

## Regimen Monograph

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## A - Regimen Name

# CISPFU+NIVL Regimen

CISplatin-Fluorouracil-Nivolumab

**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.

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.

**Rationale and Uses**      First-line treatment of HER2-negative unresectable advanced or metastatic gastric, esophagogastric junction, or esophageal adenocarcinoma

**Supplementary Public Funding** [nivolumab](#)  
 New Drug Funding Program (Nivolumab - First-line Treatment of Advanced Gastric, Esophageal, and Esophagogastric Junction Adenocarcinoma) ([NDFP Website](#))

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## B - Drug Regimen

<a href="#">nivolumab</a> <sup>1, 2</sup>	4.5 mg /kg	IV (max 360 mg)	Day 1; q21 days
<a href="#">CISplatin</a>	80 mg /m <sup>2</sup>	IV	Day 1
<a href="#">fluorouracil</a>	800 mg /m <sup>2</sup> /day	IV as continuous infusion	Days 1 to 5

<sup>1</sup> Give nivolumab before chemotherapy when given on the same day.

<sup>2</sup> Dosing based on NDFP funding criteria. Refer to NDFP form for alternative nivolumab dosing schedule (3 mg/kg IV q14 days; maximum dose 240 mg).

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## C - Cycle Frequency

**CISPFU<sup>^</sup>**: Repeat every 21 days, until disease progression or unacceptable toxicity occurs; usually up to 6 cycles due to cumulative cisplatin toxicity

**NIVOLUMAB<sup>^</sup>**: Repeat every 21 days (4.5 mg/kg)<sup>†</sup> for up to 2 years (including doses given with CISPFU), unless disease progression or unacceptable toxicity, whichever occurs first

<sup>^</sup>If chemotherapy is discontinued after at least 1 cycle due to intolerance, nivolumab may be continued as single agent (Refer to NIVL(MNT)) for up to 2 years, unless disease progression or unacceptable toxicity.

<sup>†</sup>Alternative nivolumab dosing schedule is 3 mg/kg IV q14 days.

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## D - Premedication and Supportive Measures

**Antiemetic Regimen:** High (CISPFU)

### Other Supportive Care:

Standard regimens for Cisplatin premedication and hydration should be followed. Refer to local guidelines.

Also refer to [CCO Antiemetic Recommendations](#).

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## J - Administrative Information

Approximate Patient Visit 3 to 4 hours; 5FU only: 0.5 hour

Pharmacy Workload (average time per visit) 40.012 minutes

Nursing Workload (average time per visit) 69.833 minutes

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## K - References

CADTH Reimbursement Recommendation: Nivolumab (For the treatment of adult patients with human epidermal growth factor receptor 2–negative advanced or metastatic gastric, gastroesophageal junction, or esophageal adenocarcinoma). March 2022.

Dank M, Zaluski J, Barone C, et al. Randomized phase III study comparing irinotecan combined with 5-fluorouracil and folinic acid to cisplatin combined with 5-fluorouracil in chemotherapy naive patients with advanced adenocarcinoma of the stomach or esophagogastric junction. *Ann Oncol* 2008;19(8):1450-7.

Janjigian YY, Shitara K, Moehler M, et al. First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial. *Lancet* 2021 Jul 3;398(10294):27-40.

Kang YK, Kang WK, Shin D, et al. Capecitabine/cisplatin versus 5-fluorouracil/cisplatin as first-line therapy in patients with advanced gastric cancer: a randomised phase III noninferiority trial. *Ann Oncol* 2009;20(4):666-73.

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Ohtsu A, Shimada Y, Shirao K, et al. Randomized phase III trial of fluorouracil alone versus fluorouracil plus cisplatin versus uracil and tegafur plus mitomycin in patients with unresectable, advanced gastric cancer: The Japan Clinical Oncology Group Study (JCOG9205). *J Clin Oncol* 2003;21(1):54-9.

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

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

**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 acute 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.

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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**

*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.

*The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.*

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