Submission Template

Pharmaceutical Benefits Advisory Committee (PBAC)
PD-1 and PD-L1 checkpoint inhibitor immunotherapies: options for subsidy consideration for multiple cancer types

Cover sheet

This submission template should be used to provide comments on the Background paper relating to the PBAC consideration of PD-1 and PD-L1 checkpoint inhibitor immunotherapies: options for subsidy consideration for multiple cancer types

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Category of submitting individual/organisation	Are you (select one only) ☐Patient ☒Consumer organisation ☐Pharmaceutical industry ☐Healthcare Provider ☐Professional organisation ☐Researcher ☐Government Body ☒Other (please outline) – The National Oncology Alliance is a broad cancer community alliance. The four core membership pillars are patients and carers, patient groups, industry, and clinical advisors.
Confidentiality and publishing of submissions	Please note - all submissions received will be published on the PBS website at the conclusion of the public submission period, unless otherwise requested. Where submissions indicate commercial-in-confidence or sensitive personal information, this is redacted before publication. Please ensure any commercial –in-confidence or sensitive information is clearly marked.

Submission Instructions

Submissions should be made by **5pm AEST on 29 June 2018**. The PBAC will not consider late submissions.

Submissions should be lodged electronically, preferably in this template, in Microsoft Word or other text based formats, to the email address pbac@health.gov.au

PD-1 and PD-L1 checkpoint inhibitor immunotherapies: options for subsidy consideration for multiple cancer types

General/overall comments

Please note, comments that are beyond the scope of PD-1 and PD-L1 checkpoint inhibitor immunotherapies: options for subsidy consideration for multiple cancer types will not be considered

This submission is presented on behalf of the newly established National Oncology Alliance (NOA). The NOA membership is comprised of patient groups, clinicians, researchers, industry representatives and most importantly, patients and carers that deal with the realities of cancer every day. Insights and contributions from each of these stakeholder groups have informed this submission.

There is consistent agreement across NOA that Australia's health care system is world class, and that this investigation represents an opportunity to begin advancing reimbursement processes in line with technological change. The TGA's recently adopted expedited pathways (Priority Review and Provisional Access) provide much needed regulatory expediency. Subsidy consideration across multiple cancer types will provide complimentary benefits on the reimbursement and access side of the process.

Innovative oncology medicines are slow to be reimbursed compared to other PBS listings. This is due to a myriad of factors including the comparatively higher price of these medicines compared to current alternatives, and resource intensiveness for industry, the PBAC and government in producing and assessing applications and listing medicines. Acknowledging the commercial and budgetary realities surrounding the listing of medicines, this submission focuses on the broad cancer community rationale for subsidy consideration across multiple cancer types and presents options to address follow-on indications as well as access options for neglected rare cancers, and rare subtypes of more common cancers, whose minority status creates market failures, inequity and poorer health outcomes.

PD-1 and PD-L1 checkpoint inhibitors are in some ways the 'first cab off the rank' in terms of rapidly developing immunotherapies that are showing positive application across multiple indications of cancer, particularly relevant to advanced (metastatic) disease. They will also likely be the first to be positively affected by any reform in this area. It is understandable then, that this investigation has chosen to focus on options relating to the PD-1/PD-L1 checkpoint inhibitors as a pilot, because they are considered to represent the first wave of monotherapies, have the most regulatory approvals to date and have the most publicly available evidence of efficacy. The answers below are made with reference to these medicines, however, they are intended to be suitable across multiple innovative oncology treatments.

Background and rationale

Since its inception, the PBS has provided Australians with broad access to essential medicines at an affordable price, so that, in line with the overarching National Medicine's Policy, 'cost [does] not constitute a substantial barrier to people's access to the medicines they need.' [1] Although Australia has the highest incidence of cancer in the world, the commendable functioning of the PBS up to this point has enabled high survival outcomes – although importantly, this figure is as an aggregate. Access to new cancer medicines has become an issue of community concern in recent years with over 500 submissions to two recent Senate Inquiries investigating the state of play for research funding and medicines access for cancer patients.[2][3] Part of this community pressure is based on the large volume of potential indications for many IO treatments, including PD-1/PD-L1 medicines, and whether or not reimbursement exists, or is likely to be pursued, for many of these indications.

