Regimen Monograph

A - Regimen Name

CISPFU+PEMB+TRAS Regimen

Cisplatin-Fluorouracil-Pembrolizumab-Trastuzumab

FU+PEMB+TRAS Regimen

Fluorouracil-Pembrolizumab-Trastuzumab

Disease Site

Gastrointestinal
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 patients with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive gastric or

gastroesophageal junction (GEJ) adenocarcinoma, whose tumours express PD-L1 (CPS ≥ 1) as determined by a validated test

(Refer to the NDFP eligibility form for detailed funding criteria)

Supplementary Public Funding

pembrolizumab
New Drug Funding Program (Pembrolizumab and Trastuzumab (Biosimilar) - First-line Treatment of Advanced HER2-Positive Gastric or Esophagogastric Junction Adenocarcinoma) (NDFP Website)

trastuzumab
New Drug Funding Program (Pembrolizumab and Trastuzumab (Biosimilar) - First-line Treatment of Advanced HER2-Positive Gastric or Esophagogastric Junction Adenocarcinoma) (NDFP Website)

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B - Drug Regimen

Note: Different trastuzumab products are **NOT INTERCHANGEABLE**

Cycles 1 to 6:

pembrolizumab[1, 2]	2 mg /kg	IV (max 200 mg)	Day 1
trastuzumab	8 mg /kg	IV	Day 1 (Cycle 1 only)
trastuzumab	6 mg /kg	IV	Day 1 (Cycles 2-6)
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
trastuzumab	6 mg /kg	IV	Day 1
fluorouracil†	800 mg /m²/day	IV as continuous infusion	Days 1 to 5

[1]Dosing based on NDFP funding criteria. Alternative pembrolizumab dosing schedule is 4 mg/kg IV (max 400 mg) q6 weeks.

[2]Administer pembrolizumab prior to trastuzumab and chemotherapy when given on the same day.

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

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C - Cycle Frequency

REPEAT EVERY 3 WEEKS

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

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

†Patients who complete 2 years of pembrolizumab may continue trastuzumab with fluorouracil (FU+TRAS) for one additional year.

Refer to NDFP form for funding criteria for retreatment.

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D - Premedication and Supportive Measures

Antiemetic Regimen: High (Cycles 1-6)
Low – No routine prophylaxis; PRN recommended (Cycles 7+)
No routine prophylaxis for capecitabine

Other Supportive Care:

- **Screen for hepatitis B virus in all cancer patients starting systemic treatment.** Refer to the hepatitis B virus screening and management guideline.
- Also refer to CCO Antiemetic Recommendations.
- Standard regimens for Cisplatin premedication and hydration should be followed. Refer to local guidelines.
- Avoid the use of corticosteroids or immunosuppressants before starting pembrolizumab treatment.

Premedication (prophylaxis for infusion reactions):

Pembrolizumab:

- Routine pre-medication is not recommended.
- May consider antipyretic and H1-receptor antagonist in patients who experienced a grade 1-2 infusion reaction.

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J - Administrative Information

Approximate Patient Visit

CISPFU+PEMB+TRAS	4.5 to 5 hours; 5FU only: 0.5 hour
FU+PEMB+TRAS	2 hours

Pharmacy Workload **(average time per visit)**

CISPFU+PEMB+TRAS	32.713 minutes
FU+PEMB+TRAS	31.139 minutes

Nursing Workload **(average time per visit)**

CISPFU+PEMB+TRAS	72.083 minutes
FU+PEMB+TRAS	47.500 minutes

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K - References

CADTH Reimbursement Recommendation: Pembrolizumab (Keytruda). Canadian Journal of Health Technologies. July 2024

Cisplatin drug monograph, Ontario Health (Cancer Care Ontario).

Fluorouracil drug monograph, Ontario Health (Cancer Care Ontario).

Janjigian YY, Kawazoe A, Bai Y, et al; KEYNOTE-811 Investigators. Pembrolizumab plus trastuzumab and chemotherapy for HER2-positive gastric or gastro-oesophageal junction adenocarcinoma: interim analyses from the phase 3 KEYNOTE-811 randomised placebo-controlled trial. Lancet 2023 Dec 9;402(10418):2197-208.

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.

Pembrolizumab drug monograph, Ontario Health (Cancer Care Ontario).

Trastuzumab drug monograph, Ontario Health (Cancer Care Ontario).

December 2024 Updated Rationale and Uses, Supplemental Public Funding, Drug Regimen, and Cycle Frequency sections

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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).

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

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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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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