

Medicines Access Programs to cancer medicines in Australia and New Zealand: An exploratory study

Abstract

Medicines Access Programs (MAP) offer access to publicly unfunded medicines at the discretion of pharmaceutical companies. Limited literature is available on their extent and scope in Australia and New Zealand. This study aims to identify MAPs for cancer medicines that were operational in 2014-15 in Australia and New Zealand and describe their characteristics. A preliminary list of MAPs was sent to hospital pharmacists in Australia and New Zealand to validate and collect further information. Pharmaceutical companies were contacted directly to provide information regarding MAPs offered. Key stakeholders were interviewed to identify issues with MAPs. Fifty-one MAPs were identified covering a range of indications. The majority of MAPs were provided free of charge to the patient for medicines that were registered or in the process of being registered but were not funded. Variability in the number of MAPs across institutions and characteristics was observed. Australia offered more MAPs than New Zealand. Only two of 17 pharmaceutical companies contacted agreed to provide information on their MAPs. Eight stakeholder interviews were conducted. This identified that while MAPs are widely operational there is lack of clinical monitoring, inequity to access, operational issues and lack of transparency. Our results suggest a need for a standardised and mandated policy to mitigate issues with MAPs.

1. Introduction

Granting access to new cancer medicines is a growing challenge for pharmaceutical insurance institutions because of the high cost of these medicines [1]. Both Australia and New Zealand have implemented national medicines policies that aim for equitable and sustainable access to medicines [2]. Funding decisions are based on a rigorous value for money assessment that ensures subsidised access to medicines that have been estimated to be cost-effective. However, concerns have been raised on the delays in the regulatory approval and funding of new cancer medicines in these two countries compared to similar countries in Europe and the United States of America [3-5]. At the same time, the rise of targeted, individualised cancer medicine, promoted by mass media and social media campaigns has increased the demand for access to new cancer medicines.

Outside clinical trials, compassionate use programs may be the only way for cancer patients to access expensive, new cancer medicines that are not yet approved by regulatory authorities or funded by a government. Internationally, there is no agreed terminology or nomenclature for compassionate use programs. In Australia, Medicine Access Programs (MAP) is an umbrella term for programs made available at the discretion of pharmaceutical companies that supply new and publicly unfunded medicines to patients either free of charge or at a reduced cost (Figure 1) [6]. These programs facilitate access in various situations such as the use of unapproved medicines, off-label use (use in a non-approved indication), lack of access to clinical trials (no active clinical trials are available or the patient does not meet the eligibility criteria), or 'bridging' time between the end of the clinical trial development, regulatory approval, funding recommendation and listing. They may also allow a pharmaceutical company to supply an approved but publicly unfunded medicine to prescribers within certain parameters. In Australia, pharmaceutical companies can offer free medicines following registration in a Product Familiarisation Program which allows a health care professional to enroll a maximum of ten patients in the program [7].

MAPs may have both benefits and risks. The patient may benefit from an otherwise inaccessible medicine and the pharmaceutical company may get to promote its medicine, develop a future market share and lobby to obtain a successful recommendation for funding. However, critics argue that MAPs are usually not sustainable, create equity issues for those unable to get access to the program or cannot afford the costs that may be incurred, and there is the potential for inadequate

enrolment of patients [6]. New medicines do not have a well-established safety profile, may have uncertain clinical benefit and carry a risk of toxicity [8]. However, since MAPs in Australia and New Zealand are not required to be formally monitored, unlike clinical trials, there may be limited or no systematic recording of health outcomes and adverse drug events.

Concerns have also been raised that some of these programs may be accessed by cancer patients who are desperate and vulnerable [9]. These programs may have a significant financial cost for the patients, provide questionable tangible benefits and place the patient at risk of severe toxicity. In 2015, Australian oncologists reported discussing unfunded cancer medicines with an average of 2.5 patients per month and prescribed them to an average of 0.9 patients per month [10]. Furthermore, it was observed that oncologists were prepared to recommend a cancer medicine that would cost their patients an average of AUD\$ 9,395 per each additional month of survival [11].

