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December 20, 2023

Dear Mr. Digby;

On behalf of the Myeloma Canada community, I am pleased to provide you with a response to the call for public consultation on the '*Scoping paper for the consultations on the Board's Guidelines'* released November 2023. Myeloma Canada is fortunate to be supported by patients and caregivers deeply engaged in health policy discussions which have a direct and undeniable impact on their lives— such as those affecting drug access. Alongside members of our dedicated patient community, Myeloma Canada has participated extensively in the various consultations, calls for feedback, stakeholder education sessions, and webinars held by the PMPRB over the last seven years on the proposed modernisation of the PMPRB guidelines, engaging with the development process at all stages to ensure the patient voice remains at the forefront of these conversations.

Many of the questions asked by the scoping paper are highly hypothetical, specific, and cannot be effectively answered without the benefit of research into that particular question. As a patient organization we lack the resources to conduct the necessary analyses thus our answers to the following questions are limited by the information available to us. Nevertheless, we greatly appreciate the opportunity to provide our feedback to the PMPRB, and continue participating in this process.

Regards,

Martine Elias
Executive Director Myeloma Canada

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General Recommendations

Recommendation 1: *Engagement, Collaboration, and Transparency*

The PMPRB has an opportunity with the drafting of new guidelines to benefit from active collaboration with other government agencies, such as Health Canada, Canadian Agency for Drugs and Technologies in Health (CADTH), pan-Canadian Pharmaceutical Alliance pCPA, the new Canadian Drug Agency, and provincial regulatory/funding bodies. By fostering strong partnerships, the PMPRB can ensure a coordinated approach to issues relating to drug access and leverage expertise from various stakeholders. The PMPRB should similarly maintain regular communication channels with patient and industry stakeholders to provide updates and solicit feedback on new draft guidelines, impact assessments, monitoring plans, and, on an ongoing basis, its activities, and decisions. Transparency in decision-making processes and determinative pricing methodologies can help build trust and foster collaboration with stakeholders in the bio/pharmaceutical ecosystem.
In crafting the new guidelines, we hope the PMPRB will take into consideration current and upcoming initiatives from other agencies (i.e. CADTH and pCPA's new Time-Limited Reimbursement Recommendations process, CADTH's Post-Market Drug Evaluation system, the National Strategy for Drugs for Rare Diseases, the newly created Canadian Drug Agency, and National Pharmacare.

Recommendation 2: *Flexibility, and Adaptability*

The PMPRB should maintain flexibility in its guidelines to adapt to the rapidly changing landscape of drug development, particularly for rare diseases, including the emergence of gene and cellular therapies. The pharmaceutical therapy ecosystem in Canada has changed considerably since the adoption of Bill C22 (the Patent Act) and the creation of the PMPRB in 1987 and will continue to evolve over the coming years. As well, PMPRB's experience thus far in the process of drafting and re-drafting new guidelines is indicative of this issue's complexity, thus we recommend an iterative process with built-in opportunities for adjustment of the guidelines based on real-world practice. Similarly, crafting the new guidelines within a framework that necessitates continuous monitoring and reassessment the impact of its guidelines, their efficacy, and the changing needs of the healthcare system, will allow the PMPRB to make timely adjustments to its approach.

Recommendation 3: *Patient Voice, and Patient Value*

Consideration of a drug's value to Canadian patients should be one key principle underpinning the new guidelines, and similarly a point of reference to which the PMPRB and its staff may return in moments of uncertainty. As well, the PMPRB must ensure that any changes to drug pricing regulations protect or improve individual access to therapies. This includes safeguarding access to medically necessary therapies for all residents of Canada, recognizing the discrete needs of people with rare, life-threatening and serious illnesses, and valuing patient input and real-world evidence in determining therapeutic value.

Scoping Questions

1: Efficient Monitoring of Prices Without Price Setting

As noted previously in our submission, without extensive research and expert consultation, Myeloma Canada is not in a position to respond in detail to these questions. (1.1,1.2,1.3,1.5)

- *Question 1.1.* What elements of the 2010 Guidelines should be retained? Which ones and why?
- Question 1.2: Should new Guidelines continue to categorize medicines by therapeutic class comparator characteristics such as the Level of Therapeutic Improvement?
- Question 1.3: Should the Board accord more weight to one or more of the factors set out in s. 85 of the Act in designing the Guidelines?
- Question 1.5: How should the PMPRB conduct an initial review and monitor the prices of patented medicines that have few or no international prices?
- Question 1.6: Would an expedited price review (e.g., within 90 days after initial Form 2 submission) of a new medicine based solely on international prices being below the MIP accelerate introduction of innovative medicines? How soon after an expedited review should a full price review take place?
- *Question 1.4:* If international prices are used as the initial triage measure for commencing investigations, what price levels within the PMPRB11 should be used as the triage measure? (e.g. Highest International Price (HIP) or Median International Price (MIP)?)

The choice between using the Highest International Price (HIP) or Median International Price (MIP) as the initial triage measure for commencing investigations depends on the objectives of the PMPRB. If the goal is to ensure that Canadian prices are not at the extreme end of the international spectrum, using the HIP could be a starting point. However, if the aim is to align more closely with the median international standards, then the MIP would be a more appropriate benchmark. It should be ensured that the objectives of the chosen triage measure align with the PMPRB's (narrow) legislative mandate of controlling excessively priced patented medicines.

2: Transition to PMPRB11 – New Versus Existing Medicines

In order to answer these questions, it is necessary to first understand the consequences of carrying forward a distinction between 'new' and 'existing' medicines, and how each are defined. If drawing this distinction is decreased access to lifesaving drugs medications for patients, then the distinction should not be made. In keeping with legislative and regulatory norms, the PMPRB11 should only apply to new drugs, not retrospectively. However, if post-market price reviews are conducted on 'existing' medicines the choice of comparators should be made on a case-by-case basis ensuring consideration of, among other factors, the type of drug, its target population and its market status in Canada.

- *Question 2.1:* Should the Guidelines distinguish between medicines that existed as of July 2022 (existing medicines) and medicines introduced afterwards (new medicines)?
- *Question 2.2:* What approach should the Board take with respect to existing medicines with prices above the HIP of the PMPRB11? Should the Board review these prices, and if so, how soon?

3: Price Reviews during Product Life Cycle

We are not in a position to respond in detail to the questions below (3.1, 3.4, 3.5). From the patient perspective, the 'ideal' choices of policy features are those which improve patients' timely access to safe and effective treatments.

- Question 3.1: How often should price reviews be conducted? (1-5 years).Should they be different for small molecules (average 10-year exclusivity period) versus biologics (average 20+ year exclusivity period)? Should they be different for medicines for rare diseases?
- Question 3.4: How should the PMPRB treat the allowable Consumer Price Index increase in the context where international list prices are decreasing?
- Question 3.5: What is the ideal timing for scientific review and therapeutic comparator identification? At what price review stage(s) should scientific review be applied?
- *Question 3.2:* What criteria besides time should be used to trigger a price review? Approval of a significant new indication? Significant change to the therapeutic class comparators? Availability of new/stronger evidence related to benefit vis-à-vis therapeutic class comparators? Departure from identified pricing thresholds?

The criteria for triggering a price review should be comprehensive, taking into account various clinical, economic, and patient-centered factors impacting the value and cost-effectiveness of a medicine. This approach ensures that the pricing of medicines remains appropriate in the context of their overall value to patients and the healthcare system.

- *Question 3.3:* Should the relative weighting given to different section 85 (Patent Act) factors change over the lifecycle of a medicine?

Providing an evidence-based response to the above question would require us to conduct a detailed multi-scenario assessment analysing the comparative real-world impact of affording more weight to different s. 85 factors and combinations of factors. Thus, without the information gained from such an assessment, we are unable to answer the question thoroughly. As the PMPRB has identified this question to be 'within scope' for the upcoming guideline re-drafting, we recommend that such an assessment (of the different combinations of variously weighted factors) be carried out by an independent investigator.

For patients, the real-world impact of any scenario can be defined as timely access to needed therapies that are safe and effective. Any real-world analysis must therefore rely on this definition as a key measure of success.

4: Investigations and Referral to Hearing

We cannot provide a thorough response to the questions without a set of draft guidelines to contextualize our answer, and impact assessments to illuminate the implications of using, the 2010 investigation commencement criteria, and of Voluntary Compliance Undertakings as an investigation closure mechanism.

- *Question 4.1:* Are the criteria published in the 2010 Guidelines for commencing an investigation still appropriate (assuming adjustment to PMPRB11)?

Without a set of draft guidelines to assess we cannot respond thoroughly. In future draft guidelines, however the PMPRB choses to address this issue we would ask that the answers to the following questions be provided to contextualize their decision.

