Regimen Monograph

A - Regimen Name

DOCEGEMC Regimen

Gemcitabine-DOCEtaxel

Disease Site

Gynecologic - Uterine Sarcoma
Sarcoma - Soft Tissue
Sarcoma - Uterine
(Metastatic Uterine Leiomyosarcoma)

Intent

Palliative
Adjuvant

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.

back to top

B - Drug Regimen

gemcitabine	900 mg /m²	IV over 30 to 90* minutes	Days 1 and 8
DOCEtaxel	100 mg /m²	IV	Day 8

(*Some clinical trials used an infusion rate of 10 mg/m^2/min.) (Continued on next page)

Reduce dose for patients with prior radiation therapy:

gemcitabine	650 mg /m²	IV over 30 to 65* minutes	Days 1 and 8
DOCEtaxel	75 mg /m²	IV	Day 8

(*Clinical trials used an infusion rate of 10 mg/m^2/min)

back to top

C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until disease progression or unacceptable toxicity

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Low

Other Supportive Care:

- Dexamethasone 8 mg bid po for 3 days starting 1 day prior to docetaxel (prevent anaphylaxis / fluid retention).
- Some clinical trials have used filgrastim on days 9 to 16.
  Hematological toxicity is common; consider the use of granulocyte growth factor (G-CSF). If G-CSF is not available, consider prophylactic antibiotics or dose reduction.

back to top

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

Dosing based on worst toxicity in previous cycle:

Non-Hematologic Toxicity		**Hematologic Toxicity**	**Gemcitabine (% Full Dose)**	**DAY 8 Docetaxel (% full dose)**
Grade 3	or	Grade 4 neutropenia ≥ 7 days or Febrile neutropenia or Thrombocytopenic bleeding	75%*	75%* Discontinue if recurs
Grade 3 neurotoxicity			100%*	75%*, Discontinue if recurs
Any occurrence of cystoid macular edema			No change	Hold and investigate; refer patient promptly to an ophthalmic examination. Discontinue if confirmed.
• Pneumonitis • Hemolytic Uremic Syndrome (HUS) • Stevens-Johnson syndrome (SJS) • Toxic epidermal necrolysis (TEN) • Capillary Leak Syndrome (CLS) • Grade 4 neurotoxicity			Discontinue	Discontinue

Non-Hematologic Toxicity (Continued)		Hematologic Toxicity (Continued)	Gemcitabine (% Full Dose)	Day 8 DOCEtaxel (% Full Dose)
Grade 4 other toxicity			Discontinue, or ↓ to 75%*	Discontinue, or ↓ to 75%*
Day 8 holds on > 1 cycle			Discontinue, or ↓ to 75%*	100%*

*Do not start new cycle until ANC ≥ 1500x 10^6/L, platelets ≥ 100,000 x 10^6/L and non-hematologic toxicity ≤ grade 2.

On Day 8 of Cycle:

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

Hepatic Impairment

	AST and/or ALT		Alk Phosp		Bilirubin	Gemcitabine	Docetaxel dose
Mild-moderate	> 1.5 X ULN	AND	> 2.5 x ULN			Use with caution	Do not treat
Severe	> 3.5 x ULN	OR	> 6 x ULN	OR	> ULN	Consider ↓ or Discontinue	Do not treat. Discontinue if treatment already started.

Renal Impairment

Drug	Renal Impairment
Gemcitabine	Use with caution; close monitoring for occurrence of hemolytic uremic syndrome is required. No specific recommendations found
Docetaxel	No dose adjustment required

Dosage in the Elderly

For gemcitabine, clearance is lower in the elderly but no dose adjustment necessary.

For docetaxel, no adjustment required, but caution should be exercised in elderly patients with poor performance status.

back to top

F - Adverse Effects

Refer to DOCEtaxel, gemcitabine 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 or bleeding (may be severe) • Hypersensitivity reactions (may be severe) • Fatigue, flu-like symptoms • Fluid retention (may be severe) • Neuropathy (motor or sensory) • Cutaneous effects (including nails, may be severe) • Alopecia • Proteinuria • GI (stomatitis, nausea/vomiting, diarrhea) • Musculoskeletal pain • ↑ LFTs (may be severe) • Lacrimation/tear duct obstruction	• Secondary malignancies • Pneumonitis/ARDS • Capillary leak syndrome • Cardiotoxicity, arrhythmia • Venous thromboembolism • Arterial thromboembolism • DIC • Seizures • Hemolytic uremic syndrome • Vasculitis • GI obstruction, perforation • Cystoid macular edema

back to top

G - Interactions

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

Gemcitabine is a known radiosensitizer.

back to top

H - Drug Administration and Special Precautions

Refer to gemcitabine, DOCEtaxel 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; at each visit
- Liver function tests; baseline and regular
- Renal function tests; baseline and regular
- Clinical toxicity assessment, including infection, bleeding, neurotoxicity, fatigue, fluid retention, flu-like symptoms, hypersensitivity, cutaneous changes, thromboembolism, ophthalmic, cardiovascular, musculoskeletal pain, GI or pulmonary effects; at each visit.

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

back to top

J - Administrative Information

Approximate Patient Visit	Day 1: 0.75 hour; Day 8: 2 to 3 hours
Pharmacy Workload (average time per visit)	29.323 minutes
Nursing Workload (average time per visit)	47.917 minutes

back to top

K - References

Docetaxel and gemcitabine drug monographs, Cancer Care Ontario.

Hensley ML, Blessing JA, DeGeest K, et al. Fixed-dose rate gemcitabine plus docetaxel as second-line therapy for metastatic uterine leiomyosarcoma: A Gynecologic Oncology Group phase II study. Gyne Oncol 2008;109:323-8.

Hensley ML, Blessing JA, Mannel R, Rose PG. Fixed-dose rate gemcitabine plus docetaxel as first-line therapy for metastatic uterine leiomyosarcoma: a Gynecologic Oncology Group phase II trial. Gynecol Oncol 2008 Jun;109(3):329-34.

Hensley ML, Maki R, Venkatraman E, Geller G, Lovegren M, Aghajanian C, et al. Gemcitabine and docetaxel in patients with unresectable leiomyosarcoma: results of a phase II trial. J Clin Oncol 2002;20:2824-31.

Pautier P, Floquet A, Penel N, et al. Randomized multicenter and stratified phase II study of gemcitabine alone versus gemcitabine and docetaxel in patients with metastatic or relapsed leiomyosarcomas: a Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC) French sarcoma group study (TAXOGEM study). Oncologist 2012;17(9):1213-20.

PEBC Advice Documents or Guidelines

- Chemotherapy for Inoperable, Locally Advanced, Recurrent, or Metastatic Uterine Leiomyosarcoma

December 2017 added infusion time for gemcitabine

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.

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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.

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back to top