

Australian Cancer Patients Deserve Timely Access to the Best Therapies

Merck Sharp & Dohme (MSD) Australia's submission to the Senate Inquiry into
the availability of new, innovative and specialist cancer drugs in Australia

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Executive Summary

The Senate Inquiry into the availability of new cancer drugs in Australia could not have come at a better time. Cancer treatment is on the cusp of a major transformation, particularly with the availability of new immunotherapies and targeted medicines. Yet Australia's system for reviewing cancer medicines is outdated and leads to unacceptable delays in patients accessing the treatments that they need.

In this submission, we outline our experience with the existing framework and identify areas for improvement. We consider other countries' attempts to accelerate access and propose four recommendations that will help Australian cancer patients get the medicines that they need in a timely manner:

1. **Introduce provisions for fast-tracking the registration of cancer therapies that address an important unmet need.** Many regulatory authorities have implemented expedited registration processes. Expedited reviews are used in these countries for breakthrough or life-saving medicines, or where there is a high unmet need to speed up patient access to medicines, in most cases to under 6 months.
 - a. Introduce an expedited registration process.
 - b. Adopt overseas evaluation reports for drugs granted breakthrough status.
 - c. Introduce Adaptive Pathways (AP).
2. **Equip the PBAC review process to accelerate patient access to oncology medicines.** Current PBAC systems are outdated and not appropriate for assessing innovative cancer treatments. This is primarily because of over-reliance on overall survival data.
 - a. The PBAC should tailor the evidentiary requirements for oncology medicines.
 - b. A framework for an outcomes-focussed Managed Access Program (MAP) should be developed and implemented collaboratively with sponsors.
3. **Unnecessary delays to access can and should be avoided by reducing red tape in the system.** Most cancer drugs are listed on the PBS only after two or more submissions to the PBAC. This is in part due to inefficiencies in the PBAC processes that can be addressed.
 - a. The Medical Services Advisory Committee (MSAC) should make all co-dependant technology decisions simultaneously within the PBAC review.
 - b. Transparency, flexibility and ongoing dialogue throughout the process would ensure that redundant bureaucracy doesn't affect first time approvals.
4. **The value of truly innovative medicines should be recognised early and measured over time.** Innovation requires investment; patients deserve this and bureaucratic processes should not prevent the continued development of new drugs and access to the best available therapies.
 - a. Apply a 'shadow price' mechanism to new cancer medicines.
 - b. Establish a National Chemotherapy Registry to continually assess the efficacy of medicines.

This review presents an opportunity to address the imbalance Australian patients with cancer face in gaining timely access to life-saving medicines. Thank you for considering this submission. We would be delighted to expand on any of the recommendations that we have put forward and we would welcome the opportunity to appear before the Senate to provide evidence.

Introduction

Merck Sharp & Dohme (MSD) has been bringing innovative medicines to Australians for more than 60 years. MSD also has experience in accelerating the development and availability of breakthrough medicines such as CRIXIVAN, which was a paradigm shift for HIV patients who had previously been under a death sentence from the disease.

In this submission, we will outline our experience with the existing framework and the opportunities for improvement. We will then detail what other agencies internationally have introduced – recognising the nuances that exist in the approval of cancer medicines – and propose four recommendations that will ensure patients with cancer can access medicines in a timely and efficient manner:

Recommendation 1: Introduce provisions for fast-tracking the registration of cancer therapies that address an important unmet need.

Many regulatory authorities already have expedited registration processes, including the USA (Federal Drug Administration – FDA), Canada (Health Canada – HC) and Europe (European Medicines Agency – EMA). Expedited reviews are used in these countries for breakthrough or life-saving medicines, or where there is a high unmet need to speed up patient access to medicines, in most cases to under 6 months. In contrast, Australia has no formal expedited registration process. The TGA registration process does not allow for evaluations to be speeded up beyond the standard registration period of 14–15 months. This one-size-fits-all regulatory framework stops Australians from getting timely access to life-saving medicines that are already available in comparable countries overseas.

