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February 14, 2020

Dr. Mitchell Levine
Chair, Patented Medicine Prices Review Board (PMPRB)
333 Laurier Avenue West, Suite 1400
Ottawa, Ontario K1P 1C1

Dear Dr. Levine:

Re: Patented Medicine Prices Review Board (PMPRB) Guideline Consultations

On behalf of Eisai Limited (Eisai), we would like to take the opportunity to provide our input on the draft guidelines developed by the Patented Medicine Prices Review Board (PMPRB) to operationalize the recent amendments to the *Patented Medicines Regulations*.

Eisai is the Canadian subsidiary of Eisai Co. Ltd., a *human health care (hhc)* company seeking innovative solutions in disease prevention, treatment and care for the health and well-being of people in Canada and around the world. Our company's *hhc philosophy* is based on a clear understanding that patients as well as their caregivers are the key players in healthcare, and at Eisai, we strive to develop new drug therapies that meet the needs of these patients and their caregivers while improving their quality of life. Since opening its doors in Canada in 2010, Eisai has been working hard and responsibly to help facilitate health system adoption of its medicines for cancer, epilepsy and in other areas of high unmet needs.

As a member of BIOTECanada (BTC), we have contributed and supported the association's submission in response to the draft PMPRB guidelines. The intention of this letter is to highlight how the proposed guidelines will pose a significant challenge for our organization in making innovative therapies available to Canadian patients now and into the future.

Principle areas of concern with the draft guidelines include the following:

1. Unintended consequences of applying excessive downward pricing pressure on existing medicines deemed compliant by the PMPRB and affordable by public and private payers
2. Significant uncertainty is created when "no price floor" is specified
3. Innovation or levels of therapeutic benefit no longer being recognized

1. Unintended consequences of applying excessive downward pricing pressure on existing medicines deemed compliant by the PMPRB and affordable by public and private payers

Eisai made drug launch decisions and significant investment decisions in Canada based on the current, reasonably predictable pricing environment. Our current portfolio of products was thoroughly reviewed and approved by PMPRB, CADTH, pCPA, provincial drug programs, and private insurers. It is not

appropriate for the PMPRB to re-review pricing of medicines that are currently compliant with PMPRB regulations and have already been deemed cost effective and affordable.

For example, Lenvima (lenvatinib) is a novel tyrosine kinase inhibitor (TKI) that treats patients with radioactive iodine-refractory differentiated thyroid cancer (RAIR DTC) and is also the first TKI in over 10 years to treat unresectable hepatocellular carcinoma (HCC). Lenvima received its notice of compliance (NOC) for RAIR DTC in Dec 2015. Lenvima subsequently received a positive pCODR recommendation, successfully negotiated a price and reimbursement criteria which was deemed affordable by provincial drug programs and funded across the country, including being listed broadly in the private payer market. This health technology assessment process took 25 months from pCODR submission to listings and came at significant resourcing and opportunity costs. By listing Lenvima, the payers recognize its value to the healthcare of Canadians. Applying the proposed guidelines to products that have already been assessed on multiple levels, including PMPRB disregards a well-established process federally and provincially.

It was stated that PMPRB's intention was to reduce excessive pricing and bring Canada's prices in line with the median of the OECD countries. PMPRB's proposed guideline does not take into account the significant rebates that the manufacturers pay to the provinces for existing medicines, despite mandating manufacturers to report them. In Eisai's case, we have an innovative product in epilepsy that has been on the market for 5 years that may have to take a price reduction significantly beyond the OECD median. We believe that this reduction was not the intended result PMPRB was seeking. In fact, this product has already been extensively assessed by PMPRB and has always remained in compliance. In addition, this product was assessed by CADTH and the pCPA, and negotiated significant confidential price rebates with drug programs across the country, which deemed it affordable. Further price reductions suggested in the guidelines are excessive for this product and unnecessary. They unduly penalize Eisai who, by all accounts has been a good partner and good corporate citizen with all our stakeholders including all payers and the PMPRB. The unintended consequence of excessive downward price pressure significantly beyond the OECD median will not only hurt the commercial viability of this asset in Canada but could extend globally.

Eisai is in agreement that PMPRB has a role to play in managing excessive pricing. That is in the interest of all Canadians. However, it is our position that PMPRB has created an unintended consequence in introducing these proposed guidelines. The PMPRB's goal of reducing medication prices in Canada is based on an inaccurate assessment of the actual prices due to the fact that actual rebated prices are much lower, and were not considered in this assessment. This has significant impact and we believe goes beyond the stated intent of the PMPRB. Further price reductions mandated by the new guidelines are punitive and will unfairly impact companies who have agreed to rebates in good faith with the provinces.

This introduces significant business uncertainty and sends the wrong signal to companies looking to continue to invest in the life sciences sector. We believe that all medicines currently marketed in Canada should be exempt from the application of the proposed guidelines, including the revised basket of countries.