There is limited literature on the extent and scope of MAPs in Australia and New Zealand . A report funded by Medicines Australia (the peak body representing pharmaceutical companies in Australia) suggested that the MAPs for cancer medicines were widespread. It reported this from a sample of nine pharmaceutical companies in Australia that provided 28 cancer medicines via MAPs to more than 4,700 patients in 2011 – 2012 [12]. However, it did not list the names of these medicines or the characteristics of those programs; nor did it gauge stakeholders' perceptions and experiences of these programs. The objectives of the current exploratory study were to establish a list of MAPs and their characteristics (types of cancer/patient population covered, patient co-payment and the number of patients enrolled) in Australia and New Zealand in the 2014-15 period. The stakeholders' perceptions of MAPs were also investigated by surveying key stakeholders in the provision of MAPs in these countries.

This study focused on formal MAPs organised by pharmaceutical companies which catered to more than one patient at a time. Information on one-off compassionate supply requests was not sought.

2. Methods

2.1 List of MAPs for cancer medicines

A list of MAPs to cancer medicines and their respective characteristics in Australia and New Zealand was established through a survey of hospital pharmacists working in the area of oncology and a survey of pharmaceutical companies that market cancer medicines.

2.1.1 Development of a preliminary list of MAPs

A preliminary list of MAPs available in Australia and New Zealand was developed using a literature review of published and unpublished reports, approaching key informants likely to have information on these programs and reviewing applications for new cancer medicines made to the Pharmaceutical Benefits Advisory Committee (PBAC) (which examines applications for funding in Australia) for subsidy between July 2013 and June 2015. The informants (oncologists, oncology pharmacists, members of drug and therapeutics advisory committees) were identified through the research team's professional contacts. They were subsequently sent an email to explain the project and invited to provide information on MAPs. The objective of this step was to identify a preliminary list of cancer medicines that were offered through MAPs rather than focus on their characteristics.

2.1.2 Survey of hospital pharmacists

The preliminary list of MAPs was formulated into an online questionnaire using SurveyMonkey®. The preamble explained that the focal point of the survey was on formal programs offered to more than one patient at a time rather than a one-off supply to a particular patient. The questionnaire sought information on MAPs for cancer medicines available in Australia or New Zealand between January 2014 and July 2015, programs still operational at the time the questionnaire was sent, the number of patients enrolled per program, types of cancer/patient population covered and the charge to the patient. Participants had the opportunity to add details of programs that were not on the list. The online survey was subsequently sent to members of The Society of Hospital Pharmacists of Australia (approximately 3,400 members) through the society's newsletter and to the Cancer Pharmacist Group of The Clinical Oncology Society of Australia (157 members) and New Zealand's Hospital Pharmacists' Association (340 members) via email. The pharmacists were given two weeks to respond after which a reminder notification was sent. The survey instructions stated that a single response per institution was sufficient.

The exact number of cancer centres in each country could not be established. Based on the national 'Australian Hospital Statistics Report 2012-13' there are likely to be fewer than 137 major hospitals in Australia [20]. New Zealand has 31 hospitals with pharmacy services [21].

2.1.3 Survey of pharmaceutical companies

Pharmaceutical companies were approached directly to offer information on MAPs they provided. A list of pharmaceutical companies in Australia likely to be involved in marketing of cancer medicines was obtained through Medicines Australia's website and funding applications to the PBAC. The company's contact details were obtained from their Australasian website and a telephone call was made to identify the key team/personnel with which to liaise. Subsequently, an email was sent requesting information about the MAPs they provided in Australia and New Zealand. Companies were given two weeks to respond after which a reminder telephone call was made or an email sent to follow-up. All companies were given a time of four weeks to respond.

