

CADTH Reimbursement Review

Patient Input

daratumumab (Darzalex)
(Janssen Inc.)

Indication: Light chain (AL) amyloidosis

CADTH received patient input from:
Myeloma Canada

August 9, 2021

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Myeloma Canada Patient Input—Daratumumab (Darzalex) combined with bortezomib (Velcade), cyclophosphamide and dexamethasone *for the treatment of adult patients with light chain amyloidosis.*

Name of the Drug and Indication	Daratumumab (Darzalex) combined with bortezomib (Velcade), cyclophosphamide and dexamethasone
Name of the Patient Group	Myeloma Canada
Author of the Submission	
Name of the Primary Contact for This Submission	
Email	
Telephone Number	

1. About Your Patient Group

AL or “light chain” amyloidosis is a very rare systemic disorder closely related to myeloma. Some people with myeloma will have or develop amyloidosis. Amyloidosis is usually treated with chemotherapy, using the same drugs that are used to treat myeloma. Although some people with myeloma will have or develop amyloidosis, it is rare for people with amyloidosis to develop myeloma. To know more about Myeloma Canada, see registration information or visit www.myeloma.ca.

2. Information Gathering

Over the years, Myeloma Canada has conducted several patient and caregiver surveys to collect data on the impact of myeloma and its treatments on patients and caregivers. Myeloma Canada is presently sharing patient input regarding the treatment combination of bortezomib (Velcade), cyclophosphamide and dexamethasone with daratumumab (Darzalex) for light chain (AL) amyloidosis.

Myeloma Canada shared the survey with our community, and with the Leukemia & Lymphoma Society of Canada who similarly shared it with their community, via email and through social media. The survey was available from July 12th to July 25th 2021. Eligibility for the survey was determined by patients either being newly diagnosed with light chain (AL) amyloidosis displaying measurable hematologic damage (abnormal light chain protein with one or more affected organs and being eligible to receive a combined treatment of bortezomib (Velcade), cyclophosphamide and dexamethasone; OR were currently receiving a combined treatment of bortezomib (Velcade), cyclophosphamide and dexamethasone. The survey received 40 responses, 12 of which were subsequently deemed eligible. These eligible patients were then divided into 3 subsets based on their experience with the combination under review, and questions posed to them accordingly.

- Subset A patients (7) were currently receiving bortezomib (Velcade), cyclophosphamide and dexamethasone alone; and were from Alberta (2) British Columbia (1), New Brunswick (1) Ontario (3).
- Subset B patients (2) were from British Columbia (1) and Ontario (1); and are presently waiting to begin treatment for their light chain (AL) amyloidosis.

- Subset C patients (3) were *currently receiving the treatment combination under review*, bortezomib (Velcade), cyclophosphamide and dexamethasone with daratumumab (Darzalex); and were from Alberta (1) and Quebec (2).

3. Disease Experience

This section presents results from Subset A, Subset B, and Subset C—all eligible respondents. To the question, “How important is it for you to control various aspects of your light chain (AL) amyloidosis? Please rate on a scale of 1 (not important) to 5 (extremely important)”, at least 4 patients (of 12) described every disease aspect as ‘5—extremely important’. Two thirds (8) of respondents indicated ‘kidney problems’ were ‘5-extremely important’, making it the most important aspect to control for them, followed by ‘neuropathy’ (7). Half of the respondents (6) felt ‘mobility’ to be ‘5-extremely important’, and 5 patients indicated the same for ‘cardiac problems’ and ‘digestive system disorders’ respectively. Thus, by a slim margin, ‘shortness of breath’ (4), and ‘fatigue’ (4) were of least importance.

Respondents were asked to rate on a scale of 1 (not at all) to 5 (significant impact), “How much do symptoms associated with light chain (AL) amyloidosis impact or limit your day-to-day activities and quality of life?” Viewing the responses from Subset A, B, and C in combination, indicate that amyloidosis has a ‘5—significant impact’ on the most patients’ ‘ability to work’ (7). Half of all patients (6) reported a ‘5-significant impact’ on their abilities to travel, exercise, and conduct household chores. A ‘5-significant impact’ was described by 4 patients on their ability to volunteer, 3 patients on their ‘ability to concentrate’ and 2 respondents said the same for both the abilities to ‘fulfill family obligations’ and to ‘spend time with friends and family’. As these shows, amyloidosis has a significant impact on *all activities listed* [for each one, at least 2 patients felt amyloidosis had a ‘5—significant impact’]; and therefore, on patients’ overall quality of life.

