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

FLUD(PO) Regimen

Fludarabine (oral)

Disease Site	Hematologic - 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 as a single agent in patients with CLL who have failed or are intolerant to chlorambucil.
Supplementary Public Funding	**fludarabine** ODB Limited Use (fludarabine - For second-line therapy of patients with CLL who have failed or are intolerant to chlorambucil (tablets))

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B - Drug Regimen

fludarabine	40 mg /m²	PO daily	Days 1 to 5

(Outpatient prescription available in 10mg tablets)

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C - Cycle Frequency

REPEAT EVERY 28 DAYS

For a usual total of 6 cycles unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low – No routine prophylaxis; PRN recommended

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

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

Consider antiviral and PCP prophylaxis.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations are in use at some centres.

Dosage with toxicity

Do not re-escalate previously reduced doses.

Toxicity / Counts x 10^9/L	Action	Fludarabine Dose next cycle (% full dose)

Grade 4 hematologic, or 1-2 week delay in previous cycle	Hold*	75%
Febrile neutropenia, thrombocytopenic bleeding, or grade 4 myelosuppression ≥ 7 days	Hold*	50%
Grade 3 non-hematologic / organ	Hold*	50-75%
Any grade neurotoxicity, pneumonitis or hemolysis	Discontinue	Discontinue
Grade 4 non-hematologic/organ or > 2 week delay in previous cycle	Discontinue	Discontinue

* Do not restart until non-hematologic/organ toxicity ≤ grade 2, platelets ≥ 100 x 10^9/L and ANC ≥ 1.5 x 10^9/L (or, recovered to baseline)

Hepatic Impairment

No data available; use with caution.

Renal Impairment

Creatinine Clearance	Fludarabine (% usual dose)
30 - 70 mL/min	REDUCE to 50%
< 30 mL/min	DISCONTINUE

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F - Adverse Effects

Refer to fludarabine 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 • GI (nausea/vomiting, stomatitis, diarrhea)	• Autoimmune disorders (e.g.hemolytic anemia, TTP) • Tumour lysis syndrome • Encephalopathy, CNS toxicity (e.g. seizures, confusion, agitation) • Pulmonary fibrosis/pneumonitis

• Fever • Fatigue • Rash (may be severe) • Visual changes	• MDS (with alkylating agents) • Bleeding • Heart failure, arrhythmia

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G - Interactions

Refer to fludarabine drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to fludarabine 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 fever or infection, autoimmune, dehydration, pulmonary, GI, 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

Outpatient prescription for home administration

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K - References

Boogaerts MA, Van Hoof A, Catovsky D, et al. Activity of Oral Fludarabine Phosphate in Previously Treated Chronic Lymphocytic Leukemia JCO,2001; 19(22): 4252-4258

Eichhorst BF, Busch R, Stilgenbauer S, et al. First-line therapy with fludarabine compared with chlorambucil does not result in a major benefit for elderly patients with advanced chronic lymphocytic leukemia. Blood 2009; 114: 3382-91.

Fludarabine drug monograph, Cancer Care Ontario.

Johnson S, Smith AG, Löffler H, et al. Multicentre prospective randomised trial of fludarabine versus cyclophosphamide, doxorubicin, and prednisone (CAP) for treatment of advanced-stage chronic lymphocytic leukaemia. The French Cooperative Group on CLL. Lancet 1996; 347 (9013): 1432-8.

Keating MJ, Kantarjian H, Talpaz M, et al. Fludarabine: A new agent with major activity against chronic lymphocytic leukemia. Blood, 1989; 74: 19-25

Keating MJ, O'Brien S, Kantarjian H, et al. Long-term follow-up of patients with chronic lymphocytic leukemia treated with fludarabine as a single agent. Blood, 1993; 81: 2878-2884

Leporrier M, Chevret S, Cazin B, et al.: Randomized comparison of fludarabine, CAP, and CHOP in 938 previously untreated stage B and C chronic lymphocytic leukemia patients. Blood 2001; 98 (8): 2319-25.

Rai KR, Peterson BL, Appelbaum FR, et al. Fludarabine compared with chlorambucil as primary therapy for chronic lymphocytic leukemia. N Engl J Med 2000; 343(24); 1750-7.

Rossi JF, Van Hoof A, De Boeck K, et al. Efficacy and safety of oral fludarabine phosphate in previously untreated patients with chronic lymphocytic leukemia. J Clin Oncol 2004; 22:1260-7.

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M - Disclaimer

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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.

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