2.1.4 Registration and funding status of medicines provided in MAPs.

The registration and funding status of medicines provided in MAPs was ascertained in Australia and New Zealand by examining information posted on the medicine regulatory websites (Medsafe in New Zealand and the Therapeutic Goods Administration (TGA) in Australia) and the public funding agencies (PHARMAC in New Zealand and the Department of Health which administers the Pharmaceutical Benefits Scheme (PBS) in Australia including the Public Summary Documents pertaining to funding recommendations made by the Pharmaceutical Benefits Advisory Committee (PBAC)). MAPs were classified into three main categories: "no registration", "no funding", and "outside funding restrictions" for both countries. "No registration" applied to medicines that were not registered for the indication in the MAP until the end of the study period in July 2015. "No funding" applied to medicines that were registered but not funded for the indication during the study period. "Outside funding restrictions" applied to medicines that were both registered and funded for the indication and inferred to be used outside funding indications in MAPs (e.g. as a second-line treatment instead of first-line treatment or for patients who do not fulfil the clinical criteria outlined in the listing requirements).

2.2 Interview with key stakeholders

Members from each key stakeholder group in Australia or New Zealand were invited to participate in a semi-structured interview. The stakeholder groups included oncologists, hospital pharmacists, cancer consumer organisations, cancer patients using MAPs, the Department of Health and Medicines Australia. The members were identified either through the research team's professional contacts or through information available in the public domain. Interviews were either conducted face-to-face or through Skype®. All interviews were recorded with permission. Questions focused on exploring interviewees' understanding of MAPs, their benefits, risks, processes around implementation and future prospects.

2.3 Data analysis

Data on MAPs obtained from key informants in the preliminary stage, the hospital survey and the pharmaceutical companies' survey was compiled to develop a list of MAPs. Characteristics of MAPs were summarised using descriptive analysis. Interviews were analysed using descriptive thematic analysis. Initially, the recordings were listened to by two members of the research team to identify the themes that emerged from the interviews. Following this, a group analysis session involving members of the research team was conducted to further refine the themes.

2.4 Ethics approval

Ethics approval for the study was granted by The University of Notre Dame's Human Research Ethics Committee (reference 015060F).

3. Results

3.1 List and characteristics of MAPs

Twenty-eight cancer centres in Australia and New Zealand responded to the survey. Nineteen responses were received from cancer centres in Australia and nine responses from centres in New Zealand. Fifty-one MAPs were identified as available in Australia and 36 in New Zealand in 2014-15. All programs available in New Zealand were also available in Australia. The programs covered a wide range of cancer types and patient population. A list of MAPs and their respective characteristics can be found in the Appendix.

The median number of MAPs available per centre in Australia and New Zealand in 2014-15 was 12.5 (range 1-34) overall, 17 in Australia (range 4-34) and 10 in New Zealand (range 1-14). The average number of patients per program in that period was 22.

Most (33, 65%) of the MAPs were provided free of charge to the patient while 12 (23%) had a cost-share arrangement between the patient and the pharmaceutical company with patient costs ranging from AUD \$1,200 to \$150,000. The payment arrangements for the remaining six (12%) MAPs could not be determined.

Most MAPs in Australia were for medicines that were registered or in the process of being registered but were not funded (47.0%) or were likely to be used outside funding restrictions (39.2%) (Table 1). A higher proportion of MAPs in New Zealand compared to Australia was for medicines that were not registered (33%). The registered medicines in MAPs were not funded (41.6%) or were likely to be used outside funding restrictions (19.4%) (Table 1).

3.2 Survey of pharmaceutical companies

Australian branches of 17 pharmaceutical companies marketing cancer medicines were contacted. Over 50 telephone calls were made and more than 70 emails were sent to obtain responses. Two pharmaceutical companies, Gilead® and Bristol-Myers Squibb®, agreed to participate and provided the majority of the information requested. Bristol-Myers Squibb chose not to disclose the number of patients enrolled in its access programs. Thirteen companies declined to participate in the study citing commercial reasons for their decision. A response could not be obtained from the remaining two pharmaceutical companies despite numerous attempts at contact.

