Regimen Monograph

A - Regimen Name

BMP+DARA Regimen

Bortezomib-Melphalan-Prednisone-Daratumumab

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 good performance status
Supplementary Public Funding	**bortezomib** New Drug Funding Program (Bortezomib - Previously Untreated - Multiple Myeloma) (NDFP Website) **melphalan**

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

prednisone
ODB - General Benefit (prednisone) (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.

Cycle 1^:

daratumumab	16 mg /kg	IV	Days 1*, 8, 15, 22, 29, 36

* For cycle 1 day 1, splitting the first dose over 2 days has been described (8 mg/kg days 1 and 2) and may be considered.

bortezomib†	1.3 mg /m²	IV / Subcut	Days 1, 4, 8, 11, 22, 25, 29, 32
melphalan	9 mg /m²	PO	Days 1 to 4
prednisone	60 mg /m²	PO	Days 1 to 4

Cycles 2 to 9^:

daratumumab	16 mg /kg	IV	Days 1, 22
bortezomib†	1.3 mg /m²	IV / Subcut	Days 1, 8, 22, 29
melphalan	9 mg /m²	PO	Days 1 to 4
prednisone	60 mg /m²	PO	Days 1 to 4

^Dosing based on ALCYONE trial. Other BMP schedules may be considered.

†Missed doses should not be made up. A minimum of 72 hours is required between bortezomib doses.

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C - Cycle Frequency

REPEAT EVERY 42 DAYS

For 9 cycles, unless disease progression or unacceptable toxicity

Refer to DARA(MNT) for CYCLES 10 AND BEYOND (Daratumumab monotherapy REPEAT EVERY 28 DAYS until disease progression or unacceptable toxicity)

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low
Minimal (Cycle 1, days 15 and 36)
No routine prophylaxis for melphalan 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.

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. Additional regimen-specific corticosteroids (e.g., prednisone) should not be taken on injection days when dexamethasone is given as pre-medication.

**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.

Post-infusion medications (prevention of delayed reactions):

- Prednisone as per BMP regimen***
- Consider bronchodilators (e.g. short and long acting) and inhaled corticosteroids (for patients with a history of COPD)&****

*** Or alternative corticosteroids (e.g. oral methylprednisolone (≤20 mg) or equivalent) the day after

infusion as per physician discretion.

&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)	32.794 minutes
Nursing Workload (average time per visit)	47.208 minutes

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K - References

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

Mateos MV, Cavo M, Blade J, et al. Overall survival with daratumumab, bortezomib, melphalan, and prednisone in newly diagnosed multiple myeloma (ALCYONE): a randomised, open-label, phase 3 trial. Lancet 2020 Jan 11;395(10218):132-41.

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.

PEBC Advice Documents or Guidelines

- Treatment of Multiple Myeloma: ASCO and CCO Joint Clinical Practice Guideline

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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.

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