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Collective Oncology Network for Exchange, Cancer Care Innovation, Treatment Access and Education

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Réseau collectif d'oncologie pour échange, innovation en soin du cancer, accès aux traitements et éducation

November 6th, 2020

Dear HESA Members,

We, the signatories to this letter, are writing with regards to the Patented Medicine Prices Review Board (PMPRB) Final Guidelines issued on October 23rd, 2020 to support the amended *Patented Medicines Regulations* which come into force on January 1st, 2021. The purpose of this letter is to provide our feedback on these Guidelines as well as recommendations. In support of these recommendations, we will include oncology case studies as well as an analysis of the impact of novel oncology therapies on improving life expectancy and quality of life for countless cancer patients living in Canada.

First, we would like to commend the federal government for the leadership that it is showing during this terrible pandemic, domestically and internationally. As you are aware, oncology patients have suffered profoundly because of the redeployment of healthcare services and delivery mechanisms along the care continuum ranging from prevention and screening, to end-of-life care.

We recognize that the need for government policies that promote a sustainable, effective, and efficient healthcare system are more important today than ever. As such, the regulation of drug prices is an important element in the overall strategy to accomplish this aim.

We have been closely following the regulatory changes and the consultations with stakeholders. The oncology patient community has actively engaged in all available processes to provide input. Through the process, we have seen some recognition of the concerns we have raised reflected in amendments to each iteration of the draft Guidelines.

In the final Guidelines, we were encouraged to see vaccines moved to a "complaints only" process. We also recognize the importance of modernizing the PMPRB basket of countries to include countries more aligned with Canada's drug pricing and healthcare systems. There continue to be concerns, however, about the impact of the final Guidelines on access to innovative and much needed oncology treatments for patients in Canada.

These concerns include the potential for a delay in launch of important oncology therapies and, in some cases, a decision by manufacturers not to launch in Canada at all due to the potential impact on other markets. In our submission, patients in Canada deserve the same standard of care as other comparable countries. In addition, looking solely at price without a consideration of the value of the treatment to the health of patients and their caregivers, and the resultant economic and societal benefits, is a false dichotomy.

We would like you to consider asking the PMPRB to make amendments to the Guidelines that will ensure that our concerns are addressed. In support of this request we are including an evidence-based analysis of multiple cancers and their corresponding treatments that shows the overall impact of innovative cancer treatments. Additionally, we have attached case studies of the potential outcome of the Guidelines on access 6 oncology drugs recommended by the Canadian Agency for Drugs and Technologies in Health (CADTH), prepared by a leading Canadian health economist.

Basis for our position

As patients and patient groups, we recognize the challenges of a dual federal/provincial jurisdiction that underlines the healthcare system for people across Canada.

We are also aware that there are inequities in coverage for medications across the country due to several factors. Public systems are the responsibility of provinces and territories and of course each has its own economic engine, priorities, demographics, and other factors that drive decisions about how much to spend, what to fund and what funding models to implement. In addition, employers, unions, and individuals who can afford them have private plans that provide additional access.

Patients accepts that this is the construct we have. We understand that public plans cannot afford to provide access to all drugs that we might need although we trust that they will use instruments that will help make fair, objective and evidence-based choices. We all want a sustainable system; we want the prices of drugs to permit sustainability. This is no doubt the appeal of a universal single payer pharmacare plan. We are not against it, but it needs to fairly ensure Canadians have access to the care they deserve.

Patient groups, such as the one we represent, continue to support health technology assessment agencies, CADTH and INESSS, and also pCPA. They each play a key role for the constituents they serve and do follow the values of providing better health to Canadians.

In the case of PMPRB, we continue to believe its mandate can be modernised at this time by reassessing the current basket of reference countries proposed in the current review. The other agencies listed above have the role of determining and negotiating confidential reimbursement prices to reach a mutually agreed drug price with the drug manufacturers and the provinces.

It is important to remember the history of cancer management in Canada, as it serves as a guiding principle to our position:

- In 2007 the House of Commons Standing Committee on Health heard evidence that cancer treatments required their own health technology assessment process to ensure that value is analyzed based on factors relevant to that complex group of diseases. The Committee agreed with these recommendations. The result of those hearings was the creation of pCODR with a four-part deliberative Framework as its HTA process.
- The federal government also created a cancer strategy stewarded by the Canadian Partnership Against Cancer.
- Provinces have cancer agencies to manage cancer generally, including drug reimbursement, separately from other treatments.

