October 6, 2008

Dr. Brien Benoit
Chairperson
Patented Medicine Prices Review Board
Box L40
Standard Life Centre
333 Laurier Avenue West, Suite 1400
Ottawa, Ontario K1P 1C1

Re: Response to Draft Revised Excessive Price Guidelines

Dear Dr. Benoit:

I am writing to you regarding the PMPRB's Draft Revised Excessive Price Guidelines released in August 2008 (the "Draft Guidelines"). As the matters addressed in the Draft Guidelines are of great importance to stakeholders, particularly the biotechnology industry, AMGEN Canada Inc. ("AMGEN") appreciates the opportunity to provide comment on these matters. AMGEN's comments on each issue will be addressed individually.

Levels of Therapeutic Improvement

AMGEN is of the view that there is no need for different categories of drugs. A single definition of excessive pricing should apply to all new patented medicines (see discussion below concerning introductory price tests). Such a simple definition would foster an environment in which all stakeholders would be afforded a high degree of certainty as to what constitutes excessive pricing in Canada. This, in turn, may improve the investment climate for the biotechnology industry in Canada, while permitting the PMPRB to carry out its mandate under the *Patent Act*.

Subject to the foregoing comment, AMGEN believes that the creation of four levels of therapeutic improvement for new patented medicines versus the three levels employed under the current Excessive Price Guidelines, represents a positive development. The creation of four levels of therapeutic improvement provides recognition that that there are medicines that represent moderate improvement over existing medicines which should afford patentees more flexibility in its pricing decisions.

The primary concern with the four categories of improvement is the lack of a clear definition of a "substantial improvement" versus a "moderate improvement". The Working Group on Therapeutic Improvement concluded that "it is difficult to quantify substantial improvement versus moderate improvement, versus slight or no improvement" and that this distinction is best left with HDAP which should "set the standard by their decisions". However, setting standards by relying on the precedents set by HDAP is problematic for a biotechnology company like AMGEN which develops medicines for serious and grievous illnesses. In many circumstances, the efficacy and

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safety of current therapies used to treat such diseases have not been demonstrated in large scale clinical trials, nor do these therapies have Health Canada approval to be used in that setting. It is AMGEN's contention that these circumstances would represent a "substantial" therapeutic improvement.

Also, there is no need for further scientific review by HDAP regarding the level of therapeutic improvement if Health Canada has already conducted its assessment and made the determination that a new therapy fulfills an unmet medical need and is granted a priority review. Any new therapy that is granted a priority review by Health Canada should automatically be categorized as a "substantial improvement" or "breakthrough".

Because of the difficulties distinguishing between various levels of improvement and the consequential administrative burden, AMGEN recommends that a single definition of excessive pricing be applied to all new patented medicines, as outlined below. If, instead, four categories of therapeutic improvement are adopted, a clear definition of what constitutes a "substantial improvement" versus "moderate improvement" should be developed prior to implementation. Specifically, any new therapy should be deemed a "substantial improvement" if the efficacy and safety of the comparator(s) have not been demonstrated in phase III clinical trials and if a Health Canada approval has not been granted for the comparator(s). In addition, any new therapy that has been granted a priority review by Health Canada should automatically be considered as a "breakthrough" or "substantial improvement".

Introductory Price Tests

It is AMGEN's position that the price of any new patented medicine should be considered excessive if its price is higher than the prices of the same medicine in all comparator countries and is higher than then CPI-adjusted price of local comparator medicines. This test would determine a level of excessive pricing that is simple and clear for patentees to understand. In addition, it would protect consumers from prices in Canada being the highest in the world and, in the vast majority of cases where local comparators do exist, the price of a new medicine could only be as high as its comparators. AMGEN submits that prices of patented medicines are likely to be kept below this threshold, in any event, to ensure formulary inclusion, given the requirement that value for money be demonstrated to payers. Competitive pressures will also result in prices below this threshold.

Therefore, AMGEN recommends the implementation of a simple introductory price test; specifically, that the price of any new patented medicine should only be considered excessive if its price is higher than the prices of the same medicine in all comparator countries and is higher than the CPI-adjusted price of local comparator medicines.

International Therapeutic Class Comparison Test

AMGEN supports the use of the International Therapeutic Class Comparison Test as a method of dispute resolution between patentees and the PMPRB. However, the Draft Guidelines should state that only medicines that remain under patent protection in other countries may be used in the conduct of an International Therapeutic Class Comparison Test. To compare the price a patented medicine in Canada to that of a generic version

available outside of Canada is an unfair comparison. AMGEN recommends that it be explicitly stated in the Guidelines that only the prices of patented medicines available in other countries be used in an International Therapeutic Class Comparison Test.

De-Linking of the ATP from the MNE Price

The proposal for a de-linking methodology is a positive step forward compared to the current CPI-adjustment methodology. However there are several operational issues associated with the methodology proposed by the PMPRB.

The proposed methodology still links the MNE to a previous non-excessive net ATP; instead, AMGEN supports a true "de-linking" of the ATP and MNE price. A true "de-linking" of the ATP and MNE price requires a change in the CPI-Adjustment Methodology whereby MNE prices in years following introduction of a medicine would be based on the MNE price in a previous year, adjusted for changes in the CPI.

