Government of **Western Australia**
Department of **Health**

Post-market review of the Life Saving Drugs Programme

Office of Population Health Genomics Perspective

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Introduction

The post marketing review of the Life Saving Drugs Programme (the review) represents an important discussion and a significant opportunity for Australia to develop a sustainable system for orphan drug access. The review will enable Australia to draw on the experiences of European Union member states (EU), the United Kingdom (UK), Canada and the United States of America (US) to develop international best-practice frameworks and orphan drug policies. Importantly, the current consultation process will ensure that the review draws upon the wealth of experience within Australia. In line with this, the following is a response to the terms of reference of the review from the Western Australian Department of Health, Office of Population Health Genomics.

Very few rare genetic diseases (RD) have an effective treatment and almost none are curable; most are also complex, chronic, debilitating and progressive. As such, RD have a huge impact on the lives of people living with a rare disease, the wider community and the health care system [1-3]. Further, studies have shown that people living with a rare disease, their carers and families, experience significant health, social, financial and emotional stress not associated with more common diseases [4-6].

Orphan drugs are defined by the Therapeutic Goods Administration as a medicine, vaccine or *in vivo* diagnostic agent that is intended to treat, prevent or diagnose a rare disease; or is not commercially viable to supply, treat, prevent or diagnose another disease or condition [7]. They are costly for pharmaceutical companies to produce and there is only a limited market. This means they are often extremely expensive to purchase. This cost often prohibits them from being listed on the Pharmaceutical Benefits Scheme (PBS), which aims to provide timely access to medicines at a cost individuals and the community can afford [8] . In line with this aim, the criteria for receiving funding under the PBS includes a measure of cost effectiveness, which most orphan drugs do not meet.

Given that orphan drugs may continue to fail to meet the cost effectiveness criteria within the PBS, the Life Saving Drugs Programme (LSDP) is vital to ensuring equity of treatment for people with a rare disease. The LDSP provides subsidised access, for eligible patients, to expensive drugs for rare life-threatening conditions [9]. The LSDP has grown since its establishment in 1995 from providing access to treatment for one rare condition, to providing access to seven orphan drugs treating nine rare diseases [10]. Currently, the LSDP is a program without a legislative basis and requires approval by Cabinet to subsidise additional orphan drugs. Recent precedent suggests that the LSDP criterion of the orphan drug being life-saving has been applied stringently without consideration of potential to prolong or improve quality of life, preventing new treatments from being funded through the LSDP [11]. Anecdotally there are concerns with the transparency of the LDSP process and its sustainability.

The review is an important step to strengthen the processes around orphan drug availability in Australia. It is essential that a mechanism remains in place, post this review, that will ensure vulnerable patients with a rare disease do not fall through gaps in the Australian health system. In doing so, this review, and the development of a transparent framework for orphan drug access, will support a sustainable LSDP and ensure orphan drugs will be affordable for the vulnerable Australians who need them.

Responses to terms of reference

Review the clinical effectiveness and safety of medicines currently subsidised through the LSDP

This submission will not directly respond to the clinical effectiveness and safety of medicines currently subsidised through the LSDP.

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

Examination of emerging treatments that may be included in the LSDP is an important aspect of the review. This key issue will not be addressed in the current submission as other organisations are best placed to provide information in this area.

Conduct an international comparison of subsidisation of drugs for rare diseases and the definitions for a rare/ultra-rare disease

International definitions of a rare disease vary but most include reference to the low prevalence of rare diseases in the population. For example, in the US a rare disease is defined as a condition that affects fewer than 200,000 people nationwide (approximately 1 in 1,500) [12]; in Japan a rare disease is defined as one that affects fewer than 50,000 patients nationwide (approximately 1 in 2,500) [13], while in Australia a rare disease is defined as affecting no more than 2000 people (approximately 1 in 10,000) [14].

Using a solely numerical description to define a rare disease omits other critical elements and misdirects attention from the needs of patients. Most RD are chronic, debilitating, progressive, have no cure and are difficult to diagnose. Further, people living with a rare disease, their carers and families, experience significant health, social, financial and emotional stress not associated with more common diseases [4-6].

It has been proposed that Australia adopts the European Union consumer endorsed definition of a rare disease, which refers to both prevalence and severity of burden [15]. This definition states that RD are “life-threatening or chronically debilitating diseases which are of such low prevalence (1 in 2000 people) that special combined efforts are needed to address them” [16]. Adopting a definition of a rare disease that goes beyond a numerical description has important implications for assessing its cost effectiveness. An Australian orphan drug access framework, that incorporates such a definition, would provide a basis for funding criteria that consider burden of disease as well as cost effectiveness.

