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White Paper

# ACCESS TO NEW THERAPIES: PERSPECTIVES AND BEST PRACTICE ON AUSTRALIAN EARLY ACCESS MECHANISMS

*15 best practice considerations for healthcare value chain stakeholders*

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# INTRODUCTION

Access to required medicines is considered part of the *Right to Health,* which was declared a social right in the World Health Organization Constitution (1946) and the United Nations' Universal Declaration of Human Rights (1948). Within the realm of access lies the question: is regulatory approval enough for access? With the growing trend towards specialised medicines, therapies are becoming increasingly complex to develop but also more expensive to commercialise to the point of unaffordability for individual patients. This makes coverage under a universal healthcare offering ever more difficult, with delays to reimbursement often occurring to ensure cost-effectiveness. Hence, although a medication may be available after regulatory approval, it is not necessarily accessible to patients.

*Disclaimer: Early access to medicines has been a controversial subject in the media with claims of solely commercial motivations behind providing access to medications prior to government reimbursement. However, the perspectives of both patients and healthcare professionals (HCPs) indicate not only an expectation of early access but a need for easier access to medicines awaiting both approval and reimbursement. In this white paper, IQVIA will provide various perspectives from three different groups of stakeholders.*

This report includes a comprehensive analysis of the Australian landscape of early access mechanisms including quantitative analyses and perspectives from pharmaceutical companies, healthcare practitioners, and patient representatives based on stakeholder interviews and internal expertise. The quantitative analyses are based on IQVIA's Medibus panel surveys of pharmacists and physicians. Included in this paper are hospital pharmacists (n=27), medical oncologists (n=30), and haematologists (n=30). In addition to landscape analysis, the report also highlights 15 best-practice considerations that are recommended when providing early access to new therapies in Australia.

While the naming of early access mechanisms has not been clearly defined, the scope of the report includes those which bridge the gap between clinical testing and reimbursement. These include special access schemes, authorised prescribers, expanded access, compassionate supply, and product familiarisation programs.

Although off-label use and the personal import scheme will be defined in the report, they are excluded from the analyses and best practice considerations. Not included in this report are alternative routes to reimbursement such as managed-access programs or the Life Saving Drugs Program. Additionally, marketing strategies, such as sampling, are also excluded from the report.

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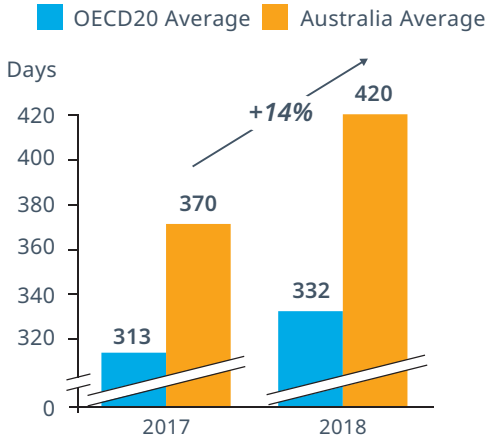
# OVERVIEW OF EARLY ACCESS MECHANISMS

The trend towards specialty care products, especially in markets with high unmet need, such as immunology, haematology, oncology, and rare diseases has prompted regulatory bodies to facilitate quicker approvals. In many cases reimbursement bodies have yet to follow suit.

In recent years, the length of time between approval of new medicines and their subsequent reimbursement across the top 20 Organisation of Economic Cooperation and Development (OECD) countries have been increasing, inadvertently delaying wider access to patients in need. The average time to reimbursement has been increasing at a rate of 1% per year with a dramatic increase from 313 to 332 days between 2017 and 2018. Australia has seen an even larger increase of 3% since 2015 and a 2017-18 increase from 370 to 420 days to reimbursement, 88 days longer than the OECD average (*Fig. 1*).[1]

Providing medicines to patients who could benefit from them, prior to their reimbursement, lies within the *Right to Health*, as does providing unapproved medicines which have proven safety and efficacy yet are still awaiting local market authorisation. The Therapeutic Goods Administration (TGA) has provided multiple mechanisms by which patients and prescribers can access safe and effective, or last-resort, medicines which have yet to be TGA approved. The pharmaceutical industry representative, Medicines Australia, in combination with company policies, have also established alternative mechanisms by which patients can access essential and unfunded therapies, ensuring more accessible medicines for the unmet need of patients.

**Figure 1: Australian and OECD20 average time from registration to reimbursement (2017-2018)**

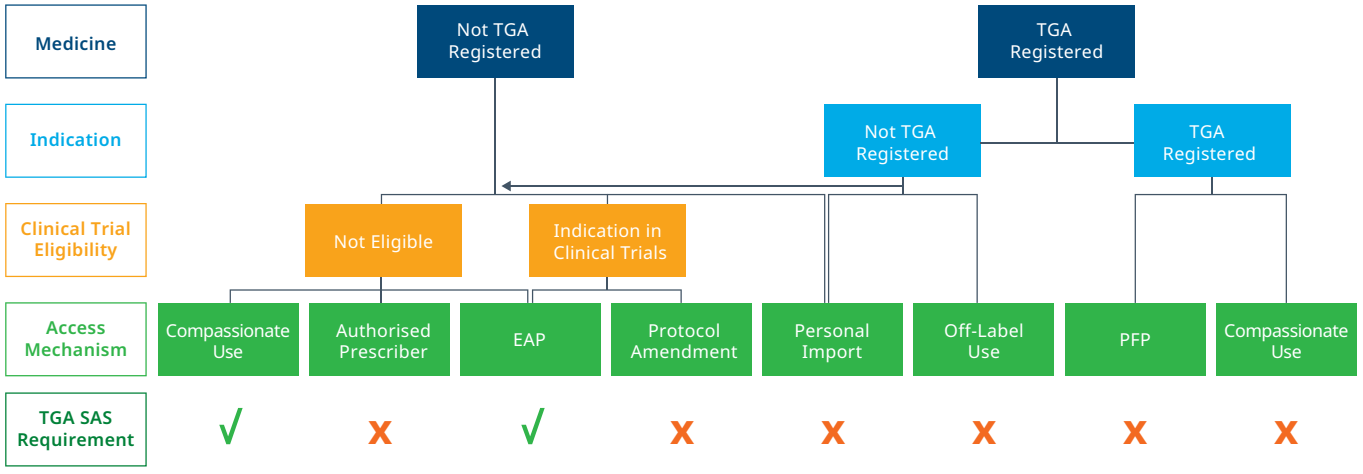



The OECD20 average time from registration to reimbursement over a four year period from 2015-18 has been **increasing by 1%** while **AU has been increasing at 3%** and **14% from 2017-2018**

## PRE-TGA ACCESS MECHANISMS

Prescribing physicians can initiate access to TGA unapproved medicines through both the Special Access Scheme (SAS) or Authorised Prescribing (AP). Alternatively, patients who have benefited from their clinical trial therapy and are awaiting regulatory approval have the right to continue treatment under the World Medical Association's Declaration of Helsinki which states that "sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial." [2] However, when patients are well informed on new therapies available, they can approach their physician regarding the Special Access Scheme (SAS), although the prescribing physician needs to ultimately notify or apply to the TGA.