3.3 Interviews with stakeholders

Eight interviews were conducted to explore issues with MAPs. These included interviews with two oncologists, a group interview with five hospital pharmacists from the same hospital, another hospital pharmacist, a pharmaceutical policy adviser at the Department of Health, a MAP consumer, a senior manager at a national cancer charity and a representative from Medicines Australia. One pharmacist sent back written answers to the interview questions.

Upon analysis of the stakeholders' interviews, six major themes regarding MAPs were identified as described below.

3.3.1 Benefits of MAPs

Stakeholders acknowledged that MAPs fulfil an area of unmet access to medicines for certain patients. They facilitated access when the medicines were not routinely available for the patient or were needed as a “last-resort” treatment option. It was noticed that these medicines sometimes offered benefit to patients in terms of longevity and quality of life. These programs were also reported to familiarise prescribers, through Product Familiarisation Programs, with medicines that were not yet routinely available.

“Patients who are expecting them and don’t have other options, don’t have to wait for as long. Side benefits include doctors become familiar with using them [medicines] and managing their patients on it.” (Representative from Medicines Australia)

3.3.2 Ethical concerns

As is evident from the quotes below, stakeholders were concerned about the ethical issues with access to MAPs. Stakeholders reported inequities of access as there was no organised forum for them to find out which programs were operational, eligibility criteria and processes to access them. The cost-share arrangement associated with some MAPs precluded certain patients with cancer from affording them. Whilst the majority of the MAPs were found to be provided free of charge to the patient, some attracted a high charge costing a patient up to AUD \$150,000 per year (e.g. ruxolitinib (Jakavi®)).

Some stakeholders also raised concerns about the potential discontinuation of supply of medicine to the patient post cessation of the program.

“There are no contractual obligations to my knowledge for the company to keep supplying it [medicine].” (Oncologist)

“Access would vary enormously based on clinician, company, therapeutic area and product development. I do not have enough visibility on similarities and differences between them.” (Representative from Medicines Australia)

3.3.3 Administrative burden

Pharmacists and prescribers reported increased administrative workload associated with MAPs without recognition of it or acknowledgement. The workload, at a pharmacy level, included setting up operating procedures for procurement, storage and

dispensing of medicines. At a prescriber level it meant filling out applications to pharmaceutical companies for individual patients to procure the medicine, applying to the hospital's drug and therapeutics committee for approval to prescribe the medicine, complying with the companies' requirements for continued supply and writing prescriptions for repeat supply.

"There is no awareness certainly at a prescriber and executive level that these programs are a different process at a pharmacy level than a regular medicine." (Pharmacist)

3.3.4 Lack of clinical monitoring

Stakeholders expressed concern that there were no mandated and standardised policies for patients to be clinically monitored whilst on these programs. These medicines have limited data on their safety and efficacy and a lack of adequate monitoring was reported to place patients at risk of toxicity and harm. Contrary to clinical trials there were also concerns that there were no formal requirements to collect any clinical data on patient outcomes.

"Collection of data should be a condition of access." (Pharmaceutical policy adviser)

"My understanding of most of the programs is that clinical data is collected but the level and variety will depend on therapeutic area, product [medicine] and clinician. The difficulty is mandating clinicians to collect data." (Representative from Medicines Australia)

3.3.5 Lack of transparency

There was general consensus amongst stakeholders that there was a lack of transparency from pharmaceutical companies on aspects of MAPs. There was no clear information on which MAPs existed, types of cancer/patient population covered and ways to access them for individual patients. Some stakeholders also reported being bound by confidentiality agreements that did not allow them to discuss MAPs of which they had knowledge. The research team found, as noted above, that obtaining information from pharmaceutical companies on MAPs was challenging. However, the representative from Medicines Australia anticipated challenges that would be associated with greater marketing of MAPs.

