Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

FLUD(PO)+R Regimen

Fludarabine (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)

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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.

riTUXimab	375 mg /m²	IV *	Day 1
fludarabine	40 mg /m²	PO	Days 1 to 5

(Outpatient prescription in 10 mg tablets)

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

Rituximab IV:

riTUXimab	500 mg /m²	IV *	Day 1

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

(Prior authorization is required for PDRP funding of this drug within this regimen)

PLUS FLUD(PO) chemotherapy:

fludarabine	40 mg /m²	PO	Days 1 to 5

* Consider slower infusion rate or split dosing over days 1-2 (± corticosteroids) for any cycle where high tumour load or WBC > 25 x 10^9/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, in the absence of disease progression or unacceptable toxicity

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J - Administrative Information

FLUD(PO): Outpatient prescription for home administration

Approximate Patient Visit	1-5 hours
Pharmacy Workload (average time per visit)	20.946 minutes
Nursing Workload (average time per visit)	69.167 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.

Boogaerts MA, Van Hoof A, Catovsky D, et al. Activity of Oral Fludarabine Phosphate in Previously Treated Chronic Lymphocytic Leukemia JCO 2001; 19(22): 4252-8.

Byrd JC, Peterson BL, Morrison VA, et al. Randomized phase 2 study of fludarabine with concurrent versus sequential treatment with rituximab in symptomatic, untreated patients with B-cell chronic lymphocytic leukemia: results from Cancer and Leukemia Group B 9712 (CALGB 9712). Blood 2003 Jan 1;101(1):6-14.

Byrd JC, Rai K, Peterson BL, et al. Addition of rituximab to fludarabine may prolong progression-free survival and overall survival in patients with previously untreated chronic lymphocytic leukemia: an updated retrospective comparative analysis of CALGB 972 and CALGB 9011. Blood 2005; 105(1): 49-53.

Del Poeta G, Del Principe MI, Consalvo MA, et al. The addition of rituximab to fludarabine improves clinical outcome in untreated patients with ZAP-70-negative chronic lymphocytic leukemia. Cancer 2005 Dec 15;104(12):2743-52.

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, 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.

Schulz H, Klein SK, Rehwald U, et al. Phase 2 study of a combined immunochemotherapy using rituximab and fludarabine in patients with chronic lymphocytic leukemia. Blood 2002 Nov 1;100(9):3115-20.

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.

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.

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