**Figure 2: Australian early access mechanism schematic overview**



## SPECIAL ACCESS SCHEMES (SAS) [3]

The SAS is a regulated arrangement whereby a single patient accesses TGA unapproved therapeutics on a case-by-case basis.

There are three pathways for access, depending on the circumstances of both the patient and the therapeutic.

### Category A

Category A provides prescribing medical practitioners (or a health practitioner on behalf of a prescribing medical practitioner) the ability to access therapies for patients if the:

1) Patient is seriously ill, and death is likely within months or,
2) Patients' premature death is likely without access to early treatment

Category A only requires that the medical practitioner provides notification to the TGA within 28 days.

### Category B

Category B provides health practitioners the ability to request access therapies for patients if the:

1) Patient does not fit the Category A description or,
2) Unapproved therapy does not have an established history of use (Category C)

Category B requires an application to the TGA but is generally only granted to medical and dental practitioners.

### Category C

Category C provides health practitioners the ability to access therapies for patients that:

1) Have an established history of use and,
2) Are included on the TGA Authorised Supply list for the specific indication

Category C only requires that the health practitioner provides notification to the TGA within 28 days. No drugs Schedule 8 or higher can be accessed through the Category C SAS.

## AUTHORISED PRESCRIBING (AP) [4]

Authorised Prescribers are medical practitioners who hold specific expertise, and who have applied and been granted the authority to prescribe a specific product to certain patients that require access to an unapproved therapy. This authority only allows the prescribing of a specific therapeutic or class of therapeutics to a specific type of patient or class of recipients with a particular indication. The AP must be able to properly assess the patient and monitor them following therapy.

Once granted the authority of Authorised Prescriber, the practitioner no longer needs to give notification to the TGA when prescribing but are required to report the number of patients they have treated every six months.

## EXPANDED ACCESS (EA) [5,6]

Offered by the pharmaceutical company, expanded access after a clinical trial is generally used for the indication that is yet to be approved by the TGA but under clinical investigation. Therapies through EA are generally offered free of cost and can also be given to patients that do not meet the inclusion criteria of clinical trials or have finished their clinical trial and require continued supply of the beneficial, yet unapproved therapy.

Many hospitals or trial sites will ensure that patients' enrolment in a clinical trial includes provisions to ensure all patients that require continuation do so until it is funded by the PBS. Alternatively, data can continue to be collected like in the clinical trial through a protocol amendment. This requires the sponsoring company to resubmit the amendment to human resources and ethics committee, complete an additional ethics application, renegotiate the clinical trial agreement, re-notify the TGA, pay an additional site fee, and update study plans in the databases to extend the period of study.

## UNFUNDED ACCESS MECHANISMS

After regulatory approval, there are less stringent regulations surrounding patient access of approved-but-unfunded therapies. As the therapy is then legally allowed to be sold in Australia, the access is generally negotiated between the company and the patient's prescriber. However, Medicines Australia (MA) have strict guidelines surrounding Product Familiarisation Programs (PFPs) as described in the MA Code of Conduct, which is Medicines Australia's complement and extension of the Therapeutic Goods Act 1989 (Cth), setting the standard for ethical pharmaceutical marketing and promotion. Importantly for companies, PFPs are the only early access mechanism, other than those pre-registration mechanisms defined by the TGA, that are defined by an external authoritative body (Medicines Australia).

They are conducted on a relatively large scale, where prescribers can enrol up to ten patients each but can be confined by company requirements. Alternatively, compassionate supply can be made accessible on a case-by-case basis if approached by patients or prescribers, but if set up in a program-like fashion similar to a PFP without a compassionate justification, a complaint can be registered with Medicines Australia by prescribers, companies or other industry stakeholders. According to the Medicines Australia Code of Conduct Annual Reports, there have yet to be breaches in the Code for Product Familiarisation Programs (Section 8). However, the fact that non-PFP early access programs have been investigated, and subsequently cleared by Medicines Australia, shows they acknowledge and allow other early access mechanisms between registration and reimbursement, *i.e.* larger scale compassionate use programs, but these programs will need clear evidence that their primary purpose is not to give HCPs familiarity of the new therapy.

### PRODUCT FAMILIARISATION PROGRAM (PFP)[7,8]

Product Familiarisation Programs are offered by the sponsoring pharmaceutical company to allow prescribers to evaluate and become familiar with a product. While it is not mandated that the product be seeking reimbursement, the PFP will generally occur while PBAC analysis and recommendation are in progress. In Australia, these programs are generally self-regulated with manufacturers abiding by the Medicines Australia Code of Conduct (Ed. 18) around the use of PFPs, the Council of Australian Therapeutic Advisory Groups' (CATAG) guiding principles for the governance of medicine access schemes in Australian hospitals, whilst also ensuring any personal information collected is used, stored and disclosed in accordance with the Australian Privacy Principles in the Privacy Act 1988. In general, PFPs must:

1) Treat patients for only the TGA approved use of the medicine
2) Enrol patients for a fixed period (no longer than 6 months) and after, will only continue enrolment if there is significant clinical rationale
3) Provide free packs to prescribers for use by the patient or pharmacy
4) Only enrol 10 patients per HCP in the program
5) Only collect individual patient data when a formal protocol complying with the relevant legislation regarding patient consent and de-identification has been constructed by the company

### COMPASSIONATE SUPPLY/COMPASSIONATE USE (CU) [9]

Compassionate use programs are initiated by the sponsoring pharmaceutical company and provide medicines that are not reimbursed or part of another funding scheme. Generally, medicines are offered to patients as a rescue treatment, or to those with serious/life-threatening conditions, but patients should be enrolled on a carefully selected case-by-case basis.

Generally, compassionate supply is offered free of charge, however this is not always feasible for the company, so a cost-sharing arrangement may be agreed upon between the patient and company. These types of agreements can include buying a set number of months treatment and receiving the rest free, buying two packs for the price of one, general discounts, or even outcome-based payment terms. Compassionate mechanisms are not formally defined by any Australian authority, with the CATAG Guiding Principles giving a definition to assist hospitals in interpretation of their principles, however companies are not required to follow these. This lack of a clear, universal definition creates varying terminology used in industry, and often the umbrella term of "early access program" is used.