To the question, “How important is it to you to have access to effective treatments for light chain (AL) amyloidosis? Please rate on a scale of 1 (not important) to 5 (extremely important).” *all* patients from Subset B (2) and Subset C (3) selected ‘5-extremely important’. Similarly in Subset A, patients most frequently chose ‘5-extremely important’.

1 - NOT IMPORTANT	2 - SOMEWHAT IMPORTANT	3 - IMPORTANT	4 - VERY IMPORTANT	5 - EXTREMELY IMPORTANT	N/A	TOTAL	WEIGHTED AVERAGE
0.00%	0.00%	14.29%	28.57%	57.14%	0.00%	7	4.43
0	0	1	2	4	0		

Figure 1—How important is it to you to have access to effective treatments for light chain (AL) amyloidosis? Please rate on a scale of 1 (not important) to 5 (extremely important). (Subset A)

When asked, “What is the number one financial implication related to your present treatment? Check all that apply,” 2 respondents from Subset C indicated “parking costs” and one patient selected “lost income due to absence from work”. One respondent from Subset B answered, ‘I have no financial implications related to my treatment’, and one chose ‘other’, providing the explanation “Travel to get stem cell transplant in future.” In Subset A respondents felt that ‘drug costs’ (2) and ‘medical supply costs’ (2) were the most significant financial implications.

ANSWER CHOICES	RESPONSES	
Drug costs	28.57%	2
Travel costs	0.00%	0
Accommodation costs	0.00%	0
Parking costs	0.00%	0
Drug administration fees	0.00%	0
Medical supply costs	28.57%	2
Lost income due to absence from work	14.29%	1
I have had no financial implications related to my treatment	28.57%	2
Other (please specify)	0.00%	0
TOTAL		7

Figure 2—What is the number one financial implication related to your present treatment? Check all that apply. (Subset A)

4. Experiences With Currently Available Treatments

All but one respondent in Subset A (6) indicated they had been on the treatment combination of bortezomib (Velcade), cyclophosphamide and dexamethasone alone for 1 to 6 months; the 1 remaining respondent answered they had been taking the treatment combination for 7 to 12 months.

Subset A respondents were asked to rank from 1 (most important) to 6 (least important) what their expectations of the treatment combination were before taking bortezomib (Velcade), cyclophosphamide and dexamethasone. Responses demonstrate ‘disease control’ followed by ‘improved quality of life’ then ‘prolonged life’ were patients’ most important treatment expectations.

	1	2	3	4	5	6	N/A	TOTAL	SCORE
Improved quality of life	0.00% 0	57.14% 4	42.86% 3	0.00% 0	0.00% 0	0.00% 0	0.00% 0	7	4.57
Disease control	71.43% 5	0.00% 0	0.00% 0	0.00% 0	28.57% 2	0.00% 0	0.00% 0	7	4.86
Remission	0.00% 0	0.00% 0	16.67% 1	16.67% 1	33.33% 2	33.33% 2	0.00% 0	6	2.17
Prolonged life	33.33% 2	0.00% 0	16.67% 1	0.00% 0	33.33% 2	16.67% 1	0.00% 0	6	3.50
Minimal side effects	0.00% 0	20.00% 1	0.00% 0	40.00% 2	0.00% 0	40.00% 2	0.00% 0	5	2.60
Enjoy a normal life	0.00% 0	20.00% 1	20.00% 1	40.00% 2	0.00% 0	20.00% 1	0.00% 0	5	3.20

Figure 3—Before taking bortezomib (Velcade), cyclophosphamide and dexamethasone alone, what were your expectations of this treatment combination? Please rank from most important (1) to least important (6). (Subset A)

Subset A respondents were asked, “Which of your expectations has your treatment combination of bortezomib (Velcade), cyclophosphamide and dexamethasone alone fulfilled? Please select all that apply.” Respondents indicated that their expectation of ‘minimal side effects’ (4) was best fulfilled, followed by the expectation of ‘disease control’ (3), and of ‘improved quality of life’ (1).