[1] Australian Government, Department of Health and Ageing. *National Medicines Policy.* Retrieved from: http://www.health.gov.au/internet/main/publishing.nsf/Content/B2FFBF72029EEAC8CA257BF0001BAF3F/$File/NMP2000.pdf p. 2

[2] Senate Community Affairs References Committee, Parliament of Australia, *Availability of new, innovative and specialist cancer drugs in Australia* (2015).

[3] Senate Select Committee, Parliament of Australia, *Funding for Research into Cancers with Low Survival Rates* (2017).

Where reimbursement does not exist for medicines that clinicians recommend based on their expert opinion of likely effectiveness, inequality arises, and patient care and outcomes are determined by one's bank balance. This investigation offers an opportunity to begin to close this gap.

The NOA conducted a survey of oncologists and haematologists around access to medicines in preparing this submission, of which there were over 70 respondents, and whose insights around unmet medical need in their patients, supports this submission. Particularly notable were comments around the frequency of conversations with patients about non-PBS listed cancer medicines including PD-1/PD-L1 medicines. Clinicians noted that such conversations were;

- *'Regular…mostly around I/O therapies*
- *'Very common'*
- *'At least once a week'*
- *'Almost a daily occurrence'*

Despite a significant volume of conversations, there was significantly lower prescription of such medicines due to financial access issues. Regarding patients and the discussed non-PBS listed medicines, of which a high proportion were PD-1, PD-L1 checkpoint inhibitors, clinicians noted that;

- *'Several patients could not afford the medication'*
- *'Most cannot afford non-PBS prices, unless on trial or compassionate access'*
- *'Mostly only prescribed if on an access program. Many drugs are unaffordable to patients'*
- *'Mostly via patient access schemes but some who've self-funded medications'*

There has been a dramatic increase in the timely availability of information around drug development to patients via the internet, and the pace of FDA registration of drugs in the U.S. vis-à-vis Australia has added to this. Despite more informed patients, the survey found that clinicians were still the primary instigators of conversations about non-PBS listed cancer medications, including PD-1 and PD-L1 checkpoint inhibitors. Clinicians consistently note for IO treatments, there is a disconnect between what they wish to prescribe to patients in their care, and what is available on the PBS. In such an environment, decisions clinicians and patients are able to make around treatment, are increasingly constrained by economic and social indicators rather than clinical expertise.

Considerations and core recommendations

In an environment where the community is eager for more efficient and equitable access to cancer medicines, it is still important that clinical and cost effectiveness is maintained, ensuring the sustainability of the PBS and the integrity of the health system in which it operates.

Challenges

- High costs and budget uncertainty for 'pan-cancer' listing – alternatively, expedited successive consideration for relevant 'follow-on' indications can be provided within a framework that allows for the early assessment of cost-effectiveness and enables faster listings.
- Uncertainty around rare indications under current processes often rules out registration and reimbursement for many rare cancers where there may be clinical benefit. Small patient populations, minimal global trials, no commercial incentive, and insufficient data (according to standard processes) all contribute to systemic exclusion from drug development and evaluation processes, creating high unmet medical need and poorer health outcomes across these patient populations. While contributing to around 30% of cancer diagnosis, rare and less common cancers account for 50% of cancer deaths, and seven per cent of Australia's total disease burden. Over the last 20 years, survival rates in many rare and less common cancers have only improved marginally, if at all.
- There is not always perfect information provided to the public via popular media, around the complex cost/benefit analysis of new medicines. This is true in the case of PD-1/PD-L1 medicines and other immunotherapies. The two main areas of information asymmetry are around the point of intervention, and side effects. Fewer trials of immunotherapies have been conducted in early stage disease, therefore, where

there is compelling evidence of clinical benefit, this has generally been associated with advanced (metastatic) disease. Additionally, perhaps due to immunotherapies' mechanism of action in enabling the immune system, there can be misconceptions around these medicines having a drastically lower chance of side effects than an existing first line comparator (eg. chemotherapy).

- Rapid advancements in molecular classification of cancers are disrupting traditional models of cancer care. Adapting Australia's health system to tackle precision medicine is essential to maintaining our country's excellent reputation in health, and ensuring patients are receiving the best care available at the right time. Randomised trials become possible in multi-tumour indications due to growth in aggregate number of molecularly defined cancers versus rarer histologically defined cancers. The proliferation of targeted molecular screening will be essential to identifying accurate effectiveness and cost-effectiveness levels.