**OFF-LABEL USE** [10]

It is unlawful for companies to promote medication for use in indications that have not been approved by the TGA. Therefore, it can be very difficult for prescribers to find guidance on off-label prescriptions. Although there are no legal prohibitions on off-label prescribing, the prescriber must have a significant defence for their choice of therapy.

**PERSONAL IMPORT SCHEME** [11]

Personal import of medicines occurs when an individual either arranges for a therapeutic good to be posted to Australia or personally brings the good into the country. These goods cannot be sold and cannot be supplied to any persons outside the immediate family of the individual. Many regulations surround the use of this scheme and the circumstances under which the personal import scheme can be used:

- Must be used by importer or immediate family,
- Must not contain prohibited substances,
- Cannot be an injection of animal or human origin excluding insulin,
- Must not exceed 3 months' supply per import and the total import for the year must not exceed 15 months' supply at the manufacturer's recommended maximum dosage, and
- If prescription medicine, must be subject of a State/Territory registered medical practitioner prescription

# PERSPECTIVES

## PATIENT REPRESENTATIVE PERSPECTIVES

***Early Access is wanted and needed by patients***

As innovative therapies continue to take over a year to achieve reimbursement in Australia (*Fig. 1*), access to medicines is extremely important for patients suffering from life-threatening or life-altering conditions who may not have the time to wait. New medicines that are available could remain unfunded for over triple the time patients have been given to live. When given poor prognoses, and when all treatment options have been exhausted, the unmet need is undeniable. For many of these patients, immediate access to new medicines through early access mechanisms could mean the difference between life and death.

Patients and their families that are in the position of a very poor prognosis can be well-read on their condition and actively investigate their options. Of the three patient organisations that generously contributed their insights to this research, each one clearly expressed the extent to which patients have researched their condition and the new innovations in the area. Moreover, in most cases, treatments approved by the FDA before reimbursement is obtained in Australia would have dedicated websites authorised in the USA that could enable patients to access this information ahead of time.

Although newly diagnosed patients do approach patient organisations for information on their condition, services available, or for disease education, patients that are searching for early access to therapies are generally those that have exhausted all options which are currently accessible to them. Patients will try all available routes before searching for a new therapy. Interviews with patient advocacy groups show that actively involved patients will identify products that will be beneficial to their care, but the process of access is difficult to navigate. Richard Vines, CEO of Rare Cancers Australia, finds this with their advocacy and patient support, commenting that "hardly a day goes by without a patient looking for access to an unfunded drug." This is where physicians can initiate the conversation and guide the patient towards early access, as is most often the case with how patients end up on these programs (*Appendix 1*), with patient advocates noting that sometimes patients will not even know they are on an early access program. Alternatively, there are patients who directly contact the company in the hope of compassionate supply directly which further exemplify the need and desire for early access.

*The lack of formality, the metro-centred healthcare environment, and the lack of patient inclusivity can be highly stressful. Additional support surrounding treatment as well as the harmonised system can facilitate easier access for both patients and their prescribers.*

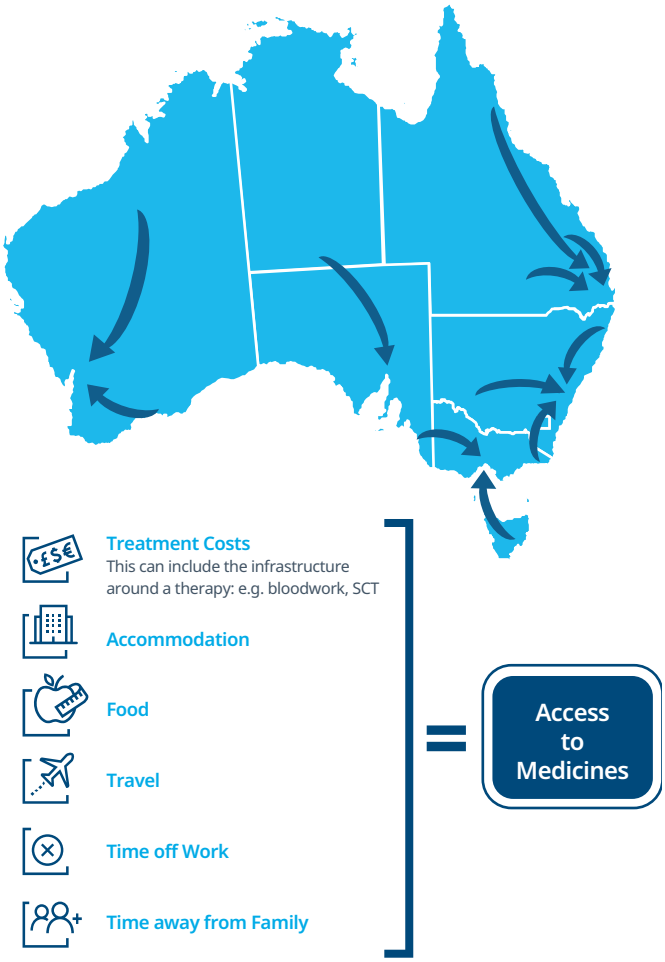
***Early Access is metro-centred***

With specialty centres being concentrated in the main metropolitan cities in Australia, many patients find that they are making substantial sacrifices to gain access to essential medicines. However, these sacrifices, such as transportation, overnight cost, and time off work, often end up making the treatment unaffordable or impractical to access. Patient advocates commented that a common barrier observed is the travel to metropolitan hospitals for regional patients, as for instance, the bloodwork required before treatment or the treatment itself is often not done by regional hospitals. Although this may not be feasible for the manufacturer to coordinate on top of free therapy, patient advocates hope for improvements to patient barriers so that all can receive equal access, with additional support from the company known to positively impact patient satisfaction.

