Submission to TGA consultation on Repurposing of Prescription Medicines via online survey

1. What is your name?

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2. What is your email address?

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3. What is your organisation?

The Society of Hospital Pharmacists Australia (SHPA)

4. Which of the following statements best reflect your situation?

(Required)

I represent a group of health professionals/organisations.

5. Can we publish your response?

Yes, I agree my responses can be published

6. What are the critical concerns and challenges/barriers to repurposing medicines in Australia?

The Society of Hospital Pharmacists of Australia (SHPA) is the national professional organisation for more than 5,000 pharmacists, pharmacists in training, pharmacy technicians and associates working across Australia's health system. SHPA members are progressive advocates for clinical excellence, committed to evidence-based practice and passionate about patient care.

SHPA convenes 30 specialty practice groups of pharmacists with specialised expertise in various therapeutic areas and they have informed our submission on this complex area of medicines use for non-approved indications. Our members provide pharmacy care to the most unwell patients in hospitals, who may have exhausted conventional first and second-line therapies, thus requiring the use of off-label medicines and medicines that are not registered in Australia. SHPA members concur with the challenges and barriers outlined in the TGA's consultation paper to repurposing of prescription medicines in Australia.

SHPA members have vast experience with off-label use of medications and acknowledge that it is poorly understood by clinicians and patients. The lack of regulatory approval for these indications impacts on clinician confidence and ability to safely provide evidence-based and transparent care. SHPA's Medicines Information Speciality Practice Leadership Committee members noted that approximately two-thirds of all medicines information inquiries they received in hospitals were in relation to the off-label use of medicines.

SHPA members also raise concerns that transparency, patient consent and relevant documentation regarding the use of off-label medicines, is another area posing challenges with the current system.

SHPA members believe that expanded regulatory approval of medicines used for off-label indications, where supported by evidence or reputable overseas medicines regulators, would be of great benefit to clinicians and patients. Improving this process will result in these medications being used more appropriately where indicated, alleviate practitioner concerns and allow patients to be more informed involved with their healthcare.

SHPA members support a combination of all the options presented by the TGA, as each of them are required to achieve a regulatory environment for repurposing medicines and off-label use of medicines that supports clinicians to provide optimal care to patients. This multi-pronged approach is required to address various

weaknesses along a medicine's regulatory journey that prevent the safer and quality use of currently off-label medicines. Option 1 is required to reduce regulatory burden, Option 2 supports greater access and transparency to off-label medicines use data and Option 3 supports corresponding PBS listing of medicines to support appropriate uptake of medicines where appropriate.

7. Are there additional challenges/barriers to repurposing that need consideration?

Additional challenges or barriers raised by SHPA members were concerning sponsor liabilities and revenue.

At present, the liabilities pertaining to the off-label use of a medication sits with the health practitioner. A prescriber or pharmacist may suggest the use of medicine for off-label indications, where supported by clinical trial data and literature. Sponsors may not be keen to shoulder that risk should they seek approval for expanded indication of medications with what they may believe to be insufficient evidence.

Many low-cost medications that do not have patent protection are commonly used as off-label for unapproved indications, for example domperidone for lactation insufficiency. Despite sponsors' full awareness that these medicines hold regulatory approval for that indication by a reputable overseas medicines regulator, the low-cost and lack of market exclusivity for these medications provides little incentive for sponsors to submit an application to the TGA for expanded indications.

Option 1. Reduce regulatory burden

8. What would be the functional impact of these options in incentivising medicines repurposing?

SHPA members do not believe Option 1 is a suitable standalone option proposed by the TGA, and should be considered along with other options presented. Whilst providing enhanced and structured regulatory support for applicants seeking to repurpose medicines may encourage some sponsors – particularly sponsors of generic medicines that lack regulatory experience with respect to expanding indications – SHPA members do not believe it would significantly alter the current situation in isolation as a regulatory reform.

Furthermore, SHPA members believe this option should not lead to unintended consequences that may limit access to medicines. SHPA members raised concerns regarding the provision of exclusivity periods for new indications of repurposed off-patent medicines. They note that a similar approach in the United States of America, where recent laws state that pharmaceutical drug companies can receive patent extensions to study medicines in children, resulted in a range of unnecessary trials taking place to maximise the exclusivity periods.

Medicines repurposing by the TGA must also be considered in the context of the Pharmaceutical Benefits Scheme (PBS) and the restrictions or lack of restrictions of that PBS medicine's listing, as currently many medicines are prescribed on the PBS inappropriately for off-label use, however their unrestricted PBS listing means this is difficult to detect. Hence, this is why a combination of Options 1, 2 and 3 are required to address this complex issue.

9. Are there additional options for the Department to consider to reduce the regulatory or cost burden for repurposing of medicines?

SHPA members state that where there is product information and evidence available for medications approved overseas for indications that are yet to be approved by the TGA, the TGA should accept this as evidence in a sponsor's application. This would significantly reduce the regulatory burden on sponsors seeking to apply for expanded indication.

Option 2. Further support the development of repurposed drugs through information access

10. Would access to data on real word use data lead to more repurposing of medicines? What sources exist and would be useful?

Whilst SHPA members do not believe that access to real world use data alone will lead to more repurposing of medicines in isolation, they do support the intent and need of having a collective repository of data on the use and safety of unapproved medicines.

