Submission re Life Saving Drugs Programme

Introduction

I welcome the opportunity to provide a personal insight into the way I have assessed the Life Saving Drugs Programme (LSDP) as an operation since my involvement as a member of the Gaucher Disease Advisory Committee (GDAC) from 1996 and as inaugural chair of the PNH Disease Advisory Committee (PDAC). In addition, I have the perspective of a treating physician in both of these disease groupings, having the largest numbers of patients with treatment facilitated by the LSDP on both of these programs in the region.

My views are well known: I have been a speaker and educator both nationally and internationally about both of these diseases and have been an almost outspoken advocate for the LSDP every time I have spoken. When describing the Programme overseas, the principles on which it was based have raised envy amongst my colleagues in a number of jurisdictions, particularly in the United States, Canada and a number of South East Asian countries. I believe that the funding mechanism and administration, as it was prior to May 2014, represented world class management of rare diseases in a nation where few if any true Centres of Excellence in rare diseases exist. Even as a treater with relatively large numbers of patients, I appreciated the views of my colleagues on the committees. They frequently assisted in management decisions and improved the care and optimised the outcomes for my patients. I am sure that this was even more so for physicians that looked after relatively few patients (in Gaucher disease, the median number of patients per treater was one, when I last was able to look). I always felt that the Disease Advisory Committees represented the finest of clinical decision making in the management of ultra-rare diseases that was possible.

The central oversight of data enabled management of the enzyme shortage resulting from the Genzyme production events, in a world leading and equitable manner in which few patients with Gaucher disease were permanently clinical disadvantaged. This required almost day-to-day involvement of the committee and resulted in an unprecedented ability to document (and publish in the international literature) the process and outcome. This in itself, was a positive advertisement for the LSDP.

Arguments for disbanding the Disease Advisory Committees

I understand that there may have been a perception that the LSDP committee structure was a cumbersome, expensive and inefficient way to manage the approval, maintenance, disposition and advisory function of the LSDP. In particular, the sitting fees for the committees and the vigilant control of ordered and dispensed medications may have become regarded unnecessarily expensive and perhaps better done without clinical oversight using a mechanism similar to the Highly Specialised Drug Program (HSDP, S100) of the Pharmaceutical Benefits Scheme (PBS). I also understand that there may be a departmental desire or even requirement to merge the functions and funding of the LSDP into the general PBS mechanisms to unify oversight (particularly financial) over all pharmaceutical funding for purposes of presumed efficiency and uniformity.

Arguments against disbanding and for strengthening the previous LSDP structures

Costs of the committees

For some years, members of the Disease Advisory Committees have been paid sitting fees for their diligent work in managing the various programs. I am aware that there is required an administrative backbone for these committees which has its own expense to maintain. Speaking personally and based on discussions with members of the committees on which I sat, the work we did exceeded the payments logarithmically and were never the primary (or even secondary) motivation for participation or doing the work. Every individual to whom I spoke would have willingly worked on these committees with no payments. We all recognised the national importance of the work we did and in particular the clinical supporting role that was provided to practitioners with few patients under their direct care. Particularly for the PNH Disease Advisory Committee, the work that was done by the committee in rapidly transitioning patients onto the program with a January 1 deadline over the Christmas period, far exceeded the hours nominally paid and made the institution of the program efficient and rapid for the staff in Canberra. We recognised how important this was and effectively gave up the end of year break and holidays willingly. In addition, PDAC was able to turn around urgent applications in under 48 hours, further reflecting the unpaid out-of-session work the members of the committee willingly performed. That is the nature of medical experts working in these fields: recognition of the importance of the optimal care of patients with rare diseases and a disregard for compensation for such work.

The administration of the LSDP was much more cumbersome in the early days: everything was paper-based and kilograms of materials were distributed to the members multiple times per year. The office staff entered data into registries directly and this too was labour intensive. In recent years, data have been provided by physicians on spreadsheet templates and aggregated data have been provided by the office to Committee members electronically. This must have cut down the workload centrally dramatically.

Uncontained expenses of the program

I speak without access to actual financial data but I do know that in Gaucher Disease, the projected numbers of patients at the very start of the program in the 1990s have never been reached, even today. In addition, the Gaucher Disease Advisory Committee worked tirelessly to minimise dose of enzyme to the patients to the minimum effective dose, effectively minimising costs. As a member of that committee for many years. I also know that the decision to manage the program this way, was done without any specific instruction from the Department but was made possible by central clinical oversight of individual patient data and rapid response to clinical changes. We have the lowest median dose of enzyme administered in the world for Gaucher Disease (or at least in those parts of the world where drug supply is appropriately funded). The dose is less than the minimum labelled dose and approximated (the last time we had data available to look at) 20U/kg/2 weeks. The labelled dose is 30-60U/kg of both approved enzyme products. Without the oversight of a clinical committee, functioning as did the Gaucher Disease Advisory Committee, it would be clinically appropriate for physicians to prescribe the maximum labelled dose to most or all patients, effectively increasing the cost to Government by a factor of 3. Physicians would be correct in suggesting that this disease was approved, that the treatment is non-toxic and that maximising dose would reduce the risks of patients deteriorating given the lack of central oversight that a Centre of Excellence (or Disease Advisory Committee) would provide.