***Further patient-centricity is needed***

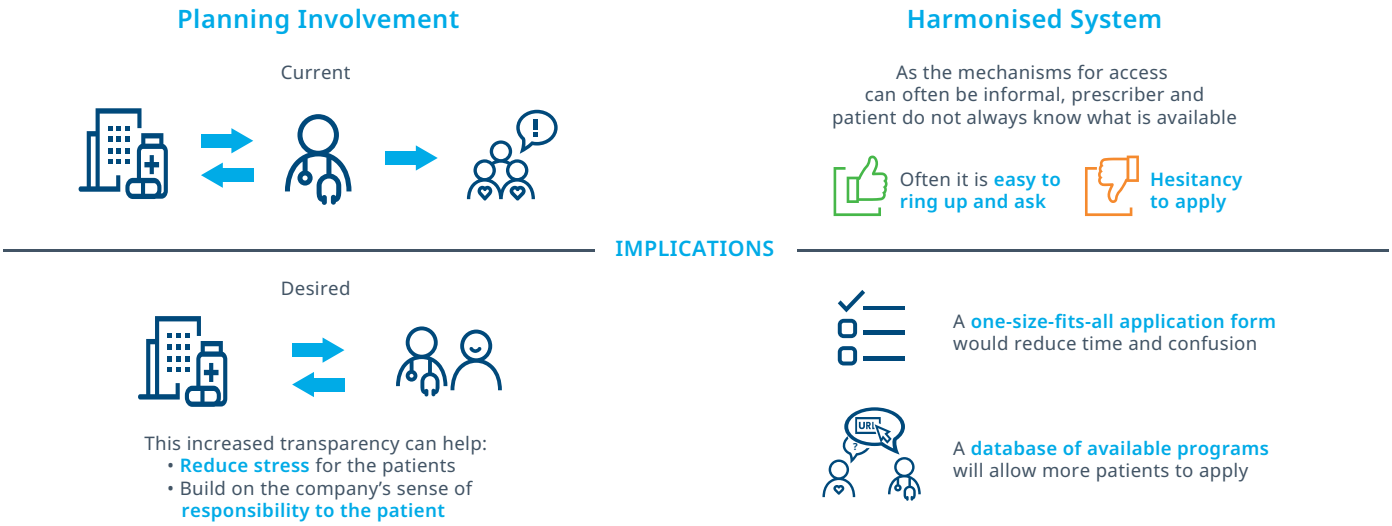
As manufacturers interact more with prescribers than with patients, early access programs may logically be focussed on the prescriber. Therefore, there is a desire from patient advocates that patients should be more involved in the treatment planning which could reduce stress by creating greater transparency between the company and patient, further building upon the company's sense of responsibility to the patient. This type of planning and involvement is understandably hard for the prescriber to involve the patient considering the informal nature of these programs. This kind of informality contains both pros and cons.

Figure 3: The real cost of early access to patients




Sometimes all it requires is a request to the company and access to therapy can be arranged but commonly it is difficult for patients or physicians to know of an access program or availability of access hence they may be reluctant to apply. Consequently, there is also call for a more harmonised system to aid patients, such as databases of available programs and a one-size-fits-all form that patients and prescribers can send to manufacturers to apply for access. According to IQVIA's Medibus panel and the patient advocates interviewed, it can take up to three hours currently to complete an application. The lack of formality, the metro-centred healthcare environment, and the lack of patient inclusivity can be highly stressful. Additional support surrounding treatment as well as the harmonised system can facilitate easier access for both patients and their prescribers.

**Figure 4: Improvements to early access as desired by patients**




## HEALTHCARE PRACTITIONERS PERSPECTIVES

Patients are the main priority for healthcare providers. Physicians and pharmacists act as the liaisons for the patient with the manufacturers when it comes to early access, and as experts in their practice, are extremely important stakeholders in the process. In fact, of the 60 prescribers on medical oncology and haematology panels that IQVIA surveyed, 57 (95%) had applied to the TGA to become Authorised Prescribers in their respective specialties. This confirms the patient organisations' experience that prescribers are taking initiative to give access to their patients and hints to the extent that Australian specialty prescribers are up-to-date with new and innovative therapies. Prescribers expect that manufacturers provide an avenue for their patients to access these therapies, if required, before TGA approval or PBS reimbursement. There is a consensus between prescriber and manufacturer, that a doctor would not request early access for their patient unless it was needed. This was confirmed in market research, where haematologists and medical oncologists responded that they would initiate early access for patients with the most advanced and severe forms of their disease (*Fig. 6*). Although there is no legal obligation to provide the therapy, from an ethical and reputational standpoint, the manufacturers tend to provide this service.

However, a barrier that has been identified in interviews with patient organisations, HCPs, and manufacturers is the paperwork burden on the healthcare staff that could already be time poor. The introduction of the online TGA portal in July of 2018 was a positive step in attempting to reduce the paperwork burden for HCPs. Although, pharmacists are still transitioning to the new technology, with only 40% of the 27 hospital pharmacists in the IQVIA Medibus panel indicating they use the portal when applying for special access. However, when used, it has been shown to significantly reduce the time to fill out the required documentation, dropping from over an hour in paperwork to ~20 minutes online for pharmacists. It is likely the online portal will begin to be more widely accepted as there are further benefits: the portal allows tracking of SAS approvals, their expiry date, and facilitates renewal submission, whilst also ensuring physicians correctly complete the form initially, avoiding the submission-rejection-resubmission cycle which can delay patient access.

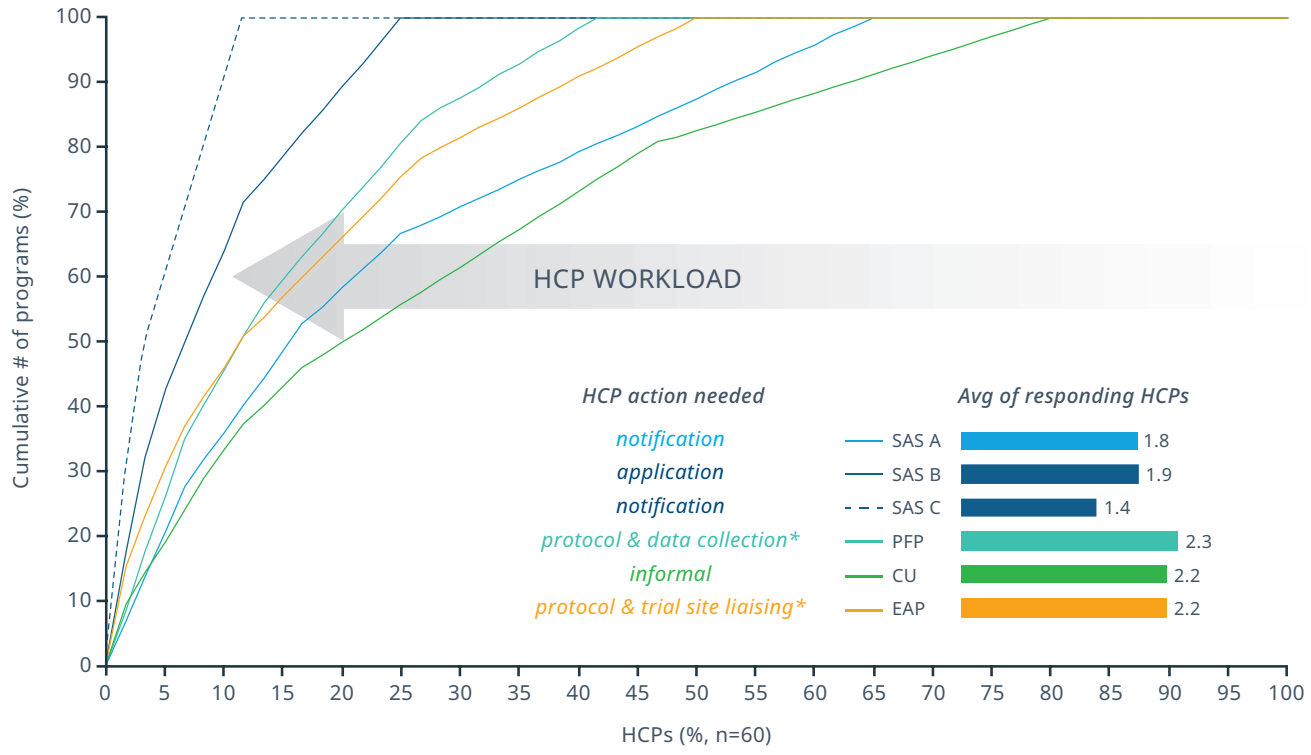
***Regardless of the amount of paperwork, patients, physicians and pharmacists are still willing to invest the time to obtain early access to medicines.***

