Regimen Monograph

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

A - Regimen Name

CYBORD+DARA(SC) Regimen

Cyclophosphamide-Bortezomib-Dexamethasone-Daratumumab (subcut)

Disease Site

Hematologic
Amyloidosis

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 newly diagnosed light-chain amyloidosis.

Supplementary Public Funding

bortezomib
New Drug Funding Program (Daratumumab and Bortezomib in combo with Cyclophosphamide and Dexamethasone - Previously Untreated Light Chain (AL) Amyloidosis) (NDFP Website)

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

daratumumab (subcut)
New Drug Funding Program (Daratumumab and Bortezomib in combo with Cyclophosphamide and Dexamethasone - Previously Untreated Light Chain (AL) Amyloidosis) (NDFP Website)

cyclophosphamide
ODB - General Benefit (cyclophosphamide - oral tablets)

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B - Drug Regimen

Note: Different daratumumab products are NOT INTERCHANGEABLE

Cycles 1 and 2:

daratumumab (subcut)	1800 mg	Subcut	Days 1, 8, 15, 22
cyclophosphamide†	300 mg /m²	PO (max 500 mg)	Days 1, 8, 15, 22
bortezomib†	1.3 mg /m²	Subcut	Days 1, 8, 15, 22
dexamethasone^	40 mg	PO	Days 1, 8, 15, 22

Cycles 3 to 6:

daratumumab (subcut)	1800 mg	Subcut	Days 1 and 15
cyclophosphamide†	300 mg /m²	PO (max 500 mg)	Days 1, 8, 15, 22
bortezomib†	1.3 mg /m²	Subcut	Days 1, 8, 15, 22
dexamethasone^	40 mg	PO	Days 1, 8, 15, 22

See DARA(MNT-SC) for Cycles 7 and beyond

† Missed doses should not be made up. For bortezomib, there should be a minimum of 72 h between doses.

^The dexamethasone dose should be reduced in elderly patients.

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C - Cycle Frequency

REPEAT EVERY 28 DAYS

For up to 6 cycles, unless disease progression or unacceptable toxicity

Refer to DARA(MNT-SC) for CYCLES 7+ (after CYBORD is completed) for daratumumab maintenance.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low
Consider prophylaxis daily for cyclophosphamide PO

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.

Pre-medications for Daratumumab (subcut) (prophylaxis for administration-related reactions (ARRs)):

To be given at least 1 hour prior to each dose:

- 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)
- Montelukast 10 mg PO‡

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

‡Montelukast 10 mg was optional on Cycle 1 Day 1 during clinical trials of daratumumab (subcut). The addition of montelukast given prior to the first daratumumab IV infusion numerically reduced the incidence of respiratory infusion reactions in the study by Nooka et al.

Post-Injection Medications for Daratumumab (subcut) (prevention of delayed ARRs):

- Dexamethasone 20 mg PO for 1 day post-injection¶,§
- Consider bronchodilators (e.g., short and long acting) and inhaled corticosteroids (for patients with a history of COPD) ‖ #

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

§May be discontinued after the 3rd injection if no major systemic ARRs occurred (excluding regimen-specific corticosteroids).

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

#May be discontinued after the 4th injection if no major ARRs occurred.

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J - Administrative Information

Cyclophosphamide and Dexamethasone: Outpatient prescription for home administration

Approximate Patient Visit	1.5 hours
Pharmacy Workload (average time per visit)	18.388 minutes
Nursing Workload (average time per visit)	41.531 minutes

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K - References

Bortezomib and cyclophosphamide drug monographs, Cancer Care Ontario.

Kastritis E, Palladini G, Minnema MC, et al. Daratumumab-based treatment for immunoglobulin light-chain amyloidosis. N Engl J Med. 2021;385(1):46-58.

Palladini G, Kastritis E, Maurer MS, et al. Daratumumab plus CyBorD for patients with newly diagnosed AL amyloidosis: safety run-in results of ANDROMEDA.Blood. 2020;136(1):71-80.

September 2022 Added NDFP form (bortezomib and daratumumab); modified Rationale/uses, Drug regimen and Cycle frequency sections

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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,

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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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