Regimen Monograph

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

A - Regimen Name

FCM+R Regimen

Fludarabine-Cyclophosphamide-mitoXANTRONE-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)

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
mitoXANTRONE	6 mg /m²	IV	Day 1
fludarabine	25 mg /m²	IV	Days 1 to 3
cyclophosphamide	200-250 mg /m²	IV	Days 1 to 3

Cycle 2 and onwards: (For a usual 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 FCM chemotherapy:

mitoXANTRONE	6 mg /m²	IV	Day 1
fludarabine	25 mg /m²	IV	Days 1 to 3
cyclophosphamide	200-250 mg /m²	IV	Days 1 to 3

* 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

Approximate Patient Visit	Day 1: 2.5-6.5 hours; Days 2-3: 1 hour
Pharmacy Workload (average time per visit)	30.755 minutes
Nursing Workload (average time per visit)	57.722 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.

Bosch F, Abrisqueta P, Villamor N, et al. Rituximab, fludarabine, cyclophosphamide, and mitoxantrone: A new, highly active chemoimmunotherapy regimen for chronic lymphocytic leukemia. J Clin Oncol 2009; 27:4578-84.

Bosch F, Ferrer A, Villamor N, et al. Fludarabine, cyclophosphamide, and mitoxantrone as initial therapy of chronic lymphocytic leukemia: high response rate and disease eradication. Clin Cancer Res 2008; 14(1): 155-61.

Bosch F, Ferrer A, Lopez-Guillermo A et al. (2002) Fludarabine, cyclophosphamide and mitoxantrone in the treatment of resistant or relapsed chronic lymphocytic leukaemia. British Journal of Haematology 2002. 119: 976 –984.

Faderl S, Wierda W, O'Brien, S. Fludarabine, cyclophosphamide, mitoxantrone plus rituximab (FCM-R) in frontline CLL <70 Years. Leukemia Research 2010; 34: 284–8.

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.

Schmitt B, Franke A, Burkhard O, et al. Fludarabine, mitoxantrone and cyclophosphamide combination therapy in relapsed chronic lymphocytic leukemia with or without G-CSF: results of the first interim analysis of a phase III study of the German CLL Group. Blood 2002;100:364b (abstract 5015).

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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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.

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.

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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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