Regardless of the amount of paperwork, patients, physicians and pharmacists are still willing to invest the time to obtain early access to medicines. Of the pre-TGA access mechanisms, continuation on therapy post-clinical trials and notification to the TGA for life-saving treatment (SAS category A) are used most commonly. However, IQVIA's Medibus panel indicates that the most commonly used access scheme overall is compassionate supply. Haematologists and medical oncologists from all states and a mix of metropolitan and regional areas were surveyed due to their familiarity with early access to medicines, both of which responded similarly to the survey. Mechanisms that require less HCP workload are more likely to be used by a broad number of prescribers, and mechanisms that have higher paperwork burden are more likely to be concentrated in few prescribers (*Fig. 5*). SAS category C is slightly different, and although it requires minimal workload, it has not been readily used by many prescribers most likely due to the recency of its introduction in July 2017. Furthermore, although pharmacists play no part in placing a patient onto therapy, they are responsible for the background work to make sure the patient receives the therapy.

Pharmacists' responsibilities can differ depending on the mechanism used to access therapy. For instance, before the patient is given a SAS prescription, the doctor will enquire about drug availability, and an individual patient use form will be submitted to the ethics committee (patient background, past therapies, reasoning for this therapy, cost, etc). Additional paperwork required by some manufacturers will need to be completed, along with a quote from supplier (time-frame for delivery and price) and SAS approval from the TGA if required. However, unfunded access mechanisms such as compassionate use and PFPs are arranged between the prescriber and the manufacturer, with less work required from the pharmacist.

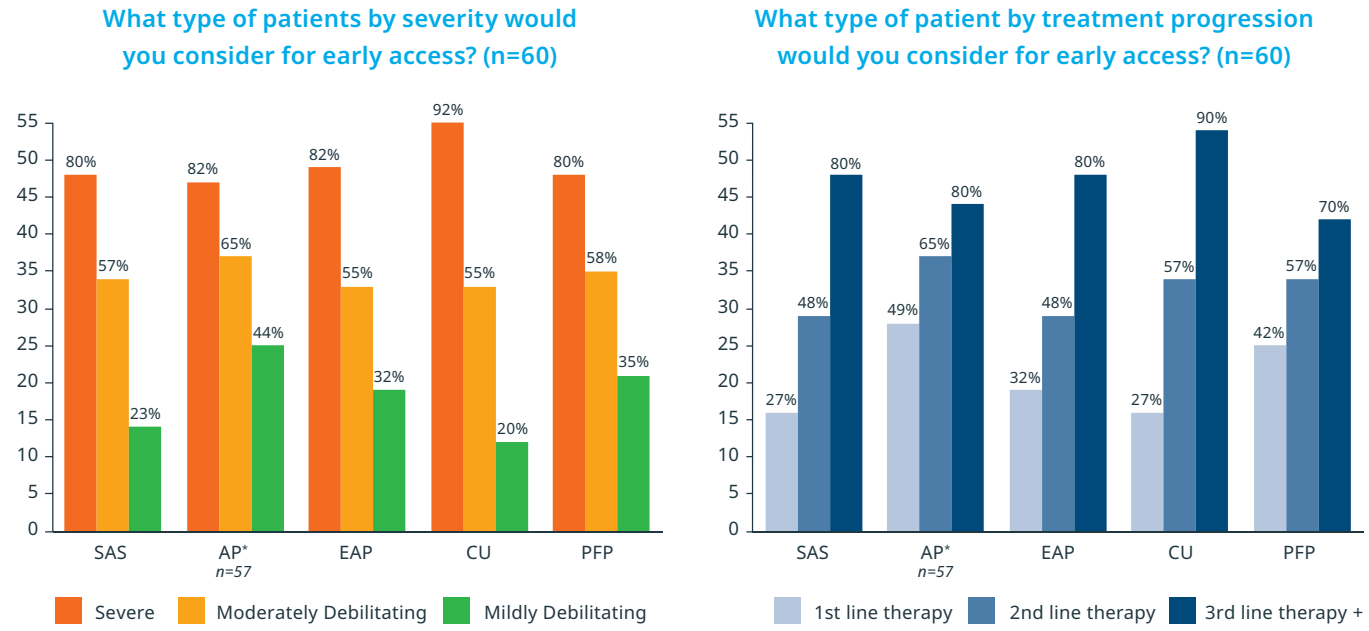
Although PFPs are manufacturer initiated, specialty physicians do expect companies to be proactive in allowing them familiarity with the product. As the only manufacturer-initiated access program, it is important to remember that PFPs, although a benefit to the patient, are geared towards prescribers and allowing them familiarity with the product. However, in the past some prescribers have expressed concerns toward the larger PFPs where a

**Figure 5: Medibus responses - How many programs have been seen or initiated within your hospital in the past month? (n=60, 30 medical oncologists, 30 haematologists)**




Source: IQVIA Medibus *workload is not always this formal but may contain up to this amount of HCP work

**Figure 6: Medibus responses - What type of patients would you consider for early access medicines? (n=60, 30 medical oncologists and 30 haematologists)**




Note that physicians could select more than one option, so totals will not add to 100%.
Source: IQVIA Medibus