- Why were the 2010 criteria originally deemed appropriate for the previous basket of comparator countries?
- Were the 2010 criteria serving their purpose effectively for the previous basket of comparator countries? (serving the purpose of the PMPRB's mandate)
- Would the adjustment to the PMPRB11 confound or nullify these criteria, or the ability to measure them?
- Does the overall redrafting of the guidelines (changes in process, guiding principles, re-distribution of duties amongst government agencies etc..) impact any of the criteria's relevance or value?
- Are there any additional criteria that should be added based on the overall redrafting of the guidelines?

- *Question 4.2:* How much detail should the Guidelines set out regarding what happens once an investigation is opened?

The Guidelines should provide sufficient information to facilitate meaningful engagement with stakeholders and should prioritize transparency in order to minimize uncertainty in the process. All possible outcomes of an investigation should be understood by all parties from the outset, as should the opportunities for engagement and how resulting feedback will be used.

- *Question 4.3:* Should the PMPRB continue to use Undertakings as an investigation closure mechanism?

If this mechanism has worked well for all involved parties, there is no glaring reason it would need to be changed. If VCUs are still used to close investigations under the new Guidelines, the PMPRB should ensure that its decisions related to the acceptance of undertakings, are made public along with an explanation of the PMPRB's reasoning for their decision which reflects that it has resulted from a fair, evidence-based process, and is in alignment with the PMPRB's mandate.

5: Relation to Pan-Canadian Health Partners, Insurers (Private and Public); And Alignment With Broader Government Initiatives

- *Question 5.1:* What efficiencies could be gained by co-ordinating decisions and timelines of the PMPRB with those of the Canadian Agency for Drugs and Technologies in Health (CADTH), Institut national d'excellence en santé et services sociaux (INESSS) and pan-Canadian Pharmaceutical Alliance (pCPA) or insurers (public and private)?

By streamlining and aligning the timelines and decision-making processes of health organizations, such as the Health Technology Assessment (HTA) agencies, the Canadian Agency for Drugs and Technologies in Health, and the Institut Nationale d'Excellence en Santé et Services Sociaux, a reduction in duplicated efforts could be achieved. At present, multiple organizations are reviewing the same

information, over-examining identical data, creating additional administrative load for all parties involved, including pharmaceutical companies. An integrated approach could limit tedious redundancies and create an efficient system of determining value, while eliminating the needless expenses of taxpayer money.

As we have stated past submissions, w*e recommend that all health technology agencies (CADTH, INESSS and pCPA) be consolidated into one body, responsible for determining access including* cost-effectiveness, value, reimbursement schemes, and overall access to medicinal drugs. This unified organization, along with all government levels, should prioritize the creation of a single cost-effectiveness evaluation process to evaluate the therapeutic worth of a medicine.

A coordinated review could expedite access to drugs following their approval, which is critical for patients awaiting treatment, especially in areas like oncology where time is of prime essence. A more harmonized process of drug review and pricing could establish a consistent decision-making system, ensuring aligned evaluation criteria of drug efficacy, safety, and cost-effectiveness across different organizations. This would mean more predictable results for drug manufacturers and patients.

An integrated system could enable enhanced scrutiny of the impact of drug pricing policies on drug launches, access to medicines, and consequently, health outcomes, ensuring the healthcare system's goals are met. For patients, a coordinated process could simplify their navigation through the system and improve their understanding of accessing new medicines. This being said, PMPRB must still adhere to the rules regarding quasi-judicial bodies, and cannot base its timelines solely on those of another government body.

- *Question 5.2:* How can the PMPRB optimize its presence within the Canadian bio/pharmaceutical ecosystem to support a whole of government approach to issues relating to patented medicines?

The PMPRB is only obligated to fulfill its legislative mandate, not to optimize its presence. Broadly though, the PMPRB can support the ecosystem within which it operates by fostering stakeholder engagement, balancing patient access to lifesaving drugs with system sustainability, supporting Research & Development, centring the principle of patient-value, promoting transparency, and being adaptable to change. These principles will help the PMPRB to effectively contribute to a comprehensive and cohesive whole-of-government approach to managing patented medicines in Canada.

6: Engaging With Patients, Health Practitioners, Pharmacy, and Other Stakeholders

- *Question 6.1: What is your experience with innovative medicines and their list prices in Canada?*

Canadians living with myeloma have significant and varying experience with innovative medicines and their list prices; n working alongside and advocating for these patients Myeloma Canada has also gained considerable experience. There is no cure for myeloma, and as a relapsed-refractory cancer, any one treatment can only control the myeloma for so long, meaning myeloma patients will always be in need of another treatment option. Only 3 lines of therapy are approved and funded by formularies across the country, yet the myeloma research space has been extremely productive over the past 15 years, leading to an ever-growing number of new therapies (like CAR T-cell therapy and bispecific antibodies) on the horizon for myeloma patients. Yet, these are new treatments, innovative therapeutic mechanisms, and the myeloma patient population is relatively

small, meaning the cost of these treatments is without exception, extremely high. To access the innovative medicines they need, myeloma patients frequently rely on the availability of clinical trials in their area, funding from industry-backed Patient Support Programs (PSPs), a patchwork of provincial funding mechanisms, federal compassionate access, and, unfortunately, their own savings. As such, Myeloma Canada is invested in supporting public and private initiatives which can reduce the cost of treatment for patients, facilitate their access, yet ensures system sustainability, including the continued and timely introduction of new medicines to the Canadian market.
Myeloma Canada, as a member of CONECTed (a group of aligned patient organizations), engaged an independent organization to conduct a case study investigating the impact of proposed new PMPRB guidelines on new and existing oncology drugs (previously submitted to the PMPRB in 2020; full report attached for reference). Included in the case were two drugs for the treatment of myeloma, daratumamab, and venetoclax. The study showed that a vast price reduction would have been required for both drugs, to the tune of 39-100% of the list price. Considering the research and development costs for medicines treating a smaller patient population, this reduction would be unfeasible for industry, and would in all likelihood discourage them from bringing similar therapies to Canada in the future. Based on the previous draft guidelines this reduction was necessary for daratumamab, which although expensive, currently plays an integral role in the treatment of myeloma. It has been able to become a standard of care, in no small part due to the real-world evidence collected through its administration to actual patients, which demonstrated in no uncertain terms the magnitude of improvement in outcomes achieved with daratumumab treatment, and thus confirmed the value of the drug to both patients and the overall healthcare system. CAR T-cell therapy, despite providing the closest thing to a 'cure' myeloma patients can presently get, and the only one-time treatment available (no ongoing or maintenance therapy required), is even more expensive. Though the first CAR T-cell therapy in myeloma, Ciltacabtagene autoleucel (cilta-cel), was approved for reimbursement by CADTH in 2022 and INESSS this year, we are hopeful that new PMPRB guidelines could expedite the listing of therapies like cilta-cel on public formularies, though concerned that the guidelines' impact could limit future opportunities for breakthrough medicines to be brought to Canadian patients.
Myeloma Canada and our patient community are always available and eager to share with the PMPRB further details of our experiences with innovative medicines and their list prices, or respond to specific questions.

- ~~*Question 6.2: What role do the PMPRB Guidelines play in your decision-making process in Canada and globally (if applicable)?*~~
- *Question 6.3: Canada and the world are facing a generation of new high-priced drugs for the treatment of rare diseases.*
    - *Should the PMPRB view the question of whether the prices of these medicines are "excessive" through a different lens than other types of medicines?*

Yes. To account for the many factors which differentiate drugs for rare diseases including (but not limited to) market size, therapeutic value, and availability of appropriate comparators, the PMPRB should adopt a transparent, flexible, and value-based approach to assessing excessiveness of price. Such an approach would consider the broader value these medicines provide to patients, caregivers, and the healthcare system, through factors such as improved quality of life, increased

life expectancy, and potential cost savings from reduced hospitalizations or other healthcare interventions. The 'lens' should not merely be a different set of measures or metric benchmarks and should instead provide a holistic approach to assessment that is flexible to the individual nature of rare disease populations, treatment landscapes, and the key factors which distinguish them. The PMPRB's approach to medicines for rare diseases should also be crafted in alignment with the *National Strategy for Drugs for Rare Diseases.*

In developing this lens, the PMPRB should engage with a wide range of stakeholders, including patient groups, healthcare providers, and rare disease experts, to understand the impact of these medicines and to ensure that the pricing review process is informed by those directly affected.

- *What quality of evidence should the Board consider when conducting its scientific review of these medicines?*

When approaching evaluation of the prices of drugs for rare diseases, the quality of evidence considered should be comprehensive and inclusive of various types of data in addition to phase 3 Randomized Control Trial (RCT data). Some examples being RWE, RWD, evidence from other countries, and phase 2/2b trial data that can provide critical insights into the value and impact of these medicines.

- *Question 6.4: How can the PMPRB better engage with you?*

Engagement In Process

We are grateful to the PMPRB for acknowledging the need for, and pursuing, public consultation throughout the process of developing new guidelines and monitoring mechanisms. We recommend the PMPRB continue to leverage a robust and mutually receptive engagement process, consulting with key stakeholders like patients, healthcare providers, industry representatives, and other relevant parties along the way. This will ensure that the PMPRB's choices/actions regarding the new guidelines are informed and shaped in an integrative process by a diverse range of perspectives, and expertise.

