Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Dose Modifications | Adverse Effects | Interactions | Drug Administration and Special Precautions | Recommended Clinical Monitoring | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

FC Regimen

Fludarabine-Cyclophosphamide

Disease Site	Hematological - Leukemia - Chronic Lymphocytic (CLL)
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	Second-line treatment in patients with CLL

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B - Drug Regimen

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

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C - Cycle Frequency

REPEAT EVERY 28 DAYS

For 6 cycles in the absence of disease progression or unacceptable toxicity

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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 (e.g. WBC > 25 x 10^9/L), consider prophylaxis for tumour lysis

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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]	↓ 1 dose level or G-CSF (for isolated neutropenia) [1]
Grade 3 non-hematologic / organ	↓ 1 dose level [1]	↓ 1 dose level [1]
Grade 4 non-hematologic / organ	Discontinue	Discontinue

Any grade autoimmune, neurotoxicity, pneumonitis, or > 2 week delay prior cycle	Discontinue	Discontinue
1. Do not retreat until non-hematologic / organ toxicity recovered to ≤ grade 2, ANC to ≥ 1 x 10^9/L and platelets ≥ 80 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)
>50 - 70	50%	100%
30 - 50	50%	75%
10 - <30	Discontinue	75%
<10		Use with extreme caution or Discontinue

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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,	• Autoimmune disorders (e.g. hemolytic anemia, TTP) • Encephalopathy, CNS toxicity (e.g. seizures, confusion, agitation)

anorexia) • Fever • ↑ LFTs • Fatigue • Rash (may be severe) • Visual changes • Cystitis • Reproductive risks	• Pneumonitis • Heart failure, arrhythmia • Arterial thromboembolism • Venous thromboembolism • SIADH • DIC • Secondary malignancies • VOD, HUS • Tumour lysis, renal failure • Pancreatitis • Rhabdomyolysis • Transfusion-associated graft-versus-host disease

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G - Interactions

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

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H - Drug Administration and Special Precautions

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

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I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- CBC; baseline and before each cycle. Interim counts should be done in first cycle and repeated if dose modification necessary.
- Baseline and regular liver and renal function tests.
- Clinical toxicity assessment (including gastrointestinal, infection, autoimmune, dehydration, cystitis, pulmonary, skin, CNS effects); at each visit

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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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

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K - References

Fludarabine and cyclophosphamide drug monographs, Cancer Care Ontario.

Hallek M, Fingerle-Rowson G, Fink A, et al. Immunochemotherapy with fludarabine (F), cyclophosphamide (C), and rituximab (R) (FCR) versus fludarabine and cyclophosphamide (FC) improves response rates and progression-free survival (PFS) of previously untreated patients (pts) with advanced chronic lymphocytic leukemia (CLL). Blood (ASH Annual Meeting Abstracts) 2008; 112: Abstract 325.

Robak T, Dmoszynska A, Solal-Celigny P, et al. Rituximab plus fludarabine and cyclophosphamide prolongs progression-free survival compared with fludarabine and cyclophosphamide alone in previously treated chronic lymphocytic leukemia. J Clin Oncol 2010; 28: 1756-65.

April 2016 Replaced regimen category with evidence-informed

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M - Disclaimer

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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