SHPA response to the Medicines Repurposing Program – proposed program framework and criteria, February 2024

The Society of Hospital Pharmacists of Australia (SHPA) is the national, professional organisation for the 6,100+ Hospital Pharmacists, and their Hospital Pharmacist Intern and Hospital Pharmacy Technician colleagues working across Australia's health system, advocating for their pivotal role in improving the safety and quality of medicines use. Embedded in multidisciplinary medical teams and equipped with exceptional medicines management expertise, SHPA members are progressive advocates for clinical excellence, committed to evidence-based practice and passionate about patient care.

SHPA welcomes the opportunity to provide input into the proposed program framework and criteria for the Medicines Repurposing Program (MRP) and commends the Therapeutic Goods Administration (TGA) and the Australian Government on their continuing commitment to enhance timely access to medicines in Australia.

SHPA members have vast experience with off-label use of medications and acknowledge that its definitions, evidence base and application to clinical practice is poorly understood by clinicians and patients, yet often off-label use of medicines is required to treat patients who are acutely unwell and/or have rare and uncommon diseases and conditions.

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.

The lack of regulatory approval for these indications impacts on clinician confidence and ability to safely provide evidence-based and transparent care. There is a heavier reliance on off-label use of medicines particularly in vulnerable populations such as in children and in the treatment of rare or uncommon diseases. Combined with differences amongst clinician confidence in off-label prescribing across the nation, the increase in off-label use of medicines exacerbates inequities in medicines access. Given this current environment, the introduction of the Medicines Repurposing Program (MRP) is a welcome direction in securing safe and equitable access to medicines for all Australians, in line with the commitments made in the *Strategic Agreement 2022-2027*[1].

In this submission, SHPA identifies potential areas for improvement in the proposed MRP framework and criteria, taking into consideration the relevance of the recently released *Health Technology Assessment (HTA) policy and methods review – consultation options paper*[2], striving to support early, equitable, and person-centred quality use of medicines for all Australians.

If you have any queries or would like to discuss our submission further, please do not hesitate to contact Jerry Yik, Head of Policy and Advocacy on jyik@shpa.org.au.

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Program framework

1. Are any changes needed to the medicines repurposing framework? If so, where and why?

Ensure clarity and guidance on the nomination process for stakeholders of all levels

SHPA supports the inclusion of any stakeholders to submit a nomination for medicines repurposing in the proposed MRP framework. This is an acknowledgement that all stakeholders, including patients, consumers, and clinicians, and not limited to pharmaceutical companies, can provide valuable insight and information to the repurposing of medicines in Australia. It also aligns with the commitment to the *Enhanced Consumer Engagement Process*[3] within the *Strategic Agreement 2022-2027*[1], to elevate patient and consumer voice in accessing medicines in Australia.

Following on from recognising the value of input from all stakeholders in any medicines access pathways, it is then important that we maximise the potential benefits of inviting all stakeholders to freely make nominations under the MRP framework. This includes ensuring that the initial nomination process is streamlined and simplified for the applicant so that meaningful information can be provided in the first instance.

One of the key learnings of the ongoing HTA review, identified in the recently released *HTA policy and methods review – consultation options paper*[2], was the issues surrounding transparency and clarity in the overall HTA process, with stakeholders having unequal knowledge in understanding the application, evidence collation and eligibility assessment procedures. Similar concerns may arise in the MRP framework, especially regarding the ability of consumers and clinicians to navigate what could potentially be a complex system when they may have minimal exposure to the Australian medicines regulatory landscape. This is a particular challenge highlighted where there may be a stark difference in the resourcing and capacity of a single consumer or a clinician making a nomination application, in comparison to a pharmaceutical company who are more familiar with the regulatory environment and is well-resourced to create a robust application.

To ensure the MRP framework incorporates a person-centred approach that is fit-for-purpose and minimises any barriers for all stakeholders in making appropriate nominations, SHPA recommends there is clear guidance and explanation, provided in plain language, of the MRP application pathways and on how to complete the publicly available nomination form, allowing both experts and non-experts to navigate the system more easily.