Engagement *As* Process

It is critical that the new guidelines incorporate patient engagement as an integral part of the PMPRB's price review process, to inhere patients' perception of the value offered by new health innovations in the decision. Particularly if the PMPRB plans to incorporate cost-effectiveness and QALYs in its evaluation, there should similarly be a process for patient input associated with this review. PMPRB may look to CADTH and INESSS for best practices, both of which have established mechanisms and procedures for reviewing patient input. Considering the significance of the "willingness to pay" factor for PMPRB, it should formulate a patient input process that reflects diverse population perspectives, such as those from the public and privately insured patient populations.

SEE 2019 ONCOLOGY DRUGS CASE STUDY BELOW

PMPRB ceiling price proposed guidelines – November 2019 Oncology Case Studies (2020-02-13 ver1.1)

Introduction

The PMPRB proposed guidelines of November 2019 are used in this analysis to estimate plausible MRPs (maximum rebated prices) of six oncology drugs that have recently been reviewed by CADTH and are now being covered in Canada. These estimates of the MRP these drugs may have gained under the proposed guidelines are compared with plausible estimates of the prices at which these drugs have been covered in Canada (the actual prices at which these drugs are covered are confidential and, thus, estimates of these prices are best guesses). This comparison results in an estimate of the price reduction from our best guess of current prices that would be required for each drug to be considered compliant with the PMPRBs proposed pricing regulations. Depending on the size of these price reductions, we estimate whether or not the drug is very likely, likely, unlikely or very unlikely to have been supplied in Canada had these guidelines been in place when these drugs were considering entering the Canadian market. This judgement has as an underlying assumption that the PEP, and subsequently the MRP, will be, in effect, transparent to the world under the proposed guidelines.

The value of this analysis is to look at drugs that are now currently available and providing real known benefits to Canadians but are very likely to be assessed as providing poor value for money (under a cost effectiveness framework). Their potential loss to the Canadian health system would have tangible and known effects. By comparison, analysis of drugs that are not yet in our market would have unknown effects, effects in principle, and thus, an unknown sense of loss. We believe this assists us in understanding the value to patients (and society) of drugs that appear to be of low value when assessed solely through the Cost Effectiveness Analysis lens.

The six drugs reviewed to date are:

- Vencexta (venetoclax) – a drug for treating chronic lymphocytic leukaemia (CLL) among patients who have failed at least one prior therapy (and, therefore, have no further treatment options);
- Opdivo (nivolumab) – for (among many other indications) adjuvant treatment of fully resected melanoma;
- Darzalex (daratumumab) – for treatment (in combination with other medicines) of multiple myeloma in patients who have failed at least one other prior therapy (and, therefore, have few further options);
- Blincyto (blinatumomab) – for treatment of pediatric patients with Philadelphia chromosome-negative relapsed or refractory B precursor acute lymphoblastic leukemia (a small group of patients - 40 a year - who face no alternatives and a very high likelihood of death);
- Unituxiini (dinutuximab) – for use in combination with other drugs for the treatment of pediatric patients with high-risk neutoblastoma who achieve at least a partial response to prior therapy (a group of around 25 to 35 children a year); and
- Tagrisso (Osimertinib) - for the first-line treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) whose tumours have epidermal growth factor receptor (EGFR) mutations (a relatively large group of around 2,000 patients annually).

Venclexta (venetoclax)

Estimation of MRP

Indication (coverage requested): As monotherapy for the treatment of patients with chronic lymphocytic leukemia (CLL) who have received at least one prior therapy and who have failed a B-Cell Receptor Inhibitor (BCRi)

Item	CADTH Base Case	CADTH Best Case	CADTH Worst Case
ICER threshold (a)		60,000	60,000
Incremental QALYs (b)		2.59	0.05
Incremental costs (c)		359,506	69,300
Treatment costs (d)		355,409	62,181
PharmacoEconomic Price - PEP (e*(a*b+d-c)/d) - $/mg		0.289	-0.047
Likely current market price - $/mg		0.476	0.476
Submitted public price (e) - $/mg		0.680	0.680
Percent reduction of likely current price			
At PEP		39%	>100%
Where revenue at $37.5M a year		41%	>100%
Where revenue at $62.5M a year		45%	>100%

NOT AVAILABLE

Assumptions:
- Estimation of MRP would be determined from the stated indication.
- Treatment cost is not reported in the CADTH reports so treatment cost is estimated from reported median treatment duration and dosing regimen for the submitted base case and then used as a proportion of the incremental treatment costs reported for the best and worst cases.
- Likely current market price is estimated at 30% price submitted to CADTH [anecdotally, this is considered conservative].

Interpretation of results

The proposed guidelines intend to use the CADTH Base Case estimates to determine the PEP. Never-the-less, CADTH do not report base case estimates for venetoclax indicating that a base case was not deliberated on or, in essence, adjudicated by an expert committee independent of the PMPRB.

The negative estimate of the PEP under the CADTH Worst Case deliberations indicates that venetoclax would have to be supplied along with a payment from the supplier for it to be considered compliant with the proposed pricing regulations. Clearly, this is not a possible price for a drug in a market and indicates there are some situations where the proposed formula does not work.

The best and worst case deliberations reported by CADTH indicate that the price reduction from best estimates of the current price would need to be somewhere between 39% and near 100% to be compliant with the proposed regulations.

At the mid-point between these estimates – a 70% price reduction from our best guess of the current price or an equivalent internationally visible price at around 80% below the publicly submitted price, we judge that it would be **very unlikely** that venetoclax would have been submitted for consideration of supply into the Canadian market.

Opdivo (nivolumab)

Estimation of MRP

Indication (coverage requested): as monotherapy, for the adjuvant treatment of adult patients after complete resection of melanoma with regional lymph node involvement, in transit metastases/satellites without metastatic nodes, or distant metastases.

Item	CADTH Base Case	CADTH Best Case	CADTH Worst Case
ICER threshold (a)		60,000	60,000
Incremental QALYs (b)		1.31	0.92
Incremental costs (c)		87,974	87,191
Treatment costs (d)		96,062	102,856
PharmacoEconomic Price - PEP (e*(a*b+d-c)/d) - $/mg		17.732	13.538
Likely current market price - $/mg		13.755	13.755
Submitted public price (e) - $/mg		19.650	19.650
Percent reduction of likely current price			
At PEP		0%	2%
Where revenue at $37.5M a year		0%	5%
Where revenue at $62.5M a year		0%	10%

NOT AVAILABLE

Assumptions:
- Estimation of MRP would be determined from the stated indication.
- Likely current market price is estimated at 30% price submitted to CADTH [anecdotally, this is considered conservative].

Interpretation of results

The proposed guidelines intend to use the CADTH Base Case estimates to determine the PEP. Never-the-less, CADTH do not report base case estimates for **opdivo** indicating that a base case was not deliberated on or, in essence, adjudicated by an expert committee independent of the PMPRB.

The best and worst case deliberations reported by CADTH indicate that the price reduction from best estimates of the current price would need to be somewhere between 0 and 10% to be compliant with the proposed regulations.

At the mid-point between these estimates – a 5% price reduction from our best guess of the current price or an equivalent internationally visible price at around 25% below the publicly submitted price, we judge that it would be **likely** that nivolumab would have been submitted for consideration of supply into the Canadian market.

Darzalex (daratumumab)

Indication (coverage requested): In combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.

In combination with lenalidomide and dexamethasone

Item	CADTH Base Case	CADTH Best Case	CADTH Worst Case
ICER threshold (a)		60,000	60,000
Incremental QALYs (b)		3.76	0.71
Incremental costs (c)		622,746	422,874
Treatment costs (d)		498,197	338,299
PharmacoEconomic Price - PEP (e*(a*b+d-c)/d) - $/mg		1.213	-0.742
Likely current market price - $/mg		4.186	4.186
Submitted public price (e) - $/mg		5.980	5.980
Percent reduction of likely current price			
At PEP		71%	>100%
Where revenue at $37.5M a year		72%	>100%
Where revenue at $62.5M a year		74%	>100%

NOT AVAILABLE

In combination with bortezomib and dexamethasone

Item	CADTH Base Case	CADTH Best Case	CADTH Worst Case
ICER threshold (a)		60,000	60,000
Incremental QALYs (b)		1.72	0.91
Incremental costs (c)		189,690	178,583
Treatment costs (d)		151,752	142,866
PharmacoEconomic Price - PEP (e*(a*b+d-c)/d) - $/mg		2.572	0.790
Likely current market price - $/mg		4.186	4.186
Submitted public price (e) - $/mg		5.980	5.980
Percent reduction of likely current price			
At PEP		39%	81%
Where revenue at $37.5M a year		41%	82%
Where revenue at $62.5M a year		44%	83%

NOT AVAILABLE

Assumptions:
- Estimation of MRP would be determined from the stated indication.
- Treatment cost is not reported in the CADTH reports so treatment cost is assumed to be a constant proportion (80%) of the incremental cost.
- Likely current market price is estimated at 30% price submitted to CADTH [anecdotally, this is considered conservative].

