

## Regimen Monograph

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## A - Regimen Name

## IRIN(Wx4) Regimen

Irinotecan

**Disease Site**      Gastrointestinal  
                                     Esophagus  
                                     Gastric / Stomach

**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.

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## B - Drug Regimen

**Weekly x 4 Schedule:**

[irinotecan](#)                      125 mg /m<sup>2</sup>                      IV                      Day 1, 8, 15, 22

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## C - Cycle Frequency

### REPEAT EVERY 42 DAYS

Until disease progression or unacceptable toxicity.

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## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Moderate

### Other Supportive Care:

Also refer to [CCO Antiemetic Summary](#)

Irinotecan - Cholinergic adverse effects (early diarrhea)

- Prophylactic atropine may be considered in patients who have experienced cholinergic symptoms
- Diarrhea (including abdominal cramps) 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
- Loperamide must be provided

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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.

Patients should not be treated with irinotecan until they have recovered from prior toxicity: platelets  $\geq 100 \times 10^9/L$ , ANC  $\geq 1.5 \times 10^9/L$ , GI toxicity recovered to baseline (without loperamide for at least 24 hours) and all other toxicities to Grade  $\leq 1$ .

Patients with ileus, fever or febrile neutropenia should receive antibiotics.

Consider a reduction in the starting dose described below for:

- elderly patients ( $\geq 70$  years)
- patients with prior abdominal or pelvic irradiation
- patients with a poor performance status (ECOG of 2)

- patients with mild increases in bilirubin (including Gilbert’s syndrome)
- patients homozygous for UGT1A1\*28 allele or patients with a history of myelosuppression with previous treatment.

**Dosage with toxicity**

All dose adjustments should be based on the worst preceding toxicity.

Dose Level	Dose (mg/m <sup>2</sup> )
0	125
-1	100
-2	75
-3	50

Toxicity grade <sup>3</sup>	Suggested dose During treatment course of Weekly schedule <sup>2</sup>	At start of subsequent course <sup>1</sup>
		Weekly schedule <sup>2</sup>
1	No change	No change
2	↓ 25mg/m <sup>2</sup>	Diarrhea alone – no change
		Hematologic alone – no change
		Other <sup>3</sup> : ↓ 25mg/m <sup>2</sup>
3	Omit, then ↓ 25mg/m <sup>2</sup> when ≤ grade 2	↓ 25mg/m <sup>2</sup>
4 or febrile neutropenia	Omit, then ↓ 50mg/m <sup>2</sup> when ≤ grade 2	↓ 50mg/m <sup>2</sup>
Pneumonitis	Hold; investigate and if confirmed, discontinue.	
<sup>1</sup> Relative to the starting dose used in the previous cycle. Start a new cycle when the parameters below are met. <sup>2</sup> Patients should not be retreated until GI toxicity resolved to baseline (without loperamide for at least 24 h), platelets ≥ 100 x 10 <sup>9</sup> /L, ANC ≥ 1.5 x 10 <sup>9</sup> /L and other toxicities recovered to ≤ grade 1. If no recovery after a 2-week delay, consider discontinuing treatment. <sup>3</sup> Excludes alopecia, anorexia, and fatigue		

**Hepatic Impairment**

Elimination is decreased in hepatic impairment with increased exposure to SN-38. Patients with bilirubin 1-1.5 x ULN or Gilbert’s syndrome are at an increased risk of myelosuppression.

Bilirubin <sup>1</sup>		Transaminases	Irinotecan dose
22-35 µmol/L (1-1.5 x ULN) or with Gilbert’s syndrome			Monitor closely; may consider dose reduction
> 35 µmol/L	or	>3 x ULN (without liver metastases) or >5 x ULN (with liver metastases)	Not recommended.
<sup>1</sup> Consider investigating for reversible causes such as biliary obstruction and re-evaluate after stent			

**Renal Impairment**

No specific studies, but as the kidney is not a major route of excretion, no adjustment anticipated to be required.

**Dosage in the Elderly**

Monitor patients ≥ 65 years closely for increased risk of diarrhea. Patients ≥ 70 years of age should receive 100mg/m<sup>2</sup> for weekly dosing.