Core recommendations

- 'Follow-on indication' pathway for applications for additional indications of PD-1/PD-L1 → streamlining resource burdens on PBAC, DoH and industry, will allow for faster access to evidence based, cost-effective medicines.
- Rare and neglected cancers pathway → managed access pathway in situations where there is high unmet medical need. A provisional PBS listing through managed access could be a solution in situations where there is a high level of uncertainty in a PBAC submission for a rare cancer indication, with additional real-world evidence collection helping to build the case for eventual PBS listing. This approach would build on current risk share arrangements or managed access either currently in use or being developed (with Medicines Australia). [4]
- The NOA stresses the importance of the compatibility of PBAC/MSAC evaluation processes with biomarker-led therapies to maintain Australia's reputation as a leader in cancer care. A framework surrounding molecular testing and classification needs to be developed. Such a framework also enables aggregation across rare cancers – preserving the role of randomised trial evidence and addressing areas of high unmet medical need.

This inquiry provides a starting point from which to address the challenges to equitable access to medicines.

[4] Rare Cancers Australia. Rare Solutions: A Time to Act. Retrieved from https://bit.ly/2uBrXq4

Specific responses

Please insert your comments against the consultation questions below.

Question 1

What do you/your organisation see as the potential advantages of the PBAC considering the PD-1 and PD-L1 checkpoint inhibitors for multi-tumour listings?

There are several advantages to multi-tumour listings for PD-1/PD-L1 checkpoint inhibitors, many of which will be amplified by a more wholesale application of a multi-tumour listing process to encompass the wide range of innovative oncology treatments already on the market and in development. The NOA believes this investigation to be a step in the right direction towards addressing our changing understanding of the biology of cancer.

The following suggestions address options to significantly increase speed of access to clinically and cost-effective medicines to patients who need them;

- The PBAC is an application-driven body. There are known to be over 900 ongoing Phase 2 & 3, industry-sponsored clinical trials into PD-1/PD-L1 medicines across over 20 tumour types. There has been a disproportionately small number of applications presented to the PBAC for reimbursement thus far (26 applications over 7 indications). A more 'fit-for-purpose' follow-on subsidy consideration process addresses some of the commercial and administrative challenges that can stall applications, and thus access for patients. The adoption of a streamlined process will additionally help mediate the volume of future applications for PD-1/PD-L1 and other innovative oncology treatments.
- Rare cancer patients and patients with rare subtypes of more common cancers face unique challenges and a greater burden of high unmet medical need than their common counterparts. There are structural challenges that cause this inequity, and affirmative action via a managed access approach for PD-1/PD-L1 medicines and beyond, will begin to address these challenges and make the system fair for rare.
- A successful process will begin to bridge the wealth gap that is growing larger in Australia around access to medicines.
- An investigation into multi-tumour listings brings us closer to a system that embraces use of real world data in analysing and deciding on cost-effectiveness (managed access pathway).

While subsequent answers in this submission address some of the points of delay in the submission/listing process, the real focus of the NOA's response is to illuminate what happens for patients and their families when listing for their indication is delayed, or in the many cases where there is no listing in sight.

The exact figure for those self-funding PD-1 and PD-L1 inhibitors for indications that are not currently PBS listed, is presumed to be quite significant. Patient groups within NOA note that in many cases, self-funding can result in financial destitution for cancer patients and their families. In these cases of self-funding – the data of their experience and health outcomes with these medicines is not being collected in a way that advances options for future listings and patients. Essentially, the information is lost. Countless stories emerged of families having to re-mortgage/sell their houses, and accessing their superannuation and life insurance policies, as well as crowd-funding, just to receive the treatment recommended by their specialist. It is important to note that when exclusively self-funding occurs for a medicine that is reimbursed for one indication, and not another where it has application, patients lose out in several ways. First, a patient has to be able to find the often tens of thousands of dollars, and even >$100, 000 required for treatment – whether this is by the methods mentioned previously or via private savings. Secondly, the taxes such patient has paid throughout their life, are used to fund other people's use of that medicine where it *is* reimbursed, yet not their own. Finally, the individual patient, unlike the government, is unable to act as a monopsony to negotiate a lower price. So, unless on a compassionate access program, the patient is likely paying a significantly higher price to the pharmaceutical company than the government would be if the treatment was subsidised through the PBS. This includes issues around GST on transport and dispensing of the drug. There are also the countless number of patients for which no money can be found, they have no choice but to go without. These are both dire situations for patients and families already dealing with the trauma of a cancer diagnosis.