Also, greater clarity is required regarding the definition of a "benefit" that will engage the de-linking methodology. Without a clear definition, patentees will offer benefits without knowing if the Board will accept them for the purposes of de-linking. In addition, fluctuations in ATPs due to the granting and expiry of multiple benefit programs offered to different classes of trade customers in different markets will further tax the resources of patentees who will need to justify these fluctuations and the PMPRB that will need to investigate them. Furthermore, AMGEN points out that many benefits are not offered on a DIN or even single product level basis and that the realization of a benefit often does not correspond to PMPRB reporting periods, which further complicates the application of the de-linking methodology. During recent discussions, Board Staff provided to patentees with several examples of how the de-linking methodology would work, however this limited set of examples is likely far less complicated and much less varied than what is offered to customers in the real world.

Given the issues noted above, the implementation of the de-linking methodology, as proposed, will require AMGEN to employ incremental resources solely for PMPRB reporting purposes. Furthermore, it is expected that the PMPRB will be required to conduct more investigations and hearings, due to the complexity of what has been proposed.

Ideally, implementation of a true de-linking methodology would be most appropriate. According to a true de-linking methodology, MNE is unlinked to ATP and the only inquiry is whether the ATP is below MNE (adjusted for CPI), in which case prices are deemed to be not excessive. Subject to the foregoing, if the de-linking methodology proposed in the Draft Guidelines is to move forward, AMGEN recommends that its implementation be delayed until an agreement can be made amongst the PMPRB and patentees on the definition of a benefit, how to report a benefit, and when to report benefits that do not coincide with the PMPRB reporting periods.

AMGEN also notes the PMPRB's decision not to implement a de-linking methodology in situations where the introductory ATP of a medicine is below the MNE. It is when a product is introduced on the market (and prior to formulary inclusion) that the offering of compassionate and support programs is most critical for patients. To penalize patentees

by allowing special introductory programs to exert downward pressure on the MNE, will almost certainly discourage the offering of such programs.

"Any" Market Price Review

There has not been any evidence provided that prices of *new* medicines are excessive when reviewed at the customer class or provincial level. Therefore the provision of an any market price review at the time of launch of a new patented medicine does not seem warranted. As noted in previous submissions, the PMPRB's Discussion Guide released in May 2006 demonstrates that the vast majority of drugs are priced within 5% of the MNE within each market.

In addition, clarity is required as to what markets will be included in an "any" market price review. The Board's position in the Notice and Comments released in August is that it "is important to ensure that introductory prices are not excessive for any class of customer or in any *province/territory"* (emphasis added). However, the Draft Guidelines state "Board Staff will calculate an ATP for each of the three classes of customers (hospital, pharmacy and wholesaler)". Provincial level price reviews are specifically excluded in the Draft Guidelines, and it was communicated by Board Staff in a teleconference with patentees that provincial level price reviews would not be conducted.

AMGEN's position is that the current policy of the PMPRB is sufficient with respect to reviewing prices in "any market", as there does not appear to be excessive pricing when prices are reviewed in this manner. AMGEN does ask for clarification that provincial level price reviews will not be conducted in an "any" market price review. In terms of calculating excess revenues for a particular class of customer, AMGEN supports the calculation being based on the average price across all markets in Canada.

Re-Setting of the MNE

AMGEN notes the omission from the Draft Guidelines of a provision for re-setting the MNE price in the case of a drug being sold under the Special Access Program (SAP), which is a significant deviation from the current Excessive Price Guidelines. No explanation has been given for this change.

The provision in the current Excessive Price Guidelines is appropriate because patentees often receive requests from health care providers and patients to make drugs available under a SAP at no charge prior to drug approval or formulary inclusion. The existing provision recognizes that the inability to re-set the MNE price in these circumstances would force manufacturers to charge the full commercial price on SAP sales, to the detriment of patients. Removal of this provision, coupled with the absence of a de-linking methodology in situations where the introductory ATP of a medicine is below the MNE (see discussion above), will act as a disincentive for the provision of medicines free of charge through a SAP.

The PMPRB has indicated that it will further analyze the implications of a de-linking methodology in situations where the introductory ATP of a medicine is below the MNE. Until such time as such a methodology is implemented, AMGEN recommends that the

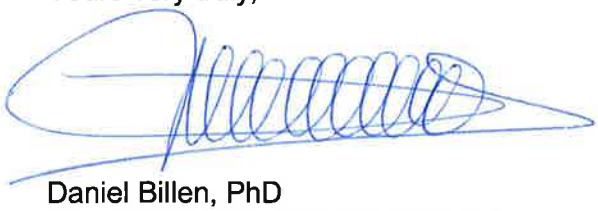
existing provision on re-setting the MNE prices of drugs sold under SAP be reinstated in the Guidelines.

Conclusion

The changes to be effected through the Draft Guidelines are wide -ranging and will increase the bureaucratic burden on patentees to the point that additional human resources will need to be employed, along with extensive modifications to existing financial reporting systems in order to meet with the new reporting obligations. In addition, greater clarity is required in the Draft Guidelines, particularly with respect to the de-linking methodology and the definition of the levels of therapeutic improvement. It is anticipated that there will be an increase in the number of investigations and hearings as both patentees and Board Staff will be forced to work without clear guidance on the reporting of benefits using the de-linking methodology and what constitutes a "substantial" versus "moderate" improvement for newly introduced patented medicines.

It is our hope that you will delay implementation of the Draft Guidelines to permit further consultation with stakeholders to address the issues noted in this letter. We look forward to your response, and to working with the PMPRB to ensure that changes to the Draft Guidelines respect the PMPRB's mandate under the *Patent Act* and provide the biotechnology industry a clear understanding of the regulatory framework it is to work under.

Yours very truly,



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