The statistics regarding cancer certainly make the case for this specific focus on cancer:

- It is the number 1 cause of death in Canada.[1]
- It is estimated that 1 of 2 people in Canada will be diagnosed with cancer in their lifetime.[2]
- 1 in 4 will die from it, or 821,000 in Canada this year alone.[2]

This is a huge public health issue that requires a discreet policy approach, as the governments have recognized.

In addition, as we know, there is not just one type of cancer, one stage of cancer or one cause of cancer:

- There are cancers that are uncommon and those that are more common.
- There are cancers for which research has found genetic links that inform prevention and treatment and those that have not.
- There are cancers that can be cured.
- There are cancers that can be effectively and have been transformed into chronic illnesses with newer, more effective treatments; yet there are many that continue to be a certain death sentence within months of diagnosis.

Key Statistics on Cancer in Canada

Melanoma: Melanoma is one of the most common types of cancer people from 15-49 years of age, and is the 7th most diagnosed type of cancer in Canada.[3] It is estimated that in 2020, about 8000 Canadians will be diagnosed with melanoma, and approximately 1300 will die from it.[3]

Breast Cancer: The most common cancer among women, both young and older people alike, is breast cancer. In 2020, an estimated 27,400 women will be diagnosed with breast cancer and 5,100 will die of this disease. Additionally 240 men will also be diagnosed with breast cancer.[4] Among women, between 5 and 10% of breast cancers are thought to be hereditary. The BRCA1 and BRAC2 have been known to be linked with a higher link of breast cancer.[5] More recently, a study in 2017 found 72 new genetic mutations linked to breast cancer and now under study.[6]

Colorectal Cancer: Colorectal cancer: Among cancers, Colorectal Cancer is the second leading cause of death in men, and the third leading cause of death in women.[7] About 50% of cases were found to be diagnosed at stages III and IV,[8] and an estimated 9700 will die of this cancer in 2020.[7]

Lung Cancer: It is estimated that this year, 29,800 Canadians will be diagnosed with lung cancer, and 21,200 will die from it.[9] It is the leading cause of cancer deaths for males and females at 25.2% and 26.1% respectively.[10] Contrary to public opinion, it is not just a disease of those who smoke. Unlike breast cancer, most cases of lung cancer are not related to inherited genetic changes.[11] There are certain “signatures” within the lung cancer cell that determine which oral cancer therapies to use.[12] It has a 19% five year survival rate compared to 93% in prostate cancer, 88% in breast and 65% in colorectal.[8]

Pediatric Cancers: Every year, around 880 children under the age of 15 are diagnosed with cancer, and 150 die from it. Cancer is the second most common cause of death for children aged 1-14 in the developed world, after accidents.[13] Due to access to new treatments, the five-year survival rate for Canadian children has improved from 71% to over 82%.[14] Without treatment these cancers are fatal.[15]

Uncommon Cancers: There are also uncommon cancers. Gastrointestinal Stromal Tumours (GIST) with unclear prevalence and incidence levels in Canada,[16] but estimated to be about 500 new cases per year.[17] Genetic testing is recommended to guide treatment decisions for high risk resected and advanced GIST.[18] Another class of uncommon cancers are Neuroendocrine Tumours (NETs), which affect thousands of Canadians and are increasing year by year.[19,20]

Analysis of Select Innovative Cancer Drugs and their Impact on Patient Lives

1. Melanoma, Breast, Lung and Colorectal Cancer

These three cancers represent over 50% of new cancer cases in Canada.[21] Up until the introduction of innovative treatments including pembrolizumab, nivolumab, trastuzumab and afatinib, overall survival in these patients was very low. For example, only 25.1% of women diagnosed with breast cancer survived for 10 years after their diagnosis. Following the introduction of these targeted protein and inhibitor based treatments, survival is now in excess of 75%.[22]

In addition, studies have shown a dramatic increase in the quality of life of patients and the speed of recovery for people treated with these innovative drugs. Colorectal and Lung cancer patients treated with pembrolizumab reported substantial improvement in wellbeing compared to patients treated with older chemotherapy-based drugs.[23,24] A rapid improvement in overall wellbeing means that people are able return to their normal activities including work within a remarkably short period of time. Pembrolizumab also brought with it a remarkable improvement in survival for melanoma patients, even when the disease has spread.[25]