We recite the story of a young mother and cancer patient who told of her frustration with her disease, delays and inequity in access to listed medicines, and the cost she needed to come up with for treatment with a PD-1/PD-L1 drug. Speaking to a Parliamentary Friends of Cancer Causes event at Parliament House in 2015, just prior to the first listing of a PD-1, (albeit not for her indication – under the current processes – it is unlikely that listing for her indication would ever be possible); these are some of the powerful insights she shared:

'There is a devastating, bewildering feeling a diagnosis like this brings, to those [who haven't experienced it] it is very difficult to describe, but I liken it to stepping off a cliff and going into a freefall that you never come out of. You can't really comprehend what's happening to you, but you do know that life will never ever be the same. As a parent I also experience utter terror at the thought that I may not be around to raise my children…Over the past year I have undergone four types of IV chemotherapy, one brief week on oral chemo and two rounds of radiotherapy. Unfortunately, the chemotherapy didn't have a big impact on my cancer, in fact the last one we tried had no effect at all'

'Put yourself in our place, you've been fighting for so long and you are so so tired, but you will do anything to stay alive for your family. You are presented with a new kind of treatment, a new hope, when you thought that actually all hope might be gone. This could be your big chance, but only if you have a spare $100, 000 up your sleeve. If you are like me you think, but wait, doesn't that stuff only happen in America? And haven't I been through enough already without having to find such a huge amount of money? There's a whole lot of politics involved in me getting my treatment. None of which I really understand and quite honestly, I never will, I have a lot of other stuff on my mind. Here are some things that I do understand… I understand that I've happily paid my taxes for years, like all of the patients here, and I am a staunch believer in combining resources for the greater good. It is the foundation of a good society. But when I desperately need those resources I can't access them. I understand that [my oncologist], is the leading expert in his field and one of the best in the world. But even though he thinks I should have this treatment, and there is a good chance that it will prolong my life, I have to wait until someone sitting in an office somewhere, who I suspect is not a world expert in [my disease], decides it is safe for me to have, and it's put on the PBS. But that could take them a few years to fill out the right forms, and until that happens I'm going to have to find the equivalent of a house deposit every year just to stay alive. I'm told that if you have [PBS listed indication] instead of [my cancer], you will soon be able to access the same drug on the PBS, because the right kind of paperwork has been done, and to that I say 'huh? how come it is ok for them and not for me?', that bit I don't understand. Some of you may come to me later and say you know, you are really oversimplifying the situation, to which I say – to me it is simple. I am a hardworking, taxpaying Australian, yes, I still manage to work, and I still pay tax, whose greatest goal in life is to live long enough for my two-year-old daughter to remember me. For the first time in a long time I really do feel like I have a shot at reaching that goal, and I am asking my country for help to do that. We have to find a way to make this process faster so that whether we live or die is not determined by the size of our bank balances.'

A process that can mitigate some of the issues in the above patient story is advantageous by anyone's standard, and we should all strive to do better by Australian cancer patients.

Question 2

What do you/your organisation see as the potential disadvantages of the PBAC considering the PD-1 and PD-L1 checkpoint inhibitors for multi-tumour listings?

The disadvantages of multi-tumour listings fall more appropriately under the heading of 'Challenges'.

Challenges

- PBS listing has only been able to traditionally occur when the medicine is first registered with the TGA for the matching indication. The pathways suggested here addresses, along with the TGA's Provisional Approval and Priority Review reforms, a way forward for indications previously unlikely candidates for registration/reimbursement.
- There may be individual patients who do not respond to multi-tumour listed medicines for reasons unknown, however, the same level of uncertainty applies to histologically classified listings. Strong focus on the rollout of molecular screening for advanced disease will help reduce some of this uncertainty further.
- Testing and classifying – there needs to be a universally accessible platform identifying common property among anatomically disparate cancers. For example; for dMMR biomarker – this means the establishment of an accessible program for testing for *all* patients with advanced or incurable cancers. This molecular profiling is not yet available without discrimination.[5]
- There are disadvantages to restricting any reform to only one class (PD-1/PD-L1), a narrow agenda for PBAC flexibility around multi-tumour listings is beneficial only in its ability to act as a pilot for precision medicines, other immunotherapy and innovative oncology treatments. The rapid evolution of molecular testing means the limited current investigation won't be sufficient on its own to tackle future technology and treatments. To this point, NOA again strongly recommends a platform for the proliferation of screening, enabling more targeted and therefore increasingly cost-effective use of medicines.