We therefore propose the following processes as options that would serve the purpose:

- a. **Introduce an expedited registration process.** The TGA should acknowledge the considerable resources that other agencies invest in granting a medicine breakthrough status, by recognising this designation in Australia. We suggest that the review process for breakthrough medicines should be accelerated by:
 - i. Accepting limited clinical data based on surrogate end-points
 - ii. Designating priority review with accelerated review timelines, with a target approval date of six months from submission
 - iii. Granting conditional approval for applications assessed on limited clinical data (with relevant post-approval follow-up)
 - iv. Allowing for the submission of additional data during the evaluation of an application.
- b. **Adopt overseas evaluation reports for drugs granted breakthrough status,** thus reducing replication by leveraging the investment of other agencies. The option should be available, in extreme cases, for the TGA to streamline the registration process by adopting recommendations from an overseas regulatory agency as the basis for an Australian approval. Evaluation reports from an approved regulatory authority would be assessed before an independent sovereign decision by the TGA. Through leveraging international experience and resources, patients in Australia could secure timelier access to much-needed medicines. Through other regulatory agencies' work, new medicines could be made available to patients in as little as 3 months after overseas approval.
- c. **Introduce Adaptive Pathways (AP).** The EMA has begun AP pilots in an attempt to reduce the significant time and resources that are required for the approval of drugs for rare diseases, with the aim of faster approvals for a niche population. Access would then be gradually broadened as more safety and efficacy data became available. Australian patients with rare cancers often face

significant delays in getting access to medicines because it is difficult for companies to do individual studies in these small cancer types. This would encourage further research in this area of high unmet need. AP should be implemented in Australia to help this often neglected group. This is particularly relevant for immunotherapies because they have broad applicability in a range of cancer types.

More information on fast-track review options for Australia is available in: *Proposal for TGA actions in accelerating product development and review for critical life-saving medicines* (Supplement one) and *A Visionary New Regulatory Scheme for Medicines* (Supplement two).

Recommendation 2: Equip the PBAC review process to accelerate patient access to oncology medicines.

The current PBAC systems are outdated and not appropriate for assessing innovative cancer treatments. It takes more than two years on average to achieve a PBS listing for an approved oncology medicine. This is primarily because of over-reliance on overall survival data, which takes time to accrue and is very difficult to estimate in the oncology space, due to the impact of crossover and/or the influence of other therapies used post-progression. Once a medicine starts to show significant benefit versus the standard of care, it should be made available; the following processes would enable the PBAC to do this:

- a. **The PBAC should tailor the evidentiary requirements for oncology medicines to particular tumour types.**
 - i. Currently, oncology medicines are evaluated in the same way as other drugs. For instance, there is a requirement for a new medicine to demonstrate an overall survival benefit. Whilst overall survival is a meaningful endpoint for patients and clinicians, waiting for patients to die leads to unnecessary delays, especially when the therapy being trialled offers a significant benefit versus the standard of care. Overall survival is also notoriously difficult to measure in oncology trials as results are confounded by trial patients switching to a new medicine as soon as they fail on the previous trial medicine.
 - ii. Trial endpoints which are equally meaningful to oncology patients, such as significant improvement in the quality of life and progression free survival, receive only peripheral consideration by the PBAC. The lack of overall survival data increases PBAC uncertainty about the oncology medicine's cost effectiveness and leads to delays in gaining a positive recommendation. This was exemplified in the case of a melanoma medicine, Yervoy. Despite a high clinical need for new therapies, over five years' worth of overall survival data and three PBAC submissions were required to convince the PBAC of the effectiveness of this medicine.
- b. **A framework for an outcomes-focussed Managed Access Program (MAP) should be developed collaboratively with each sponsor and based on the principle of shared risk.**
 - i. In 2010, the Department of Health and Medicines Australia attempted to enable early patient access to new medicines through the establishment of a MAP framework called the 'Managed Entry Scheme'. This framework provided a pathway for reimbursement based on a limited dataset, with a view to providing a higher price once more mature evidence became available. However, the scheme was not taken up due to perception that all risk in participating in the scheme would be borne by companies, with little hope of price increases even if conclusive evidence was forthcoming.