Clinical Decision Making Without Clinical Experts

Both the Gaucher Disease Advisory Committee and PNH Disease Advisory Committee regularly made recommendations for dose modifications in individual patients to optimise clinical outcomes and ensure that the large sums of money spent on the pharmaceutical products were put to best advantage for the patients. The nature of rare diseases is that each patient teaches us something new and that individualised and often unpredictable decisions need to be made. This was clearly so in Gaucher Disease and despite the constraints based on the funding model for the treatment of patients with PNH, that committee frequently made recommendations for exceptions that were usually approved by the Ministerial Delegate. There is under the current structure, no possible mechanism whereby regular, longitudinal assessment of these patients is possible and this would be less so under a HSDP process.

Dangers of incorporating the LSDP into the PBS Highly Specialised Drug Program.

Haematologists in particularly are very familiar with the HSDP process managed through the Tasmanian office of Medicare. This program is managed through an application and follow-up process based on tick boxes, data provision and relatively slow turn-around time except for those few agents that have transitioned to telephone authority.

The system is "*gameable*" by physicians in order to maximise the chances of patients in need receiving subsidised medications. While wholesale fabrication of data must be rare, it is possible in some situations to provide data limited to the requirements of the scheme that do not tell the whole clinical picture and enable access where in reality, if all facts were made clear, a patient may not qualify.

The system is *rigid* at times to the point of producing detrimental outcome for patients. A personal experience is of a patient I still care for with multiple myeloma who was treated with Velcade under S100 whose therapy was ceased because of neurotoxicity. Retreatment with the agent was not permitted at the time but subsequently became possible for patient who had achieved a strictly defined biochemical partial remission with initial therapy. My patient had a reduction of the marker protein to 53% of the baseline level, not quite achieving the 50% required by the program for retreatment. Despite multiple well-argued submissions by me that this patient, whose renal function was rapidly deteriorating would end up on chronic dialysis without intervention with the drug, all of my applications were rejected because of the rigid interpretation of the numbers. The patient's life is now miserable on dialysis which, while funded through a separate mechanism, has cost the community dearly in terms of funds and resources. Had a Disease Advisory Committee or something similar, been following this patient longitudinally, I am quite sure that the clinical outcome would have been different.

I did not describe this clinical vignette to recommend a change to the S100 administration scheme but more to show what could happen to the management of patients with diseases far less common than multiple myeloma

There is also the potential for real clinical risk that patients who are not specifically mentioned in the guidelines but were well known and discussed in the Committees will suffer adverse events without committee input. Examples that have been dealt with by committees but may lack a mechanism for discussion in a different environment include:

- patients with PNH not meeting eligibility criteria for funded eculizumab who require treatment through pregnancy and may be able to stop after delivery;
- patients on eculizumab treatment for PNH who require dose increases during and after pregnancy;
- patients with type IIIB Gaucher disease.

Potential Personal Conflicts of Interest

Yes, I have undertaken education activities and given advice to all companies involved in Gaucher Disease and PNH drug marketing. The dissolution of the Disease Advisory Committees has freed up a significant amount of time for me but despite this, I remain a strong advocate for their reinstitution. In addition, the stated rationale for disbanding the committees, namely that I (and my colleagues) would be able to participate in this review more freely. I can state without reservation, that the opinions I express in this submission would have been identical had I still been a committee member and chair.

Personal Recommendations

I believe that the LSDP is (and most certainly was) a jewel in the crown of the Australian healthcare delivery system and should not be disbanded but rather strengthened. The rest of the rare-diseases world would look on us with bemusement if we disbanded the best management scheme for rare disease on Earth.

I recommend that

1. The disease advisory committees be reconstituted to evaluate every patient on application and longitudinally and thereby provide expert clinical support to the LSDP.
2. The chairs of these committees be charged with the responsibility to maintain oversight of outcome data to ensure appropriate use of rare medications
3. The committees be given a voice into changes in the management of these patients over time, based on follow-up data analysis
4. The Department regards these committees as partners in the management of ultra-rare diseases
5. The current programs NOT be incorporated into the HSDP of the PBS as there are clinical (and possibly financial) risks in such a move.

The primary aim of any change to the LSDP should be improving the care of these patients and the appropriate expenditure of public moneys on expensive treatments for rare diseases. I have argued that strengthening the LSDP rather than its weakening or disbandment is vital for the future of the rare disease space and the preservation of the most efficient and well managed part of the health system in Australia.

October 25, 2014

Professor Jeff Szer AM B Med Sc MB BS FRACP
Professor/Director, Department of Clinical Haematology and BMT Service
The Royal Melbourne Hospital VIC 3050