2. Significant uncertainty is created when "no price floor" will be specified for a majority of new medicines under the proposed guideline

Price certainty is a key driver for businesses to determine whether to launch a product into the marketplace or not. Companies should not be arbitrarily penalized for bringing to market an effective therapy that is addressing an area of high unmet need and provides patients with additional therapeutic options.

We have outlined key examples to illustrate how the level of price uncertainty introduced by the proposed PMPRB guidelines will impact our business:

- Pricing referenced to incremental cost effectiveness ratios (ICERs)
- Pricing referenced to net sales over time
- Pricing referenced to the median domestic therapeutic class comparison (dTCC) or international therapeutic class comparison (iTCC)
- Variability in price over time

ICER adjustments made by economic reviewers can vary immensely from the manufacturers' model, making it very challenging for companies to predict what will be considered acceptable prices in Canada prior to launching. This is especially true in the absence of a price floor. In addition, novel therapies would be subject to arbitrary price reductions based on market size, which effectively will limit revenues of an innovative medicine. Market size should not be used to determine the excessiveness of prices as it is dependent on market dynamics that varies year over year, often outside our control (i.e. launch or exit of a competitor), and are difficult to predict. In the context of the guideline consultations, we recommend, that the ICER and market size factors be removed from referencing pricing in order to allow for price certainty during a medicines patent life.

The choice of comparators to calculate the dTCC and iTCC are completely at the discretion of the PMPRB, which makes it very challenging for companies to understand the pricing limits that could be imposed. Under the current guidelines, the highest comparator in the basket is used to reference price, while in the draft guidelines it is the median price in the class comparison that is referenced. This key differentiator is compounded by the fact that generics may be included in the comparison and force innovative therapies that represent a new class of treatments to be benchmarked to generic pricing.

This would pose a significant barrier to entry, particularly in high unmet need therapeutic areas where innovation has not occurred for a long period of time and the market has become genericized. An example of this is Fycompa (Perampanel), which is an innovative antiepileptic drug that treats patients with partial-onset seizures (POS) and primary generalized tonic-clonic seizures (PGTCS), and received it's NOC in 2014. Fycompa has been on the market for over 5 years, considered cost-effective and affordable by payers, and if launched under the draft guidelines, would be benchmarked to generic pricing. The current guidelines had the prices set to the highest in the comparator basket, which aligns to the PMPRB mandate of not being excessive, but going to the median would force Eisai as a manufacturer to go to prices that are not economically sustainable.

In addition to the price uncertainty outlined above at time of launch, allowable price levels could continue to vary with time in an unpredictable manner. Under the proposed guidelines, the interim maximum list price (MLP) maybe adjusted yearly. The MRP may also be adjusted based on difficult to predict reevaluated ICERs and/or market sizes where no pricing floor exists. Price reassessments could also occur arbitrarily at the discretion of the PMPRB staff, who are not bound by the guidelines.

Having these factors applied to any business model poses significant uncertainty throughout the medicine's patent life.

3. Innovation or levels of therapeutic benefit no longer being recognized

At Eisai, we pride ourselves on introducing novel, innovative therapies to market in very difficult to treat disease areas. Introducing innovative therapies in areas of high unmet need provides patients and

physicians with further treatment options that improve patient survival, outcomes, and improves patient's quality of life, as we have heard from many Lenvima DTC and HCC patients.

Under the current PMPRB guidelines, prices can be differentiated based on the level of therapeutic improvement provided (breakthrough, substantial, moderate, or slight/no improvement). It is disappointing that under the proposed guidelines, the PMPRB is categorizing treatments based solely on treatment cost and market size thresholds. This failure to continue to recognize innovation will limit the introduction of novel therapies into the Canadian market, as the level of therapeutic benefit is no longer being recognized. Eisai Canada is already engaged in discussions with our parent company to justify why we should launch new therapies in this new environment.

Clear rules of engagement are needed that provide pharmaceutical companies with a predictable commercial pathway for innovative medicines and to help attract health research investments. Companies need to be able to evaluate expected revenues in a market before deciding whether to and when to launch a medicine.

Additionally, trends globally suggest collaboration amongst international regulators may allow patients to receive earlier access to potentially life-changing medications and make these available as quickly as possible. A recent precedent setting example of this is "Project Orbis" whereby the Lenvima + Keytruda combination product underwent an accelerated review with three regulators simultaneously (USFDA, Health Canada and Australian TGA). This was undertaken in Endometrial Cancer because there have been no new therapies to treat these women for 30 years. We hoped to provide this combination to patients in need as quickly as possible. Health Canada, in concert with the PMPRB, is being counterproductive by simultaneously implementing price controls that are difficult to predict and will prevent and delay health system adoption of new therapies with significant duplication of government resource and efforts.

As significant uncertainty and questions remain under the proposed guidelines, we recommend the PMPRB take the necessary time to engage with stakeholders in meaningful discussions to fully understand how these proposed guidelines will significantly challenge companies in bringing innovative therapies to Canadian patients.

Sincerely,

Pat Forsythe
President and General Manager
Eisai Limited