Regimen Monograph

A - Regimen Name

FC Regimen

Fludarabine-Cyclophosphamide

Disease Site	Hematologic - Lymphoma - Non-Hodgkin's Low Grade
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.
Rationale and Uses	Treatment of recurrent follicular or other non-Hodgkin’s indolent B-cell lymphoma

back to top

B - Drug Regimen

fludarabine (Round to nearest 2.5 mg)	25 mg /m²	IV	Days 1 to 3
cyclophosphamide (Round to nearest 10 mg)	250 mg /m²	IV	Days 1 to 3

back to top

C - Cycle Frequency

REPEAT EVERY 28 DAYS

For a usual total of 4 to 6 cycles in the absence of disease progression or unacceptable toxicity

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

Other Supportive Care:

Also refer to CCO Antiemetic Summary

- Consider prophylactic growth factor support, antiviral and PCP prophylaxis (according to local practice).
- If high volume disease consider prophylaxis for tumour lysis

back to top

E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated

Dosage with toxicity

Suggested dose levels for fludarabine are 25 mg/m^2 , 20 mg/m^2 and 15 mg/m^2
Suggested dose levels for cyclophosphamide are 250 mg/m^2 , 200 mg/m^2 and 150 mg/m^2

Toxicity	Fludarabine (% previous dose)	Cyclophosphamide (% previous dose)
Febrile Neutropenia; Grade 4 myelosuppression ≥ 7 days; Thrombocytopenic bleeding; 1-2 week delay prior cycle	↓ 1 dose level or G-CSF (for isolated neutropenia)*	↓ 1 dose level or G-CSF (for isolated neutropenia)*
Toxicity	Fludarabine (% previous dose)	Cyclophosphamide (% previous dose)
Grade 3 non-hematologic / organ	↓ 1 dose level*	↓ 1 dose level*
Grade 4 non-hematologic / organ	Discontinue	Discontinue
Any grade autoimmune, neurotoxicity, pneumonitis, or > 2 week delay prior cycle	Discontinue	Discontinue
*Do not retreat until non-hematologic / organ toxicity recovered to ≤ grade 2, ANC to ≥ 1 x 10^9/L and platelets ≥ 100 x 10^9/L (or to baseline levels).		

Hepatic Impairment

Bilirubin		**AST / ALT**	**Fludarabine (% usual dose)**	**Cyclophosphamide (% usual dose)**
1-2 x ULN			No data available; use with caution	No change
>2-4 X ULN	and/or	>2-4 X ULN		Caution
> 4 x ULN	and/or	> 4 x ULN		Caution

Renal Impairment

Creatinine Clearance (mL/min)	**Fludarabine (% usual dose)**	**Cyclophosphamide (% usual dose)**
30 - 70	50%	100%
10 - <30		50-75%
<10	Discontinue	50% or Discontinue

back to top

F - Adverse Effects

Refer to fludarabine, cyclophosphamide drug monograph(s) for additional details of adverse effects.

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Myelosuppression ± bleeding • Infection; including opportunistic (may be severe) • GI (nausea/vomiting, diarrhea, anorexia) • Fever • ↑ LFTs • Fatigue • Rash (may be severe) • Visual changes • Cystitis	• Autoimmune disorders (e.g. hemolytic anemia, TTP) • Encephalopathy, CNS toxicity • Pneumonitis • Cardiotoxicity, arrhythmia • Arterial thromboembolism • Venous thromboembolism • SIADH • MDS, Secondary malignancies • Tumour lysis syndrome • Renal failure • Pancreatitis • Rhabdomyolysis

back to top

G - Interactions

Refer to fludarabine, cyclophosphamide drug monograph(s) for additional details

back to top

H - Drug Administration and Special Precautions

Refer to fludarabine, cyclophosphamide drug monograph(s) for additional details

back to top

I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- CBC; baseline and at each visit
- Liver and renal function tests; baseline and at each visit
- Clinical toxicity assessment (including infection, bleeding, hypersensitivity, cystitis, pulmonary, skin, GI and CNS effects); at each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

back to top

J - Administrative Information

Approximate Patient Visit	1 hour
Pharmacy Workload (average time per visit)	23.541 minutes
Nursing Workload (average time per visit)	41.667 minutes

back to top

K - References

Eucker J,Schille C,Schmid P, et al. The combination of fludarabine and cyclophosphamide results in a high remission rate with moderate toxicity in low-grade non-Hodgkin's lymphomas. Anti-Cancer Drugs 2002;13:907–13.

Fludarabine, cyclophosphamide drug monographs, Cancer Care Ontario.

Tam CS, Wolf MM, Januszewicz EH, et al. Fludarabine and cyclophosphamide using an attenuated dose schedule is a highly effective regimen for patients with indolent lymphoid malignancies. Cancer 2004;100:2181–9.

Thomas DW, Owen RG, Johnson SAN, et al. Superior quality and duration of responses among patients with mantle cell lymphoma treated with fludarabine and cyclophosphamide with or without rituximab compared with prior responses to CHOP. Leukemia & Lymphoma 2005;46(4):549 – 52.

June 2021 removed fludarabine NDFP funding info

back to top

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.

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.

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.

While care has been taken in the preparation of the information contained in the Formulary, 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.

CCO and the Formulary's content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person's use of the information in the Formulary.

back to top