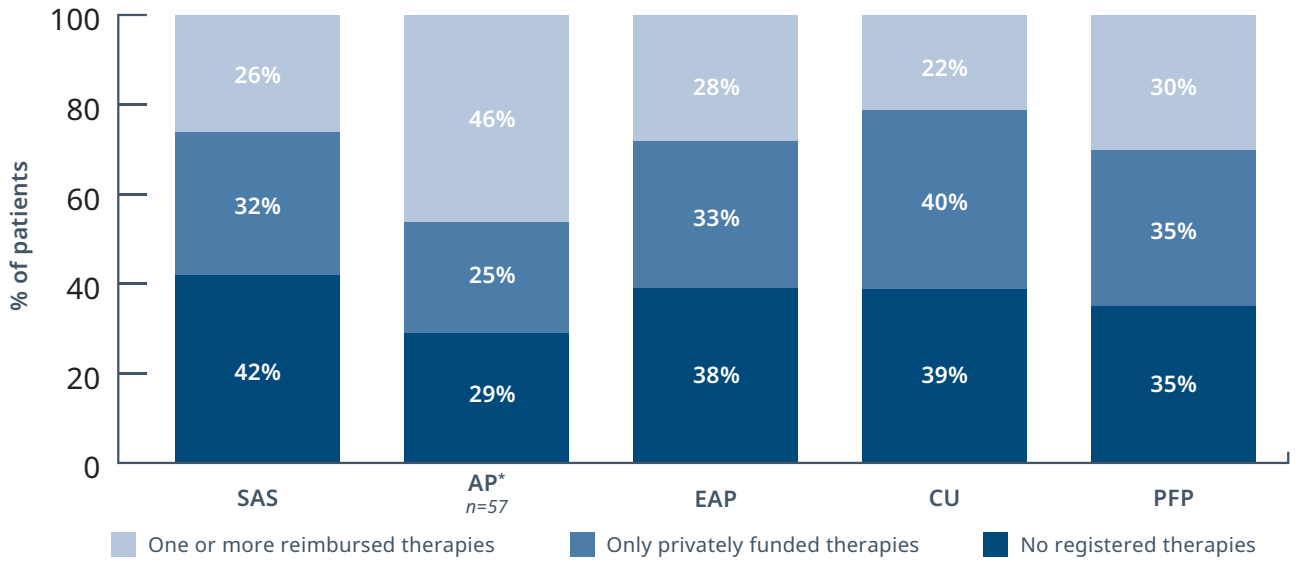
large amount of patients can be grandfathered across to reimbursed treatment for a therapy with low incremental clinical benefit.[12] Despite this apprehension, when there is an unmet need, providing access to the patients while familiarising the prescriber benefits all involved. As indicated by respondents, physicians are most likely to initiate early access for patients that have exhausted at least three lines of therapy or more. Although, this does not mean that physicians will not initiate patients that are only on their first line of therapy (*Fig. 6*).

***A PFP that is well-managed by the manufacturer ensures prescriber confidence in the medicine, and that the enrolled patients will be grandfathered onto reimbursed therapy which serves to recover the cost of the program.***

Similarly, although specialists are more likely to initiate early access for patients with the most severe form of their disease, there is a significant proportion of physicians that initiate access for patients with mildly debilitating chronic conditions (*Fig. 6*).

Interestingly, not all specialty physicians preferred initiating access for those patients with no reimbursed options left. Actually, authorised prescribers (APs) are more likely to initiate access for patients with reimbursed options which may highlight their enthusiasm for early access prescribing *(Fig. 7*). They also benefit from less paperwork burden once they have gone through the effort of becoming an AP. Another explanation could be that APs are known in the prescribing community, and so patients with subtypes of diseases who can benefit from newer unregistered therapies are funnelled to the APs in the therapeutic area. Overall however, aligning with what is seen by patient organisations, more severe patients that have exhausted all therapy options are more likely to be given early access to medicines.

**Figure 7: What types of treatment options are remaining for the patients by access mechanism? (n=60, 30 medical oncologists, 30 haematologists)**




Note some totals exceed 100% due to rounding
Source: IQVIA Medibus

## MANUFACTURER PERSPECTIVES

PFPs play an important part of launching a new medicine into Australia for manufacturers. Essentially, it is the only early access program that has commercial motivations and so focus is put on increasing the patient pool, prescriber familiarity and considering the risk of delays. Early access mechanisms are offered for most specialty Australian launches as providing early access is increasingly becoming a "cost of doing business". From their perspective, this is the most mutually beneficial mechanism by which patients can access new medicines. In general, most other access mechanisms provide patients free medicines on a case-by-case basis. For the manufacturer, this can introduce a cost burden, especially for newer manufacturers or companies that have a limited portfolio, and as a result, limited revenue to cover the manufacturing, importing and/or supply costs. For the patients, this also can be very difficult to access. PFPs allow physicians and their patients to gain access to a medicine free of charge before it is listed on the PBS. However, the patient is not the only party to benefit in this case as the patients will be grandfathered onto the PBS listed product when the time comes, and the key prescribers will have ideally become familiar with the therapy, its dosing, side effects, administration, and management.

The therapy should be provided to patients for which it will work best to avoid adverse events and insufficient efficacy. A PFP that is well-managed by the manufacturer ensures prescriber confidence in the medicine, and that the enrolled patients will be grandfathered onto reimbursed therapy which serves to recover the cost of the program.

Although expanded access after clinical trials has no commercial incentives, the act of conducting a clinical trial in Australia needs to be considered from more than just a clinical perspective, as a trial can bolster a product's launch by providing familiarity to prescribers. With the Research and Development Tax Incentive, and the relative ease of implementing a clinical trial, Australia is an important clinical trial location especially for prescriber familiarity, but the population and its dispersion need to be considered with regards to recruitment. Consequently, as part of the *Right to Health*, this also means that patients finishing clinical trials and awaiting both TGA approval and PBS listing should be given expanded access to beneficial medications. However, providing access following clinical trials via expanded access does not have any commercial considerations or motivations. The cost-burden of supplying therapy for years until reimbursement, the likely low number of patients that would be grandfathered and the fact that it is a universal social right indicates a solely compassionate reason behind keeping patients on expanded access.

Furthermore, PBS reimbursement at the end of Phase 3 clinical trials is not certain, as is TGA approval. With the uncertainty of if, and when the product will be made available to the wider market, expanded access remains a compassionate gesture that inevitably follows conducting clinical trials in Australia.