While an international comparison of the subsidisation of drugs for rare diseases is not specifically addressed here, it is recognised that the cost of orphan drugs to treat RD are significant. However, it is argued that patients with a rare disease should be entitled to the same quality of treatment as patients with more common diseases [17]. Specifically, people living with a rare disease should be able to access, at an affordable cost, a drug that could lengthen and/or improve the quality of their life; similar to people who have a chronic condition who can access affordable treatments. Therefore, there is an ongoing need for a mechanism to subsidise orphan drugs.

Compare the subsidisation and equity principles of the PBS and the LSDP

Treatment of a rare disease can often be complex and costly. Despite this, European governments have argued that patients with a rare disease should be entitled to the same quality of treatment as other patients [17]. Following this principle, it is essential that patients with a rare disease have timely access to the best therapies available, including affordable access to orphan drugs that will enable them to live the best life possible.

The Australian Government subsidises an extensive range of drugs under the PBS [8]. Funding criteria for the PBS is based largely on cost effectiveness. However, the PBS also includes assessment of other factors, where needed, including severity of disease, comparative health gain, patient affordability in the absence of PBS subsidy and presence of effective alternatives [18, 19].

The PBS can also apply a “rule of rescue” where funding applications are marginally outside acceptable cost effectiveness thresholds and meet four criteria. These criteria are: 1) no

alternative exists in Australia to treat patients with the specific circumstances of the medical condition, 2) the medical condition is severe, progressive and expected to lead to premature death, 3) the medical condition defined by the listing only applies to a very small number of patients and 4) the proposed drug produces a worthwhile clinical improvement sufficient to qualify as a rescue for the medical condition. Due to their high prices, the majority of orphan drugs fall far outside traditional cost effectiveness standards and therefore do not qualify for the "rule of rescue".

In the current system, medical products that do not receive approval for funding under the PBS may be recommended for consideration under the LSDP. The LSDP aims to provide subsidised access for eligible patients to expensive and lifesaving drugs for serious and rare medical conditions [9]. Criteria for making a recommendation to fund under the LSDP have been developed, however final approval of funding must be approved by Cabinet [9, 10]. Recent precedent suggests that the criterion of being life-saving has been applied stringently without consideration of potential to prolong or improve quality of life, preventing new treatments from being funded through the LSDP [11].

This review provides an important opportunity to recognise that health benefits from orphan drugs can only be realised if patients are able to access them. Currently, a gap exists between what can be funded under the PBS due to cost-effectiveness thresholds and the strict criteria for funding under the LSDP. A mechanism is needed that better meets the needs of vulnerable patients, such as those living with RD.

Balance is needed to ensure that subsidisation of drug therapies is not based solely on disease rarity, cost effectiveness or a drug being lifesaving, but rather on better responding to the unmet needs of patients. A survey of 1,000 Western Australians aged 18 years and over provided evidence that this would likely be supported by the public. When asked about government spending on rare disease initiatives, 96% (CI: 94-97) of respondents agreed that patients should be able to access treatments that have been developed. 86% (CI:84-88) agreed that government should pay for expensive rare disease treatments [20]. Similarly, a study of value based pricing criteria in the UK has identified that diseases for which no other treatments are available represent an unmet need and should be prioritised [21]. While it is recognised that the health budget is finite, and that it is not possible to fund every disease and treatment, the current mechanism appears to be overly prohibitive.

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

The value for money of the medicines currently subsidised under the LSDP will not be evaluated in this submission. However, it is important to note that people living with a rare disease, their carers and families, experience significant health, social, financial and emotional stress [4-6]. Therefore, in assessing the value for money of medicines funded through the LSDP it may be of benefit to assess value against the burden of disease on patients as well as by standard cost/benefit analysis.

Drug funding decisions made by governments usually take into consideration a drug's effectiveness and its cost-effectiveness. However, for rare diseases, it is often difficult to conduct clinical trials of adequate sample size to rigorously assess a drug's effectiveness. In addition, orphan drugs are often very expensive and, with little or no confirmatory data on their effectiveness, are rarely found to be cost-effective.

A number of concerns have been raised around funding of access to orphan drugs. Major among these concerns is the high price of orphan drugs, the sustainability of subsidising such prices and the ultimate impact on government health budgets. In Europe, growth in the cost of orphan drugs, as a proportion of total pharmaceutical expenditure, is predicted to plateau by 2020 [22, 23]. This

suggests that fears of the growth in orphan drug expenditure leading to unsustainable cost escalation may not be justified.

