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Myeloma Canada Input on: ***Shaping the Future: A Discussion Guide for PMPRB Phase 2 Consultations on New Guidelines"*** (2024).

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On behalf of Myeloma Canada and our patient community, we would like to express our gratitude to the PMPRB for this opportunity to engage with them on the development of New Guidelines and provide our feedback. We appreciate the efforts made to include diverse perspectives throughout the many stages of this process, particularly those of patients, who are ultimately the intended beneficiaries of the PMPRB's overarching goal— curtailing excessive drug prices. We fully support this goal and are very hopeful that the new Guidelines developed through these consultations will effectively balance the need to limit excessive drug prices, with consideration of the potential impact of proposed changes on patients' access to live-saving and life-changing treatments.

Our broad reccomendations, responses to the Topics outlined in the discussion guide, and outstanding questions are presented below.

1 Broad Recommendations:

Recommendation 1: While respecting its mandate, structure as a quasi-judicial body, confidentiality requirements, and the limitations on potential stakeholder engagement imposed by these factors, we recommend that PMPRB endeavour to find a formal or informal mechanism through which patient input can be received and considered in the in-depth review process.

Patient groups recognise that (due to the aforementioned factors) direct involvement in PMPRB decision-making is not possible. Based on our experience with existing patient input processes at organizations like CDA and INESSS, we do not expect nor require that the PMPRB's consideration of patient input entails our involvement in decision-making, or direct communication with PMPRB Review Staff.

Recommended mechanisms:

Formal – Expand the role of the HDAP, using its preexisting ability to solicit advice from outside experts to gather patient input. (Topic 7)

Informal – Allow Rights Holders to inform relevant patient groups when an in-depth review is initiated and request their input. This input could be submitted to Staff by Rights Holders in their comments or, if deemed more appropriate, could be sent 'unsolicited' to Staff by patient groups, on the basis of a notification by Rights Holders that the in-depth review has commenced. (Outstanding questions).

Recommendation 2: Implementation of the new guidelines should involve an iterative learning period of 8 months, 18 months, and 4 years, during which the real-world function and impact of certain processes changed by the new guidelines are reviewed with stakeholders at each interval.

Predefining opportunities for the guidelines to be reviewed and minor improvements made would increase stakeholder confidence in supporting the adoption of new guidelines, despite elements that may increase uncertainty for patients and Rights Holders. Additionally, this would demonstrate the PMPRB's own confidence in their new guidelines by ensuring that if stakeholders' fears regarding their impact *are* realized, there will be concrete opportunities to express these concerns and consult on possible changes to remedy the situation. This recommendation aligns with the proposed three-year transition period (Topic 2) and strengthens PMPRB's suggestion of holding twice-yearly dialogue sessions with patient groups, by establishing transparent expectations for the intent, and possible outcomes of such discussions.

Recommendation 3: Implement a six-month learning period following the introduction of new guidelines, during which complaints (from any party) would be amassed without triggering in-depth reviews. This would allow time to assess the nature and volume of complaints and, in consultation with stakeholders, develop an appropriate triage process or evaluation standard for handling them efficiently. (Topic 4)

Recommendation 4: The new guidelines should emphasize and clearly describe the PMPRB's self-perception of its primary role as a "monitoring" body, as has been well expressed by members of PMPRB staff. This will help the general public (patients) better understand how the function of the Guidelines differs from that of the Board itself.

Recommendation 5: As proposed on page 7 of the discussion guide, hold a twice-yearly consultative discussion group with patient groups to "share information about the issues and decisions before the Board, particularly on the structure and implementation of the Guidelines, and their expected impact." These meetings should not be restricted to 'expected impact' but should continue through the first years following the

implementation of new Guidelines, particularly beyond the transition period (Topic 2), to ensure that any *actual* impacts can be discussed and addressed. If our Recommendation 2 is adopted, less frequent meetings may be appropriate as consultation will be ongoing. If not, PMPRB should clarify if and how it plans to respond to the comments shared in these meetings and apply them to its work developing and administering the new guidelines.

Recommendation 6: In the interest of validating a transparent methodology for the in-depth review process, we recommend the PMPRB publish reports on all completed in-depth reviews (with any sensitive information redacted), regardless of their outcome. (Outstanding Questions).

2 Topics / Option Selection:

Topic 1: Price level within the PMPRB11 to be used in the initial and post-initial price review:

Option 2: HIP, or

Option 3: midpoint between the MIP and HIP

Using the MIP would likely have the most negative impact on patients' access to new drugs and is least consistent with the 'excessive' pricing standard laid out in the PMRPB's mandate. While using HIP may not capture all instances of *potential* excessive pricing in need of further review, it is in greater alignment with the standard of excessiveness.

