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RE: Amgen Canada response to Regulations Amending the Patented Medicines Regulations published on the Canada Gazette on December 2, 2017

The following document constitutes the response from Amgen Canada Inc. (Amgen) to the proposed draft regulatory changes to the Regulations published in Canada Gazette Part 1, December 2, 2017 ("CG1"). We begin by noting that we strongly support and endorse the response to these draft regulations submitted on behalf of Innovative Medicines Canada. For that reason our response here is largely focussed on providing additional information, context and perspective and on reinforcing certain key messages that we believe are of particular importance.

The Rationale for Change is Not Supported by the Evidence

The recent pharmaceutical price regulatory reforms proposed by Health Canada represent the most disruptive changes in price regulation policy since the creation of PMPRB in 1987. Before addressing the individual elements of the proposed reforms we believe it is important to underscore that the rationale for initiating such a dramatic reform is founded on inaccurate and exaggerated claims that leave the mistaken impression that (1) Canadian patented drug prices are dramatically out of line with those in other developed economies, and (2) that growth in expenditures on patented prescription drugs constitutes an affordability crisis and poses an existential threat to publicly funded healthcare systems. Neither premise is consistent with the evidence, including the government's own published data.

Despite claims from PMPRB as recently as 2017 that Canada's patented prescription drug prices were "among the highest in the world"[1], the most recent PMPRB analysis[2] confirms that Canada's patented prescription drug prices ranked 4th highest out of its 7 reference markets, squarely in the middle of the pack. When patented medicines that have generic competition are removed from the comparison, Canada's prescription drug prices

[1] Regulatory Impact Analysis Statement, Canada Gazette, December 2, 2017
[2] 2016 PMPRB Annual Report

ranked even lower, at 6th highest in the basket of 7 reference countries[3]. The 2016 PMPRB annual report also shows that the changes in the prices of patented medicines have consistently been below the rate of inflation in Canada. With respect to the alleged growth in expenditures, a recent analysis[4] reports that per capita patented prescription drug expenditures, expressed in real terms, have remained essentially unchanged over the past decade as have these expenditures when expressed as a share of national GDP (<1%). Furthermore, as a share of overall health expenditures, patented prescription drug expenditures have actually declined over the past 10 years. As for the issue of affordability, patented prescription drugs represent an estimated 3.7% of total public healthcare expenditures in Canada[5].

We recognize and understand the fiscal and policy challenges associated with ensuring a sustainable healthcare system. Amgen has consistently demonstrated a willingness and ability to work constructively with provincial and private payers to help address these challenges. However, we strongly object to the way in which patented prescription drug prices have been characterized as a major contributing factor to rising healthcare costs when all of the available evidence clearly demonstrates otherwise. For this reason it is unclear to us why reform of prescription drug price regulations has become a priority of the federal government at this time.

Lack of consultation and speed of reform is unacceptable

In consideration of the enormous scope and potential implications of the proposed regulatory changes that are addressed below, there is every reason to take a measured approach, to ensure that all proposed changes are subjected to extensive consultation and that they be assessed in the context of clear policy objectives with due consideration of any unintended consequences. Unfortunately this has not been the case. Until very recently, consultation consisted of the solicitation of a single round of written submissions from stakeholders with no opportunity for dialogue, despite repeated requests from the industry. Furthermore, the recently issued draft regulations do not appear to have addressed any of the material issues raised in written submissions from industry leaving the impression that the outcome of the current "consultation" process has been predetermined. Equally concerning is that the requisite regulatory impact (cost benefit) analysis produced by the Ministry of Health is deeply flawed and highly oversimplified. It grossly understates the potential impact of the proposed changes on the industry, the economy and most importantly, the healthcare of Canadians.

For all of the reasons noted above, we are extremely concerned about the proposed reforms and the process by which they are being advanced. We continue to advocate for more meaningful consultation and a more considered assessment of their implications. However, in accordance with the opportunity afforded us under the circumstances we are providing the following comments on the proposed reforms as outlined in CG1.