2. Uncommon Cancers:

For Gastrointestinal Stromal Tumours (GISTs), novel targeted therapies such as sunitinib can shrink these tumours sufficiently to make them removable by surgery.[18] In the area of Neuroendocrine Tumours (NETs), innovative radiation-based drugs like Lutetium Lu 177 dotatate allow us to treat previously deadly and untreatable neuroendocrine tumours in the intestines.[26]

3. Pediatric Cancers:

Due to innovative treatments, pediatric cancers have some of the highest survival rates in the country ranging from 66% to 99%.[14] In addition to improved survival, these new treatments such as bortezomib, vorinostat, sorafenib, tipifarnib and erlotinib, are safer for children than older therapies.[27]

Conclusions

In our submission the PMPRB, as a federal government agency must recognize that government policy has determined that oncology is a discreet group of diseases for public policy purposes. Oncology patient groups and other stakeholders strongly support this policy as good health policy that is strongly supported in many other countries.

Until the draft Guidelines were issued in late November 2019, patient groups had no defined concrete formula or processes by which to determine whether the planned changes will consider public policy regarding oncology and, therefore, whether it will be a good public policy instrument or not.

When the November 2019 draft Guidelines were released, in order to ensure an objective evidence based and expert analysis of the Guidelines, we asked an external health economist to assist us understand how those formulas in the proposed guidelines would be applied. Specifically, we asked him to look at six oncology drugs for different types of cancer that have been reviewed by pCODR fairly recently and to compare the outcomes they received through that process with the outcomes we can predict they would have had under the November 2019 Guidelines release with the information available to us. The results of these analyses and recommendations based on them were presented to PMPRB during a meeting on February 13, 2020 and submitted formally on February 14, 2020 as a response to the open consultation. The case studies indicate that at least 4 of the 6 oncology drugs analyzed would be very unlikely to be launched in Canada, despite all 6 being recommended by CADTH.

When the second draft Guidelines were issued in June 2020, the health economist reanalyzed the 6 drugs. The conclusions indicated that at least 2 of the 6 oncology drugs analyzed were still unlikely to be launched in Canada, despite all 6 being recommended by CADTH.

A copy of these case studies and the analysis is attached.

It remains clear that oncology needs its own approach in these Guidelines, as the federal and provincial governments have recognized in other health policies.

It also remains clear that this approach must be flexible enough to recognize the differences between uncommon and more common cancers, different stages of cancer, genetic factors, paediatrics versus adults, comorbidities, Indigenous populations and social determinants of health, to name a few.

It is not the role of patient groups to determine what decisions a pharmaceutical company will make about launching new drugs into Canada based on such reductions. It will probably be a case by case decision based on factors which are specific to the business environment and expectations. Decisions not to launch or to delay launch will directly impact access to needed therapies for oncology patients. The uncertainty remains about the availability of a new therapy still exist.

CADTH's deliberative framework for oncology drugs, with four considerations, including clinical benefit, cost effectiveness, patient values and feasibility of adoption, has recognized this nuanced, flexible and pragmatic health technology assessment required for oncology drugs. This is a recognition that there are limitations of using a single outcome measure for economic evaluation, since doing so means that important health consequences are excluded. INESSS also takes into account societal and patient values in its health technology assessment considerations.

Conversely, PMPRB only analyzes price, utilization, and cost trends so that Canada's healthcare system has more accurate information on how medicines are being used and on sources of cost pressures. In oncology, PMPRB analyzes oncology sales, market distribution and treatment costs in Canada.