Q12 Which of your expectations has your treatment combination of bortezomib (Velcade), cyclophosphamide and dexamethasone alone fulfilled? Please select all that apply.

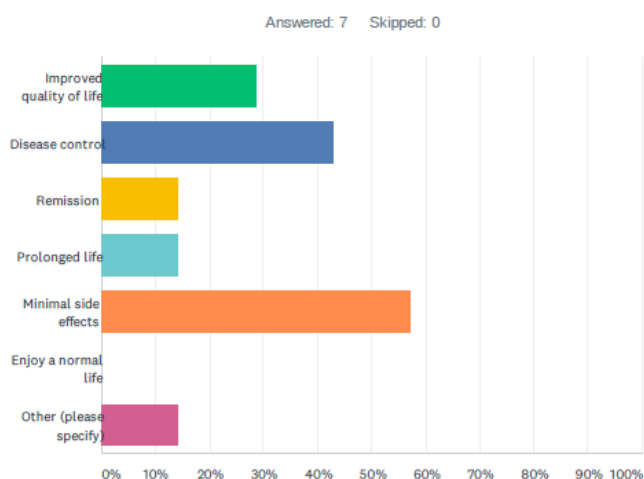


Figure 4—Expectation-fulfillment for bortezomib, cyclophosphamide & dexamethasone alone. (Subset A)

To the question, “Based on your personal experience with the combination of bortezomib (Velcade), cyclophosphamide, and dexamethasone, how would you rate their overall side effects, from 1 (completely intolerable) to 5 (extremely tolerable)?” three [Subset A](#) respondents reported the side effects to be ‘2-somewhat intolerable’, another three indicated ‘3-tolerable’ and one patient selected ‘4-very tolerable’.

[Subset A](#) respondents were asked, “How would you rate the common side effects that you have experienced with bortezomib (Velcade), cyclophosphamide, and dexamethasone?” Responding on the same scale of 1 (completely intolerable) to 5 (extremely tolerable), responses indicate ‘fatigue’ and ‘neuropathy’ to be the least tolerable side effects.

	1 - COMPLETELY INTOLERABLE	2 - SOMEWHAT INTOLERABLE	3 - TOLERABLE	4 - VERY TOLERABLE	5 - EXTREMELY TOLERABLE	N/A	TOTAL	WEIGHTED AVERAGE
Neutropenia	0.00% 0	0.00% 0	50.00% 3	16.67% 1	16.67% 1	16.67% 1	6	3.60
Neuropathy (pain, numbness, tingling, swelling or muscle weakness)	14.29% 1	14.29% 1	42.86% 3	0.00% 0	14.29% 1	14.29% 1	7	2.83
Anemia	0.00% 0	0.00% 0	57.14% 4	28.57% 2	0.00% 0	14.29% 1	7	3.33
Cardiac failure	0.00% 0	0.00% 0	14.29% 1	14.29% 1	14.29% 1	57.14% 4	7	4.00
Breathing difficulties (shortness of breath, asthma, apnea)	0.00% 0	14.29% 1	28.57% 2	0.00% 0	0.00% 0	57.14% 4	7	2.67
Upper respiratory tract infection	0.00% 0	0.00% 0	14.29% 1	14.29% 1	14.29% 1	57.14% 4	7	4.00
Peripheral edema	0.00% 0	16.67% 1	66.67% 4	16.67% 1	0.00% 0	0.00% 0	6	3.00
Diarrhea	0.00% 0	28.57% 2	42.86% 3	0.00% 0	14.29% 1	14.29% 1	7	3.00
Nausea/vomiting	0.00% 0	0.00% 0	28.57% 2	14.29% 1	0.00% 0	57.14% 4	7	3.33
Fatigue	14.29% 1	42.86% 3	42.86% 3	0.00% 0	0.00% 0	0.00% 0	7	2.29
Insomnia	0.00% 0	14.29% 1	57.14% 4	14.29% 1	0.00% 0	14.29% 1	7	3.00

Figure 5 — On a scale of 1 (completely intolerable) to 5 (extremely tolerable), how would you rate the common side effects that you have experienced with bortezomib (Velcade), cyclophosphamide, and dexamethasone? (Subset A)