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[3] Analysis from IMC on the international prices of its member companies, first presented on a submission in a response to PMPRB consultation in October 2016

[4] Skinner, Brett J (2017). Does Canada need a Patented Medicine Prices Review Board? *Canadian Health Policy*, working paper posted October 23, 2017. Access to Innovative Medicines (AIM) series. Toronto: Canadian Health Policy Institute (CHPI). URL: www.canadianhealthpolicy.com

[5] Skinner, Brett. "How Ottawa's using a fake drug crisis to force through damaging pharmaceutical policy." *Financial Post*. January 16, 2018. http://business.financialpost.com/opinion/how-ottawas-using-a-fake-drug-crisis-to-force-through-damaging-pharmaceutical-policy

The proposed reforms introduce high levels of uncertainty and will delay and/or discourage new product launches.

Overall Amgen disagrees with the introduction of new economic-based factors proposed. Section 85 of the Patent Act already gives PMPRB four factors to consider in order to determine whether a price is excessive. Additionally, Section 85 gives the Board the freedom to use any other factors deemed relevant. It is not apparent why the existing four factors are not sufficient to allow PMPRB to determine whether prices of patented drugs in Canada are excessive. For patentees, the introduction of additional factors would greatly increase the complexity of reporting and maintaining compliance as well as of assessing the feasibility of launching new drugs in Canada. We call specific attention to the following issues and concerns with the proposed factors:

Pharmaco-economic assessments are not an appropriate basis for setting price.

Pharmaco-economics is one of a number of tools that can be helpful in healthcare decision making. However, it is intended to assist in informing choices related to resource allocation from the perspective of a single decision body with a fixed pool of resources. Two assessments of the same drug can result in markedly different conclusions depending on the perspective of the assessment. In other words the conclusion of a pharmaco-economic review is not generalizable to all settings or circumstances. An assessment by CADTH can differ markedly from an assessment of the same product by INESSS or by a third party payer. To our knowledge, no other jurisdiction in the world uses a cost effectiveness assessment to set the ceiling price of a drug; rather it is used to inform a funding/reimbursement decision.

To further illustrate this issue, consider a pharmaco-economic assessment conducted by CADTH. CADTH takes the perspective of a publicly funded healthcare system. Such a system is assumed to have a fixed pool of resources (budget) to manage the health of a specific population and wishes to use them in a manner that generates the most benefit for that population. In this simple example a choice needs to be made between paying for a new Drug A or for the currently funded standard of care, Drug B. Such an assessment would model the “relevant” costs and benefits of each option. Using the current CADTH HTA guidelines, only benefits which accrue to the health system would be included in its analysis. Benefits external to the health system, such as, the impact on or cost to caregivers at home, convenience for the patient or the impact on workplace productivity or absenteeism, or other downstream societal benefits would not be included in CADTH’s analyses.

Now consider the same assessment undertaken by a private insurance company on behalf of its customer (an employer or a trade union). Its assessment of Drug A would also need to consider the currently funded standard of care, but in this case that might be quite different from what a public plan covers. For example, the employer may be paying for multiple drug treatment options which include but are not limited to Drug B. The population insured is quite likely also different in terms of demographics, disease prevalence, comorbidities and other factors. The employer would also be very concerned about other costs and benefits that are not relevant to the publicly funded plan such as the impact on workplace productivity, absenteeism, or utilization of other employer funded benefits such as massage, physiotherapy, nursing or psychotherapy. To complicate matters further, the employer or union would likely also look at such decisions in the context of an overall

benefits/compensation package designed to attract and retain staff or to satisfy a collective agreement. Given this example of two very different perspectives, it is not difficult to see why the recommendations of a single pharmaco-economic review cannot be generalized to all the relevant stakeholders.

In addition to the complexity noted above, it is also important to note that pharmaco-economic analyses are conducted using models or simulations of what is presumed or predicted to happen in the course of diagnosis and treatment. As such, they rely on assumptions about the relationships between a selected subset of variables in the model and invariably understate the complexity that exists in the real world. Generally speaking the output of such models is summarized as cost per Quality Adjusted Life Year ($/QALY). However, the $/QALY value generated by such models is often highly sensitive to the assumptions used in the model. With many of these assumptions there will be a high level of uncertainty which means that there will also be a high level of uncertainty about the cost/benefit determination.