- ii. The original intent of the scheme, to enable earlier access to new medicines, was not realised. There have been two more recent MAPs, for crizotinib and trametinib. In these cases proof of cost effectiveness and at least two PBAC submissions were required to gain listing. On top of that, in terms of this arrangement, once further data has been collected (real world data or clinical trial data), the cost effectiveness would be reviewed, with penalty interest and rebates required if the claimed clinical benefit was not delivered, but with no opportunity for the sponsors to be rewarded if the clinical benefit was better than expected.
 - iii. The Department of Health (DoH) and Medicines Australia have been developing a new MAP framework through the Australian Medicines Working Group (AMWG) that will hopefully formalise a more effective way of giving patients access to new products. To be fully operational, this new framework will need the full support and understanding of the Pharmaceutical Benefits Advisory Committee, its Economic Sub-Committee and its evaluators. Moreover, sufficient time will be needed for sponsors and government officials to discuss and finalise the provisions of future MAP arrangements.
- c. **The PBAC should pay greater attention to patient and clinician input in making its recommendations.** When making recommendations on innovative cancer medicines the PBAC should add more weight in its deliberations to the experience of patients and clinicians. PBAC recommendations would benefit greatly from the real world insights that these stakeholders can provide into the issues of greatest importance in providing effective treatment.

Recommendation 3: Unnecessary delays to access can and should be avoided by reducing red tape in the system.

Most cancer drugs are listed on the PBS only after two or more submissions to the PBAC. Although each cycle is 17 weeks, it is not possible to do back to back cycles and each cycle missed adds another 17 weeks. Each rejection leads to an eight month delay (Appendix one). This is often due to inefficiencies in the PBAC processes that can be addressed:

- a. **The Medical Services Advisory Committee (MSAC) should make all co-dependant technology decisions simultaneously with the PBAC review**, reducing unnecessary delays and duplication that extend the time taken before listing on the PBS. The number of options assessed should also be reduced, saving significant resources and time during the pre-work process.
- b. **Ongoing dialogue throughout the process can improve the quality of PBAC decision making.** An example of this relates to the clinical or economic uncertainties that can arise in evaluating medicines through the PBAC process. Such uncertainties can be managed through dialogue between the evaluator and the sponsor on what steps can be taken to manage these uncertainties and give the PBAC greater confidence in the analysis provided. The process followed for the melanoma medicine Yervoy is a good example of where uncertainties played an important role in delaying a positive PBAC recommendation. Yervoy was first assessed by the PBAC at the July 2011 meeting, at which it was rejected. It was rejected a second time at the March 2012 meeting, before finally receiving a positive recommendation at the November 2012 meeting. Further delays in the post-recommendation process meant that it was only listed on the PBS in August 2013. That means it took over 2 years from the initial submission before it was available to patients on the PBS.

Recommendation 4: The value of truly innovative medicines should be recognised early and measured over time.

The initial cost of cancer medicines is based on the significant investment in research and development to bring the medicines to market. Over time, the cost becomes comparatively lower, because drugs are not subject to price increases, unlike all other health care costs, and once generic they will be available at a significantly reduced price. For instance, as of 1 April 2015, docetaxal will be 98.5 percent cheaper than its original price. Innovation requires investment; patients deserve this and no pricing systems should prevent the continued development of new and improved medicines.

It should also be born in mind that the true cost of cancer is often grossly underestimated, as many cancers have a social and economic impact beyond the patient, such as carers and lost productivity for example. The government should introduce the following processes to ensure that patients in Australia gain timely access to the most effective treatments:

- a. **Apply a ‘shadow price’ mechanism** to better reflect the fair value of innovative medicines. Judging cost effectiveness of new cancer medicines by referencing against older chemotherapy agents, which continue to erode in price, is not recognising the true value. A shadow price would be a CPI adjusted price of the reference medicine when it was launched. Cost effectiveness analyses would then be undertaken versus the shadow price.

- a. **Establish a National Chemotherapy Registry to continually assess the efficacy of medicine** and thus help to show the true value that medicines bring to society. At present, despite significant expenditure on cancer medicines, no comprehensive picture exists of what happens to patients once they are placed on therapy, as no national database exists which captures this information. As well as empowering clinicians with information to improve cancer care, such data provides a framework to monitor real world cost effectiveness and to support Managed Access Schemes. This would enable the health community to continually monitor whether it is getting value for money out of its investment.

While the government is making some progress in the right direction, for example through the MAP policy discussed above, there is still much work to do to ensure Australia has rapid access to new medicines. This is especially true for cancer patients who cannot wait for therapies to undergo lengthy assessments.

This inquiry presents a timely opportunity to address this imbalance and for Australia to become a global leader in giving swift and affordable access to essential medicines.

Thank you for the opportunity to provide this submission. We would be delighted to expand on any of the recommendations that we have put forward and we would welcome the opportunity to appear before the Senate to provide evidence.

Appendices

Appendix 1.

The impact of a single rejection from the PBAC



The impact of a single rejection is an 8 month delay