"Lack of transparency inevitably means there is inequity." (Pharmaceutical policy adviser)

“The concern I have with complete transparency is the pressure it will put on clinicians and pharmaceutical companies to provide access to everyone even if it is not suitable for them.” (Representative from Medicines Australia)

3.3.6 Future of MAPs

Stakeholders urged that MAPs should be operated with greater patient monitoring and transparency from pharmaceutical companies. Most stakeholders were in favour of clinical data on patient outcomes being systematically collected and reported. Some suggested the establishment of a registry of MAPs allowing for uniformity in the awareness of operational MAPs, mitigating some issues around inequity of their access. Additionally, pharmacists suggested that remuneration for the administrative workload around MAPs was warranted.

“They have to be run like trials. We run them like trials except we don’t charge.”
(Pharmacist)

These [MAPs] don’t go through the registry as far as I know. There is no data, I would prefer to see them run like clinical trials.” (Senior manager at a national cancer charity)

“Current systems must be flexible enough in a transparent way to address community expectations with access in areas of high unmet clinical need.” (Pharmaceutical policy adviser)

4. Discussion

A total of fifty-one MAPs were available in Australia and New Zealand in the 2014-2015 period. This is substantially greater than the 28 MAPs identified in Medicines Australia's report in 2011-2012 [12]. Several reasons may explain this higher number. The present study compiled information from different sources including from hospital pharmacists directly involved in the administration of these programs in cancer centres. Also, there is a possibility that the data reported by the respondents may have included information on cancer medicines provided to patients on an individual basis rather than in comprehensive programs organised by pharmaceutical companies.

Most MAPs involved registered medicines or medicines close to registration but still publicly unfunded. MAPs are thus generally different from Expanded Access Programs in the United States of America [13] or Compassionate Use programs in European states [14, 15] which involve investigational medicines exclusively. There are a number of reasons for this. In Australia, registration submissions are made later than to the U.S. Food and Drug Administration (FDA) or to the European Medicines Agency and registrations are even more delayed in New Zealand [3, 4]. Also, the time to positive funding decisions and actual listing appears to be longer in Australia and New Zealand than in some other countries [16]. For cancer medicines registered between 2010 and 2016 in Australia, the average time between registration to the date of PBS listing was 18.6 months [17]. The existence of these MAPs is implicitly recognised by the PBAC as recommendations for funding may include grandfathering provisions. For example, vorinostat was recommended by the PBAC and included grandfathering provisions for patients who had accessed the medicine through the sponsor's "Expanded Access Program" [18]. Furthermore, the PBAC may impose restrictions on the use of funded medicines considering that patients who do not fulfil the criteria may receive the medicine under a MAP. For example, the PBAC restricted the use of pembrolizumab to patients with metastatic melanoma who had not been previously exposed to ipilimumab while considering that the company will continue providing pembrolizumab to ipilimumab-refractory patients through a MAP [18]. In a number of cases, MAPs may start while the medicine has not been registered yet and access would need to be notified through the Special Access Scheme pathway. Once the medicine is registered but still unfunded, access may be provided under compassionate use or as a Product Familiarisation Program in Australia.

MAPs can also be provided for medicines that are registered and funded but prescribing restrictions may limit use to specific indications or to patients who fulfil some conditions. For example, abiraterone was listed on the PBS in August 2013 but it had to be used in combination with the specified steroids only [19]. Enzalutamide was listed in December 2014 for metastatic prostate cancer but only as a second-line agent in patients who had received prior chemotherapy [20]. MAPs could then be provided at different stages during the regulatory life cycle of a medicine. For example, pembrolizumab could be provided before registration, between registration and PBS listing, and after listing to patients who do not fulfil the clinical restrictions of the PBS listing (i.e. who have not been previously exposed to ipilimumab).