Additionally, non-PFP early access mechanisms such as compassionate use, expanded access and SASs are more important for ethical and compassionate reasons than commercial reasons. Prior to TGA approval, there are no tangible commercial incentives to provide access to patients or prescribers who have requested the therapy as a last resort. Prior to approval, many companies feel it their duty to the patient to provide life-saving therapies free of cost or highly subsidised, especially when there is a delay in Australian availability as compared to the rest of the world. Similarly, compassionate use after approval but prior to reimbursement, also stems from its namesake, compassion. All interviews IQVIA conducted with manufacturers mentioned their drive to help patients as one of the main factors in the rush to get product to market. Manufacturers will want to get their product to market – and to their patients – as quickly as possible, but when reimbursement will not come soon enough for some, compassionate supply can be given.

However, complexity lies in many factors that a company needs to account for when considering if a PFP should be provided, and how best to implement. As PFPs are the only commercially driven, and mutually beneficial, early access mechanism, there are specific considerations that need to be discussed by the manufacturer:

## Green Light | Timing | How to Implement

**Is large-scale access program right for this launch?**

The first question is whether the company should offer a large-scale early access program as it is not necessarily the key to success for every launch. The following questions are recommendations of what can be discussed internally during launch preparation:

| Market Access & Reimbursement | Product Profile | Market Landscape |
|---|---|---|
| **1. Do the cost of goods permit such a program?** Expensive products to manufacture/import may leave the company in a financially difficult situation or there may not be enough resources. | **4. Will the product end up on the PBS or on hospital formularies?** Negotiation with individual hospitals will be needed in the case of the latter. | **6. Is the product for acute or chronic conditions?** Large-scale programs could potentially cure a large portion of the patient pool, leaving the manufacturer with no return on the large sum they have invested. |
| **2. Is reimbursement likely for a broad or specific patient population?** Without confidence in the indication that the PBAC will accept, patients may be removed from the therapy if only a small subset of patients have the condition variant listed on the PBS. | **5. What is the prevalence of the condition in Australia?** With smaller patient pools, large-scale programs may not be feasible or achievable. | **7. How strong is the clinical unmet need that the product is servicing?** Prescribers and patients may be less interested in "me too" products and generics. |
| **3. Is reimbursement reasonably likely within a reasonable timeframe?** The product will most likely need to be provided until the product is listed on the PBS. | | |

Many of these questions may lead to the answer that providing access on a large-scale is not needed or feasible. However, smaller-scale access can be given to patients on a case-by-case basis if they or their physician approach the company. In many of the interviews conducted for this paper, it was mentioned that there is an expectation from the prescribers and patients for some level of early access to be made available to patients prior to launch. For many of the reasons above, a PFP may not be feasible, but this does not mean that compassionate supply or even pre-TGA access will not be granted if and when the manufacturer is approached.

**How would this be implemented?**

When discussions, evidence and the aforementioned considerations all point towards implementing an early access program, one of the largest considerations is the timing of the offering(s). Key Australian prescribers, especially specialists, are particularly up to date with the latest literature on new therapies and are coming to expect access to new medicines for their patients. The first question that a company must answer is when to initiate the program(s). Discussions of how best to implement and manage the program is recommended at cross-functional team meetings once the product has been TGA approved, approximately a year before launch, and the following considerations accounted for:

| Market Access & Reimbursement | Product Profile | Market Landscape |
|---|---|---|
| **8. How much confidence is in the PBAC positively recommending the product under the indication chosen?** This is the most important consideration for conducting an access program, as misaligning the indication of the access program with the indication suggested by the PBAC can prove costly for company and patient. Those patients outside the reimbursed indication will either need continued support from the company or, if this is not feasible for the company, will need to be taken off free therapy, which is not ideal for either party. | **9. How long can the program be run based on the resources that have been allotted?** This will limit how early before reimbursement a company can roll out a large-scale access offering. This decision will also link into the decision around sizing of the program and how many patients should be enrolled to the program. | **10. How high is the unmet need in this disease area?** Where there is a large unmet need for therapies that prolong survival, many companies feel the moral obligation to provide these medicines early to their patients. Where there is lower unmet need, prescriber familiarity will be the major consideration, and so the marketing strategy becomes important for the company to maximise the impact of the product's access program.<br><br>**11. How competitive is the product in the market?** Products which are superior may end up being used by prescribers to switch patients from other therapies, where comparable products may just capture new patients where uptake would be slower. If a competitor is also close to launching, providing access of a comparable product earlier can capture a larger portion of the patient pool. |

Once there has been a decision around the timing of the access program, further consideration is needed for the size and strategy of the product's offering(s). The size of the early access offering (*i.e.* total patient number to reach) is influenced by the following:

## Market Access & Reimbursement

**12. What resources are available and allotted?**

The number of patients enrolled, in combination with the program length, is directly linked to the resources that will be needed. The larger the patient number, the larger the initial outlay required, and so again, being confident of time of reimbursement is imperative for success.

## Product Profile

**13. What type of product is being launched?**

Programs with lower patient to prescriber ratio may be better suited to products that are high cost with low patient numbers (*e.g.* oncology biologics). Programs with higher patient to prescribers ratios may be better suited to products that low cost with high patient numbers (*e.g.* primary care products) to maximise exposure. If the company already has a product in this market, consideration will need to be taken around the cannibalisation of the company's own market share.

**14. Will data collection be required or warranted?**

Recently, Medicines Australia updated their guidelines of PFPs to allow the collection of patient data with a formal protocol. Data collection during early access can provide the first real world evidence (RWE) generated for the product in Australia, to be used internally to gauge real-world usage, externally in publications as evidence for stakeholders, but also to use as a supplement to reimbursement submissions and pricing negotiations if needed. Most of the interviews IQVIA conducted with manufacturers in the Australian pharmaceutical industry mentioned the lack of data collection while providing early access to patients and prescribers. A point that was brought up repeatedly was the concern of over-burdening the physicians with paperwork, which can frustrate prescribers and may lead to poor first impressions of the drug and subsequent disfavour for continuing the enrolment. These prescriber considerations should be balanced against the rich RWE these programs can provide.

Further to considering how many patients a company wishes to reach in its offerings, a strategy regarding the breadth and depth will need to be decided upon also. A "broad" early access program employs a strategy to include as many prescribers that resources will allow, leading to a higher number of prescribers, each with a lesser number of patients. A "deep" early access program employs a strategy to allow each prescriber in the program to include a maximum of their patients, in an effort to get prescribers as familiar as possible with the product.