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**F - Adverse Effects**

Refer to [irinotecan](#) 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

## IRIN(Wx4)

<ul style="list-style-type: none"><li>• Diarrhea (both early and late), may be severe</li><li>• Nausea and vomiting</li><li>• Fatigue</li><li>• Alopecia</li><li>• Abdominal pain</li><li>• Anorexia</li></ul>	<ul style="list-style-type: none"><li>• Constipation</li><li>• Cholinergic symptoms</li><li>• Myelosuppression ± infection, bleeding (may be severe)</li></ul>	<ul style="list-style-type: none"><li>• Cough, dyspnea (may be severe)</li><li>• Rhinitis</li><li>• Headache/insomnia/dizziness</li><li>• Musculoskeletal pain</li><li>• Increased LFTs (may be severe)</li><li>• Rash</li><li>• Mucositis</li><li>• Dyspepsia</li><li>• Edema</li></ul>	<ul style="list-style-type: none"><li>• Arterial/venous thromboembolism</li><li>• GI obstruction, perforation</li><li>• Hypersensitivity</li><li>• Pancreatitis</li><li>• Pneumonitis</li><li>• Tumour Lysis Syndrome</li><li>• Renal failure</li></ul>
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### G - Interactions

Refer to [irinotecan](#) drug monograph(s) for additional details

- Azole antifungals are contraindicated with irinotecan (discontinue one week before the first dose of irinotecan)
- Avoid concomitant use of strong CYP3A4 inhibitors and inducers with irinotecan
- Avoid concomitant use of prochlorperazine (on same day of irinotecan treatment), turmeric and azatanavir with irinotecan

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### H - Drug Administration and Special Precautions

Refer to [irinotecan](#) drug monograph(s) for additional details

#### Administration:

- Mix in 500mL bag (D5W-preferred or NS) in a concentration range between 0.12 to 3 mg/mL; infuse IV over 90 minutes
- Do not refrigerate admixtures in NS (may result in precipitation)
- Avoid freezing irinotecan and its admixtures since this may result in drug precipitation
- Do not admix with other drugs
- Protect from light

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- Prior to the initial irinotecan treatment, patients should be given a sufficient supply of loperamide and instructed on its appropriate use
  - Avoid grapefruit, starfruit, Seville oranges, their juices or products during irinotecan treatment

**Contraindications:**

- Patients with a known hypersensitivity to the product or any of its ingredients
- Irinotecan should not be co-administered with azole antifungals (ketoconazole etc, see Interactions section)
- Avoid in patients with hereditary fructose intolerance since the product contains sorbitol
- Avoid the use of live or live attenuated vaccines

**Other Warnings/Precautions:**

- Not recommended for use in patients with ECOG performance status 3 or 4, or in patients with moderate or severe increases in bilirubin.
- Carefully monitor and consider dose reduction for elderly patients, patients with poor performance status (= 2), limited marrow reserve, 3rd space accumulation, Gilbert's syndrome and patients with reduced UGT1A1 activity; they may be more susceptible to the toxic effects of irinotecan.
- Concurrent administration of irinotecan with irradiation is not recommended. Patients with prior pelvic or abdominal irradiation are at an increased risk of severe myelosuppression following irinotecan therapy.

**Pregnancy/Lactation:**

- Irinotecan is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least **6 months** after the last dose.
- Breastfeeding is not recommended.
- Fertility effects unknown

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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 dose
- Liver function tests; Baseline and monthly
- Toxicity rating of diarrhea and other GI effects, cholinergic symptoms, pneumonitis, neurological, bleeding, infection, dehydration, fatigue, pancreatitis, thromboembolism; At each visit
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

### Suggested Clinical Monitoring

- Blood glucose, especially in patients with diabetes; Baseline and as clinically indicated
- Renal function tests; periodic

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## **J - Administrative Information**

Approximate Patient Visit	1.5 to 2 hours
Pharmacy Workload (average time per visit)	16.162 minutes
Nursing Workload (average time per visit)	37.083 minutes

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## **K - References**

Chun JH, Kim HK, Lee JS, et al. Weekly irinotecan in patients with metastatic gastric cancer failing cisplatin-based chemotherapy. *Jpn J Clin Oncol* 2004;34(1):8-13.

Enzinger PC, Kulke MH, Clark JW, et al. A phase II trial of irinotecan in patients with previously untreated advanced esophageal and gastric adenocarcinoma. *Dig Dis Sci* 2005;50(12):2218-23.

Irinotecan drug monograph, Cancer Care Ontario.

### **PEBC Advice Documents or Guidelines**

- [Systemic Therapy for Advanced Gastric and Gastro-Esophageal Carcinoma](#)

**November 2022** Added PEBC guideline link

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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.*

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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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