The average number of patients per MAP in this study was 22 which is much lower than the average of 169 patients per medicine found in Medicines Australia's report [12]. This may be due to the fact that programs proposed in the period studied were used by a lower number of people on average though it is also likely that our results underestimated the number of patients actually on MAPs in Australia and New Zealand because of the low response rate in our survey. According to documents released under the Freedom of Information Act 1982, the number of applications to the Australian Special Access Scheme for pembrolizumab was 170 between the 1st of January 2014 and 31 January 2015 [21]. Although it is not known how much of this usage was provided through MAPs, this number is higher than the estimate that can be drawn from the responses received in the present study (36). The PBAC application for vorinostat indicated "less than 10,000 active patients with CTCL [cutaneous T-cell lymphoma] receiving vorinostat treatment through the MSD [Merck Sharpe & Dohme] Expanded Access Program (EAP)" [18]. It is likely that MAPs actually cater to many more patients than what was observed in this study. However, the exact numbers are not made available publicly including in the Public Summary Documents released by the PBAC where these numbers are blacked out [18].

Australia had more MAPs than New Zealand. The two countries differ significantly in their funding practices [2, 22]. New Zealand operates on a capped budget and spent less than half of Australia's per capita medicine expenditure in 2011. Additionally, new cancer medicines in New Zealand were found to be less likely to be funded than in Australia [3, 23, 24]. Therefore, there may be less incentive for pharmaceutical companies to offer a medicine through MAPs as there is less chance of getting a

positive funding decision. Patients may get subsidised access to unfunded medicines only in exceptional circumstances [25].

Interviews of stakeholders in this study confirmed previous reports in the literature that MAPs facilitated access to new cancer medicines for patients who had exhausted funded treatment options [8,26]. While enrolment in clinical trials of new medicines could still be a possibility, no active clinical trial may be available or patients may not fulfil the eligibility criteria. Access to international clinical trials of cancer medicines is limited as there may be only a few places kept for Australian patients [4]. New cancer medicines may also be unavailable because of long delays before regulatory approval, and between regulatory approval, funding and listing of medicines [4].

The issue of lack of transparency on MAPs in Australia and New Zealand was a strong theme not only in the stakeholders' interviews, but also in the survey of pharmaceutical companies. Only two of the 17 pharmaceutical companies surveyed agreed to provide information on MAPs they offered. It may be that pharmaceutical companies were unwilling to discuss some aspects of MAPs as it could be seen to promote access to these programs outside specific cancer centres and could lead to an unmanageable number of requests for access from patients. Open discussion of programs could also be perceived as direct promotion of prescription medicines to consumers which is currently prohibited in Australia. It could also interfere with the financial negotiations between these companies and the funding authorities. In developing the preliminary list of MAPs, some pharmacists (including some from leading cancer centres) and oncologists were unwilling to share information citing confidentiality agreements with pharmaceutical companies as the major reason. Cancer centres may also not be willing to advertise MAPs as they cannot manage to have patients coming from all over the country. However, consumers and health professionals would likely welcome the availability of publicly available information on MAPs.

Stakeholders were concerned at the lack of clinical data collected and patient monitoring associated with MAPs. The lack of accountability, governance and scrutiny of these programs has the potential for harm to patients. Currently pharmaceutical companies are under no obligation to collect, monitor or report any clinical data on MAPs which differs from clinical trials which are governed by strict protocols [26]. Given medicines provided through MAPs can be investigational products or have only been used by a limited number of patients, their clinical benefit to patients could be uncertain and there may be a risk of toxicity. However, the collection of data within a

MAP places legal obligations on pharmaceutical companies that would need to be further defined in Australian regulations. We note that data collection by prescribers and pharmacists would increase the already significant administrative burden these programs place them under. This was echoed in the discussion with pharmacists that manage these programs. It would be important to ensure that the administrative requirements of MAPs match the resource allocation for them.

This study found large variations in the number of MAPs available at each centre. Some centres reported up to 34 MAPs had been available at some stage in 2014-15 and some only one. These findings support the concerns raised by consumers, clinicians and pharmacists during the interviews about the lack of equity of access to MAPs across centres. Variability of access to MAPs is part of a wider issue with the variability of access to high cost medicines in Australian hospitals not listed on the PBS, as previously reported [27, 28]. These medicines have to be paid from hospital budgets, and the availability of resources and processes for allocating resources vary between hospitals and between states, resulting in some medicines being available in some hospitals but not in others.