Respondents from Subset A were asked, “If you experienced side effects with the treatment combination of bortezomib (Velcade), cyclophosphamide, and dexamethasone briefly explain how you managed side effects.” Here are the comments we received: *“Reduced Dex level. Take one laxative 2 days after Velcade injection. Raise feet above heart often.”*; *“Sleep a lot”*; *“Taking pain killer to ease the pain and taking probiotic to help diarrhea.”*

Subset A respondents (7) were asked, “How would you rate your quality of life with bortezomib (Velcade), cyclophosphamide, and dexamethasone”. Responding on a scale from 1 (bad quality of life) to 5 (excellent quality of life), one patient chose ‘1-poor quality of life’, five chose ‘2-fair quality of life’, and one answered ‘4-very good quality of life’.

5. Improved Outcomes

Responding to the question “If you are taking drug treatment (or were to consider taking drug treatment) to treat your light chain (AL) amyloidosis, how important is to you to bring about improvement to your overall quality of life?” On a scale of 1 (not important) to 5 (extremely important), five Subset A respondents (7) chose ‘5-extremely important’, one chose ‘4-very important’ and one ‘3-important’. The two Subset B patients both chose ‘5-extremely important’; all three Subset C respondents answered ‘5—extremely important’.

All three Subsets were asked “What treatment side effects do you want to avoid. Please rank from 1 (the most important to avoid) to 10 (the least important to avoid)?” Responses from Subset C (3) described ‘nausea and vomiting’ (2) alongside ‘diarrhea’ (1) as the side effects they most wanted to avoid. Subset A indicated that ‘cardiac failure’ and ‘neuropathy’ were the most important side effects to avoid, then ‘diarrhea’ followed by ‘upper respiratory tract infection.’ By a significant margin Subset B patients (2) felt ‘cardiac failure’ and ‘neutropenia’ were the most important side effects to avoid.

	1	2	3	4	5	6	7	8	9	N/A	10	TOTAL
Diarrhea	33.33% 1	33.33% 1	33.33% 1	0.00% 0	0.00% 0	0.00% 0	0.00% 0	0.00% 0	0.00% 0	0.00% 0	0.00% 0	3
Fatigue	0.00% 0	33.33% 1	0.00% 0	33.33% 1	0.00% 0	0.00% 0	0.00% 0	0.00% 0	33.33% 1	0.00% 0	0.00% 0	3
Insomnia	0.00% 0	0.00% 0	0.00% 0	33.33% 1	0.00% 0	0.00% 0	33.33% 1	0.00% 0	33.33% 1	0.00% 0	0.00% 0	3
Nausea/vomiting	66.67% 2	0.00% 0	0.00% 0	0.00% 0	33.33% 1	0.00% 0	0.00% 0	0.00% 0	0.00% 0	0.00% 0	0.00% 0	3
Neuropathy (pain, numbness, tingling, swelling or muscle weakness)	0.00% 0	0.00% 0	33.33% 1	0.00% 0	33.33% 1	0.00% 0	0.00% 0	33.33% 1	0.00% 0	0.00% 0	0.00% 0	3
Breathing difficulties (shortness of breath, asthma, apnea)	0.00% 0	0.00% 0	0.00% 0	0.00% 0	0.00% 0	66.67% 2	33.33% 1	0.00% 0	0.00% 0	0.00% 0	0.00% 0	3
Neutropenia	0.00% 0	0.00% 0	0.00% 0	33.33% 1	0.00% 0	33.33% 1	33.33% 1	0.00% 0	0.00% 0	0.00% 0	0.00% 0	3
Upper respiratory tract infection	0.00% 0	0.00% 0	0.00% 0	0.00% 0	33.33% 1	0.00% 0	0.00% 0	66.67% 2	0.00% 0	0.00% 0	0.00% 0	3
Peripheral edema	0.00% 0	33.33% 1	0.00% 0	0.00% 0	0.00% 0	0.00% 0	0.00% 0	0.00% 0	33.33% 1	0.00% 0	33.33% 1	3
Cardiac failure	0.00% 0	0.00% 0	33.33% 1	0.00% 0	0.00% 0	0.00% 0	0.00% 0	0.00% 0	0.00% 0	0.00% 0	66.67% 2	3