Interpretation of results

The proposed guidelines intend to use the CADTH Base Case estimates to determine the PEP. Never-the-less, CADTH do not report base case estimates for daratumumab indicating that a base case was not deliberated on or, in essence, adjudicated by an expert committee independent of the PMPRB.

The proposed guidelines intend to calculate a weighted average of the PEP for an indication where there are clear sub-populations for which a PEP for each can be determined. However, the CADTH reports do not provide any information to enable a weighted average to be calculated in this instance.

The negative estimate of the PEP under the CADTH Worst Case deliberations for the lenalidomide with dexamethasone combination indicates that daratumumab would have to be supplied along with a payment from the supplier for it to be considered compliant with the proposed pricing regulations. Clearly, this is not a possible price for a drug in a market and indicates there could be some situations where the proposed formula does not work.

The best and worst case deliberations reported by CADTH indicate that the price reduction from best estimates of the current price would need to be somewhere between 39% and near 100% to be compliant with the proposed regulations.

At the mid-point between these estimates – a 70% price reduction from our best guess of the current price or an equivalent internationally visible price at around 80% below the publicly submitted price, we judge that it would be **very unlikely** that daratumumab would have been submitted for consideration of supply into the Canadian market.

Blincyta (blinatumomab)

Estimation of MRP

Indication (coverage requested): For the treatment of pediatric patients with Philadelphia chromosome-negative relapsed or refractory B precursor acute lymphoblastic leukemia (ALL).

And for the treatment of all adult patients with Philadelphia chromosome-negative relapsed or refractory B-precursor acute lymphoblastic leukemia (ALL), including those who have had one prior line of therapy (i.e., adult patients who are refractory or patients who are in first or later relapse)

Item	CADTH Base Case	CADTH Best Case	CADTH Worst Case
ICER threshold (a)		60,000	60,000
Incremental QALYs (b)		1	0
Incremental costs (c)		158,224	158,270
Treatment costs (d)		154,919	154,964
PharmacoEconomic Price - PEP (e*(a*b+d-c/d) - $/vial		757.72	121.33
Likely current market price - $/vial		2,091.08	2,091.08
Submitted public price (e) - $/vial		2,987.26	2,987.26
Percent reduction of likely current price			
Where revenue < $12.5M		46%	91%
Where revenue at $20M		54%	93%
Where revenue at $40M		61%	94%

NOT AVAILABLE

Assumptions:
- Estimation of MRP would be determined from the adult indication given its likely greater prevalence.
- Blinatumomab would qualify as rare and thus its MRP would be adjusted under rules for rare disease drugs.
- Treatment cost is not reported in the CADTH reports but median treatment cycles and cycle cost is reported for the submitted base case. Treatment costs under the best and worst cases are assumed to be the same constant proportion of the incremental cost calculated from the median cycles and cycle costs reported for the submitted base case.
- Likely current market price is estimated at 30% price submitted to CADTH [anecdotally, this is considered conservative].

Interpretation of results

The proposed guidelines intend to use the CADTH Base Case estimates to determine the PEP. Never-the-less, CADTH do not report base case estimates for blinatumomab indicating that a base case was not deliberated on or, in essence, adjudicated by an expert committee independent of the PMPRB.

The best and worst case deliberations reported by CADTH indicate that the price reduction from best estimates of the current price for blinatumomab would need to be somewhere between 46% and near 94% to be compliant with the proposed regulations.

At the mid-point between these estimates – a 70% price reduction from our best guess of the current price or an equivalent internationally visible price at around 75% below the publicly submitted price, we judge that it would be **very unlikely** that blinatumomab would have been submitted for consideration of supply into the Canadian market.

Unituxiini (dinutuximab)

Estimation of MRP

Indication (coverage requested): for use in combination with GM-CSF, IL-2 and Retinoic acid (RA) for the treatment of pediatric patients with high-risk neuroblastoma who achieve at least a partial response to prior first-line multi-agent, multimodal therapy (a very small group of patients numbering around 25 to 35 a year in Canada).

Item	CADTH Base Case	CADTH Best Case	CADTH Worst Case
ICER threshold (a)	60,000		
Incremental QALYs (b)	4.74		
Incremental costs (c)	347,793		
Treatment costs (d)	313,014		
PharmacoEconomic Price - PEP (e*(a*b+d-c/d) - $/vial	10,247.56		
Likely current market price - $/vial	8,995.00		
Submitted public price (e) - $/vial	12,850.00		
Percent reduction of likely current price			
Where revenue < $12.5M	0%		
Where revenue at $20M	0%		
Where revenue at $40M	0%		

Assumptions:
- Dinutuximab would qualify as rare and thus its MRP would be adjusted under the rules for rare disease drugs.
- Treatment cost is not reported in the CADTH reports but the individual costs of the combination treatment are itemised for a full 6 cycles of treatment. Thus the proportion that dinutuximab (90%) makes up of these costs (less isotretinoin) is used to estimate treatment costs as a proportion of incremental costs.
- Likely current market price is estimated at 30% price submitted to CADTH [anecdotally, this is considered conservative].

Interpretation of results

The base case reanalysis by CADTH indicates that the submitted public price would be below the MRP (assuming market size falls below $12.5M as estimated) and, therefore, compliant with the PMPRB regulations.

Given no price reductions would have been required to be compliant with the PMPRB regulations, we judge that it would be **very likely** that dinutuximab would have been submitted for consideration of supply into the Canadian market.

Tagrisso (osimertinib)

Estimation of MRP

Indication (coverage requested): For the first-line treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) whose tumours have epidermal growth factor receptor (EGFR) mutations.

Compared with gifitinib

Item	CADTH Base Case	CADTH Best Case	CADTH Worst Case
ICER threshold (a)		60,000	60,000
Incremental QALYs (b)		0	0
Incremental costs (c)		142,401	141,598
Treatment costs (d)		131,147	130,408
PharmacoEconomic Price - PEP (e*(a*b+d-c/d) - $/vial		0.48	0.36
Likely current market price - $/vial		2.58	2.58
Submitted public price (e) - $/vial		3.68	3.68
Percent reduction of likely current price			
At PEP		87%	90%
Where revenue $200M		88%	91%

NOT AVAILABLE

Compared with ofatinib

Item	CADTH Base Case	CADTH Best Case	CADTH Worst Case
ICER threshold (a)		60,000	60,000
Incremental QALYs (b)		0	0
Incremental costs (c)		138,459	137,686
Treatment costs (d)		130,882	130,152
PharmacoEconomic Price - PEP (e*(a*b+d-c/d) - $/vial		0.53	0.42
Likely current market price - $/vial		2.58	2.58
Submitted public price (e) - $/vial		3.68	3.68
Percent reduction of likely current price			
At PEP		86%	89%
Where revenue $200M		87%	90%

NOT AVAILABLE

Assumptions:
- Treatment cost is not reported in the CADTH reports but median treatment duration is provided for the submitted base case. Together with estimated monthly cost, a cost of treatment with osimertinib is estimated. This cost, as a proportion of incremental costs in the submitted base case, is assumed to be constant in all other cases.
- Likely current market price is estimated at 30% price submitted to CADTH [anecdotally, this is considered conservative].
- Market size is assumed to be significant for this drug because of the incidence and the duration and price of treatment.

Interpretation of results

The proposed guidelines intend to use the CADTH Base Case estimates to determine the PEP. Never-the-less, CADTH do not report base case estimates for osimertinib indicating that a base case was not deliberated on or, in essence, adjudicated by an expert committee independent of the PMPRB.

The proposed guidelines intend to calculate a weighted average of the PEP for an indication where there are clear sub-populations for which a PEP for each can be determined. However, the CADTH reports do not provide any information to enable a weighted average to be calculated in this instance.

The best and worst case deliberations reported by CADTH indicate that the price reduction from best estimates of the current price for osimertinib would need to be somewhere between 86% and 91% to be compliant with the proposed regulations.

At the mid-point between these estimates – a 88% price reduction from our best guess of the current price or an equivalent internationally visible price at around 91% below the publicly submitted price, we judge that it would be **very unlikely** that osimertinib would have been submitted for consideration of supply into the Canadian market.

Administrative and technical observations

- The guidelines anticipate that the cost effectiveness analysis required to make the PEP and MRP calculations will be available from recognised public authorities (i.e. the public HTA bodies used by Canadian jurisdictions) in the form required to make the calculations. Currently, not all the information required to make the calculations is available in the public records from CADTH (note: information from INESSS was not reviewed in this project). While the information may be available in information shared between these public bodies and the PMPRB, these case studies illustrate that the missing information will not have been deliberated on by CADTH's expert committees unless its assessment processes are changed. Thus, unless the assessment processes change, it won't be able to be claimed that all the information used to calculate the PEP has, in effect, been adjudicated by the recognised public HTA body.