**15. Broad vs Deep access program**

| | BENEFIT | DOWNSIDES |
|---|---|---|
| BROAD | • Maximum number of prescribers are familiarised<br>• Reduces the workload per prescriber | • One adverse event is more likely to persuade the doctor negatively than when they have many patients<br>• The prescribers may fail to use the product on the 4-6 patients needed for general familiarity with the product |
| DEEP | • The most influential prescribers are involved and familiar<br>• One AE does not persuade the doctor negatively when there are many more patients with no AEs<br>• Provides greater company resources per prescriber – better training on administration, dosage, *etc.* to avoid AEs | • Results in less prescribers familiar with the product<br>• Risk of disappointing prescribers who were not given early access |

Both PFPs and compassionate use, as initiated and implemented by manufacturers, are important aspects of launch and should be discussed as an option by the brand team for every launch in Australia. IQVIA's global expertise in launch and analysis of over 12,000 launches worldwide to determine fundamental factors for an excellent launch. Both company-initiated unfunded access mechanisms are included in IQVIAs Launch Excellence Framework as key aspects of Launch Excellence.

## IQVIA PERSPECTIVE

Considering the perspectives of the stakeholders described, thematic elements emerge as being important to implementing and providing early access to medicines in Australia.

### PATIENT-CENTRICITY

The concept of designing a service or solution around a patient emerges as a key thematic element, not only from the prescribers, but from manufacturers as well. This concept has been circulating through the pharmaceutical industry in recent years, aligning with the desire of pharmaceutical companies to work with the prescriber to facilitate early access, and easier access to those that need it most. This is important in the Australian setting, as innovative therapies tend to launch later than in larger foreign markets like the US or the EU, although the TGA and PBS are making efforts to speed up both the registration and reimbursement pathways though priority reviews. It is apparent that when feasible, the company will facilitate access, exemplifying the mantra of patient-centricity. However, some improvements are sought after from the patient perspective, particularly services to overcome the barriers faced by patients receiving early access, as it is known they exist. Providing these services to overcome the barriers faced by regional patients trying to access metro-centred PFPs can improve patient satisfaction. Additionally, answering the calls for a more harmonised system, such as maintaining a database of available programs that patients and prescribers can use to find programs, will also help improve current practice in the hope of allowing more patients access when required.

Also, working with industry stakeholders to provide a one-size-fits-all application form, suitable for all manufacturers, would reduce stress and improve patient experience.

## IMPORTANCE IN LAUNCH EXCELLENCE

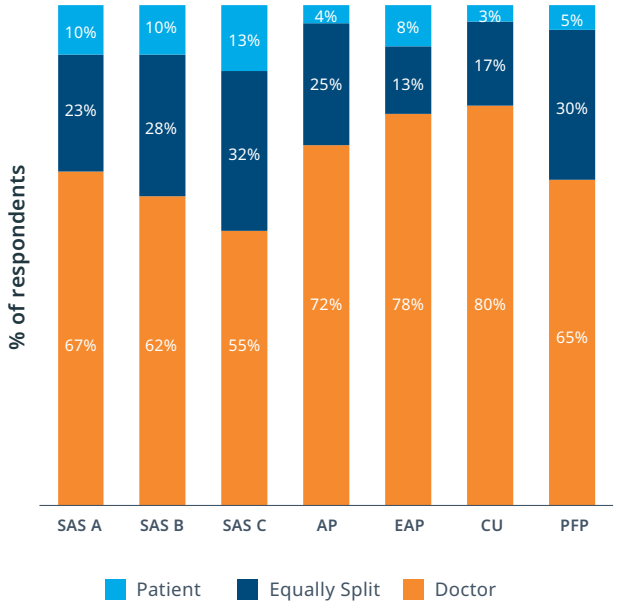
Another thematic element emerging is the important role these programs play for Launch Excellence in Australia. Providing early access to these medicines not only helps the patient but can satisfy the prescriber's plea for beneficial medicines and so can help strengthen the underlying relationship with prescribers. Unfunded early access mechanisms (PFPs) allow many patients to gain access to affordable therapy and build a patient base before launch, whilst allowing time for the prescriber to get familiar with the product's intricacies in the most appropriate patients. Once PBS listed, patients on a PFP can be grandfathered onto the reimbursed product allowing patients to continue with affordable access and allow manufacturers to start with a significant number of patients immediately upon launch. In this way, each party benefits in specific ways: patients gaining access early, prescribers becoming familiar with new/innovative products and increased uptake of the product following launch providing a higher starting market share with the hope of long-term commercial success: market share achievement relative to the promotional share of voice investment, market rank achievement and a superior launch uptake curve.

## CAREFUL IMPLEMENTATION

To ensure an excellent launch, it is important that the long list of considerations be discussed in deciding if, when and how they implement early access. Foremost, it is apparent that timing, which closely ties into aligning the program's indication with that which will be listed by the PBS, is imperative to a successful PFP. Neither the company, prescriber, nor the patient want to have to discontinue the therapy if their condition is not a PBS listed indication so higher certainty around the PBAC recommended indication is important. During IQVIA's information gathering, cautionary tales regularly surfaced including PFPs designed with indications too broad for the product, which led to an undesirable rate of AEs or patients that could not be grandfathered across to reimbursed treatment. Other cautionary tales are programs for products which get delayed or rejected by the PBAC, having a negative commercial impact, leading to the premature end the program, which disappoints patient and prescriber. Consequently, it can pay to hold off on initiation until positive signals are given by the PBAC. Another area of interest is how industry use the data generated by these programs. Given the latest update of Medicines Australia Code of Conduct on PFPs which allowed for more individual patient data to be collected, which acknowledges this data as an untapped resource. In the PFP setting, data usage is a risk versus reward conversation for the company. Although increasing the paperwork for the prescriber may burden them and push them away from enrolling further patients, the formal protocol allows in-depth real-world evidence (RWE) generation to understand patient needs. This data could prove useful, for instance in a contingency strategy where in-depth RWE data was collected to satisfy the PBAC or Health Minister in pricing negotiations in the case of drawn out submissions.

In summary, providing early access to therapies is deep-seated and important in the Australian setting, however there is complexity in doing so. Manufacturers provide access to satisfy the ethical considerations of the prescriber and their patients, but also in the hope of benefiting from more familiar prescribers with patients that are grandfathered across to reimbursed treatment.

**Appendix 1: Is the motivation behind seeking out these programs generally driven by yourself, or the patient? (n=60, 30 medical oncologists, 30 haematologists)**




Note some totals exceed 100% due to rounding

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Quentin manages IQVIA Consulting practice area and team in Australia and New Zealand, managing project teams including both internal and external resources in the design, development and delivery of client deliverables and leveraging business experience and acumen in identifying strategic alternatives and project approach to client questions. He brings 8 years of consulting experience working across commercial excellence, market access, portfolio management and brand strategy in the healthcare sector.

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