Figure 6—Important treatment side effects to avoid (Subset C)

Patients in Subset A and Subset B were both asked “If you were eligible to receive bortezomib (Velcade), cyclophosphamide, and dexamethasone with daratumumab (Darzalex), what do you believe the benefits would be for you (compared to the type of treatment you are currently receiving, or have already received)?” Subset A respondents primarily felt that ‘prolonged

remission’ and ‘all of the above’(less side effects, better control of myeloma symptoms, prolonged remission, better quality of life, better overall health) were the benefits they would receive, followed by ‘better quality of life’. The two respondents in Subset B both chose, ‘all of the above’.

When asked if they felt “ ... receiving bortezomib (Velcade), cyclophosphamide, and dexamethasone with daratumumab (Darzalex) to treat your light chain (AL) amyloidosis could improve your health and well-being?” of (7) Subset A respondents, 5 responded ‘yes’ and 2 responded ‘I don’t know’. Subset B respondents (2) were posed the same question, to which 1 replied, ‘yes’ and 1 ‘I don’t know’.

6. Experience With Drug Under Review

This section presents results from Subset C. Respondents were asked to evaluate on a scale of 1 (not effective) to 5 (extremely effective), “How would you rate the combined effectiveness of bortezomib (Velcade), cyclophosphamide, and dexamethasone with daratumumab (Darzalex) as a treatment regimen in controlling your light chain (AL) amyloidosis?” Two responded it was ‘3—effective’ and one respondent answered ‘4—very effective’. When asked if ‘the administration (by injection) of daratumumab (Darzalex) had a negative effect’ on them, all three respondents said ‘no’.

To the question “Based on your personal experience with the combination of bortezomib (Velcade), cyclophosphamide, and dexamethasone with daratumumab (Darzalex), how would you rate their overall side effects, from 1 (completely intolerable) to 5 (extremely tolerable)?” one respondent respectively, indicated ‘2—somewhat tolerable’, ‘3—tolerable’, and ‘4—very tolerable’. On (the same) scale of 1 (completely intolerable) to 5 (extremely tolerable), respondents from Subset C were asked “How would you rate the common side effects that you have experienced with bortezomib (Velcade), cyclophosphamide, and dexamethasone with daratumumab (Darzalex)?” The responses indicated that they found ‘breathing difficulties’, ‘neutropenia’ and ‘cardiac failure’, to be the least tolerable side effects.

	1 - COMPLETELY INTOLERABLE	2 - SOMEWHAT INTOLERABLE	3 - TOLERABLE	4 - VERY TOLERABLE	5 - EXTREMELY TOLERABLE	N/A	TOTAL	WEIGHTED AVERAGE
Neutropenia	33.33% 1	0.00% 0	0.00% 0	0.00% 0	33.33% 1	33.33% 1	3	3.00
Upper respiratory tract infection	0.00% 0	0.00% 0	33.33% 1	33.33% 1	0.00% 0	33.33% 1	3	3.50
Diarhea	0.00% 0	0.00% 0	33.33% 1	66.67% 2	0.00% 0	0.00% 0	3	3.67
Nausea/vomiting	0.00% 0	0.00% 0	33.33% 1	0.00% 0	66.67% 2	0.00% 0	3	4.33
Anemia	0.00% 0	0.00% 0	33.33% 1	0.00% 0	66.67% 2	0.00% 0	3	4.33
Neuropathy (pain, numbness, tingling, swelling or muscle weakness)	0.00% 0	33.33% 1	33.33% 1	33.33% 1	0.00% 0	0.00% 0	3	3.00
Breathing difficulties (shortness of breath, asthma, apnea)	33.33% 1	0.00% 0	0.00% 0	33.33% 1	0.00% 0	33.33% 1	3	2.50
Peripheral edema	0.00% 0	0.00% 0	66.67% 2	33.33% 1	0.00% 0	0.00% 0	3	3.33
Cardiac failure	33.33% 1	0.00% 0	0.00% 0	0.00% 0	33.33% 1	33.33% 1	3	3.00
Infusion-related reaction	0.00% 0	0.00% 0	33.33% 1	0.00% 0	33.33% 1	33.33% 1	3	4.00

Figure 7—Tolerability of treatment side effects (Subset C)

When asked how they managed these side effects, two respondents answered: ‘Perdu du poids’; ‘Burning feet restless legs—took gabapentin.’

