcitabine - Dose on Day 8 of Cycle:

Toxicity on Day 8 of cycle					Gemcitabine (% Full Dose)
Non-hematologic (related organ)		Hematologic			
		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

Capecitabine:

Toxicity†	Action During a Course of Therapy	Dose Adjustment for Next Cycle (% of starting dose)
Grade 1	Maintain dose level	Maintain dose level
Grade 2 1st appearance 2nd appearance 3rd appearance 4th appearance	Interrupt until resolved to grade 0-1 Interrupt until resolved to grade 0-1 Interrupt until resolved to grade 0-1 Discontinue treatment permanently	100% 75% 50% -

Toxicity (Continued)	Action During a Course of Therapy	Capecitabine Dose Adjustment for Next Cycle (% of starting dose)
Grade 3 1st appearance 2nd appearance 3rd appearance OR any evidence of Stevens-Johnson syndrome or Toxic Epidermal Necrolysis	Interrupt until resolved to grade 0-1 Interrupt until resolved to grade 0-1 Discontinue treatment permanently	75% 50% –
Grade 4 1st appearance, including SJS, TENS, OR cardiotoxicity OR acute renal failure 2nd appearance	Discontinue permanently OR If physician deems it to be in the patient's best interest to continue and no evidence of Stevens-Johnson syndrome or toxic epidermal necrolysis, interrupt until resolved to grade 0-1. Discontinue permanently	Discontinue OR 50% -

† Dose adjustment mandatory for gastrointestinal, dermatological toxicity and hyperbilirubinemia. Practitioner may elect not to reduce dose for other toxicities unlikely to become serious or life-threatening. Doses should not be re-escalated if reduced for toxicity.

Hepatic Impairment

Gemcitabine: Use with caution in patients with hepatic impairment (cirrhosis, hepatitis, metastases, etc.); initial dose reduction should be considered if the patient is treated, especially in hyperbilirubinemia.

Capecitabine: Use dose modification table above for increases in bilirubin. In patients with mild to moderate hepatic impairment due to liver metastases exposure is increased, but no dose adjustment is necessary, although caution should be exercised. The use of capecitabine in patients with severe hepatic impairment has not been studied.

Renal Impairment

Creatinine clearance (mL/min)	Gemcitabine (% previous dose)	Capecitabine (% previous dose)
51-80	100%	100%
30-50	100%	75%
<30	Consider discontinuing or ↓	Discontinue

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F - Adverse Effects

Refer to [gemcitabine](#), [capecitabine](#) drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
<ul style="list-style-type: none"> • Myelosuppression ± infection, bleeding • Fatigue, flu-like symptoms • Musculoskeletal pain • Rash (may be severe) • Edema • Proteinuria • Hand-foot syndrome • Stomatitis • Diarrhea • Edema & Proteinuria • Nausea or vomiting • Elevated LFTs (may be severe) 	<ul style="list-style-type: none"> • Pneumonitis/ARDS • Hemolytic-uremic syndrome • Arrhythmia • Cardiotoxicity • Venous/arterial thromboembolism • Capillary leak syndrome • Hypersensitivity • Vasculitis

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G - Interactions

Refer to [gemcitabine](#), [capecitabine](#) drug monograph(s) for additional details

Gemcitabine is a known radiosensitizer.

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H - Drug Administration and Special Precautions

Refer to [gemcitabine](#), [capecitabine](#) 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 and on day 8. Interim counts should be done in first cycle and repeated if dose modifications necessary.
- Baseline and regular liver and renal function tests
- Clinical toxicity assessment (flu-like symptoms, fatigue, edema, pulmonary, rash, hand-foot syndrome, diarrhea, dehydration, infection, bleeding, stomatitis); at each visit
- INR or PT; baseline and regular if on anticoagulants
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

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J - Administrative Information

Approximate Patient Visit	0.75 hour
Pharmacy Workload (average time per visit)	22.85 minutes
Nursing Workload (average time per visit)	36.667 minutes

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K - References

Capecitabine and gemcitabine drug monographs, Cancer Care Ontario.

Knox JJ, Hedley D, Oza A, et al. Combining gemcitabine and capecitabine in patients with advanced biliary cancer: a phase II trial. *J Clin Oncol*. 2005;23:2332-8.

Riechelmann RP, Townsley CA, Chin SN, et al. Expanded phase II trial of gemcitabine and capecitabine in advanced biliary tract cancer. *Cancer* 2007;110:1307–12.

April 2023 Updated DPD deficiency information in the Dose Modifications section

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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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