MEDICINES Australia
BETTER HEALTH THROUGH RESEARCH AND INNOVATION

10 November 2014

PBS Post-Market Review team
Department of Health
MDP 900
GPO Box 9848
CANBERRA ACT 2601
Via email to: PBSpostmarket@health.gov.au

Dear Sir/ Madam

RE: THE POST-MARKET REVIEW OF THE LIFE SAVING DRUGS PROGRAMME

Medicines Australia represents the research-based pharmaceutical industry in Australia. Our members make a significant and important contribution to improving health outcomes for Australians and supply over 80% of the prescription medicines market, including some of the medicines currently funded through the Life Saving Drug Programme (LSDP) and subject to the Post-Market Review of the LSDP (herein, "the review").

Medicines Australia welcomes the opportunity to provide comment on the review and welcomes the timely evaluation of the LSDP as there is a need to review the access and equity considerations of the programme to ensure patients with rare and life threatening diseases receive access to much needed medicines. In conducting this review, the Government should remain cognisant of the ethical and evidentiary dilemmas encountered when considering the reimbursement of medicines for rare and ultra-rare diseases, including the limitations of applying stringent cost-effectiveness criteria to such therapies.

Medicines Australia recognizes that the absence of the LSDP or an equivalent funding mechanism for rare disease therapies in the future would provide a disincentive for pharmaceutical companies to bring orphan or ultra-orphan medicines to patients in Australia, and indeed would discourage R&D initiatives into rare and life threatening diseases in Australia.

Medicines Australia will not provide specific commentary against each and every Term of Reference (ToR) for the review. However, Medicines Australia will address the issues that should be considered during the review. In doing so, Medicines Australia makes three overarching recommendations to the review:

1. the review should focus on providing patients with equitable and timely access to therapies for rare and life threatening diseases and should not be focussed on cost containment;
2. the review outcomes should acknowledge the significant challenges in identifying therapies to treat rare diseases and the obvious evidentiary barriers facing sponsors when developing these treatments and seeking appropriate funding to ensure patient access; and
3. the Department of Health should follow consistent, rigorous and transparent processes for the review and for all post-market reviews.

The review

Medicines Australia acknowledges that the Terms of Reference (ToR) for the LSDP review seems to conflate two separate reviews:

a) a policy review of the LSDP and settings to enable appropriate, evidence based access to rare disease treatments (equity principles and criteria); and
b) a post-market review of all products currently provided under the programme (e.g. review of clinical efficacy, safety data and value for money etc).

In that context, Medicines Australia welcomes a review of the current policy settings to provide access to rare diseases treatments. A review of the administration, purpose, ethics and equitable access needs for the funding of

rare disease therapies should take into account the range of views of all stakeholders to ensure that Australians with rare diseases are provided access to the best medicines available to them. Medicines Australia notes that the ToR do not explicitly include attention to the criteria and conditions for funding of medicines on the current LSDP. Medicines Australia recommends that the review scrutinise the current criteria to ensure they remain fit for purpose.

Regarding the review of the products currently provided under the programme, Medicines Australia welcomes the Government's stated commitment to ensure continuity of access to treatments currently covered by the LSDP during the review for existing and new patients[1]. Patients currently receiving treatment through the LSDP should also have confidence that access to medicines currently on the LSDP will continue following the review.

Medicines Australia is pleased by commitments to that end from the Government. However, several previous post-market reviews have resulted in arbitrary pricing actions for medicines, which can, in turn, threaten access to existing and future treatments, therefore Medicines Australia encourages further commitments to ensure that any recommendations following the review support, not threaten, access by limiting any pricing actions.

1. The review should focus on providing patients equitable and timely access to therapies for rare and life threatening diseases and should not be focussed on cost containment

Medicines Australia acknowledges that the LSDP has provided an important medicinal safety net for many Australians with rare and life threatening conditions whose clinical needs are not met by medicines or other treatment modalities otherwise available through the Pharmaceutical Benefits Scheme (PBS), Medical Benefits Scheme (MBS) or public hospital system.