SHPA also recommends that sufficient information, education, and training tools are provided to support a more meaningful input and nominations made by stakeholders of all levels.

Furthermore, it may be helpful to outline a feedback system within the framework, to clarify transparency of the progress tracked by a nominated medicine. While it is in the best interest of all involved parties to avoid adding complexity and unnecessary steps into the MRP framework, it is still important to ensure that where a nominated medicine has failed to be selected, this information is made publicly accessible to help stakeholders understand how their application has contributed to the decision-making process within the MRP framework.

Implement safeguards against stakeholders who may take advantage of the proposed fee waivers

SHPA welcomes the introduction of fee waivers and dossier support for pharmaceutical companies for medicines that have been selected for repurposing. As identified in the earlier consultations, cost was a significant disincentive for pharmaceutical companies to enlist a new indication for an existing medicine, particularly when a company may no longer hold the patent.

However, with the introduction of fee waivers, there is now concern that sponsors may utilise the MRP to obtain fee waivers in listing new indications for medicines that they may have market exclusivity for, thereby overburdening the resourcing at TGA. This issue may be exacerbated if the lack of support and guidance for the nomination process leads to disparities in the quality of the nomination forms submitted by pharmaceutical companies compared to other stakeholders, potentially influencing the short-listing process.

To ensure all nominated medicines have equal visibility to the TGA in being considered as a candidate for repurposing, and to minimise the potential overburdening of TGA resources, SHPA recommends that safeguards are placed to prevent potential misuse of the MRP by larger stakeholders who may wish to take advantage of the fee waivers offered through this medicines access pathway.

While the detail of these safeguards is at the discretion of the TGA, in principle they would support a clear consideration of whether the application was made in genuine interest of public health outcomes with greatest potential to affect patient equity of access, and evidence that standard costs if it were to track on the usual registration pathways would make the application financially unviable.

2. Do you have any feedback on the feasibility of evidence collation aimed at generating a dossier robust enough to support a future application by a sponsor?

SHPA would like to seek clarification on the 'evidence collation' process referred to in this question, as the current consultation document only broadly outlines the evidence required in the initial nomination, which includes evidence on efficacy, clinical impact, and accessibility of the proposed medicine for repurposing. Without visibility on what the final nomination form would look like, it is difficult to ascertain the feasibility of evidence collation aimed at generating a robust dossier for future use by a sponsor, and how much of this responsibility lies with the applicant making the nomination.

As previously discussed, it is important that adequate support is provided for stakeholders of all levels to understand and effectively navigate the MRP application process, so that any stakeholder can confidently put forward a robust application to nominate a medicine that they may have extensive experience and knowledge in and see the potential to make significant impact on health outcomes.

Currently under the 'Identification of promising candidate medicines' section of the MRP framework, it states that the publicly available nomination form will request evidence of efficacy of proposed treatment, with reference to the *TGA's dossier requirements for literature based submissions*[4]. This guidance is highly technical and can be confusing and difficult to understand especially for stakeholders who may not be as health literate and would struggle to effectively communicate their input and experience in a meaningful way.

SHPA recommends that any responsibility placed on the applicant making the nomination to create a robust application in the first instance should be supported with tools and written guidance in plain language, to ensure both experts and non-experts can be supported to collate high quality evidence to be considered for future application by a sponsor.

Eligibility check

3. Do you agree with the proposed eligibility criteria for the program?

SHPA notes that the proposed MRP framework and criteria limits the number of medicines to be repurposed to only five medicines per year, and would like to seek clarification on how the TGA came to this limit. While acknowledging the TGA must factor in operational costs of running such a program, there are concerns that limiting the number of medicines for repurposing could create barriers to equitable access to medicines, particularly for vulnerable populations and patients requiring treatment for rare and uncommon diseases and conditions.