Though we lack the expertise to provide a more rigorous answer, on principle, *Option 3* appears to be a fair compromise between the PMPRB's previously suggested price levels (MIP and HIP), as it balance the interests of lower drug prices for Canadians with the concerns regarding new Guidelines' potential impact on access to treatments (in part through a chilling effect on industry decisions to enter the market).

The impact of any options' implementation on patients and their ability to access new treatments will determine our ultimate position, but these effects may not be clear until the Guidelines begin to operate. This supports our Recommendation 2— for the PMPRB to implement new Guidelines through an iterative consultation process, which would allow stakeholders to provide constructive input informed by their experience of the early stages of the Guidelines' application.

Topic 2: The length of time staff should wait, following the implementation of the Guidelines, to determine whether the IPC identification criterion for an existing medicine is met:

Option 3: three years

From the patient perspective, a three-year transition period for the new guidelines makes the most sense, considering the current challenges facing Canada's pharmaceutical supply chain. Our health system is already under strain, beleaguered by delays, and immediate changes could make it more difficult for patients to access the medications they need. Pharmacies, distributors, and manufacturers have made long-term plans based on the existing framework, and disrupting those plans could lead to additional delays, shortages, and/or higher prices, ultimately limiting patients' access to treatment, and harming their overall health. It is critical that Canadians who rely on patented medicines or the prospect of them, are not made to suffer due to the new guidelines.

Topic 3: In-depth review based on CPI increase criteria:

Option 1: if the list price increase is above one-year CPI

Option 2: if the cumulative increase in list price over the last two years is above the combined CPI for the past two years and the increase only took place within the last year.

We lack the expertise to effectively and thoroughly answer this question; the impact of either option's implementation on patients and their ability to access new treatments will determine our ultimate position, but these effects may not be clear until the Guidelines begin to operate. This again supports the adoption of Recommendation 2, an iterative and collaborative approach to the implementation of New Guidelines.

Topic 4: The individuals/groups permitted to submit a complaint:

Option 3: limit complaints to everyone except for Rights Holders.

OR

Option 4: no limits/restrictions.

Myeloma Canada supports either Option 3 or 4, though in the interest of fairness, our preference is for Option 4. The most important consideration here is ensuring the inclusion of a pathway for patients (as members of the general public) to submit complaints based on their own experience. Particularly considering the difficulties PMPRB has expressed regarding its limited capacity to involve patients in the review process, complaints may become the only formal process by which the PMPRB can hear directly from those personally impacted by the price of a drug.

Similarly, we feel restricting complaints to those with existing political and/or institutional power (i.e. Ministers, public drug plans, etc.) would unfairly advantage the interests of groups that already possess the connections and resources to effectively advocate for the importance of their complaint.

To avoid increasing the administrative burden on PMPRB Staff or triggering unnecessary in-depth reviews we understand this approach likely warrants developing a triage process or evaluation standard to handle incoming complaints, [1]We would suggest that this process/standard be developed after an initial learning period— 6-12 months immediately following the implementation of new guidelines. During this period no in-depth reviews would be triggered by a complaint, allowing the PMPRB to quantify the nature and volume of incoming complaints, and, in consultation with stakeholders, determine the best strategy to manage them.

Topic 5: Expanding the Scope of Products Subject to In-Depth Review Following a Complaint to Include Biosimilars and/or Vaccines

Option 2: The PMPRB should initiate an in-depth review of biosimilars and/or vaccines only when a formal complaint is received.

Patented biosimilars are typically less expensive than their reference products and help foster market competition, which tends to lower prices over time and reduce overall healthcare costs. While the price difference between a patented biosimilar and its reference product may be small in some cases, the introduction of additional biosimilars plays a crucial role in advancing the PMPRB's mandate to control excessive drug prices. Therefore, it is in the PMPRB's best interest to promote a streamlined pathway for patented biosimilars, encouraging their development and availability in Canada.

Similarly, vaccines should only be subject to an in-depth review following a complaint. Vaccine development often involves extensive clinical trials and regulatory scrutiny, leading to high initial costs. However, most vaccines are designed for large populations, and once production ramps up, economies of scale can significantly reduce vaccines' prices per-dose, which may be further reduced by negotiating bulk purchase agreements. As well, vaccines are generally one-time or limited use products with a prescribed number of doses and thus a fixed cost, unlike many patented medicines, which are designed to manage chronic conditions through ongoing use. This means even higher upfront costs can be more quickly and easily recouped in overall healthcare spending when vaccines prevent or reduce the severity of disease. Given the unique market dynamics and public health importance of vaccines, applying an in-depth review only when a complaint arises will facilitate faster market entry, ensuring Canadians have timely access to essential preventative care.