Medicines Australia acknowledges that a review of the LSDP was undertaken in 2009. The purpose of that review was intended to examine the LSDP with a view to establishing consistent and rigorous procedures and to ensuring the sustainability of the program. The terms of reference for the 2009 review specified that it was to be conducted with reference to the Government's Expenditure Review principles of appropriateness, effectiveness, efficiency, performance assessment, integration and strategic policy alignment.

There was a clear focus on cost in that review, which led to tightened criteria for the listing of medicines on the programme, and resulted in further limiting access to therapies for rare diseases in Australia.

A review of the LSDP in 2014 should not focus on cost, but should instead provide a safeguard that a programme such as the LSDP is equitable and fit for purpose to meet the needs of Australian patients and broader society now and into the future.

Since the 2009 review of the LSDP, only two new therapies have been approved for listing on the LSDP.

- Velaglucerase alfa (Vpriv®) for Gaucher Disease (type 1) was funded on the LSDP in March 2012.
- Eculizumab (Soliris®), for Paroxysmal Nocturnal Haemoglobinuria (PNH) was listed on 1 January 2011.

Access to therapies for rare diseases faces a number of barriers, which are outlined in more detail in the next section of this submission. Medicines Australia is concerned that the current LSDP program does not comprehensively address the needs, and the range of issues affecting patients with rare diseases. Other provisions, such as the '*Rule of Rescue*' also fall short of their objectives to provide access to medicines where cost-effectiveness is uncertain but clinical benefit and clinical need are high. While some companies are in a position to provide compassionate access to medicines, this is only feasible in certain circumstances, and should not be considered an alternative to publicly funded access.

Reforms to the PBS have put expenditure on a sustainable path and created headroom to enable further access to therapies, including those for rare diseases. Expenditure on the LSDP was $80 million in 2013-14[2], and the medicines component of the PBS was $9,148.5 million[3]. In August, the Parliamentary Budget Office forecast growth in PBS spending will slow to 0.3 per cent annually out to 2024-25[4]. Industry has contributed to the

[1] http://www.pbs.gov.au/info/reviews/life-saving-drugs
[2] This figure excludes funding for the Herceptin program which was established as a special fund beyond the LSDP. Advice to industry indicates that the annual cost of the core LSDP is around $80 million per annum.
[3] Australian Government Expenditure and prescriptions twelve months to 30 June 2014
[4] http://www.aph.gov.au/About_Parliament/Parliamentary_Departments/Parliamentary_Budget_Office/reports/Projections_of_Government_spending_over_the_medium_term

sustainability of these programmes through significant reforms, in particular the price disclosure reforms which will deliver in excess of $20 billion of PBS savings to government from 2007-18[5].

Regarding ToR 5: Assess the value for money of the medicines subsidised on the LSDP by evaluating the benefit of each drug's treatment outcomes, including in terms of quality of life achieved through the programme, and their cost.

Medicines Australia requests greater transparency regarding the methods that will be used to assess the value of medicines currently listed on the LSDP. Medicines are listed on the LSDP instead of the PBS because their Incremental Cost Effectiveness Ratio (ICER) has not been deemed cost-effective. It is highly unlikely that the review alone could lead to medicines for rare diseases achieving cost-effectiveness. If the purpose of this ToR is to explore removal of certain medicines from the LSDP this should be explicitly stated on the review webpage and stakeholders should have the opportunity to respond to this aim. Additionally, if the Department is intending to use this review to apply new and unexpected price reductions, this should also be made transparent. Price reductions imposed without appropriate safeguards and consultation may significantly impact on the viability of the sponsors concerned, and affect their ability to continue to provide therapies to Australian patients.