Question 3

What is urgent unmet clinical need? How should it be established? For which patient groups?

Urgent unmet medical need can be established by a variety of factors and primarily relates to two groups (of which there is often crossover); patients with advanced cancers who have exhausted conventional treatment options, and systemically excluded rare cancer patients who have limited treatment options from the outset. For those with advanced cancers, who have run out of conventional treatment options, novel options like immunotherapies are often likely to provide benefit.[6] This group also often has cross over with disease rarity. Rare and less common cancer patients, and common cancer patients with rare subtype disease, are likely to be disenfranchised from treatment in many ways. This is due to clinical trial evidence requirements being difficult to gather in small patient populations combined with disproportionately low research and treatment funding, amongst other factors.

The definition of what is a rare and less common cancer is therefore a relevant aspect when identifying relevant patient groups. The Rare Solutions Report[Error! Bookmark not defined.] defines rare, less common, and super rare cancers as follows:

• 'Less common' are defined as those cancers with an incidence of between 6 and 12 (inclusive) per 100,000 Australians per annum;

• 'Rare cancers' are defined as those with an incidence of less than 6 per 100,000 Australians per annum;

• 'Super rare cancers' are defined as those with an incidence of equal to, or less than, 2 per 100,000 Australians per annum, this equates to approximately less than 480 Australians per year.[7]

Patients disenfranchised by current processes would be brought into the fold with multi-tumour listings.

Question 4

[5] Please see Garvan submission for more information
[6] Please see Garvan submission for more information
[7] Rare Cancers Australia. Rare Solutions: A Time to Act. Retrieved from https://bit.ly/2uBrXq4

What is the minimum level of evidence of effectiveness that you/your organisation think should be required before a PD-1 and PD-L1 checkpoint inhibitors is considered for subsidy for a particular kind of cancer? Why?

As far as possible, existing PBAC mechanisms should be utilised in measuring cost-effectiveness. The TGA's recent reforms have shown flexibility in accepting evidence from comparable overseas regulators. NOA suggests similar flexibility be shown by the PBAC to contribute to efficient evidence assessment. Measures such as overall response rate (ORR) and progression free survival (PFS) should begin to play a larger role in quantifying effectiveness as we endeavour towards a future of cancer being managed as a chronic disease. Patient groups and patients have commented on how PFS measures can positively impact a patient's quality of life with advanced disease. However, where data is not available, a fair negotiated price should be agreed upon based on price for other indications, then reviewed with the benefit of real world data after 2-3 years as appropriate. A 'fair price' means that both Sponsors and the Commonwealth share the risk associated with early listing.

If a pay for performance model is pursued in the case of rare cancers, effectiveness would be determined on the individual level. The criteria for such effectiveness would need to be established prior to treatment and ideally would lean on the principles above, existing criterion for a major listed indication and advice/assessment by an independent clinical third party.

Question 5

Do you/your organisation think it is possible for the PBAC to be able to extrapolate, or apply, the evidence of effectiveness of a checkpoint inhibitor in one kind of cancer to another kind of cancer, or from late stage cancer to early stage cancer? Why? How?

Yes – for one kind of cancer to another kind of cancer by using markers such as six-month progression free survival and other efficient identification of response patterns (eg. monthly or bi-monthly testing). This kind of extrapolation is particularly important for rare cancers (where more common cancers are likely to have enough data that extrapolation isn't needed). The use of biomarker testing in this extrapolation is paramount.

No - for late stage cancers to early stage cancers. Randomised trial design necessary as many drugs that are effective in the context of advanced cancer do not have benefit in respect of early stage cancer. In these cases, randomised trials based on biomarker analysis might be the only feasible option in pan-tumour investigation.[8]

Where we can see evidence of clinical effectiveness but insufficient evidence for cost effectiveness we can draw parallels with better studied tumour types where we do have cost-effectiveness data. We should focus more on the intent of the legislation rather than the minutiae of the regulation.

Question 6

Do you/your organisation think it is possible for PBAC to satisfy itself that treatment with a PD-1 or PD-L1 checkpoint inhibitor is cost-effective without an economic model that is specific to that kind of cancer? How?

- **Is it possible to group different cancer types together based on particular characteristics that are similar, and construct a single model for the group?**
  Are other approaches to establishing cost-effectiveness across cancer types possible? What are those approaches and how would they operate?