Equally problematic is the fact that the acceptable cost per QALY (or "willingness to pay") is an arbitrary figure around which there is no consensus. As the scoping document acknowledges, even from a single payer's perspective, the acceptable ICER in one disease area often differs from that in another. While the scoping document states that the QALY threshold would be "revised periodically to reflect changing market conditions" it is instructive in this respect to note that figure of $50K which has been cited by PMPRB is the same figure cited in a publication from 1982[6]. Leaving aside that the original number was expressed in $US, simply applying a CPI adjustment[7] would raise this figure to $115K in today's terms. Yet the $50K figure persists as a commonly cited acceptable ICER threshold.

PMPRB's reference to the use of CADTH's economic assessments is also problematic for other reasons. Contrary to the statement in the scoping document, CADTH's assessments do not compare a new technology to "the least cost-effective health technology" in the healthcare system. In fact, the overwhelming majority of health technologies in the public healthcare system have never even been the subject of a cost-effectiveness assessment. The comparison is generally to the "standard of care" which can vary markedly and therefore greatly limits the generalizability of cost-effectiveness determinations as discussed above. It is also important to note that CADTH is funded by the public payers it serves. Its process is closed, its assessments are not subject to public consultation and its recommendations are not peer reviewed. Furthermore, CADTH's recommendations often choose modelling assumptions that are more likely to understate the cost-effectiveness of a new drug and which therefore provide a rationale for negotiating lower prices. The fact that, as in independent agency, CADTH is not subject to the "Access to Information" mechanisms that provide some measure of transparency into government operations only adds to list of concerns associated with the proposal to use CADTH's cost effectiveness assessments for the purpose of determining a national price.

In summary, the use of pharmaco-economic analysis to establish patented prescription drug prices in Canada would introduce an enormous level of bias, uncertainty and unpredictability into the process of forecasting and predicting ceiling prices. In making investment decisions or even feasibility assessments relating to the launch

[6] Kaplan R, Bush J. Health-related Quality of life measurement for evaluation research and policy analysis. *Health Psychology*, Vol 1(1), Win 1982, 61-80. http://dx.doi.org/10.1037/0278-6133.1.1.61
[7] Bank of Canada Inflation Calculator found at https://www.bankofcanada.ca/rates/related/inflation-calculator/

of new products, a predictable method of estimating price is absolutely critical. The uncertainty introduced by the spectre of pharmaco-economic factors being used in price setting would almost certainly delay investment and launch of new products or even discourage launch altogether. It clearly does not meet the PMPRB's expressed intent of a framework that would encompass "economically-derived, bright line tests to yield meaningful ceiling prices that are foreseeable to patentees."

Market size & GDP growth are not relevant to a determination of price

PMPRB's scoping document states that in addition to the aforementioned tests it would assess "whether a drug … should have its price further adjusted because of its expected impact on payers within the first three to five years from launch (assuming appropriate clinical utilization and no rationing of care). This test would consider the anticipated market size of the new drug against GDP growth, with the latter serving as a rough proxy for how much Canadian consumers can afford to pay for the new patented drugs that come to market on an annual basis."

This statement is problematic for several reasons. The terms "impact on payers" appear to be in reference to budget impact although that is not explicitly stated. While Amgen appreciates that budget impact is an important consideration for payers, we do not agree that this factor is in any way relevant to PMPRB's mandate of ensuring prices are not excessive and we believe that this measure would unnecessarily introduce additional risk and uncertainty for manufacturers. The price of an individual product should reflect its value to Canadian patients and the healthcare system. To the extent that the overall expenditures on a particular drug represent a budget challenge for payers, these challenges are best addressed through other existing means such as the negotiation of listing agreements with payers.

Incorporating budget impact considerations into PMPRB assessments is problematic for several reasons including but not limited to the following:

- It is extremely difficult to predict the adoption rate of new technologies or to anticipate the impact of new clinical information or emergent competing technologies on practice patterns. Were PMPRB to establish a price ceiling based on a forecast which overestimated the actual utilization of a new product, there will be no mechanism for the company to recover its economic losses.
- Furthermore, using market size for new indications as a rationale to proactively lower drug prices could discourage manufacturers from bringing new indications to market and could potentially serve as a disincentive to the launch of indications or new treatments that have the greatest impact on burden of disease.
- The additional workload required to meet this regulatory requirement would be considerable given that forecasts and budget impact analyses are not generally tracked and managed at the level of the individual DIN. Manufacturers prepare financial forecasts at the brand level that reflect realistic assumptions of drug uptake, expected entry of new competitors, access conditions and timing, etc. Currently manufacturers do not produce forecasts of extremely favourable and unrealistic potential "maximum use" of new products or new indications. Doing so would also likely result in myriad individual DIN level issues and complexities.