Cost-effectiveness is an important and legitimate tool, and underpins the payer's "value for money" premise that is the foundation for the PBS approach to Health Technology Assessment (HTA) and reimbursement decision-making. However, Medicines Australia reiterates its position that cost-effectiveness should not be applied as a criterion for funding on the LSDP.

2. The review outcomes should acknowledge the significant challenges in identifying therapies to treat rare diseases and the obvious evidentiary barriers facing sponsors when developing these treatments and seeking appropriate funding to ensure patient access

Medicines Australia recommends that specific but not necessarily separate processes be applied in the evaluation and funding of medicines to treat rare and life threatening diseases. To that end, the PBAC is the appropriate body to continue the HTA of therapies seeking inclusion on the LSDP. However, the review must ensure the *criteria for funding a drug on the LSDP*[6] is sufficiently flexible to allow timely access to medicines that treat rare diseases, whilst balancing the Government's need to ensure continued sustainability of the programme. To that end, and to ensure that the LSDP remains responsive to the needs of Australians, no cap should be placed on total LSDP expenditure.

Currently, to be funded through the LSDP, a new therapy must meet all eight criteria, and if in the view of the PBAC it does not sufficiently meet one of the criteria, access is denied to patients who would likely receive a clinical benefit. The most contentious change to the LSDP funding criteria occurred in 2010 with the additions to Criterion Four, which includes a requirement that *there is evidence acceptable to the PBAC to predict that a patient's lifespan will be substantially extended as a direct consequence of the use of the drug*[7].

In line with the National Medicines Policy, the process for evaluating therapies for rare diseases should incorporate the broader value of treatment to a patient suffering rare disease, beyond cost-effectiveness. The benefits of patients avoiding catastrophic health expenditure and costs of care, as well as their increased economic activity are overlooked in the evaluation of funding new therapies. Thousands of Australians suffering from rare diseases cannot access their therapies through the PBS, rendering the economic costs to patients with rare diseases inequitable. A utilitarian approach to universal health care will never meet the needs of all Australians with rare disease. The system needs to be accompanied by a mechanism that protects the vulnerable not covered by a universal system, in a more targeted manner, that is, a more flexible understanding of cost-effectiveness.

The following points must be considered when reviewing the stringent criteria applied when assessing medicines for funding on the LSDP; the equity of access to therapies for rare diseases; and when conducting the broader review:

- Rare diseases, by definition, are suffered by a small number of patients, and one rare disease often shows a wide variety of different symptoms, making identification difficult and drug discovery often opportunistic;

[5] Sweeney, K, Impact of Further PBS Reforms, Centre for Strategic Economic Studies, Victoria University, March 2013
[6] All 8 criteria available via http://www.health.gov.au/internet/main/publishing.nsf/Content/lsdp-criteria
[7] http://www.health.gov.au/internet/main/publishing.nsf/Content/lsdp-criteria

- Limited prior research means that the biology of a rare disease is often poorly understood, limiting the applicability of traditional clinical trial methods, such as animal or computer modelling. This reduces the ability to fully utilise prior research in the discovery phase of a rare disease;
- Once identified, developing a medicine through clinical trials is further complicated by small numbers of research participants, geographical spread and a mis-diagnosed or under-diagnosed patient population[8];
- Gold standard clinical trial designs, such as direct randomised control trials are most often not feasible, creating issues on the acceptability of data from trials, acceptability often differs across jurisdictions;
- Clinical trials for rare disease therapies create moral and ethical issues, i.e. continuing the placebo controlled arm may not be ethical where there results show significant benefits from the medicine being tested. In addition to this, patient switching can distort the measurement of the effects; and
- The very small patient numbers associated with rare diseases make requirements to demonstrate statistical significance of improved survival unfeasible and unreasonable. Alternative approaches to modelling the estimated benefit of treatment should be accepted in this context, with verification of modelled outcomes via collection of registry data, possibly with the co-operation of multiple countries.

Regarding ToR 2: Review emerging clinical treatments and diseases, including those that identify sub-groups by molecular target, which could potentially seek subsidisation through the LSDP in the future.