Subset C respondents were asked “On a scale of 1 (bad quality of life) to 5 (excellent quality of life) how would you rate your quality of life with of bortezomib (Velcade), cyclophosphamide, and dexamethasone with daratumumab (Darzalex)?” One responded they had a ‘4—very good quality of life’, one indicated ‘3—good quality of life’ and one selected ‘1—poor quality of life’.

When asked “Did your treatment of bortezomib (Velcade), cyclophosphamide, and dexamethasone with daratumumab (Darzalex) improve your health and well-being?” one responded ‘yes’, one said ‘no’ and the third indicated it was ‘too soon to tell’. In response to the question “Did your treatment of bortezomib (Velcade), cyclophosphamide, and dexamethasone with daratumumab (Darzalex) improve your long-term health outlook?” 2 respondents selected ‘yes’ and 1 responded it was ‘too soon to tell’.

To the question “Did the combination of bortezomib (Velcade), cyclophosphamide, and dexamethasone with daratumumab (Darzalex) meet your expectations in treating your light chain (AL) amyloidosis?” one respondent answered ‘yes’. Two respondents chose ‘please explain’ and provided the following comments: “Je ne sais pas, je le saurai le 3 août”; “Side effects of Velcade made life miserable”.

Finally, Subset C respondents were asked “Is there anything else about your experience with bortezomib (Velcade), cyclophosphamide, and dexamethasone with daratumumab (Darzalex) that you would like us to know?” Two respondents provided the following comments: “Plus de conseils pour les diètes sans sel.”; “I had to go on daratumab and dexamethazone only. Velcade and cyclophosphamide side effects were not tolerable”.

7. Anything Else?

Amyloidosis is a disease in which a protein accumulates in different organs of the body in the form of aggregates. The larger these deposits become, the more difficult it is for the affected organ to function. To date, there is no way to prevent amyloidosis. On the other hand, the earlier the diagnosis, the greater the chances of success of the treatment. Patients need more specific treatments to stop the progression of the disease and manage the side effects. When treatment of the disease requires suffering serious side effects, life with light chain (AL) amyloidosis is made even more difficult. The management of this pathology has to be multidisciplinary to be successful, considering patients’ outcomes and quality of life as a whole.

The data presented above makes evident that patients feel it is very important the treatments they receive are **effective**, and *not accompanied by debilitating side effects*, so they **can lead a life of best possible quality**.

To further reinforce this point, when all three subsets were asked “What is important to you when it comes to treating your light chain (AL) amyloidosis?” the majority of responses described a strong desire for a good/better quality-of-life. Their feelings about their side effects experiences were mixed, sometimes tinged with despair and sometimes with hope. Some comments to this end are as follows: “Being stable”; “Être en rémission le plus longtemps possible”; “Once per month Daratumab infusion is as much as I can handle.”; “A short wait time to start chemo”; “Numbness and pain”; “Ability to taste. Overall flaking skin and cracks in my fingernails and toenails. Muscle loss and agility. Return of a general feeling of wellness.”; “Quality of life and survival”; “Que je puisse marcher sans douleur, continuer mes exercices et faire une vie normale”.

Appendix A: pCODR Patient Group Conflict of Interest Declaration

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it. **No.**
2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it. **Yes. Indrek Koppel from the Leukemia & Lymphoma Society of Canada (Manager, Advocacy & Partnerships) assisted with the survey's translation and distribution. All analysis was done by Myeloma Canada.**
3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Amgen Canada Inc.				x
Sanofi				x
Janssen				x
Bristol-Myers Squibb Canada Co.				x
Celgene				x
Takeda Canada Inc.				x
Merck Canada Inc.			x	
Pfizer Canada			x	
Karyopharm Therapeutics				x
Novartis	x			
GlaxoSmithKline Inc.			x	
Leo Pharma Inc.		x		
Rapid Novor Inc.			x	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Martine Elias

Position: Executive Director

Patient Group: Myeloma Canada

Date: July 26, 2021