In summary, including budget impact as an overall price setting factor introduces further uncertainty into already complicated decisions by manufacturers regarding investment in and launch of new products and is likely to delay or even discourage altogether the entry of new products into the Canadian market. There are other existing less onerous and more effective mechanisms to address budgetary concerns.

The introduction of GDP growth as a factor is also puzzling. How a measure of the overall growth rate of the economy might play a role in the determination of the ceiling price of an individual drug is difficult to understand. In the absence of further explanation, we have assumed that PMPRB's underlying rationale is that the growth in drug expenditures should bear some relationship to the growth in the overall economy. This in itself is a highly contentious assertion and one which is ultimately a matter of public policy. However, even if one were to accept this premise, it is extremely difficult to envision how, in the context of its assessment of multiple new technologies in any given year, PMPRB could apply this factor to the definition of the ceiling price of an individual drug. Affordability is a matter of trade-offs and is a determination that can only be made in a specific context which itself a consequence of specific policy decisions and priorities. It is not, nor should it ever be, within PMPRB's mandate to define such public policy priorities for individual payers or Canadian consumers.

Changes in the Reference Group are acceptable provided that they facilitate "apples to apples" comparisons.

The existing pricing regulatory framework aims at having the introductory prices of patented drugs in Canada at the median of a basket of countries with similar economic standing. The current proposal references an expanded group of countries with the expressed objective of tying Canadian ceiling prices to the median prices of OECD countries. The OECD is an extremely diverse group in economic terms. Its objective is to "promote policies that will improve the economic and social wellbeing of people" and while it produces a wide range of comparative economic indicators, we are not aware of any areas of economic performance in which Canada aspires to achieve the median of the OECD countries.

A Canadian manufacturer of patented prescription drugs operates in a Canadian economy where it must compete for talent and fund its operations based on Canadian market dynamics and prices. It seems fundamentally unreasonable to base local drug price assessments on comparisons with median OECD market prices while aspiring to outperform OECD on other comparative economic indicators.

The proposed expanded reference group is an extremely diverse group in terms of the level of economic development and prosperity. Specifically the proposal to include Spain and South Korea, countries which have GDP per capita approximately 35% [8] below that of Canada, is unreasonable and inappropriate.

In addition, a comparison of international prices without a parallel comparison of the populations which are reimbursed would also be unfair. For example, where lower prices in a given reference market are accompanied by less restrictive reimbursement criteria than those applied in Canada, the use of these prices as a benchmark would be unreasonable and inappropriate.

[8] Comparison done with 2016 per capita GDP in current USD from The World Bank

While we do not object in principle to the expansion of the reference group, we believe that any countries that are added to the existing reference group should be comparable to Canada in terms of the level of economic development and prosperity. The use of per capita GDP as an economic indicator in defining reference markets would be acceptable provided that selected reference markets fall within a predefined range (+/-) relative to Canada on that measure. With respect to the application of the reference group to an assessment of any individual product, allowances should be made to exclude reference markets in which the criteria for coverage are materially different.

Requiring patentees to report price and revenues net of all price adjustments is unnecessary and will discourage innovative and beneficial product listing agreements

PMPRB claims that, in order to properly regulate prices, it needs access to confidential discounts being offered to public and private payers. We disagree with this assertion. PMPRB, under the Patent Act, has the mandate to ensure prices are not excessive and we believe it should continue to do so by focussing on establishing ceiling prices. If the list price of a drug is at or below such a ceiling, and no unit is sold in Canada at a price above that level, PMPRB can be assured that consumers are not paying an excessive price and there is no need for any further analysis.