Off-label use of medicines is especially common in the treatment of rare and paediatric diseases. As noted in *The New Frontier – Delivering better health for all Australians*[5] report published in 2021, the current HTA processes utilise models that are primarily designed for more common diseases, presenting a further disincentive for pharmaceutical companies to register medicines for repurposing. Rare diseases, generally defined as affecting less than five in 10,000 people, approximately affect two million Australians. While there may be a smaller population of Australians affected, rare diseases are associated with high level of symptom complexity, ongoing health and psycho-social challenges, and have severely limited treatment options.

One of the listed eligibility criteria looks to consider the public health benefit and patient need, including consideration of which candidates have the greatest potential impact on health outcomes and patient equity of access. For patients with rare diseases, they represent smaller patient numbers that impact cost effectiveness. Furthermore, there are often less clinical evidence available due to the challenges of conducting large-scale clinical trials, for example the ethical challenges faced in conducting clinical trials in paediatric populations, in which off-label use of medicines is prevalent.

To ensure the MRP framework is fit-for-purpose and can accommodate for the consideration of medicines in both common and rare diseases, SHPA recommends the TGA to include in their eligibility check, the broader economic benefits beyond just ‘greatest potential impact on health outcomes’, including measures that are most important to patients and their carers (e.g. availability of alternative therapies and increased out-of-pocket costs in comparison to other disease states), and acknowledge the challenges of generating large-scale evidence for treatments used in rare conditions. This will allow the MPR framework and criteria to bridge inequities in medicines access for patient populations that are already disadvantaged and have generally less therapeutic on-label choices.

4. Are there any additional eligibility criteria that you would like to see included?

As discussed, SHPA recommends that the eligibility criteria reflect the principles of equity, by ensuring it considers the challenges of treatments for rare conditions to demonstrate great impact on health outcomes for a larger population size. This may mean a revision of the current limitation on the allowed number of medicines for repurposing each year, as well as a clarification of the criteria assessing the impact of proposed medicines on health outcomes, to ensure the TGA supports equity in assessing nominated medicines for both common and uncommon diseases.

Prioritisation of candidate medicines

5. Do you agree with the proposed prioritisation criteria for the program?

Similar to the concerns outlined under the questions in the Eligibility Check section, SHPA would like to highlight that the limit of five medicines per year for repurposing, in combination with lack of adjustment where appropriate for the level of clinical trial evidence considered, may further exacerbate inequities in medicines access, particularly for vulnerable populations and those with rare or uncommon conditions. In considering evidence to support safety and efficacy of proposed new indication for rare conditions, parameters of assessment should be adjusted to accommodate the lower volume of patients involved in clinical trials, and take into account other complexities such as obtaining ethics approval to conduct large-scale clinical trials.

Additionally, the criteria to consider evidence of wide acceptance of off-label use may be difficult to justify in uncommon conditions, where the lack of regulatory approval for unregistered indications may have deterred prescribers from confidently prescribing these medicines to treat rare diseases, or financial barriers may have impeded a patient's ability to access the treatment, despite widespread use internationally. SHPA recommends that the evidence to support widespread off-label use should incorporate the availability of international use where there is lack of local evidence, to support these applications,

6. Are there any additional prioritisation criteria that you would like to see included?

No further comments.

References

[1] Australian Government. (2021). Strategic Agreement in relation to reimbursement, health technology assessment and other matters. Available from: https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2023/10/ma-strategic-agreement-22-27.pdf

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[3] Department of Health and Aged Cared. (2023). Co-design of an enhance consumer engagement process. Available from: https://www.health.gov.au/our-work/co-design-of-an-enhanced-consumer-engagement-process

[4] Therapeutic Goods Administration. (2014). Dossier requirements for literature based submissions. Available from: https://www.tga.gov.au/resources/resource/guidance/dossier-requirements-literature-based-submissions

[5] Parliament of the Commonwealth of Australia. House of Representatives Standing Committee on Health, Aged Care and Sport. (2021). The New Frontier - Delivering better health for all Australians - Inquiry into approval processes for new drugs and novel medical technologies in Australia