Despite our response to Topic 5, we would support a complaint screening process (Topic 4) that sends any product (drug, biosimilar, vaccine) with a lower standard of evidence supporting its complaint(s) to the initial review process first.

Topic 6: Use of clinical evidence to contextualize the degree of similarity of comparators identified for the TCC.

Option 2: each comparator will be assigned a level of similarity.

Of the provided options, Myeloma Canada supports the second, more nuanced approach—. assigning each comparator a level of similarity. Even within the same class of drugs, the of factors defining one comparator's level of similarity to the product under review may vary greatly from that of other comparators (in the same class), thus a grouped score approach would be incompatible with the intent of including multiple comparators in the analysis.

The definition of clinical evidence must also extend beyond the "gold standard" of phase III randomized controlled trials, which are not always feasible or appropriate due to factors like small patient populations, or limited viable treatment options, as is often the case for rare diseases. Where appropriate, the staff must also consider clinical evidence generated through alternative trial designs, and real-world data.

Finally, we believe that input from patients and clinicians is especially vital to determining comparator(s). This is particularly important in complex disease areas where there is often significant disagreement between researchers, Health Canada, Rights Holders, and HTA bodies, regarding the appropriate choice of

comparator(s). Clinical evidence is often highly specialized and requires context which both patients and practitioners are best situated to provide. (See Topic 7 below).

Topic 7: Future role of HDAP

Option 1: HDAP will be used only on an ad hoc basis when deemed necessary by staff.

Where clinical evidence is involved, we feel it is imperative that PMPRB Scientific Review Staff has access to specialist clinical expertise in the field/disease area relevant to the product under review and makes use of this advice to improve their analysis, particularly in more 'complex cases'.

In view of the provided options, only the first aligns with this principle, thus we feel the HDAP's ability to consult outside experts means it *must* be available to the scientific review staff *at least* on an ad hoc basis.

However, we would suggest the following alternative approaches:

Option 3: No HDAP—scientific review will be conducted by Staff, who will seek the input of clinical experts on an ad hoc basis.

Option 4: HDAP is redefined as Human Drug Advisory Input Office, and its role expanded.

In this configuration it could both A) administer the solicitation of input from relevant "specific subject-matter clinical experts" to advise the Scientific Review Staff and B) facilitate collection and transmission of patient input to the Staff.

As noted in the Guidelines, Scientific Review Staff (SR Staff) will have "*much of the necessary expertise to provide recommendations on comparators and comparable dosage regimens for the purposes of a TCC analysis"* (6.3.2), indicating that like HDAP members, SR Staff will have "broad general knowledge" of "drug therapy, drug evaluation, drug utilization and clinical research methodology," replicating much of the HDAP's value (though if the SR Staff lack these qualifications, the HDAP remains indispensable).

The HDAP's current capacity to consult experts is uniquely valuable as its operation has, to date, remained entirely compatible with both the PMPRB's mandate and its confidentiality obligations towards Rights Holders. We feel this existing function could be re-operationalized to solicit input from relevant patient groups for products undergoing in-depth review and provide this input to Staff.

3 Outstanding Questions

1. How will combination therapies be assessed?

2. Will the existence of ongoing price negotiations at pCPA be a factor considered by in-depth reviewers when considering if a hearing is necessary?
    a. Are there any other government institutions that would be aware of the initiation of an in-depth review (ex. pCPA)?

3. Other than a notice of hearing, will any information about in-depth reviews be made public, and when? For example, will the PMPRB share reports of completed reviews that do not advance to a public hearing?

4. Would Rights Holders be permitted to inform stakeholders such as patient groups that an in-depth review has been initiated?

    a. Could Rights Holders subsequently request input from patient groups and provide it to staff, or include it in their comments?

5. The Discussion guide states: "*in-depth reviews … for a large majority of patented medicines, will now take place at time points considerably after Canada's Drug Agency (formerly CADTH), INESSS and other international organizations have had the opportunity to conduct such assessments using a full suite of best practices. It is anticipated that going forward, the Board will have better information to ensure its s.85 (1)(b) determinations are optimal.*" CDA provides stakeholders the opportunity to prepare input and makes these reports available in full following a decision.

    Will these patient input reports be considered by staff during an in-depth review, and if so, what value might they be given? Could the Staff share with stakeholders what kind of information (within the general scope of these reports) might be valuable to them?