Leaving aside the added burden of tracking and reporting all of this additional information to PMPRB which in itself is substantial, we foresee a myriad of issues that will trigger spurious investigations and overwhelming complexity. Consider for example that many product listing agreements contain provisions for rebates that vary based on volume. How would year over year changes in the average price resulting from changes in volume or business mix be assessed and what consequences would a manufacturer face? Consider also that many PLAs contain provisions for repayment based on factors that can only be assessed retrospectively and which are unlikely to align with PMPRB's fiscal reporting periods. How would PMPRB manage annual compliance assessments under such circumstances? Consider that the evolution of drug reimbursement schemes is clearly trending rapidly toward various risk sharing agreements which involve pay-for-performance arrangements or outcomes-based-agreements where the payer and the manufacturer have already aligned on what is a mutually acceptable transfer of expenditure and performance risk. PMPRB's proposed reporting requirements would discourage the adoption of such innovative arrangements. How would average prices under such arrangements even be assessed? How would benefits associated with copay assistance or other patient oriented support programs be incorporated and how would changes or competitive differences that affect average transaction prices be managed?

Additionally, were PMPRB to utilize confidential average transaction prices for the purposes of benchmarking other products in the market place, doing so would require the disclosure of highly confidential commercially sensitive information to existing and potential competitors. How would PMPRB protect such highly confidential information? And how would PMPRB deal with differences that might arise between competing products due to changing market conditions such as, for example, where a product has a lower average price than a competitor because it enjoys a market share advantage?

The list of potential issues is frankly endless and begs the question "What benefits accrue to PMPRB or to Canadian consumers by the introduction of such burdensome and complex requirements that are not already

realized by the simple affirmation that list prices (the maximum prices that any Canadian consumer would pay) are at or below a ceiling level that is deemed acceptable?" On the other hand, the introduction of complicated reporting issues associated with these highly desirable discounting arrangements is likely to impose additional burden and risk on manufactures and introduce even further uncertainty which will ultimately discourage their introduction.

Any reform of regulations must include "grandfathering" and transition provisions

Decisions to invest in and launch existing patented prescription drugs were informed by assessments based on the existing regulatory framework and in many cases are the subject of product listing agreements with payers. The imposition of a new regulatory framework will have uncertain and potentially profound implications for in market products. For this reason, all existing products should continue to be managed in accordance with the regulations in place at the time of launch. Grandfathering is compatible with the basic principles of fairness and predictability that should be the basis for solid pricing policies.

What Can/Does Amgen Support?

Amgen is supportive of efforts by the government to work with health system stakeholders in a consultative fashion to address the policy and fiscal challenges facing Canada's healthcare system. However, the process needs involve a dialogue which has so far been absent from this policy reform initiative.

Reform of the regulations must reflect the following principles:

- Enhance health and economic wellbeing of all Canadians
- Reward and encourage innovation
- Reduce business uncertainty
- Do not stray into domains of public policy outside of mandate
- Minimize regulatory complexity and reporting burden
- Provide provisions for "grandfathering" for existing products
- Reflect the heterogeneity of the Canadian pharma market
- Do not duplicate assessments done by other regulators or payers
- Protect confidential commercially sensitive info
- Facilitate/encourage innovative reimbursement frameworks e.g. pay for performance, VBHC etc.

We can support the following elements of the proposed changes:

- Establishing a national ceiling price as a means of executing PMPRB's mandate to protect Canadian consumers from excessive prices of patented prescription drugs
- Revisions to the current reference price group provided that the additional members are similar to Canada in measures of economic wellbeing (e.g. per capita GDP) and that, for the purposes of individual drug price comparisons, the reimbursement conditions/criteria are consistent
- Shifting the focus PMPRB away from all products to a subset of drugs that represent so-called "higher risk" products which would help to reduce low-value-add regulatory burden.

Conclusions

Amgen recognizes and understands that governments face significant challenges in ensuring the sustainability of the healthcare system in Canada. While we believe that the government's characterization of patented prescription drug prices and their contribution to these challenges is not consistent with the evidence, we are willing to work with all stakeholders and we strongly support constructive dialogue that is focussed on improving the health and well-being of Canadians. Given the lack of meaningful consultation to date, we are deeply concerned that many elements of the proposed regulations will negatively impact the ability of our industry to bring innovative medicines to Canadian patients. We believe that the regulatory impact analysis presented by the government is poorly informed and lacking in rigour. For all of these reasons we strongly encourage the government to delay the implementation of the proposed regulatory reforms and allow for proper dialogue and consultation.