Regimen Monograph

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

A - Regimen Name

CISPFU+PEMB Regimen

CISplatin-Fluorouracil-Pembrolizumab

Disease Site

Gastrointestinal
Esophagus

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, in patients with good performance status, of:

- locally advanced unresectable or metastatic esophageal adenocarcinoma or squamous cell carcinoma
- HER2-negative advanced or metastatic adenocarcinoma of the esophagogastric junction

Supplementary Public Funding	**pembrolizumab** New Drug Funding Program (Pembrolizumab - First-line Treatment of Advanced Esophageal and Esophagogastric Junction Carcinoma) (NDFP Website)

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B - Drug Regimen

Cycles 1 to 6:

pembrolizumab[1,2]	2 mg /kg	IV (max 200 mg)	Day 1
CISplatin	80 mg /m²	IV	Day 1
fluorouracil	800 mg /m²/day	IV as continuous infusion	Days 1 to 5

Cycles 7 and onwards:

pembrolizumab[1,2]	2 mg /kg	IV (max 200 mg)	Day 1
fluorouracil*	800 mg /m²/day	IV as continuous infusion	Days 1 to 5

*May continue with PEMB(MNT) if fluorouracil is discontinued. Refer to PEMB(MNT) regimen for details.

[1]Dosing based on NDFP funding criteria. Refer to NDFP form for alternative pembrolizumab dosing schedule (4 mg/kg IV q6 weeks).

[2]Give pembrolizumab before chemotherapy when given on the same day.

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C - Cycle Frequency

CISPFU or FU: Repeat every 21 days

PEMBROLIZUMAB: Repeat every 21 days (2 mg/kg)†

For 6 cycles of CISPFU+PEMB^, followed by FU+PEMB^ for up to 2 years (including initial CISPFU+PEMB cycles), unless disease progression or unacceptable toxicity.

^If chemotherapy is discontinued after at least 1 cycle due to intolerance, pembrolizumab may be continued as single agent (PEMB(MNT)) for up to 2 years, unless disease progression or unacceptable toxicity.

†Alternative pembrolizumab dosing schedule is 4 mg/kg IV q 42 days.

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D - Premedication and Supportive Measures

Antiemetic Regimen: High (Cycles 1-6)
Low (Cycles 7+)

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	4 hours; 5FU only: 0.5 hour
Pharmacy Workload (average time per visit)	50.162 minutes
Nursing Workload (average time per visit)	69.833 minutes

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K - References

pCODR reimbursement review (pembrolizumab: esophageal carcinoma, gastroesophageal junction adenocarcinoma). February 2022.

Sun JM, Shen L, Shah MA, et al. Pembrolizumab plus chemotherapy versus chemotherapy alone for first-line treatment of advanced oesophageal cancer (KEYNOTE-590): a randomised, placebo-controlled, phase 3 study. Lancet 2021 Aug 28;398(10302):759-71.

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.

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.

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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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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