Regimen Monograph

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

A - Regimen Name

XELOX+PEMB+TRAS Regimen

Oxaliplatin-Capecitabine-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
Treatment of patients with locally advanced unresectable or metastatic HER2 positive gastric or gastroesophageal junction (GEJ) adenocarcinoma, whose tumours express PD-L1

Supplementary Public Funding
capecitabine
ODB - General Benefit (capecitabine) (ODB Formulary)

trastuzumab
New Drug Funding Program (Trastuzumab (Biosimilar) - Advanced Gastric, Gastroesophageal, or Esophageal Cancer) (NDFP Website)

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B - Drug Regimen

pembrolizumab[1,2]	200 mg	IV	Day 1
trastuzumab	8 mg /kg	IV	Day 1 (Cycle 1 only)
trastuzumab	6 mg /kg	IV	Day 1 (Cycle 2 and onwards)
oxaliplatin	130 mg /m²	IV	Day 1
capecitabine^	1000 mg /m²	PO	BID, Days 1 to 14

(^Total dose 2000 mg/m^2/day)

[1] Alternative pembrolizumab dosing schedule is 400 mg IV q6 weeks.

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

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C - Cycle Frequency

Repeat every 3 weeks†
Until disease progression or unacceptable toxicity^, or up to a maximum of 2 years, whichever occurs first

†Alternative pembrolizumab dosing schedule is 400 mg IV q6 weeks

^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.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate
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.
- Topical emollients (e.g. hand creams, udder balm) may ameliorate the manifestations of hand-foot syndrome in patients receiving capecitabine.
- Patients should be counselled about cold avoidance prior to receiving oxaliplatin, since cold temperatures can precipitate or exacerbate acute neurological symptoms.
- 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.

Oxaliplatin

- There is insufficient evidence that routine prophylaxis with pre-medications reduces IR rates.
- Consider corticosteroids and H1-receptor antagonists ± H2-receptor antagonists in high-risk patients (i.e. ≥ cycle 6, younger age, female gender, prior platinum exposure, platinum-free interval ≥ 3 years).

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J - Administrative Information

Outpatient prescription for home administration (capecitabine)

Approximate Patient Visit 4 hours

Pharmacy Workload (average time per visit)	26.229 minutes
Nursing Workload (average time per visit)	59.167 minutes

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K - References

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

Cunningham D, Starling N, Rao S, et al. Capecitabine and oxaliplatin for advanced esophagogastric cancer. N Engl J Med 2008;358(1):36-46. doi: 10.1056/NEJMoa073149.

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.

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

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

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

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L - Other Notes

DPD Deficiency Testing and Guidance:

Patients should be tested for DPD deficiency before starting treatment with capecitabine. 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 Capecitabine Overdose:

Uridine triacetate is a prodrug of uridine and is a specific antidote for treating capecitabine 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.

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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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.

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

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The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

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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