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 Regimen

Fludarabine

Disease Site	Hematologic - Lymphoma - Non-Hodgkin's Low Grade (including Waldenstrom's Macroglobulinemia)
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	For previously treated patients with stage III-IV low-grade lymphoma (including Waldenstrom's Macroglobulinemia)

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B - Drug Regimen

fludarabine	25 mg /m²	IV	Days 1 to 5

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C - Cycle Frequency

REPEAT EVERY 28 DAYS

For a total of 6 cycles, or 2 cycles beyond maximum response in the absence of disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

Other Supportive Care:

- Allopurinol and hydration to reduce the risk of tumour lysis syndrome are recommended.
- Consider prophylaxis for PCP (cotrimoxazole) as per local guidelines.
- Use irradiated blood products to ↓ risk of GVHD.

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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

Hematologic Toxicities: See Appendix 6 for general recommendations.

Toxicity / Grade	Action	Dose next cycle
Platelet < 100 x 10^9/L and/or ANC < 1.5 x 10^9/L	Hold until recovery	↓ 25%
Febrile neutropenia, thrombocytopenic bleeding	Hold until recovery	↓ 25%

Grade 3 non-hematologic toxicity	Hold until recovery	↓ 25%
Grade 4 non-hematologic toxicity OR Any grade neurotoxicity, hemolysis OR Suspected/proven pneumonitis/fibrosis	Discontinue	Discontinue

Hepatic Impairment

No data available; use with caution.

Renal Impairment

Creatinine Clearance	% 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 • Infection; including opportunistic • GI (nausea/vomiting, stomatitis, diarrhea) • Fever • Fatigue • Rash (may be severe) • Visual changes	• Autoimmune disorders (e.g.hemolytic anemia, TTP) • Tumour lysis syndrome • Encephalopathy, CNS toxicity (e.g. seizures, confusion, agitation) • Pulmonary fibrosis/pneumonitis • MDS (with alkylating agents) • Bleeding • Heart failure, angina

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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

- Clinical toxicity assessment (including fever or infection, hemolysis, dehydration, pulmonary, GI, CNS).
- CBC 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
- Creatinine clearance if > 70 yrs or renal dysfunction suspected
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Approximate Patient Visit	0.5 hour

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K - References

Coiffier B, Neidhardt-Berard EM, Tilly H, et al. Fludarabine alone compared to CHVP plus interferon in elderly patients with follicular lymphoma and adverse prognostic parameters: a GELA study. Annals of Oncology 1999; 10: 1191-7.

Czuczman M, Koryzna A, Mohr A, et al. Rituximab in combination with fludarabine chemotherapy in low-grade or follicular lymphoma. J Clin Oncol 2005; 23(4): 694-704.

Foran JM, Rohatiner AZS, Coiffier B, et al. Multicenter phase II study of fludarabine phosphate for patients with newly diagnosed lymphoplasmacytoid lymphoma, waldenstrom's macroglobulinemia, and mantle cell lymphoma. JCO 1999; 17: 546-53.

Klasa R, Meyer R, Shustik C, et al. Randomized phase III study of fludarabine phosphate versus cyclophosphamide, vincristine, and prednisone in patients with recurrent low-grade non-Hodgkin's lymphoma previously treated with an alkylating agent or alkylator-containing regimen. J Clin Oncol 2002; 20(24): 4649-54.

Ross SR, McTavish D, Faulds D. fludarabine. A review of its pharmacological properties and therapeutic potential in malignancy. Drugs 1993; 45(5): 737-59.

Redman JR, Cabanillas F, Velasquez WS, et al. Phase II trial of fludarabine phosphate in lymphoma: An effective new agent in low-grade lymphoma. J Clin Oncol. 1992 May; 10(5): 790-4.

Solal-Celigny P, Brice P, Brousse N, et al. Phase II trial of fludarabine monophosphate as first-line treatment in patients with advanced follicular lymphoma: a multicenter study by the groupe d'etude des lymphomes de l'adulte. JCO 1996; 14: 514-9.

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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 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

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