Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

FOLFOXIRI+BEVA Regimen

Folinic Acid (Leucovorin)-Fluorouracil-Oxaliplatin-Irinotecan-Bevacizumab

Disease Site
Gastrointestinal
Colorectal

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.

This **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). 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.

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B - Drug Regimen

bevacizumab	5 mg /kg	IV	Day 1

(This drug is not currently publicly funded for this regimen and intent)

Followed by:

irinotecan	165 mg /m²	IV over 1 hour	Day 1

then give:

leucovorin	400 mg /m²	IV over 2 hours	Day 1

concurrently with:

oxaliplatin	85 mg /m²	IV over 2 hours	Day 1

followed by:

fluorouracil	3200 mg /m²	IV continuous infusion over 48 hours only	Start on Day 1

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C - Cycle Frequency

REPEAT EVERY 14 DAYS

For a usual total of 12 cycles, followed by maintenance bevacizumab, unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

Irinotecan - Cholinergic adverse effects (early diarrhea)

- Prophylactic atropine may be considered in patients experiencing cholinergic symptoms

Diarrhea (abdominal cramp = diarrhea) may be severe and delayed with Irinotecan; use Loperamide 4mg at the onset of diarrhea, then 2mg q2h until patient is diarrhea-free for 12 hours

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J - Administrative Information

Approximate Patient Visit	First dose: 5.5 hours; Second dose: 5 hours; Subsequent: 4.5 hours
Pharmacy Workload (average time per visit)	50.556 minutes
Nursing Workload (average time per visit)	80.833 minutes

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K - References

Cremolini C, Loupakis F, Antoniotti C, et al. FOLFOXIRI plus bevacizumab versus FOLFIRI plus bevacizumab as first-line treatment of patients with metastatic colorectal cancer: updated overall survival and molecular subgroup analyses of the open-label, phase 3 TRIBE study. Lancet Oncol 2015;16(13):1306-15.

Loupakis F, Cremolini C, Masi G, et al. Initial therapy with FOLFOXIRI and bevacizumab for metastatic colorectal cancer. N Engl J Med 2014;371(17):1609-18.

Masi G, Loupakis F, Salvatore L, et al. Bevacizumab with FOLFOXIRI (irinotecan, oxaliplatin, fluorouracil, and folinate) as first-line treatment for metastatic colorectal cancer: a phase 2 trial. Lancet Oncol. 2010;11(9):845-52.

PEBC Advice Documents or Guidelines

- The Role of Primary Tumour Location in the Selection of Biologics for the Treatment of Unresectable Metastatic Colorectal Cancer

April 2023 Updated DPD deficiency and fluorouracil antidote information in the Other Notes section

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L - Other Notes

DPD Deficiency Testing and Guidance

Patients should be tested for DPD deficiency before starting treatment with fluorouracil. Refer to the DPD Deficiency Guidance for Clinicians for more information.

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

Antidote for Fluorouracil Overdose:

Uridine triacetate is a prodrug of uridine and is a specific antidote for treating fluorouracil overdose or severe early onset toxicities. If available, consider administering as soon as possible (i.e. within 96 hours) for suspected overdose. If not available, treatment is symptomatic and supportive.

For usage approval and supply, contact Health Canada's Special Access Program (SAP) (Phone: 613-941-2108. On-call service is available for emergencies). Uridine triacetate (Vistogard®) is supplied by its manufacturer in the United States (Wellstat Therapeutics).

The recommended dosing and administration for **uridine triacetate** in patients ≥18 years is:

- 10 grams (1 packet of coated granules) orally every 6 hours for 20 doses in total, without regards to meals.
- Granules should not be chewed. They should be mixed with 3 to 4 ounces of soft foods such as applesauce, pudding or yogurt.
- The dose should be ingested within 30 minutes of preparation, followed by at least 4 ounces of water.
- Refer to the prescribing information on dose preparation for NG-tube or G-tube use.

Additional resources on the management of fluorouracil infusion overdose:

- Management of Fluorouracil Infusion Overdose Guideline (Alberta Health Services)
- Management of Fluorouracil Infusion Overdose at the BCCA - Interim Guidance (BC Cancer Agency)

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M - Disclaimer

Regimen Abstracts

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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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Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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