In its October 2020 NPDUIS report of trends and international comparisons of oncology medicines in Canada from 2010 to 2019,[28] it concludes:

- Since 2010, the share of oncology medicines as a proportion of the total Canadian market has more than doubled, from 7.1% to 14.6%. Despite this rapid increase, Canada's oncology share of pharmaceutical sales remains the lowest among the PMPRB11. Recent trends show a greater international alignment in the prices of oncology medicines. Although oncology prices in Canada continue to sit above the PMPRB11 median, price levels across comparator countries have grown closer in recent years.
- Over the last decade, the Canadian oncology market has shifted significantly towards higher-cost drugs. Medicines with 28-day treatment costs over $7,500 now account for more than half of all oncology sales in Canada, a sharp increase from 16% in 2010.
- The Canadian oncology market is largely driven by new medicines. Medicines introduced after 2010 accounted for 58% of oncology sales in 2019, compared to 24% of non-oncology sales. Canadian availability for top-selling new oncology medicines is in line with comparator countries. Canada matched the PMPRB11 median for both the share of new medicines sold in 2019, and their respective share of total OECD new medicine sales.
- High-cost oncology medicines account for a growing share of drug costs in Canada's private drug plans. Shares differ greatly across jurisdictions, likely due to differences in public coverage for oral therapies, which now make up half of all oncology sales in Canada.

Failures of the PMPRB Analysis Approach

This narrow analysis fails to take into account the overall value of these medications to the healthcare system, and the beneficial socio-economic impact due to patients recovering faster, and getting back to normal daily activities, including a return to the workforce. It also fails to recognize the money saved in caregiving, long-term disability claims, drug claims, healthcare system utilization. This also ignores the contributions to the economy that recovered individuals make as they return to an active lifestyle and resume their normal purchasing habits and contributions to social programs.

Recommendations

Based on our review of the entire revised Guidelines provided on October 23rd, 2020 we are pleased to make the following recommendations that will support the modernisation of the PMPRB:

Recommendation #1 – Further consultation is required

We accept that the new Guidelines are an improvement for cancer drugs in general from the previous draft Guidelines. The Guideline changes that are proposed are significant and will have important consequences.

It must be recognized, however, that decisions about all aspects of drug pricing and launches in Canada, are exclusively within the purview of each company. The decision about whether required price reductions will be acceptable to each company will undoubtedly involve a number of factors proprietary to each company. Therefore, patient groups cannot draw conclusions as to whether these changes will encourage introduction of a drug, and if it will do so in a timely manner. The Guidelines do still create a level of uncertainty that may well discourage industry from bringing certain needed drugs to market. **Therefore, we ask that further consultations with industry should be undertaken to clarify areas of uncertainty before adoption**. To support this dialogue, we ask that PMPRB provide case studies across the 4 levels of TLC for Category 1 drugs.

Recommendation #2 – implementation in stages

The PMBRB should consider implementing the new Guidelines in a staged approach. First the implementation of the updated 11 basket of countries as of January 1, 2021. The implementation of the pharmaco-economic, GDP and market size factors to follow at a later stage closely aligned with our **Recommendation #1**. A carefully thought out and interrelated roll out with interim evaluations and course correction measures will result in better outcomes for all stakeholders.

Recommendation #3 – Multi-stakeholder evaluation and monitoring committee

The Guidelines be amended to provide a multi-stakeholder Committee responsible and accountable to oversee the monitoring and evaluation process of the PMPRB modernisation Guidelines.
This Committee should be tasked with the creation of a multi-stakeholder Panel of experts to review all drugs that are determined to be “excessive” in entry level price by the criteria set out in the Guidelines. This Panel will take into consideration factors other than MRP, including factors taken into account by CADTH in its deliberative framework.

As well a multi-stakeholder subcommittee including patients and patient representatives chosen by oncology patient groups must be implemented to review Category 1 drugs to provide advice to determine the TLC designation for each drug being evaluated.

Recommendation #4 – Maintain non-transparency for the benefit of patients

The Guidelines be amended to provide that PMPRB’s public decision will only provide information that the analysis has either met the PMPRB threshold and is not excessive or that it has not met the PMPRB threshold or other CADTH analysis and is excessive.

No specific economic data or numbers supporting this decision should be made public by PMPRB. This will ensure that the public Canadian price will not put at risk other markets and particularly the U.S. market such that companies will decline to enter, or delay, the Canadian market for that reason.

Recommendation #5 – Patient Engagement

The PMPRB develop a formal patient engagement programme following the ICER model co-created with patient groups chosen by the oncology patient community: https://icer-review.org/announcements/2020_vaf_update/. See particularly pages 50-54.[29]

Thank you for inviting us to provide our comments on the final PMPRB Guidelines revisions. We look forward to hearing back from you at your earliest convenience.

Respectfully submitted,

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