Another equity issue is the existence of cost-share arrangements as observed in approximately a quarter of these programs. High costs will preclude otherwise eligible patients from accessing medicines [30]. Unaffordable access to MAPs may represent a departure from current medicine policies that promote equitable access to medicines for all citizens [9].

In May 2015, the Council of Australian Therapeutic Advisory Groups (CATAG) launched a set of guiding principles to facilitate appropriate governance and implementation of MAPs [6]. These intend to promote quality use of MAPs and prevent the likelihood of physical and financial harm to patients and hospitals. However, it is not known whether the principles captured by these guidelines are complied with in Australia, as these are neither mandated nor regulated. Current regulations for access to unapproved medicines in Australia (Special Access Scheme) and New Zealand (Section 29) only envisage individual access to unapproved medicines and are not suited to the regulation of programs which may enrol cohorts of patients like in MAPs [29, 30]. Such regulations have been implemented in the Expanded Access Programs in the US [13] and in some European countries for compassionate use of medicines [14, 15] with the objective to improve the protection of patients and the collection of safety data. In Australia, Product Familiarisation Programs following registration can

be proposed [7]. However, no comprehensive information is publicly available on these programs. New provisions introduced in the 2015 edition of Medicines Australia's Code of Conduct allow the collection of individual patient data under a formal protocol. This, however, is not mandated or monitored.

In Australia, in response to two national reviews, the 'Expert review of medicines and medical devices regulation' and the Australian Senate's inquiry on 'Availability of new, innovative and specialist cancer drugs in Australia' [4, 5, 31], a number of policy recommendations have been or are in the process of being implemented by the Australian Government. These include shorter registration processes with the priority review pathway [32], the provisional approval pathway [33] and the consideration of comparable overseas regulators' assessment in the registration process [34]. In September 2017, Special Access Scheme processes have been improved [30]. In August 2017, a \$13 million Rare Cancers and Rare Diseases research program to stimulate clinical trial activity may provide new avenues for patients with rare cancers to benefit from the latest research [35]. The implementation of managed access programs where funding is conditional to the provision of further scientific evidence may also decrease the need for MAPs in the future by bridging the gap between regulatory approval and the listing of medicines [2, 36].

In New Zealand, a recent study funded by PHARMAC concluded that, in the absence of clinically significant health benefits provided by cancer medicines funded in Australia but not in New Zealand, "*a policy of funding more new cancer medicines in order to achieve numerical parity with Australia or other countries would not result in substantive health improvement... and would not represent good value for money in terms of delivering the best health outcomes for all New Zealanders*" [37].

The results of this study demonstrate a compelling need for greater transparency and accountability for MAPs. The findings create a strong case for collaboration between the stakeholders to promote safe, equitable and monitored use of MAPs. The existence of these programs is well recognised by all stakeholders including by the PBAC [38]. However, there is no legal or regulatory framework for MAPs. The use of unapproved medicines by significant number of patients outside clinical trials should be regulated as it is in other countries, for example the Expanded Access Programs for investigational drugs in the United States of America. Product Familiarisation Programs for approved medicines that are currently controlled under Medicines Australia's code of conduct have no legal recognition. It is not clear whether the rules

of Medicines Australia's code of conduct also apply to medicines that are provided for compassionate use after registration. Ideally, the rules related to these programs should comply with the provisions outlined in the CATAG guidelines including: "any MAP should ensure uninterrupted supply, free of charge ... for as long as the patient's treating clinician determines that there is a clinical benefit and no equivalent or tolerated therapeutic alternative for the patient remains available Australia" [6]. There should be an open access registry for MAPs, which provides detailed information on the medicines and processes to follow, within a regulated framework as suggested by the CATAG guidelines.