Review the administration of the LSDP, including the Guidelines with which the programme is administered for each condition, and assess alternative administration systems

A robust and transparent governance framework to support the LSDP is important. Specifically, there is the need for a strong system to deal with the complex issues surrounding orphan drug access. It is recommended that Australia learn from governance structures in place overseas that assess orphan drugs, to develop a sustainable framework for orphan drug access. Australia should also work to strengthen networks and expertise that exist within the current LSDP.

Under the current LSDP system several Disease Advisory Committees (DAC) monitor and review therapeutic strategies for patients being treated with drugs funded through the LSDP. The advisory groups have worked well as they have the advantage of concentrating expertise at a national level. This allows allowing ongoing monitoring and review of therapeutic strategies for drugs funded through the LSDP [11]. Of particular note is the quality of the experts and the commitment they have provided in the rigorous assessment and review of submissions to the LSDP. The DAC system benefits those patients being treated under the LSDP and also enables centralised data collection which supports optimal use of expensive orphan drug therapies [11]. This approach would sit well in an Australian framework for orphan drug access that used expert assessment to review suitability of rare diseases and orphan drug treatments.

In Canada, a framework has been established for public funding of orphan drugs [24, 25]. Included in the framework is a seven step process that enables consideration of available evidence, patient need and current funding gaps. This framework considers diseases for which it is considered that randomised trials would be impossible to complete within a reasonable period of time, based on current knowledge of the disease. This was done so as to not create a policy that decreased motivation to conduct randomised trials in conditions that were simply uncommon or difficult to study [24]. This framework was designed to address aspects unique to a particular rare disease, while being applicable to dissimilar diseases. The Canadian framework may not directly translate to Australian context; however the approach used may provide a useful basis for the development of Australian orphan drug access policy.

In a time of escalating health costs and other strains on the Commonwealth Budget, reviews of pharmaceutical spending under the PBS have shown the potential for significant savings estimated at approximately 14% of the current PBS budget [26, 27]. This saving far outweighs the cost of orphan drugs currently funded under the LSDP and projected growth in new orphan drugs for specified conditions.

Establish a framework for data collection on rare diseases in Australia and assess how this could function internationally.

A framework for data collection is an essential component of enabling Australia to best respond to RD. A framework is needed that supports national data collection and feeds into international data collection networks. A national approach could look to the work underway in Western Australia to collect robust data on people living with rare diseases.

WA Health has a strong interest in supporting the development and maintenance of patient registries for RD. Patient registries are sets of data collected, stored, retrieved and disseminated in an organised, systemic manner [28], In the context of RD these registries aim to maximise the use of scarce resources. They are important tools for: clinical planning and treatment strategies; public health surveillance; studying disease aetiology, the distribution and determinants of disease; service planning, operation and evaluation; and diagnostic classification [28]. There is a strong need to foster collaborative programs at local, national and international levels, since

research, no matter where it is conducted, will ultimately benefit people living with RD in Australia. In particular, collaboration in the performance of clinical trials is essential to reach a population size which provides sufficient statistical power to undertake studies [29].

In 1999, the European Commission mandated that every Member State in the EU should develop a rare diseases plan or Strategy by 2013, to improve the diagnosis, care and treatment of people living with a rare disease [30]. Further, the European Union Committee of Experts on Rare Diseases (EUCERD), recommended that some form of data collection should take place in all member states and that mechanisms to share data when needed should be in place [31]. EUCERD recommends that [31];

- All registries and data collections should be internationally interoperable as much as possible and procedures to collect and exchange data need to be harmonised and consistent.
- All sources of data should be considered as sources of information for RD registries and data collections, to speed up the acquisition of knowledge and the development of clinical research.
- Collected data should be utilised for public health and research purposes.
- Patient registries and data collections should adhere to good practice guidelines in the field.
- Existing and future patient registries and data collections should be adaptable to serve regulatory purposes, where required.
- Patient registries and data collections should be sustainable for the foreseeable timespan of the registries' utility.

WA Health is involved in a number of collaborations at a national and international level that are aimed at building capacity to share rare disease data collections. One important global program is the International Rare Diseases Research Consortium (IRDiRC) which was launched in 2011. It is an initiative of the European Commission and the US National Institutes of Health. These institutions recognised that there was insufficient data in the US and EU separately, and established a trans-Atlantic agreement to use the combined data of the two continents [32, 33]. Membership to IRDiRC extends beyond Europe and the US, including Australia represented by WA Health [34].

WA Health is also a partner in the RD-Connect project. This project aims to enable progress of the IRDiRC goals by developing an integrated platform that connects databases, registries, biobanks and clinical bioinformatics for RD research. RD-Connect have recently published a charter of principles for sharing bio-specimens and data that recognises the need for global collaboration and harmonized infrastructure to make optimal use or rare disease resources [35].

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