Regimen Monograph

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

A - Regimen Name

MFOLFOX6+TRAS Regimen

Folinic Acid (Leucovorin) - Fluorouracil - Oxaliplatin - Trastuzumab

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

For treatment of patients with HER2-positive advanced (non-resectable; locally advanced, recurrent or metastatic) adenocarcinoma of the esophagus, stomach, or gastroesophageal junction, who have not received prior systemic therapy for metastatic disease

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

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B - Drug Regimen

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

Trastuzumab loading dose:

trastuzumab*	6 mg /kg	IV	Day 1, Cycle 1 only

THEN trastuzumab (Maintenance dose):

trastuzumab*	4 mg /kg	IV	Day 1, Cycle 2 onwards

WITH MFOLFOX6:

oxaliplatin	85 mg /m²	IV	Day 1
leucovorin	400 mg /m²	IV	Day 1
fluorouracil	400 mg /m²	IV bolus, after leucovorin	Day 1

Then,

fluorouracil	2400 mg /m²	IV continuous infusion over 46 hours (single dose)	Start on Day 1

*Dosing based on NDFP funding criteria. Refer to NDFP form for alternative trastuzumab dosing schedule (8 mg/kg IV loading dose, then 6 mg/kg IV maintenance dose q21 days).

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C - Cycle Frequency

REPEAT EVERY 14 DAYS

Until disease progression or unacceptable toxicity

If chemotherapy is discontinued due to intolerance, trastuzumab may be continued as single agent, unless disease progression or unacceptable toxicity. (Refer to TRAS regimen.)

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Premedication (prophylaxis for infusion reactions)

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).

Other Supportive Care:

- Avoid mucositis prophylaxis with ice chip as cold temperatures can precipitate or exacerbate acute neurological symptoms of oxaliplatin.
- Also refer to CCO Antiemetic Recommendations.

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J - Administrative Information

Approximate Patient Visit	4 to 5 hours
Pharmacy Workload (average time per visit)	49.195 minutes
Nursing Workload (average time per visit)	89.167 minutes

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K - References

Al-Batran SE, Hartmann JT, Probst S, et al. Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. J Clin Oncol 2008;26(9):1435-42.

Ding X, et al. Trastuzumab and oxaliplatin exhibit a synergistic antitumor effect in HER2-postive gastric cancer cells. Anticancer drugs 2014; 25(3):315-322.

Montagnani F, et al. Effectiveness and safety of oxaliplatin compared to cisplatin for advanced, unresectable gastric cancer: a systematic review and meta-analysis. Gastric Cancer 2011;14(1):50-55.

Ter Veer E, et al. Comparing cytotoxic backbones for first-line trastuzumab-containing regimens in human epidermal growth factor receptor 2-positive advanced oesophagogastric cancer: A meta-analysis. Int J Cancer 2018;143:438-448.

Rivera F, et al. Phase II study to evaluate the efficacy of Trastuzumab in combination with Capecitabine and Oxaliplatin in first-line treatment of HER2-positive advanced gastric cancer: HERXO trial. Cancer Chemother Pharmacol 2019;83(6):1175-1181.

Ryu M, et al. Multicenter phase II study of trastuzumab in combination with capecitabine and oxaliplatin for advanced gastric cancer. Eur J Cancer. 2015 Mar;51(4):482-8.

PEBC Advice Documents or Guidelines

- Systemic Therapy for Advanced Gastric and Gastro-Esophageal Carcinoma

September 2023 Updated the "Administrative Information" section with pharmacy and nursing workload.

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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

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

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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.

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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