

Regimen Monograph

[Regimen Name](#) | [Drug Regimen](#) | [Cycle Frequency](#) | [Administrative Information](#) | [References](#) | [Other Notes](#) | [Disclaimer](#)

A - Regimen Name

FC(PO)+R Regimen

Fludarabine (oral)-Cyclophosphamide (oral)-Rituximab

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.

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 anti-CD20 antibody-naive previously untreated or second-line relapsed or refractory CLL patients, in whom fludarabine-based therapy is considered appropriate. There is insufficient evidence for the use of maintenance rituximab in CLL patients.

Supplementary Public Funding [riTUXimab](#)
New Drug Funding Program (Rituximab (Biosimilar IV) and Rituximab SC - Previously Untreated Chronic Lymphocytic Leukemia)

riTUXimab

New Drug Funding Program (Rituximab (Biosimilar IV) and Rituximab SC - Second Line - Chronic Lymphocytic Leukemia)

fludarabine

ODB Limited Use (fludarabine - For the first-line treatment of CLL in combination with rituximab (tablets; with or without cyclophosphamide))

fludarabine

ODB Limited Use (fludarabine - For second-line therapy of patients with CLL who have failed or are intolerant to chlorambucil (tablets))

riTUXimab (subcut)

New Drug Funding Program (Rituximab (Biosimilar IV) and Rituximab SC - Previously Untreated Chronic Lymphocytic Leukemia)

riTUXimab (subcut)

New Drug Funding Program (Rituximab (Biosimilar IV) and Rituximab SC - Second Line - Chronic Lymphocytic Leukemia)

cyclophosphamide

ODB - General Benefit (cyclophosphamide - oral tablets)

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B - Drug Regimen

Note: Different rituximab products are NOT INTERCHANGEABLE.

Cycle 1: All patients must receive their first dose of rituximab by IV infusion.

<u>riTUXimab</u>	375 mg /m ²	IV *	Day 1
In clinical trials, cycle 1 rituximab was given the day prior to FC			
<u>fludarabine</u>	25 mg /m ²	PO	Days 1 to 5
(Outpatient prescription in 10 mg tablets)			
<u>cyclophosphamide</u>	150 mg /m ²	PO	Days 1 to 5
(Outpatient prescription in 25 mg or 50 mg tablets)			

Cycle 2 and onwards: (For a total of 6 cycles, including initial IV rituximab cycle(s))

Rituximab IV:

riTUXimab	500 mg /m ²	IV *	Day 1
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OR

Rituximab (subcut):

The subcutaneous formulation must only be given at the second or subsequent cycles, and only after at least 1 full rituximab IV dose.

riTUXimab (subcut)	1600** mg	Subcut	Day 1
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PLUS FC(PO) chemotherapy:

fludarabine	25 mg /m ²	PO	Days 1 to 5
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(Outpatient prescription in 10 mg tablets)

cyclophosphamide	150 mg /m ²	PO	Days 1 to 5
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(Outpatient prescription in 25 mg or 50 mg tablets)

* Consider slower infusion rate or split dosing over days 1-2 (± corticosteroids) for any cycle where high tumour load or WBC > 25 x 10⁹/L.

** Note: Rituximab subcut dosing is higher in CLL compared to other indications. Ensure the proper dose is administered.

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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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J - Administrative Information

FC(PO): Outpatient prescription for home administration

Approximate Patient Visit	1-5 hours
Pharmacy Workload (average time per visit)	28.643 minutes
Nursing Workload (average time per visit)	84.167 minutes

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K - References

Assouline S, Buccheri V, Delmer A, et al. Pharmacokinetics, safety, and efficacy of subcutaneous versus intravenous rituximab plus chemotherapy as treatment for chronic lymphocytic leukaemia (SAWYER): a phase 1b, open-label, randomised controlled non-inferiority trial. *Lancet Haematol* 2016;3(3):e128-38.

Cazin B, Divine M, Leprêtre S, et al. High efficacy with five days schedule of oral fludarabine phosphate and cyclophosphamide in patients with previously untreated chronic lymphocytic leukaemia. *Br J Haematol*. 2008 Oct;143(1):54-9.

Hallek M, Fischer K, Fingerle-Rowson G, et al. Addition of rituximab to fludarabine and cyclophosphamide in patients with chronic lymphocytic leukaemia: a randomised, open-label, phase 3 trial. *Lancet* 2010;376(9747):1164-74.

Hendry L, Bowen A, Matutes E, et al. Fludarabine, cyclophosphamide and mitoxantrone in relapsed or refractory chronic lymphocytic leukemia and low grade non-Hodgkin's lymphoma. *Leuk Lymphoma* 2004 May;45(5):945-50.

Hillmen P, Cohen DR, Cocks K, et al. A randomized phase II trial of fludarabine, cyclophosphamide and mitoxantrone (FCM) with or without rituximab in previously treated chronic lymphocytic leukaemia. *Br J Haematol*. 2011 Mar;152(5):570-8.

Keating MJ, O'Brien S, Albitar M, et al. Early results of a chemoimmunotherapy regimen of fludarabine, cyclophosphamide, and rituximab as initial therapy for chronic lymphocytic leukemia. *J Clin Oncol* 2005; 23: 4079-88.

Laurenti L, De Padua L, Tarnani M, et al. Comparison between oral and intravenous fludarabine plus cyclophosphamide regime as front-line therapy in patients affected by chronic lymphocytic leukaemia: influence of biological parameters on the clinical outcome. *Ann Hematol*. 2011 Jan;90(1):59-65.

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.

Tam CS, O'Brien S, Wierda W, et al. Long-term results of the fludarabine, cyclophosphamide, and rituximab regimen as initial therapy of chronic lymphocytic leukemia. *Blood* 2008; 112(4): 975-80.

PEBC Advice Documents or Guidelines

- [Rituximab in Lymphoma and Chronic Lymphocytic Leukemia](#)

August 2020 Updated NDFP forms and interchangeability information in Drug Regimen section

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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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