- Similarly, the guidelines anticipate calculating a weighted average PEP within an indication where there are multiple treatment sub-groups. Where this occurs, the information to make these weighted averages is not discussed in the CADTH expert committee reports and, thus, is not currently adjudicated by the public HTA body.

- These case studies indicate that there are some circumstances under which the calculated PEP can be negative. While these situations have been encountered in these case studies as a consequence of having to make assumptions about the treatment cost (as this information is frequently missing), it is not valid to conclude that this is an artefact of the assumptions used here. There are realistic scenarios under which the current formula can result in negative numbers being those where the treatment cost makes up a relatively low proportion of the incremental cost. These situations are likely to arise when a new drug is used in combination therapies - which are not uncommon in oncology.

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MYELOMA CANADA
MAKING MYELOMA MATTER

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December 20, 2023

Dear Mr. Digby;

On behalf of the Myeloma Canada community, I am pleased to provide you with a response to the call for public consultation on the '*Scoping paper for the consultations on the Board's Guidelines'* released November 2023. Myeloma Canada is fortunate to be supported by patients and caregivers deeply engaged in health policy discussions which have a direct and undeniable impact on their lives— such as those affecting drug access. Alongside members of our dedicated patient community, Myeloma Canada has participated extensively in the various consultations, calls for feedback, stakeholder education sessions, and webinars held by the PMPRB over the last seven years on the proposed modernisation of the PMPRB guidelines, engaging with the development process at all stages to ensure the patient voice remains at the forefront of these conversations.

Many of the questions asked by the scoping paper are highly hypothetical, specific, and cannot be effectively answered without the benefit of research into that particular question. As a patient organization we lack the resources to conduct the necessary analyses thus our answers to the following questions are limited by the information available to us. Nevertheless, we greatly appreciate the opportunity to provide our feedback to the PMPRB, and continue participating in this process.

Regards,

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General Recommendations

Recommendation 1: *Engagement, Collaboration, and Transparency*

The PMPRB has an opportunity with the drafting of new guidelines to benefit from active collaboration with other government agencies, such as Health Canada, Canadian Agency for Drugs and Technologies in Health (CADTH), pan-Canadian Pharmaceutical Alliance pCPA, the new Canadian Drug Agency, and provincial regulatory/funding bodies. By fostering strong partnerships, the PMPRB can ensure a coordinated approach to issues relating to drug access and leverage expertise from various stakeholders. The PMPRB should similarly maintain regular communication channels with patient and industry stakeholders to provide updates and solicit feedback on new draft guidelines, impact assessments, monitoring plans, and, on an ongoing basis, its activities, and decisions. Transparency in decision-making processes and determinative pricing methodologies can help build trust and foster collaboration with stakeholders in the bio/pharmaceutical ecosystem.
In crafting the new guidelines, we hope the PMPRB will take into consideration current and upcoming initiatives from other agencies (i.e. CADTH and pCPA's new Time-Limited Reimbursement Recommendations process, CADTH's Post-Market Drug Evaluation system, the National Strategy for Drugs for Rare Diseases, the newly created Canadian Drug Agency, and National Pharmacare.

Recommendation 2: *Flexibility, and Adaptability*

The PMPRB should maintain flexibility in its guidelines to adapt to the rapidly changing landscape of drug development, particularly for rare diseases, including the emergence of gene and cellular therapies. The pharmaceutical therapy ecosystem in Canada has changed considerably since the adoption of Bill C22 (the Patent Act) and the creation of the PMPRB in 1987 and will continue to evolve over the coming years. As well, PMPRB's experience thus far in the process of drafting and re-drafting new guidelines is indicative of this issue's complexity, thus we recommend an iterative process with built-in opportunities for adjustment of the guidelines based on real-world practice. Similarly, crafting the new guidelines within a framework that necessitates continuous monitoring and reassessment the impact of its guidelines, their efficacy, and the changing needs of the healthcare system, will allow the PMPRB to make timely adjustments to its approach.

Recommendation 3: *Patient Voice, and Patient Value*

Consideration of a drug's value to Canadian patients should be one key principle underpinning the new guidelines, and similarly a point of reference to which the PMPRB and its staff may return in moments of uncertainty. As well, the PMPRB must ensure that any changes to drug pricing regulations protect or improve individual access to therapies. This includes safeguarding access to medically necessary therapies for all residents of Canada, recognizing the discrete needs of people with rare, life-threatening and serious illnesses, and valuing patient input and real-world evidence in determining therapeutic value.

Scoping Questions

1: Efficient Monitoring of Prices Without Price Setting

As noted previously in our submission, without extensive research and expert consultation, Myeloma Canada is not in a position to respond in detail to these questions. (1.1,1.2,1.3,1.5)

- *Question 1.1.* What elements of the 2010 Guidelines should be retained? Which ones and why?
- Question 1.2: Should new Guidelines continue to categorize medicines by therapeutic class comparator characteristics such as the Level of Therapeutic Improvement?
- Question 1.3: Should the Board accord more weight to one or more of the factors set out in s. 85 of the Act in designing the Guidelines?
- Question 1.5: How should the PMPRB conduct an initial review and monitor the prices of patented medicines that have few or no international prices?
- Question 1.6: Would an expedited price review (e.g., within 90 days after initial Form 2 submission) of a new medicine based solely on international prices being below the MIP accelerate introduction of innovative medicines? How soon after an expedited review should a full price review take place?
- *Question 1.4:* If international prices are used as the initial triage measure for commencing investigations, what price levels within the PMPRB11 should be used as the triage measure? (e.g. Highest International Price (HIP) or Median International Price (MIP)?)

The choice between using the Highest International Price (HIP) or Median International Price (MIP) as the initial triage measure for commencing investigations depends on the objectives of the PMPRB. If the goal is to ensure that Canadian prices are not at the extreme end of the international spectrum, using the HIP could be a starting point. However, if the aim is to align more closely with the median international standards, then the MIP would be a more appropriate benchmark. It should be ensured that the objectives of the chosen triage measure align with the PMPRB's (narrow) legislative mandate of controlling excessively priced patented medicines.

2: Transition to PMPRB11 – New Versus Existing Medicines

In order to answer these questions, it is necessary to first understand the consequences of carrying forward a distinction between 'new' and 'existing' medicines, and how each are defined. If drawing this distinction is decreased access to lifesaving drugs medications for patients, then the distinction should not be made. In keeping with legislative and regulatory norms, the PMPRB11 should only apply to new drugs, not retrospectively. However, if post-market price reviews are conducted on 'existing' medicines the choice of comparators should be made on a case-by-case basis ensuring consideration of, among other factors, the type of drug, its target population and its market status in Canada.

- *Question 2.1:* Should the Guidelines distinguish between medicines that existed as of July 2022 (existing medicines) and medicines introduced afterwards (new medicines)?
- *Question 2.2:* What approach should the Board take with respect to existing medicines with prices above the HIP of the PMPRB11? Should the Board review these prices, and if so, how soon?

3: Price Reviews during Product Life Cycle

We are not in a position to respond in detail to the questions below (3.1, 3.4, 3.5). From the patient perspective, the 'ideal' choices of policy features are those which improve patients' timely access to safe and effective treatments.

- Question 3.1: How often should price reviews be conducted? (1-5 years).Should they be different for small molecules (average 10-year exclusivity period) versus biologics (average 20+ year exclusivity period)? Should they be different for medicines for rare diseases?
- Question 3.4: How should the PMPRB treat the allowable Consumer Price Index increase in the context where international list prices are decreasing?
- Question 3.5: What is the ideal timing for scientific review and therapeutic comparator identification? At what price review stage(s) should scientific review be applied?
- *Question 3.2:* What criteria besides time should be used to trigger a price review? Approval of a significant new indication? Significant change to the therapeutic class comparators? Availability of new/stronger evidence related to benefit vis-à-vis therapeutic class comparators? Departure from identified pricing thresholds?

The criteria for triggering a price review should be comprehensive, taking into account various clinical, economic, and patient-centered factors impacting the value and cost-effectiveness of a medicine. This approach ensures that the pricing of medicines remains appropriate in the context of their overall value to patients and the healthcare system.

- *Question 3.3:* Should the relative weighting given to different section 85 (Patent Act) factors change over the lifecycle of a medicine?

Providing an evidence-based response to the above question would require us to conduct a detailed multi-scenario assessment analysing the comparative real-world impact of affording more weight to different s. 85 factors and combinations of factors. Thus, without the information gained from such an assessment, we are unable to answer the question thoroughly. As the PMPRB has identified this question to be 'within scope' for the upcoming guideline re-drafting, we recommend that such an assessment (of the different combinations of variously weighted factors) be carried out by an independent investigator.

For patients, the real-world impact of any scenario can be defined as timely access to needed therapies that are safe and effective. Any real-world analysis must therefore rely on this definition as a key measure of success.