Hospital Drug Therapeutic Committees (DTCs) regularly undertake systematic, evidence-based reviews on off-label use of medications for inclusion in the hospital formulary. This is a reliable source of data to include in a national repository of information. DTC data in some states can be challenging for health practitioners to access, for example in South Australia DTC information is not stored on a state-wide database, and in Queensland there is poor DTC transparency. State-based Therapeutic Advisory Groups (TAGs) also play a central role in evaluating data for off-label use of medications at a state level. They too, would be suitable sources of information.

It would be in the interests of the TGA to gain access and utilise this information to identify which medications they would support an application for, based on national public utilisation data.

11. Are there other non-commercial datasets that could be obtained that would assist in facilitating repurposing?

In addition to our response above regarding DTCs, hospitals also have Individual Patient Usage (IPU) application databases that contain clinical data from the use of medicines used for indications that are off-formulary. There is significant crossover between what would be considered off-label and off-formulary in a hospital.

When hospital prescribers or pharmacists require the use of a medicine that is not on the hospital formulary, typically they will need to make an IPU application that is reviewed by the DTCs that evaluates the literature for the indication that it is meant to treat, what the treatment success markers are, and the projected costs to allow for a cost-efficiency analysis.

IPUs that are approved by the DTCs require regular reporting by the applying prescriber on the patients' prognosis and measurement of the identified treatment success markers, to make the case for continued approval of the IPU.

Medicines that receive a large volume of IPU applications in a hospital, with solid in-hospital evidence that it can appropriately treat a certain condition with positive health outcomes, are then identified as candidates for formulary applications so that it can be on the hospital formulary.

Thus, SHPA believes that the IPU datasets, that are held by individual hospitals and hospital networks, are a critical and untapped database that would likely have a wealth of independent clinical evidence and information to assist facilitation of repurposing of medicines. SHPA would be keen to assist the TGA with accessing these datasets in the interests of safer care and quality use of medicines.

Option 3. Actively pursue registration and potential PBAC review of additional indications for medicines

12. What are the main barriers that would lead to sponsor refusal to apply to register a new indication?

Many low-cost medications that do not have patent protection are commonly used as off-label for unapproved indications, for example domperidone for lactation insufficiency. Despite sponsors' full awareness that these medicines hold regulatory approval for that indication by a reputable overseas medicines regulator, the low-cost of these medications and lack of market exclusivity, makes it difficult for sponsors to reclaim costs associated with a TGA application for expanded indication.

Furthermore, even if medicines sponsors were successful in expanded a medicines indication with the TGA, to achieve corresponding regulatory approval for its PBS listing to recognise those indications, would at minimum require a Category 2 submission to PBAC which costs over $160,000 on top of other PBAC fees.

For medicines without patent protection, or where the indication is for a smaller population cohort or rare disease/condition, the regulatory environment necessitating cost-recovery does not appropriately incentivise sponsors to register new indications, to the detriment of transparent, safe and quality healthcare.

13. Would there be interest from non-commercial groups to become sponsors to enable registration and reimbursement of repurposed medicines?

SHPA members believe that there may be an interest from certain non-commercial groups to become sponsors, enabling registration and reimbursement of repurposed medicines. Non-commercial groups may include medical, pharmacy, allied health and consumer organisations. However, there would be more traction from non-commercial, non-for-profit groups/organisations if they could bypass costs incurred by the TGA application process when there is a public need for expanded indication of a certain medication.

SHPA members raise an equity concern that allowing non-commercial organisations to make a submission to the TGA for expanded indication of a medication, may result in unintended equity issues. There is a risk that applications for expanded indications of interest to powerful consumer/lobby groups will be pushed through the system at a much faster rate than those less visible to the general public. For example, medications that can be used to treat certain cancers may be more likely to attract non-commercial sponsorship compared with medications to treat severe atopic dermatitis. As mentioned earlier in this submission, SHPA members believe that the TGA should analyse central usage data from the various data sources to identify the medicines that require sponsorship to apply for expanded indications and would benefit the most Australians. This would eliminate the risk of inequity across health conditions.

Another concern raised by SHPA members was in regard to liabilities associated with non-commercial sponsorship, given they do not actually manufacture the medicine nor hold all clinical trial and safety data in relation to that medicine. This is likely to act as a deterrent to many non-commercial groups if clear guidance was not given on responsibilities and liabilities.

14. Would particular measures undertaken by the Department (e.g. compelling an application or deeming a new indication) be an effective and feasible mechanism to facilitate repurposing?

As mentioned above, SHPA members believe that the responsibility should lie with the TGA to determine medicines that should be approved for expanded indications without the need for an application from a sponsor. This mechanism would ensure consistency and equity across various health conditions.

This process should also trigger an automatic referral process to PBAC since not all applications to the TGA for expanded indication result in a PBAC application, as is the case with lamotrigine, which has approved for prevention of depressive episodes associated with bipolar disorder in 2011 but has not received a PBAC application for this indication.

SHPA members believe a combination of all the options presented by the TGA are required to achieve a regulatory environment for repurposing medicines and off-label use of medicines. Option 1 is required to reduce regulatory burden, Option 2 supports greater access and transparency to off-label medicines use data and Option 3 supports corresponding PBS listing of medicines to support appropriate uptake of medicines where appropriate. This multi-pronged approach is required to address various weaknesses along a medicine's regulatory journey that prevent safer and quality use of currently off-label medicines.

15. Are there any supporting attachments you would like to provide?

No.