Regimen Monograph

A - Regimen Name

CAPEGEMC Regimen

Gemcitabine-Capecitabine

Disease Site	Gastrointestinal Pancreas
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.
Supplementary Public Funding	**capecitabine** ODB - General Benefit (capecitabine)

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B - Drug Regimen

capecitabine	650 mg /m²	PO	BID* Days 1 to 14
(*Total daily dose 1300 mg/m^2/day; Outpatient prescription in 150 mg and 500 mg tablets)			
gemcitabine	1000 mg /m²	IV	Days 1 and 8

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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%*
• 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 10^6/L, platelets ≥ 100,000 x 10^6/L and non-hematologic toxicity ≤ grade 2.

Gemcitabine - 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

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	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 capecitabine, gemcitabine drug monograph(s) for additional details of adverse effects

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• ↑ LFTs (may be severe) • Nausea, vomiting • Hand-foot syndrome	• Diarrhea (may be severe) • Fatigue • Flu-like symptoms • Proteinuria • Myelosuppression ± infection, bleeding (may be severe) • Rash (may be severe)	• Mucositis • Edema • Musculoskeletal pain • Alopecia • Abdominal pain	• Pneumonitis/ARDS • Hemolytic-uremic syndrome • Arrhythmia • Cardiotoxicity • Venous/arterial thromboembolism • Capillary leak syndrome • Hypersensitivity • Vasculitis • GI obstruction, perforation • Eye disorders, including keratitis • PRES

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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

Outpatient prescription for home administration (capecitabine)

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.

Cunningham D, Chau I, Stocken DD, et al. Phase III randomized comparison of gemcitabine versus gemcitabine plus capecitabine in patients with advanced pancreatic cancer. J Clin Oncol. 2009 Nov 20;27(33):5513-8.

Herrmann R, Bodoky G, Ruhstaller T, et al. Gemcitabine plus capecitabine compared with gemcitabine alone in advanced pancreatic cancer: a randomized, multicenter, phase III trial of the Swiss group for clinical cancer research and the central European cooperative oncology group. J Clin Oncol 2007;25:2212-2217.

April 2023 Modified Adverse Effects section; 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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