4: Investigations and Referral to Hearing

We cannot provide a thorough response to the questions without a set of draft guidelines to contextualize our answer, and impact assessments to illuminate the implications of using, the 2010 investigation commencement criteria, and of Voluntary Compliance Undertakings as an investigation closure mechanism.

- *Question 4.1:* Are the criteria published in the 2010 Guidelines for commencing an investigation still appropriate (assuming adjustment to PMPRB11)?

Without a set of draft guidelines to assess we cannot respond thoroughly. In future draft guidelines, however the PMPRB choses to address this issue we would ask that the answers to the following questions be provided to contextualize their decision.

- Why were the 2010 criteria originally deemed appropriate for the previous basket of comparator countries?
- Were the 2010 criteria serving their purpose effectively for the previous basket of comparator countries? (serving the purpose of the PMPRB's mandate)
- Would the adjustment to the PMPRB11 confound or nullify these criteria, or the ability to measure them?
- Does the overall redrafting of the guidelines (changes in process, guiding principles, re-distribution of duties amongst government agencies etc..) impact any of the criteria's relevance or value?
- Are there any additional criteria that should be added based on the overall redrafting of the guidelines?

- *Question 4.2:* How much detail should the Guidelines set out regarding what happens once an investigation is opened?

The Guidelines should provide sufficient information to facilitate meaningful engagement with stakeholders and should prioritize transparency in order to minimize uncertainty in the process. All possible outcomes of an investigation should be understood by all parties from the outset, as should the opportunities for engagement and how resulting feedback will be used.

- *Question 4.3:* Should the PMPRB continue to use Undertakings as an investigation closure mechanism?

If this mechanism has worked well for all involved parties, there is no glaring reason it would need to be changed. If VCUs are still used to close investigations under the new Guidelines, the PMPRB should ensure that its decisions related to the acceptance of undertakings, are made public along with an explanation of the PMPRB's reasoning for their decision which reflects that it has resulted from a fair, evidence-based process, and is in alignment with the PMPRB's mandate.

5: Relation to Pan-Canadian Health Partners, Insurers (Private and Public); And Alignment With Broader Government Initiatives

- *Question 5.1:* What efficiencies could be gained by co-ordinating decisions and timelines of the PMPRB with those of the Canadian Agency for Drugs and Technologies in Health (CADTH), Institut national d'excellence en santé et services sociaux (INESSS) and pan-Canadian Pharmaceutical Alliance (pCPA) or insurers (public and private)?

By streamlining and aligning the timelines and decision-making processes of health organizations, such as the Health Technology Assessment (HTA) agencies, the Canadian Agency for Drugs and Technologies in Health, and the Institut Nationale d'Excellence en Santé et Services Sociaux, a reduction in duplicated efforts could be achieved. At present, multiple organizations are reviewing the same

information, over-examining identical data, creating additional administrative load for all parties involved, including pharmaceutical companies. An integrated approach could limit tedious redundancies and create an efficient system of determining value, while eliminating the needless expenses of taxpayer money.

As we have stated past submissions, w*e recommend that all health technology agencies (CADTH, INESSS and pCPA) be consolidated into one body, responsible for determining access including* cost-effectiveness, value, reimbursement schemes, and overall access to medicinal drugs. This unified organization, along with all government levels, should prioritize the creation of a single cost-effectiveness evaluation process to evaluate the therapeutic worth of a medicine.

A coordinated review could expedite access to drugs following their approval, which is critical for patients awaiting treatment, especially in areas like oncology where time is of prime essence. A more harmonized process of drug review and pricing could establish a consistent decision-making system, ensuring aligned evaluation criteria of drug efficacy, safety, and cost-effectiveness across different organizations. This would mean more predictable results for drug manufacturers and patients.

An integrated system could enable enhanced scrutiny of the impact of drug pricing policies on drug launches, access to medicines, and consequently, health outcomes, ensuring the healthcare system's goals are met. For patients, a coordinated process could simplify their navigation through the system and improve their understanding of accessing new medicines. This being said, PMPRB must still adhere to the rules regarding quasi-judicial bodies, and cannot base its timelines solely on those of another government body.

- *Question 5.2:* How can the PMPRB optimize its presence within the Canadian bio/pharmaceutical ecosystem to support a whole of government approach to issues relating to patented medicines?

The PMPRB is only obligated to fulfill its legislative mandate, not to optimize its presence. Broadly though, the PMPRB can support the ecosystem within which it operates by fostering stakeholder engagement, balancing patient access to lifesaving drugs with system sustainability, supporting Research & Development, centring the principle of patient-value, promoting transparency, and being adaptable to change. These principles will help the PMPRB to effectively contribute to a comprehensive and cohesive whole-of-government approach to managing patented medicines in Canada.

6: Engaging With Patients, Health Practitioners, Pharmacy, and Other Stakeholders

- *Question 6.1: What is your experience with innovative medicines and their list prices in Canada?*

Canadians living with myeloma have significant and varying experience with innovative medicines and their list prices; n working alongside and advocating for these patients Myeloma Canada has also gained considerable experience. There is no cure for myeloma, and as a relapsed-refractory cancer, any one treatment can only control the myeloma for so long, meaning myeloma patients will always be in need of another treatment option. Only 3 lines of therapy are approved and funded by formularies across the country, yet the myeloma research space has been extremely productive over the past 15 years, leading to an ever-growing number of new therapies (like CAR T-cell therapy and bispecific antibodies) on the horizon for myeloma patients. Yet, these are new treatments, innovative therapeutic mechanisms, and the myeloma patient population is relatively

small, meaning the cost of these treatments is without exception, extremely high. To access the innovative medicines they need, myeloma patients frequently rely on the availability of clinical trials in their area, funding from industry-backed Patient Support Programs (PSPs), a patchwork of provincial funding mechanisms, federal compassionate access, and, unfortunately, their own savings. As such, Myeloma Canada is invested in supporting public and private initiatives which can reduce the cost of treatment for patients, facilitate their access, yet ensures system sustainability, including the continued and timely introduction of new medicines to the Canadian market.
Myeloma Canada, as a member of CONECTed (a group of aligned patient organizations), engaged an independent organization to conduct a case study investigating the impact of proposed new PMPRB guidelines on new and existing oncology drugs (previously submitted to the PMPRB in 2020; full report attached for reference). Included in the case were two drugs for the treatment of myeloma, daratumamab, and venetoclax. The study showed that a vast price reduction would have been required for both drugs, to the tune of 39-100% of the list price. Considering the research and development costs for medicines treating a smaller patient population, this reduction would be unfeasible for industry, and would in all likelihood discourage them from bringing similar therapies to Canada in the future. Based on the previous draft guidelines this reduction was necessary for daratumamab, which although expensive, currently plays an integral role in the treatment of myeloma. It has been able to become a standard of care, in no small part due to the real-world evidence collected through its administration to actual patients, which demonstrated in no uncertain terms the magnitude of improvement in outcomes achieved with daratumumab treatment, and thus confirmed the value of the drug to both patients and the overall healthcare system. CAR T-cell therapy, despite providing the closest thing to a 'cure' myeloma patients can presently get, and the only one-time treatment available (no ongoing or maintenance therapy required), is even more expensive. Though the first CAR T-cell therapy in myeloma, Ciltacabtagene autoleucel (cilta-cel), was approved for reimbursement by CADTH in 2022 and INESSS this year, we are hopeful that new PMPRB guidelines could expedite the listing of therapies like cilta-cel on public formularies, though concerned that the guidelines' impact could limit future opportunities for breakthrough medicines to be brought to Canadian patients.
Myeloma Canada and our patient community are always available and eager to share with the PMPRB further details of our experiences with innovative medicines and their list prices, or respond to specific questions.

- ~~*Question 6.2: What role do the PMPRB Guidelines play in your decision-making process in Canada and globally (if applicable)?*~~
- *Question 6.3: Canada and the world are facing a generation of new high-priced drugs for the treatment of rare diseases.*
    - *Should the PMPRB view the question of whether the prices of these medicines are "excessive" through a different lens than other types of medicines?*

Yes. To account for the many factors which differentiate drugs for rare diseases including (but not limited to) market size, therapeutic value, and availability of appropriate comparators, the PMPRB should adopt a transparent, flexible, and value-based approach to assessing excessiveness of price. Such an approach would consider the broader value these medicines provide to patients, caregivers, and the healthcare system, through factors such as improved quality of life, increased

life expectancy, and potential cost savings from reduced hospitalizations or other healthcare interventions. The 'lens' should not merely be a different set of measures or metric benchmarks and should instead provide a holistic approach to assessment that is flexible to the individual nature of rare disease populations, treatment landscapes, and the key factors which distinguish them. The PMPRB's approach to medicines for rare diseases should also be crafted in alignment with the *National Strategy for Drugs for Rare Diseases.*

In developing this lens, the PMPRB should engage with a wide range of stakeholders, including patient groups, healthcare providers, and rare disease experts, to understand the impact of these medicines and to ensure that the pricing review process is informed by those directly affected.