Yes, drug evaluation always has some degree of uncertainty. For instance, and importantly for new developments in cancer care, the current HTA modelling used does not account for molecular diversity. We have defined cost-effectiveness through the lens of current HTA regulations. We will at times have cancers with adequate evidence for

[8] Please see Garvan submission for more information

traditional cost effectiveness and will also have reasonable evidence of similar clinical effectiveness in others. With some flexibility of mind, it is not difficult to translate cost-effectiveness models based on clinical effectiveness which is then reviewed and buttressed by real world data collection. It is absolutely essential that such data collection is organised in a way that does not delay drug access where there is evidence of clinical benefit, or present an insurmountable burden to treating clinicians, which would also have the result of delayed access. Additionally, there should be a greater tolerance of uncertainty in situations of high unmet medical need, particularly where the patient population is relatively small, easily identifiable and response patterns regularly monitored.

Question 7

What do you/your organisation think is a reasonable subsidy price for Government to pay for a PD-1 or PD-L1 medicines for cancer types where the benefit is potentially very modest?

The NOA is open to the possibility of scaling price according to magnitude of benefit. In high unmet medical need and rare cancer situations that would be pursuing the managed access model; we see no impediment to a pay-for-performance mechanism in this case. An example is where the drug is provided free of charge for 3-4 cycles and if there is a positive response, it becomes subsidised ongoing whilst a patient continues to respond. The term modest is misleading in that individual patients will have a varied response and a patient who has a complete response would not consider their result modest and vice-versa

Question 8

Do you/your organisation think PD-1 and PD-L1 medicines should be made available to all patients whose cancers display a particular biomarker? Why? Which biomarker?

This question is quite narrow at an early stage. For example, we understand debate still exists around the reliability of PD-1 expression as a predictor of efficacy, and it is likely to differ by tumour type. However, where benefits reach an agreed standard (e.g. for trial patients who share property of dMMR across multiple cancer indications where the benefit is at least the same or larger than in patients with melanoma using the same therapies), it would not be equitable or rational to view otherwise. More evidence is still accumulating surrounding the efficacy of biomarker driven approaches, particularly for late stage cancers.

Question 9

Do you/your organisation think it is appropriate for the PBAC to extrapolate the evidence from one PD-1 or PD-L1 checkpoint inhibitor to other medicines in the same class(es). This could provide patients with more choice and give Government the opportunity to negotiate better subsidy prices by utilising the competition between sponsors of medicines.

Our reimbursement system is based on the production of evidence in strictly structured and controlled clinical trials. The proposition of a broad-based abandonment of evidence-based medicine is a significant departure from current medical practice. A case could only be made if future clinical trials show identical results between two or more drugs.

Question 10

Do you/your organisation think that different evidentiary requirements are appropriate for rare cancers? How do you think cost-effectiveness should be established in this case?

Yes, affirmative action is required to fairly treat any disadvantaged minority.

The current model for the discovery, development and reimbursement of treatments is not suitable for patients with rare or less common cancers. There are, for example, a number of medicines that are already available for patients with a common cancer, or likely to be pursued for reimbursement, which could, at the very least, be life-extending for

rare cancer patients. However, small patient numbers often result in fewer global clinical trials, less information about support for the disease and insufficient data to support registration and reimbursement for rare indications. Over the past 20 years, survival rates in many rare cancers have only improved marginally, if at all. It is no small coincidence that in addition to a lack of research funding, the money we spend on treatments for these patients through the PBS is also disproportionately low. Between 2010 and 2016, five medications were listed on the PBS for rare cancer indications, compared to 49 for all cancers. This is despite causing approximately 50% of cancer deaths[9]. When there are structural barriers to registration and reimbursement for rare indications, we see time and time again that one's ability to receive treatment is decided by their economic capacity, not their medical need. This is not in any way congruent with our National Medicines Policy or the purpose of the PBS.

A managed access/pay for performance pathway is highly appropriate for rare cancers. It will expedite access where there is some evidence of clinical benefit and meeting unmet medical need. Weak starter evidence can be buttressed by real world data collection.

Question 11

Do you/your organisation think PBAC should set aside one of its meetings each year to consider only PD-1 or PD-L1 inhibitors for cancer? (This would mean no other submissions for other medicines, including other cancer medicines, or other diseases would be considered at that meeting.)

