Regimen Monograph

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

A - Regimen Name

CYBORD+DARA Regimen

Cyclophosphamide-Bortezomib-Dexamethasone-Daratumumab

Disease Site

Hematologic
Multiple Myeloma

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 newly diagnosed multiple myeloma, in patients who are not suitable for autologous stem cell transplant and have a good performance status

Supplementary Public Funding

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

bortezomib
New Drug Funding Program (Bortezomib - Previously Untreated - Multiple Myeloma) (NDFP Website)

dexamethasone
ODB - General Benefit (dexamethasone) (ODB Formulary)

daratumumab
New Drug Funding Program (Daratumumab in Combination with a Bortezomib-Based Regimen for Newly Diagnosed Transplant Ineligible Multiple Myeloma) (NDFP Website)

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B - Drug Regimen

Note: Different daratumumab products are NOT INTERCHANGEABLE

Cycles 1 and 2:

daratumumabα,¶	16 mg /kg	IV	Days 1, 8, 15, 22
cyclophosphamide†	300 mg /m²	PO	Days 1, 8, 15, 22
bortezomib†	1.3 to 1.5 mg /m²	IV / Subcut	Days 1, 8, 15, 22
dexamethasone^, §	40 mg	PO	Days 1, 8, 15, 22

Cycles 3 to 6:

daratumumabα,¶	16 mg /kg	IV	Days 1 and 15
cyclophosphamide†	300 mg /m²	PO	Days 1, 8, 15, 22
bortezomib†	1.3 to 1.5 mg /m²	IV / Subcut	Days 1, 8, 15, 22
dexamethasone^,§	40 mg	PO	Days 1, 8, 15, 22

Cycles 7 and onwards:

daratumumab[α,¶]	16 mg /kg	IV	Day 1
cyclophosphamide[†]	300 mg /m²	PO	Days 1, 8, 15, 22
bortezomib[†]	1.3 to 1.5 mg /m²	IV / Subcut	Days 1, 8, 15, 22
dexamethasone[^,§]	40 mg	PO	Days 1, 8, 15, 22

[†] Missed doses should not be made up. For bortezomib, a minimum of 72 hours is required between doses

[α]Daratumumab infusion should be administered at the appropriate initial infusion rate with incremental escalation. Subsequent infusion rate escalation or dilution reduction should only be considered if the previous infusion was well-tolerated.

[¶]Splitting the first dose over 2 days has been described (8 mg/kg days 1 and 2) and may be considered. The same premedications should be administered prior to both treatment days. See Premedication and Supportive Measures section for details.

[^]The dexamethasone dose should be reduced in elderly patients.

[§]Dexamethasone may be given as 20mg pre-medication, on the days of daratumumab infusion, and 20mg post-medication, the days after the infusion.

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C - Cycle Frequency

REPEAT EVERY 28 DAYS

For up to 8-9 cycles, unless disease progression or unacceptable toxicity

After CYBORD is completed, refer to DARA(MNT). (Daratumumab monotherapy REPEAT EVERY 28 DAYS until disease progression or unacceptable toxicity.)

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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.

Supportive care:

- HBV screening should be performed in all patients prior to starting daratumumab.
- Consider antiviral prophylaxis for herpes zoster reactivation.
- Daratumumab can interfere with cross-matching for blood transfusions; type and screen and RBC genotyping tests should be done before starting this drug.
- Patients at risk of tumour lysis syndrome should have appropriate prophylaxis and be monitored closely.
- Oral hydration is encouraged to prevent dose-related hemorrhagic cystitis.
- Prophylaxis with a proton pump inhibitor and an antibiotic (e.g. quinolone) were also used in some clinical trials.
- Use of anti-fungal mouthwash was recommended in some clinical trials.

Daratumumab Pre-medications (prophylaxis for infusion reaction):

To be given at least 1 hour prior to daratumumab infusion:

- Dexamethasone 20 mg IV/PO*
- Oral antipyretic (e.g. acetaminophen 650-1000 mg)
- H1-receptor antagonist IV/PO (e.g. diphenhydramine 25-50 mg or equivalent)
- Famotidine 20 mg IV (or equivalent)
- Montelukast 10 mg PO**

*Administer IV prior to the first infusion; Oral administration may be considered prior to subsequent infusions. Dexamethasone on the day of infusion may be given as part of pre-/post-medications for daratumumab; 20 mg IV/PO on the day of daratumumab infusion and 20 mg PO on the day after infusion. For patients receiving reduced dose dexamethasone 20 mg weekly, the entire 20 mg dose has been given prior to the daratumumab infusion in some clinical trials.

**The addition of montelukast given prior to the first infusion numerically reduced the incidence of respiratory infusion reactions in the study by Nooka et al.

Daratumumab Post-infusion Medications (prevention of delayed reactions):

- Dexamethasone 20 mg PO on the day after daratumumab infusion*
- Consider bronchodilators (e.g. short and long acting) and inhaled corticosteroids (for patients with a history of COPD)&***

*Dexamethasone on the day of infusion may be given as part of pre-/post-medications for daratumumab; 20 mg IV/PO on the day of daratumumab infusion and 20 mg PO on the day after infusion. For patients receiving reduced dose dexamethasone 20 mg weekly, the entire 20 mg dose has been given prior to the daratumumab infusion in some clinical trials.

&Consider adding an H1-receptor antagonist if the patient is at higher risk of respiratory complications.

***These may be discontinued after the 4th infusion if no major IRs occurred.

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J - Administrative Information

Approximate Patient Visit	2.5 to 7.5 hours (depending on duration of daratumumab infusion)
Pharmacy Workload (average time per visit)	41.794 minutes
Nursing Workload (average time per visit)	46.843 minutes

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K - References

Bortezomib, cyclophosphamide and daratumumab drug monographs. Ontario Health (Cancer Care Ontario).

Nooka AK, Gleason C, Sargeant MO, et al. Managing Infusion Reactions to New Monoclonal Antibodies in Multiple Myeloma: Daratumumab and Elotuzumab. J Oncol Pract. 2018 Jul;14(7):414-22.

pCODR Expert review committee final recommendation: Daratumumab for the treatment of patients with newly diagnosed multiple myeloma. Aug 29, 2019.

Reeder CB, Reece DE, Kukreti V, et al. Cyclophosphamide, bortezomib and dexamethasone induction for newly diagnosed multiple myeloma: high response rates in a phase II clinical trial. Leukemia 2009; 23: 1337–41.

Yimer H, Melear J, Edward Faber E, et al. Lyra: a phase 2 study of daratumumab plus cyclophosphamide, bortezomib, and dexamethasone (Cybord) in newly diagnosed and relapsed patients (Pts) with multiple myeloma. Blood 2018;132 (Supplement 1):152.

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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.

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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.

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