- *What quality of evidence should the Board consider when conducting its scientific review of these medicines?*

When approaching evaluation of the prices of drugs for rare diseases, the quality of evidence considered should be comprehensive and inclusive of various types of data in addition to phase 3 Randomized Control Trial (RCT data). Some examples being RWE, RWD, evidence from other countries, and phase 2/2b trial data that can provide critical insights into the value and impact of these medicines.

- *Question 6.4: How can the PMPRB better engage with you?*

Engagement In Process

We are grateful to the PMPRB for acknowledging the need for, and pursuing, public consultation throughout the process of developing new guidelines and monitoring mechanisms. We recommend the PMPRB continue to leverage a robust and mutually receptive engagement process, consulting with key stakeholders like patients, healthcare providers, industry representatives, and other relevant parties along the way. This will ensure that the PMPRB's choices/actions regarding the new guidelines are informed and shaped in an integrative process by a diverse range of perspectives, and expertise.

Engagement *As* Process

It is critical that the new guidelines incorporate patient engagement as an integral part of the PMPRB's price review process, to inhere patients' perception of the value offered by new health innovations in the decision. Particularly if the PMPRB plans to incorporate cost-effectiveness and QALYs in its evaluation, there should similarly be a process for patient input associated with this review. PMPRB may look to CADTH and INESSS for best practices, both of which have established mechanisms and procedures for reviewing patient input. Considering the significance of the "willingness to pay" factor for PMPRB, it should formulate a patient input process that reflects diverse population perspectives, such as those from the public and privately insured patient populations.

SEE 2019 ONCOLOGY DRUGS CASE STUDY BELOW

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MAKING MYELOMA MATTER

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December 20, 2023

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General Recommendations

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In crafting the new guidelines, we hope the PMPRB will take into consideration current and upcoming initiatives from other agencies (i.e. CADTH and pCPA's new Time-Limited Reimbursement Recommendations process, CADTH's Post-Market Drug Evaluation system, the National Strategy for Drugs for Rare Diseases, the newly created Canadian Drug Agency, and National Pharmacare.

Recommendation 2: *Flexibility, and Adaptability*

The PMPRB should maintain flexibility in its guidelines to adapt to the rapidly changing landscape of drug development, particularly for rare diseases, including the emergence of gene and cellular therapies. The pharmaceutical therapy ecosystem in Canada has changed considerably since the adoption of Bill C22 (the Patent Act) and the creation of the PMPRB in 1987 and will continue to evolve over the coming years. As well, PMPRB's experience thus far in the process of drafting and re-drafting new guidelines is indicative of this issue's complexity, thus we recommend an iterative process with built-in opportunities for adjustment of the guidelines based on real-world practice. Similarly, crafting the new guidelines within a framework that necessitates continuous monitoring and reassessment the impact of its guidelines, their efficacy, and the changing needs of the healthcare system, will allow the PMPRB to make timely adjustments to its approach.

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Scoping Questions

1: Efficient Monitoring of Prices Without Price Setting

As noted previously in our submission, without extensive research and expert consultation, Myeloma Canada is not in a position to respond in detail to these questions. (1.1,1.2,1.3,1.5)

- *Question 1.1.* What elements of the 2010 Guidelines should be retained? Which ones and why?
- Question 1.2: Should new Guidelines continue to categorize medicines by therapeutic class comparator characteristics such as the Level of Therapeutic Improvement?
- Question 1.3: Should the Board accord more weight to one or more of the factors set out in s. 85 of the Act in designing the Guidelines?
- Question 1.5: How should the PMPRB conduct an initial review and monitor the prices of patented medicines that have few or no international prices?
- Question 1.6: Would an expedited price review (e.g., within 90 days after initial Form 2 submission) of a new medicine based solely on international prices being below the MIP accelerate introduction of innovative medicines? How soon after an expedited review should a full price review take place?
- *Question 1.4:* If international prices are used as the initial triage measure for commencing investigations, what price levels within the PMPRB11 should be used as the triage measure? (e.g. Highest International Price (HIP) or Median International Price (MIP)?)

The choice between using the Highest International Price (HIP) or Median International Price (MIP) as the initial triage measure for commencing investigations depends on the objectives of the PMPRB. If the goal is to ensure that Canadian prices are not at the extreme end of the international spectrum, using the HIP could be a starting point. However, if the aim is to align more closely with the median international standards, then the MIP would be a more appropriate benchmark. It should be ensured that the objectives of the chosen triage measure align with the PMPRB's (narrow) legislative mandate of controlling excessively priced patented medicines.

2: Transition to PMPRB11 – New Versus Existing Medicines

In order to answer these questions, it is necessary to first understand the consequences of carrying forward a distinction between 'new' and 'existing' medicines, and how each are defined. If drawing this distinction is decreased access to lifesaving drugs medications for patients, then the distinction should not be made. In keeping with legislative and regulatory norms, the PMPRB11 should only apply to new drugs, not retrospectively. However, if post-market price reviews are conducted on 'existing' medicines the choice of comparators should be made on a case-by-case basis ensuring consideration of, among other factors, the type of drug, its target population and its market status in Canada.

- *Question 2.1:* Should the Guidelines distinguish between medicines that existed as of July 2022 (existing medicines) and medicines introduced afterwards (new medicines)?
- *Question 2.2:* What approach should the Board take with respect to existing medicines with prices above the HIP of the PMPRB11? Should the Board review these prices, and if so, how soon?

3: Price Reviews during Product Life Cycle

We are not in a position to respond in detail to the questions below (3.1, 3.4, 3.5). From the patient perspective, the 'ideal' choices of policy features are those which improve patients' timely access to safe and effective treatments.

- Question 3.1: How often should price reviews be conducted? (1-5 years).Should they be different for small molecules (average 10-year exclusivity period) versus biologics (average 20+ year exclusivity period)? Should they be different for medicines for rare diseases?
- Question 3.4: How should the PMPRB treat the allowable Consumer Price Index increase in the context where international list prices are decreasing?
- Question 3.5: What is the ideal timing for scientific review and therapeutic comparator identification? At what price review stage(s) should scientific review be applied?
- *Question 3.2:* What criteria besides time should be used to trigger a price review? Approval of a significant new indication? Significant change to the therapeutic class comparators? Availability of new/stronger evidence related to benefit vis-à-vis therapeutic class comparators? Departure from identified pricing thresholds?

The criteria for triggering a price review should be comprehensive, taking into account various clinical, economic, and patient-centered factors impacting the value and cost-effectiveness of a medicine. This approach ensures that the pricing of medicines remains appropriate in the context of their overall value to patients and the healthcare system.

- *Question 3.3:* Should the relative weighting given to different section 85 (Patent Act) factors change over the lifecycle of a medicine?

Providing an evidence-based response to the above question would require us to conduct a detailed multi-scenario assessment analysing the comparative real-world impact of affording more weight to different s. 85 factors and combinations of factors. Thus, without the information gained from such an assessment, we are unable to answer the question thoroughly. As the PMPRB has identified this question to be 'within scope' for the upcoming guideline re-drafting, we recommend that such an assessment (of the different combinations of variously weighted factors) be carried out by an independent investigator.

For patients, the real-world impact of any scenario can be defined as timely access to needed therapies that are safe and effective. Any real-world analysis must therefore rely on this definition as a key measure of success.

4: Investigations and Referral to Hearing

We cannot provide a thorough response to the questions without a set of draft guidelines to contextualize our answer, and impact assessments to illuminate the implications of using, the 2010 investigation commencement criteria, and of Voluntary Compliance Undertakings as an investigation closure mechanism.

- *Question 4.1:* Are the criteria published in the 2010 Guidelines for commencing an investigation still appropriate (assuming adjustment to PMPRB11)?

Without a set of draft guidelines to assess we cannot respond thoroughly. In future draft guidelines, however the PMPRB choses to address this issue we would ask that the answers to the following questions be provided to contextualize their decision.

- Why were the 2010 criteria originally deemed appropriate for the previous basket of comparator countries?
- Were the 2010 criteria serving their purpose effectively for the previous basket of comparator countries? (serving the purpose of the PMPRB's mandate)
- Would the adjustment to the PMPRB11 confound or nullify these criteria, or the ability to measure them?
- Does the overall redrafting of the guidelines (changes in process, guiding principles, re-distribution of duties amongst government agencies etc..) impact any of the criteria's relevance or value?
- Are there any additional criteria that should be added based on the overall redrafting of the guidelines?

- *Question 4.2:* How much detail should the Guidelines set out regarding what happens once an investigation is opened?

The Guidelines should provide sufficient information to facilitate meaningful engagement with stakeholders and should prioritize transparency in order to minimize uncertainty in the process. All possible outcomes of an investigation should be understood by all parties from the outset, as should the opportunities for engagement and how resulting feedback will be used.

- *Question 4.3:* Should the PMPRB continue to use Undertakings as an investigation closure mechanism?