The recommendations in this submission aim to both reduce administrative/resourcing burdens that cause delays in access to treatment and address systemic exclusion from access to treatments for rare cancer patients. The NOA believes these recommendations will reduce 'churn' and that as long as speed and access to quality and cost-effective medicines is kept to the fore, the existing timeline of PBAC meetings would be suitable to accommodate such recommendations.

Question 12

If limited evidence is available at the time of subsidy of a PD-1 or PD-L1 inhibitor for a type of cancer, what do you/your organisation think should happen afterwards?

- **Should sponsors be required to collect more evidence?**
- **What should happen if the new evidence shows the medicine is less effective or has greater safety risks than expected?**
- **Should the medicine continue to be subsidised but at a price commensurate with its benefit? Should the sponsor be compelled to continue to make the medicine available even if it thinks the price is too low?**

Yes, sponsors should be required to continue to collect more evidence. Managed access approach with data collection achieves two things; expedited access where there is some evidence of benefit, and collection of residual data for eventual listing. There should be a prior agreement regarding the threshold of evidence of benefit under which PBAC will proceed with full listing.

We must be prepared to de-fund medicines where the evidence does not show clinical benefit, although this withdrawal should be able to be grandfathered where it is not a direct safety concern.

Question 13

(For industry/clinical groups) Clinical study information: (Please use the template provided for this information.)

- **In what indications has your organisation completed clinical trials with a PD-1 and PDL1 inhibitor? Please include both positive and negative studies.**

[9] Rare Cancers Australia. Rare Solutions: A Time to Act. Retrieved from https://bit.ly/2uBrXq4

- **In what indications is your organisation currently conducting or planning to conduct clinical trials with PD-1 or PD-L1 inhibitors? If usual PBAC processes were to be followed, when would you expect to make an application for subsidy for these indications?**
- **How does your organisation decide which indications to study and which to prioritise for registration or subsidy?**

Please refer to the answers given in individual submissions to the PBAC by clinical/industry members of the NOA.

Question 14

Are there effective international models for multi-tumour subsidy that could be applied in Australia within the current regulatory framework?

Medicines Australia's Oncology Industry Taskforce (OIT) has conducted preliminary research into innovative international models for subsidy consideration across multiple indications and found that there are various initiatives underway in overseas health systems. Elements of the those highlighted in the table below could be actioned within the existing regulatory framework; however, some legislative change would be required for many if wholesale adoption was sought. Insights around horizon scanning of upcoming indications would be immediately useful, and some learnings could be gathered from the Italian example in relation to the managed access recommendation for rare indications. A more in-depth regulatory comparison is required to make firm comment on the international models' adoptability.

	Belgium	Denmark	Netherlands	Germany	Italy
New indication delay to Market Access	Up to 30 days	Up to 60 days	Immediate	Immediate	Immediate (if deemed innovative)
Form of value assessment for each new indication at launch	None, available in one month	Mini HTA	Abbreviated HTA	None, available in one month	Risk-sharing, payment by results, Fee for efficacy
Form of agreement	2-tiered discount	PVA	PVA	None	MEA
Duration of agreement	2+1 years	2+1 years	3 years	NA	2 years
Budget allocation	✓ For IO products – €200 M (2018)	No	✓ Product specific	✓ Product specific	€ 1 billion fund for innovative therapies
Price	Price based on volume tiers	Price based on volume tiers	Price based on volume tiers	Volume-weighted average price per indication	Net price for each indication with payback depending on performance
Budget cap + payback	✓	No	✓ Product specific	✓ Product specific	✓ Product specific
Any re-assessment of new indication after launch	✓ On-going. CE study required to show impact on all indications	Possible, for any uncertainties in assessment	Possible, for any uncertainties in assessment	✓ Comparator based value assessment within 1 year.	Possible, if MEA is re-negotiated

Question 15

(For Industry) What information can you provide regarding established international agreements for multi-tumour subsidy and how could these apply in the Australian regulatory context?
As above, please consult the Oncology Industry Taskforce's submission for further information.
Question 16 **Is there anything else you/your organisation would like to add?**
There is no doubt that immuno-oncology and precision medicine will change many people's experience with cancer. It is essential that where there is clinical benefit, and especially in cases where there is high unmet medical need, patient's timely access to their oncologist recommended medicines, is not decided by their bank balance. NOA would like to thank the PBAC for conducting this inquiry, and we look forward to continuing the conversation around options for multi-tumour subsidy consideration.