Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

FCM(PO)+R Regimen

Fludarabine (oral)-Cyclophosphamide (oral)-mitoXANTRONE-riTUXimab

Disease Site Hematologic - Lymphoma - Non-Hodgkin's Low Grade

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 follicular lymphoma or other indolent histology, CD20-positive B-cell lymphoma* after disease progression following first-line treatment, in patients who:

- Have not received previous treatment with rituximab for indolent B-cell lymphoma
- Have previously received rituximab (including combination rituximab-chemotherapy and/or rituximab monotherapy or maintenance rituximab) and have sustained a response and remained disease-free for at least 6

months after the last dose of rituximab

*__excluding__ small lymphocytic lymphoma, CLL

Refer to the NDFP eligibility forms for detailed funding criteria.

Supplementary Public Funding

riTUXimab
New Drug Funding Program (Rituximab (Biosimilar IV) and Rituximab SC in Combination with Chemotherapy - Indolent B-cell Lymphoma) (NDFP Website)

riTUXimab
New Drug Funding Program (Rituximab (Biosimilar IV) and Rituximab SC - Retreatment - Indolent Lymphoma) (NDFP Website) (with combination chemotherapy)

cyclophosphamide
ODB - General Benefit (cyclophosphamide - oral tablets) (ODB Formulary)

riTUXimab (subcut)
New Drug Funding Program (Rituximab (Biosimilar IV) and Rituximab SC - Retreatment - Indolent Lymphoma) (with combination chemotherapy)

riTUXimab (subcut)
New Drug Funding Program (Rituximab (Biosimilar IV) and Rituximab SC in Combination with Chemotherapy - Indolent B-cell Lymphoma)

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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	PO	Days 1 to 5
(This drug is not currently publicly funded for this regimen and intent)			
cyclophosphamide	150 mg /m²	PO	Days 1 to 5

Cycle 2 and onwards [up to 6 cycles in total, including initial IV rituximab cycle(s)]:

riTUXimab	375 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)	1400 mg	Subcut	Day 1

Plus FCM(PO) Chemotherapy

mitoXANTRONE	6 mg /m²	IV	Day 1
fludarabine	25 mg /m²	PO	Days 1 to 5

(This drug is not currently publicly funded for this regimen and intent)

cyclophosphamide	150 mg /m²	PO	Days 1 to 5

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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

For patients who responded to induction therapy, and were rituximab-naïve prior to induction, refer to maintenance rituximab regimen - RITU(MNT) or RITU(MNT-SC).

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low
Consider prophylaxis daily for cyclophosphamide PO

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

- Consider antiviral and PCP prophylaxis
- If high volume disease, consider steroids and prophylaxis for tumour lysis
- HBsAg positive patients should receive antiviral prophylaxis during and after rituximab. HBsAg negative, but HBcAb positive patients should be considered for antiviral prophylaxis and be closely monitored for viral reactivation by a HBV expert.

Premedication (prophylaxis for infusion reactions):

Administer at least 30 minutes prior to rituximab:

- Oral antipyretic (e.g. acetaminophen)
- H1-receptor antagonist (e.g. diphenhydramine)
- Corticosteroid (e.g. methylprednisolone 80 mg IV) in patients with high bulk disease or pulmonary involvement if no corticosteroids are already being given as part of the chemotherapy regimen.
- In patients receiving **subcut rituximab** who experienced adverse effects with pre-medications, the omission of pre-medications can be considered.

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

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J - Administrative Information

Approximate Patient Visit	2 to 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

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.

Fludarabine, cyclophosphamide, mitoxantrone, rituximab drug monographs, Cancer Care Ontario.

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; 45(5): 945-50.

Hillmen P, Pocock C, Cohen D, Cocks K, Sayala H, et al. NCRI CLL201 Trial: A randomized phase II trial of fludarabine, cyclophosphamide, and mitoxantrone (FCM) with or without rituximab in previously treated CLL. (Abstract). Blood. 2007; 110:752.

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).

Davies A, Merli F, Mihaljević B, et al. Efficacy and safety of subcutaneous rituximab versus intravenous rituximab for first-line treatment of follicular lymphoma (SABRINA): a randomised, open-label, phase 3 trial. Lancet Haematol. 2017 Jun;4(6):e272-e282.

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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