If this mechanism has worked well for all involved parties, there is no glaring reason it would need to be changed. If VCUs are still used to close investigations under the new Guidelines, the PMPRB should ensure that its decisions related to the acceptance of undertakings, are made public along with an explanation of the PMPRB's reasoning for their decision which reflects that it has resulted from a fair, evidence-based process, and is in alignment with the PMPRB's mandate.

5: Relation to Pan-Canadian Health Partners, Insurers (Private and Public); And Alignment With Broader Government Initiatives

- *Question 5.1:* What efficiencies could be gained by co-ordinating decisions and timelines of the PMPRB with those of the Canadian Agency for Drugs and Technologies in Health (CADTH), Institut national d'excellence en santé et services sociaux (INESSS) and pan-Canadian Pharmaceutical Alliance (pCPA) or insurers (public and private)?

By streamlining and aligning the timelines and decision-making processes of health organizations, such as the Health Technology Assessment (HTA) agencies, the Canadian Agency for Drugs and Technologies in Health, and the Institut Nationale d'Excellence en Santé et Services Sociaux, a reduction in duplicated efforts could be achieved. At present, multiple organizations are reviewing the same

information, over-examining identical data, creating additional administrative load for all parties involved, including pharmaceutical companies. An integrated approach could limit tedious redundancies and create an efficient system of determining value, while eliminating the needless expenses of taxpayer money.

As we have stated past submissions, w*e recommend that all health technology agencies (CADTH, INESSS and pCPA) be consolidated into one body, responsible for determining access including* cost-effectiveness, value, reimbursement schemes, and overall access to medicinal drugs. This unified organization, along with all government levels, should prioritize the creation of a single cost-effectiveness evaluation process to evaluate the therapeutic worth of a medicine.

A coordinated review could expedite access to drugs following their approval, which is critical for patients awaiting treatment, especially in areas like oncology where time is of prime essence. A more harmonized process of drug review and pricing could establish a consistent decision-making system, ensuring aligned evaluation criteria of drug efficacy, safety, and cost-effectiveness across different organizations. This would mean more predictable results for drug manufacturers and patients.

An integrated system could enable enhanced scrutiny of the impact of drug pricing policies on drug launches, access to medicines, and consequently, health outcomes, ensuring the healthcare system's goals are met. For patients, a coordinated process could simplify their navigation through the system and improve their understanding of accessing new medicines. This being said, PMPRB must still adhere to the rules regarding quasi-judicial bodies, and cannot base its timelines solely on those of another government body.

- *Question 5.2:* How can the PMPRB optimize its presence within the Canadian bio/pharmaceutical ecosystem to support a whole of government approach to issues relating to patented medicines?

The PMPRB is only obligated to fulfill its legislative mandate, not to optimize its presence. Broadly though, the PMPRB can support the ecosystem within which it operates by fostering stakeholder engagement, balancing patient access to lifesaving drugs with system sustainability, supporting Research & Development, centring the principle of patient-value, promoting transparency, and being adaptable to change. These principles will help the PMPRB to effectively contribute to a comprehensive and cohesive whole-of-government approach to managing patented medicines in Canada.

6: Engaging With Patients, Health Practitioners, Pharmacy, and Other Stakeholders

- *Question 6.1: What is your experience with innovative medicines and their list prices in Canada?*

Canadians living with myeloma have significant and varying experience with innovative medicines and their list prices; n working alongside and advocating for these patients Myeloma Canada has also gained considerable experience. There is no cure for myeloma, and as a relapsed-refractory cancer, any one treatment can only control the myeloma for so long, meaning myeloma patients will always be in need of another treatment option. Only 3 lines of therapy are approved and funded by formularies across the country, yet the myeloma research space has been extremely productive over the past 15 years, leading to an ever-growing number of new therapies (like CAR T-cell therapy and bispecific antibodies) on the horizon for myeloma patients. Yet, these are new treatments, innovative therapeutic mechanisms, and the myeloma patient population is relatively

small, meaning the cost of these treatments is without exception, extremely high. To access the innovative medicines they need, myeloma patients frequently rely on the availability of clinical trials in their area, funding from industry-backed Patient Support Programs (PSPs), a patchwork of provincial funding mechanisms, federal compassionate access, and, unfortunately, their own savings. As such, Myeloma Canada is invested in supporting public and private initiatives which can reduce the cost of treatment for patients, facilitate their access, yet ensures system sustainability, including the continued and timely introduction of new medicines to the Canadian market.
Myeloma Canada, as a member of CONECTed (a group of aligned patient organizations), engaged an independent organization to conduct a case study investigating the impact of proposed new PMPRB guidelines on new and existing oncology drugs (previously submitted to the PMPRB in 2020; full report attached for reference). Included in the case were two drugs for the treatment of myeloma, daratumamab, and venetoclax. The study showed that a vast price reduction would have been required for both drugs, to the tune of 39-100% of the list price. Considering the research and development costs for medicines treating a smaller patient population, this reduction would be unfeasible for industry, and would in all likelihood discourage them from bringing similar therapies to Canada in the future. Based on the previous draft guidelines this reduction was necessary for daratumamab, which although expensive, currently plays an integral role in the treatment of myeloma. It has been able to become a standard of care, in no small part due to the real-world evidence collected through its administration to actual patients, which demonstrated in no uncertain terms the magnitude of improvement in outcomes achieved with daratumumab treatment, and thus confirmed the value of the drug to both patients and the overall healthcare system. CAR T-cell therapy, despite providing the closest thing to a 'cure' myeloma patients can presently get, and the only one-time treatment available (no ongoing or maintenance therapy required), is even more expensive. Though the first CAR T-cell therapy in myeloma, Ciltacabtagene autoleucel (cilta-cel), was approved for reimbursement by CADTH in 2022 and INESSS this year, we are hopeful that new PMPRB guidelines could expedite the listing of therapies like cilta-cel on public formularies, though concerned that the guidelines' impact could limit future opportunities for breakthrough medicines to be brought to Canadian patients.
Myeloma Canada and our patient community are always available and eager to share with the PMPRB further details of our experiences with innovative medicines and their list prices, or respond to specific questions.

- ~~*Question 6.2: What role do the PMPRB Guidelines play in your decision-making process in Canada and globally (if applicable)?*~~
- *Question 6.3: Canada and the world are facing a generation of new high-priced drugs for the treatment of rare diseases.*
    - *Should the PMPRB view the question of whether the prices of these medicines are "excessive" through a different lens than other types of medicines?*

Yes. To account for the many factors which differentiate drugs for rare diseases including (but not limited to) market size, therapeutic value, and availability of appropriate comparators, the PMPRB should adopt a transparent, flexible, and value-based approach to assessing excessiveness of price. Such an approach would consider the broader value these medicines provide to patients, caregivers, and the healthcare system, through factors such as improved quality of life, increased

life expectancy, and potential cost savings from reduced hospitalizations or other healthcare interventions. The 'lens' should not merely be a different set of measures or metric benchmarks and should instead provide a holistic approach to assessment that is flexible to the individual nature of rare disease populations, treatment landscapes, and the key factors which distinguish them. The PMPRB's approach to medicines for rare diseases should also be crafted in alignment with the *National Strategy for Drugs for Rare Diseases.*

In developing this lens, the PMPRB should engage with a wide range of stakeholders, including patient groups, healthcare providers, and rare disease experts, to understand the impact of these medicines and to ensure that the pricing review process is informed by those directly affected.

- *What quality of evidence should the Board consider when conducting its scientific review of these medicines?*

When approaching evaluation of the prices of drugs for rare diseases, the quality of evidence considered should be comprehensive and inclusive of various types of data in addition to phase 3 Randomized Control Trial (RCT data). Some examples being RWE, RWD, evidence from other countries, and phase 2/2b trial data that can provide critical insights into the value and impact of these medicines.

- *Question 6.4: How can the PMPRB better engage with you?*

Engagement In Process

We are grateful to the PMPRB for acknowledging the need for, and pursuing, public consultation throughout the process of developing new guidelines and monitoring mechanisms. We recommend the PMPRB continue to leverage a robust and mutually receptive engagement process, consulting with key stakeholders like patients, healthcare providers, industry representatives, and other relevant parties along the way. This will ensure that the PMPRB's choices/actions regarding the new guidelines are informed and shaped in an integrative process by a diverse range of perspectives, and expertise.

Engagement *As* Process

It is critical that the new guidelines incorporate patient engagement as an integral part of the PMPRB's price review process, to inhere patients' perception of the value offered by new health innovations in the decision. Particularly if the PMPRB plans to incorporate cost-effectiveness and QALYs in its evaluation, there should similarly be a process for patient input associated with this review. PMPRB may look to CADTH and INESSS for best practices, both of which have established mechanisms and procedures for reviewing patient input. Considering the significance of the "willingness to pay" factor for PMPRB, it should formulate a patient input process that reflects diverse population perspectives, such as those from the public and privately insured patient populations.

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