Regimen Monograph

A - Regimen Name

MFOLFOX6+ZOLB Regimen

Oxaliplatin-Leucovorin-Fluorouracil-Zolbetuximab

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 CLDN18.2 positive, HER2-negative locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma

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B - Drug Regimen

Zolbetuximab loading dose:

zolbetuximab[1]	800 mg /m²	IV	Day 1, Cycle 1 only

(This drug is not currently publicly funded for this regimen and intent)

THEN Zolbetuximab (Maintenance dose):

zolbetuximab[1]	400 mg /m²	IV	Day 1, Cycle 2 and beyond

(This drug is not currently publicly funded for this regimen and intent)

WITH MFOLFOX6 (All cycles):[2]

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

[1]Give zolbetuximab before chemotherapy when given on the same day.

[2]After treatment initiation, if chemotherapy is discontinued due to intolerance, zolbetuximab may be continued as single agent - ZOLB(MNT).

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C - Cycle Frequency

REPEAT EVERY 14 DAYS

Until disease progression or unacceptable toxicity

(In the SPOTLIGHT trial, mFOLFOX6 was given for 12 cycles with zolbetuximab.)

After treatment initiation, if chemotherapy is discontinued due to intolerance, zolbetuximab may be continued as single agent, until disease progression or unacceptable toxicity. (Refer to ZOLB(MNT))

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D - Premedication and Supportive Measures

Antiemetic Regimen: High

- Also refer to CCO Antiemetic Recommendations.

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

Avoid mucositis prophylaxis with ice chip as cold temperatures can precipitate or exacerbate acute neurological symptoms of oxaliplatin.

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J - Administrative Information

Approximate Patient Visit	6 hours

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K - References

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

Leucovorin drug monograph. Ontario Health (Cancer Care Ontario).

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

Product monograph: Zolbetuximab. Astellas Pharma Canada, Inc. December 14, 2024.

Reimbursement recommendation (draft): Zolbetuximab. Canada' Drug Agency. Meeting Date: December 2024.

Shitara K, Lordick F, Bang YJ, et al. Zolbetuximab plus mFOLFOX6 in patients with CLDN18.2-positive, HER2-negative, untreated, locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma (SPOTLIGHT): a multicentre, randomised, double-blind, phase 3 trial. Lancet. 2023 May 20;401(10389):1655-68.

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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

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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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