Regimen Monograph

A - Regimen Name

BORTCYCDOXPRED+R Regimen

(VR-CAP) bortezomib - cyclophosphamide - DOXOrubicin - prednisone - riTUXimab

Disease Site

Hematologic
Lymphoma - Non-Hodgkin's Low Grade - Mantle Cell

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

For treatment of patients with previously untreated mantle cell lymphoma who are ineligible for an autologous stem cell transplant

(This regimen is also known as VR-CAP.)

Supplementary Public Funding	**riTUXimab** New Drug Funding Program (Rituximab (Biosimilar IV) and Rituximab SC in Combination with Chemotherapy - Indolent B-cell Lymphoma) (NDFP Website) **prednisone** ODB - General Benefit (prednisone) **riTUXimab (subcut)** New Drug Funding Program (Rituximab (Biosimilar IV) and Rituximab SC in Combination with Chemotherapy - Indolent B-cell Lymphoma) (NDFP Website) **bortezomib** New Drug Funding Program (Bortezomib - Previously Untreated Transplant Ineligible Mantle Cell Lymphoma) (NDFP Website)

back to top

B - Drug Regimen

Note: Different rituximab products are NOT INTERCHANGEABLE.

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

prednisone[*,1]	100 mg /m²	PO	Days 1 to 5

[*]Dosing based on Robak et al. Some cancer centres give prednisone as 100 mg PO daily on Days 1 to 5. The dose may be divided as BID based on local protocols.

bortezomib[^,†]	1.3 to 1.5 mg /m²	IV / Subcut	Days 1, 8, 15
riTUXimab	375 mg /m²	IV	Day 1
DOXOrubicin	50 mg /m²	IV	Day 1
cyclophosphamide	750 mg /m²	IV	Day 1

Cycle 2 and onwards (For a total of 6 to 8 cycles including initial IV rituximab cycle(s)):

Rituximab IV:

riTUXimab	375 mg /m²	IV	Day 1

OR

Rituximab subcutaneous:

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 BORTCYCDOXPRED chemotherapy:

prednisone*,1	100 mg /m²	PO	Days 1 to 5
bortezomib^,†	1.3 to 1.5 mg /m²	IV / Subcut	Days 1, 8, 15
DOXOrubicin	50 mg /m²	IV	Day 1
cyclophosphamide	750 mg /m²	IV	Day 1

*Dosing based on Robak et al. Some cancer centres give prednisone as 100 mg PO daily on Days 1 to 5. The dose may be divided as BID based on local protocols.

1 On Day 1 to be given as part of premedication before riTUXimab

^Bortezomib was given before rituximab on Day 1 in the clinical trial (Robak et al, 2018).

† Dosing based on NDFP funding criteria. The alternative schedule for bortezomib is 1.3 mg/m^2 IV/Subcut days 1, 4, 8, 11, every 21 days.

back to top

C - Cycle Frequency

REPEAT EVERY 21 DAYS

For a usual total of 6 cycles*, unless disease progression or unacceptable toxicity

*Two additional cycles may be given if response first demonstrated at cycle 6.

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).

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate (Day 1)
Low (Days 8, 15)

Also refer to CCO Antiemetic Recommendations.

Premedication (prophylaxis for infusion reactions):

Administer at least 30 minutes prior to **rituximab**:

- Oral antipyretic (e.g. acetaminophen)
- H1-receptor antagonist (e.g. diphenhydramine)
- Give day 1 prednisone as part of pre-medication before rituximab
- In patients receiving **subcut rituximab** who experienced adverse effects with pre-medications, the omission of pre-medications can be considered.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Other Supportive Care:

- If high volume disease, consider prophylaxis for tumour lysis.
- Consider the use of antiviral prophylaxis against herpes zoster.

back to top

J - Administrative Information

Approximate Patient Visit	Day 1, 1st cycle: 6 hours; Subsequent cycles: 2-5 hours; Bortezomib-only days: 0.5 hour
Pharmacy Workload (average time per visit)	23.517 minutes
Nursing Workload (average time per visit)	49.167 minutes

back to top

K - References

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.

Robak T, Jin J, Pylypenko H, et al. Frontline bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone (VR-CAP) versus rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in transplantation-ineligible patients with newly diagnosed mantle cell lymphoma: final overall survival results of a randomised, open-label, phase 3 study. Lancet Oncol 2018;19:1449-58.

Robak T, Huang H, Jin J, et al. Bortezomib-based therapy for newly diagnosed mantle-cell lymphoma. N Engl J Med 2015 Mar 5;372(10):944-53.

Salar A, Casao D, Cervera M, et al. Rapid infusion of rituximab with or without steroid-containing chemotherapy: 1-yr experience in a single institution. Eur J Haematol 2006;77:338–40.

Salles G, Seymour JF, Offner F, et al. Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): a phase 3, randomised controlled trial. Lancet 2011;377(9759):42-51.

Sehn LH, Donaldson J, Filewich A, et al. Rapid infusion rituximab in combination with corticosteroid-containing chemotherapy or as maintenance therapy is well tolerated and can safely be delivered in the community setting. Blood 2007;109(10):4171-3.

van Oers MH, Van Glabbeke M, Giurgea L, et al. Rituximab maintenance treatment of relapsed/resistant follicular non-Hodgkin's lymphoma: long-term outcome of the EORTC 20981 phase III randomized intergroup study. J Clin Oncol 2010;28(17):2853-8.

September 2023 Updated the "Administrative Information" section with pharmacy and nursing workload.

back to top

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 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.

While care has been taken in the preparation of the information contained in the Formulary, 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.

CCO and the Formulary's content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person's use of the information in the Formulary.

back to top