Industry is well placed to assist with horizon scanning activities to determine potential therapies that may seek funding through the LSDP. This would also encourage earlier engagement with the Department on possible therapies, to facilitate streamlining of the evaluation and listing process.

3. The Department of Health and should follow consistent, rigorous and transparent processes for this review and for all post-market reviews.

Medicines Australia continues to support initiatives to ensure that medicines are prescribed, dispensed and used in a responsible, appropriate and ethical manner. Medicines Australia continues to maintain that any post-market review should have a clear focus on Quality Use of Medicines, not on arbitrary pricing measures.

Medicines Australia acknowledges that important steps have been taken towards improving the post-market review process, in addition to working towards producing an appropriate framework for their initiation and conduct through the Access to Medicines Working Group (AMWG). Medicines Australia is confident that the Department of Health's proposed framework and guidance document will bring more predictability and transparency to the post-market review programme.

Medicines Australia acknowledges that process improvements have been integrated into this review, including:

- Consultation on the terms of reference for the review;
- longer timeframes for the development of submissions; and
- publication of a review specific webpage, including a list of the review Reference Group.

Despite these positive steps, there remains some deficiency in the process for this review. To that end, Medicines Australia welcomes transparency of the following on the review webpage:

- Identify (publicly) the trigger(s) for the review;
- Identify some possible outcomes for the review (e.g. changes to policy; changes to access, etc);
- Outline further consultation steps for stakeholders and sponsors including dates and time for stakeholder meeting(s). Given the complexity and scope of this review, it may be necessary for several stakeholder meetings throughout the review process, particularly for sponsor companies with medicines on the LSDP or likely to have submissions to list a therapy for a rare disease, in addition to further consultation on the draft report of the review; and
- Provide regular updates on the progress of the review on the review webpage, including indicating timing for further consultation and the release of the draft report.

[8] A survey in the UK found that on average it takes 5.6 years and 2 to 3 misdiagnoses before a patient with a rare disease receives a proper diagnosis - Rare Diseases Impact Report: Insights from patients and the medical community, Shire (2013).

In addition to this, when acting on the advice of the PBAC following a post-market review, the Government should:

- Act in accordance with existing PBS policy and guidelines, and the National Medicines Policy;
- Utilise the most appropriate policy levers (noting that price cuts to medicines are unlikely to address findings of inappropriate prescribing/utilisation);
- Consider the administration of outcomes with sufficient time allocated for sponsors and other stakeholders to consider their positions and respond;
- Advise affected stakeholders of all the options available to them, including a mechanism for independent review or dispute resolution.
- Consider international best-practice in the evaluation of therapies for rare diseases and for breadth of therapy coverage.

Medicines Australia considers that other ongoing procedural and policy concerns with the post-market review programme and framework are currently being adequately addressed through the AMWG.

Conclusion

In conclusion, Medicines Australia contends that the Department should follow consistent, rigorous and transparent post-market review processes for all reviews. The overall intent of this review remains ambiguous and it is still apparent that this review conflates two separate and distinct analyses. Medicines Australia is of the view that the review of the programme should be separated from the review of the products currently funded through the programme.

Medicines Australia also recommends that this review be focussed on providing equitable and timely access to therapies for rare and life threatening diseases and should not be focussed on cost containment.

Finally, the review outcomes should acknowledge the significant challenges in identifying therapies to treat rare diseases and the obvious evidentiary barriers facing sponsors when developing these treatments and seeking appropriate funding to ensure patient access

Should you have any questions about this submission, please do not hesitate to contact me on (02) 6122 8525 or by email at Elizabeth.deSomer@medicinesaustralia.com.au. In the alternative, you may wish to contact Mr Sam Develin, Reimbursement Manager on (02) 6122 8507 or by email at Sam.Develin@medicinesaustralia.com.au.

Kind regards,

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