Limitations of the study

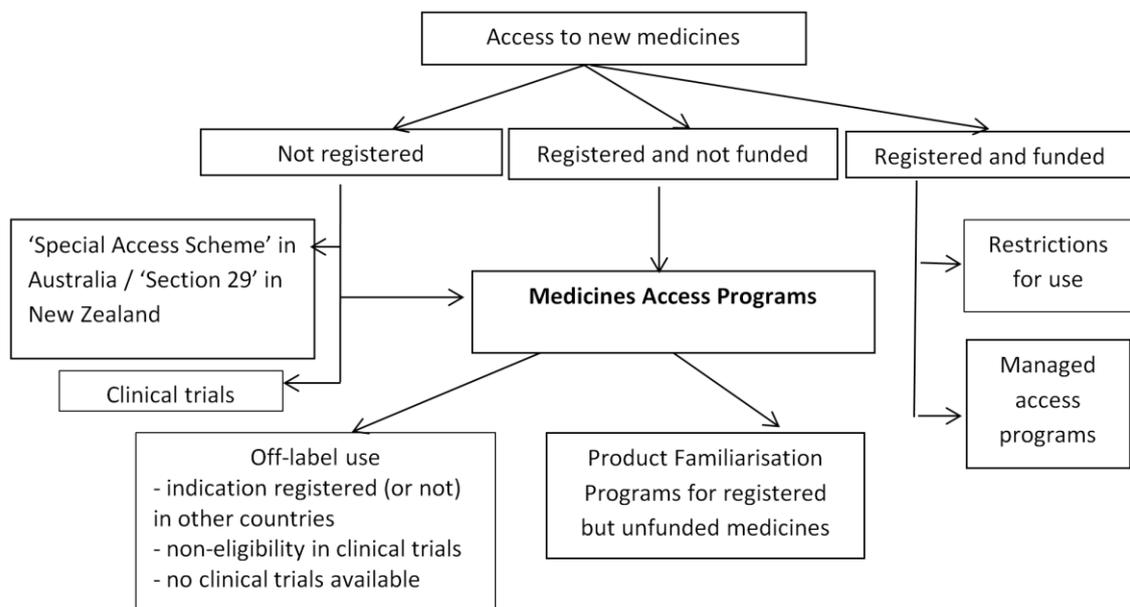
This study has a number of limitations. The small number of respondents to the pharmacist survey may underestimate the actual number of patients on MAPs. The assessment of registration and funding status of medicines provided through MAPs was done on the basis of the limited information provided in the survey. It was not always possible to identify the exact indication(s) for which medicines were used and the indications may vary among patients and over time. Only a limited number of stakeholders were interviewed and the views expressed may not be representative of that stakeholder group as a selection bias may be present. The reliability of the comparison between the availability of MAPs in Australia and New Zealand is limited by the small number of respondents in each country.

5 Conclusion

Medicines Access Programs are widely operational in Australia and New Zealand. These programs raise a number of important issues with regards to the lack of overarching regulatory policies, consistent governance, adequate information and protection of patients, outcome and safety monitoring, transparency and equity of access. A number of initiatives such as the publication of the CATAG guidelines may improve the current situation. Also, a collaborative approach is needed to drive standardised and mandated policies to mitigate issues with MAPs. Further research is required to enable a more comprehensive analysis of the MAPs in place overtime across Australia and New Zealand.

Figure 1

Access to new medicines in Australia and New Zealand



Note: the Special Access Scheme in Australia and Section 29 in New Zealand regulate access to unapproved medicines.

Table 1 Registration and funding status of medicines provided in MAPs in Australia and New Zealand

	Australia		New Zealand	
	Number	Percentage	Number	Percentage
No registration	6	11.8	12	33.3
No funding	24 (10*)	47.0	15 (6*)	41.6
Outside funding restrictions	20	39.2	7	19.4
Outside registered indications/no funding	1	2.0	1	2.8
Unknown	0	0	1	2.8
	51	100	36	100

*Registered during study period

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