

Feedback – PMPRB meeting Dec 3 2019

Some of the suggestions discussed below are not with respect to PMPRB but other aspects of the drug regulatory and reimbursement system in Canada. However, unless systemic change can be made to the system as a whole, the PMPRB will be unable to have the tools that it needs to actually regulate prices. The rapid rise in the cost of EDRDs is really an emergent situation (consider the opportunity costs for upcoming drugs such as edavarone and Zolgensma (and many other upcoming gene therapies). These costs are capable of derailing entirely the public funding system.

Many of the proposed changes are positive including changing the basket of comparator countries, including economic impact from sales and also some assessment of value in pricing. However, for EDRDs, these changes may not have the desired effects for several reasons:

1. For rare diseases, “opportunity cost” for EDRDs as averaged over total health care expenditures is always low for individual drugs due to the small number of patients on them. Thus, the proposed revisions regarding pharmacoeconomic value and market size will not result in price reductions
2. Recommendations like “reimburse with substantial price reductions” are commonly seen in CADTH evaluations for EDRDs but, for EDRDs, the “substantial reduction” could be 98%! This is simply not feasible. Similarly, putting a ceiling of 1.5X cost effective price would essentially eliminate access to any of the EDRDs, even those that work well.
 - a. In the event that these “substantial” price reductions are not obtained and thus the drug is not available for reimbursement by public plans in Canada, the timing of the pCPA negotiations (which are done after the drug receives NOC) precludes drug plans from obtaining product from other markets which may be cheaper.
 - i. There are precedents for this in other countries (UK, Netherlands) who obtain some drugs with orphan indications (Ammonul, Remicade, Humira etc) at much cheaper prices from other sources (e.g. South Korea)

Possible suggestions for systemic changes specific to EDRDs:

1. For EDRDs, rather than have a horizontal linear process (Health Canada then CADTH/INESS then pCPA then Pmprb review), the process should be vertical with simultaneous evaluation by all parties. Thus, Health Canada should not issue NOC until such time as it is determined a price that is manageable for the public health plans can be obtained. This would allow then for options to obtain drug from other markets if satisfactory price negotiations cannot be completed
 - a. Obviously, doing simultaneous evaluation is complex and cannot be done for all drugs so criteria for doing simultaneous evaluation would be needed
 - b. An alternative solution to the simultaneous evaluation approach is to amend the Special Access Programme such that alternatives available under the SAP remain available (at

least in the event that satisfactory price negotiations cannot be completed) to allow for import of drugs from less expensive sources

- i. A good example of this problem is the drug ProCysbi for nephropathic cystinosis. The previous product (Cystagon) was an SAP drug and available ~\$8000/year; when Health Canada approved ProCysbi (same active agent but a sustained release form), Cystagon was no longer available through SAP so there was no alternative but to use Procysbi despite the fact that the price/patient went up >30fold.
2. Any drug which expands its indications should be subject to review again as, with an expanded market, the price should come down. This would prevent the current process of “salami slicing” wherein a drug is brought to market for a rare indication and then those indications are progressively expanded (e.g. eculizumab)
3. Canada should develop “crisis” legislation that allows production and/or importation of drug outside an existing patent if excessive prices prevent provision of the drug to Canadians if there are not alternative drugs available. This is an option of last resort but is potentially a “stick” for negotiations that are not resolved through traditional channels.
 - a. The UK has such legislation and it was a tool used in the 2019 negotiations over a disputed cystic fibrosis drug that ultimately resulted in an agreement for reimbursement
4. HTA assessments need to develop tools proactively to address changes in therapeutic strategies for rare diseases including:
 - a. N of 1 trials – this area is likely to rapidly increase in the era of personalized medicine. Evaluation of the “platform” by which the individualized medication is developed rather than the each individual drug which is tailored to an individual mutation (e.g. Woodcock and Marks *N Engl J Med* 2019; 381:1678-1680)
 - b. Gene therapy – assessment both of efficacy and the issue of value over time given that most of the gene therapy trials are quite short so an alternative payment structure will be required if reimbursed which does not pay the entire cost up front as longer term efficacy is not known
5. There are numerous examples of political overrides of otherwise scientifically sound decisions not to reimburse a drug (e.g. MPSIV and others). In order to provide perspective which might help elected officials make difficult decisions, it may be useful to have a standing public panel of educated individuals who could provide perspectives on what the public would find reasonable. In effect, this panel would be like a “grand jury” with education in the area of rare diseases that allows them to put individual decisions in context and hopefully with members from a broad based background.
6. There is a need to review processes which allow for companies to obtain DIN numbers for products which were not previously considered drugs and then raise the price by 1000 fold or more (for example the provision of a DIN number for Cystadane). There are many products for rare diseases that are at risk of this approach including thiamine, riboflavin, biotin etc