SENATE COMMUNITY AFFAIRS REFERENCES COMMITTEE

INQUIRY INTO THE AVAILABILITY OF NEW, INNOVATIVE AND SPECIALIST CANCER DRUGS IN AUSTRALIA

SUBMISSION

PHARMACEUTICAL BENEFITS ADVISORY COMMITTEE

MARCH 16 2015

SUMMARY

The role of the Pharmaceutical Benefits Advisory Committee (PBAC)

The role of the PBAC is defined by the National Health Act: to provide advice to the Minister about new medicines for serious health problems, including cancer, so that the community can have prompt and equitable access to effective and safe medicines. According to this legislation, the PBAC is required to recommend listing on the Pharmaceutical Benefits Schedule (PBS) only those drugs whose price is aligned to the benefits they deliver.

The members of the PBAC and its subcommittees are clinicians, pharmacists, health economists and consumers. The underpinning principle of the committee's operations is that all Australians are equally entitled to community support for the costs of new medicines. The PBAC therefore considers drugs for cancer on the same basis as drugs for other illnesses. This includes assessment of the evidence from scientific studies about benefits and harms, the cost of a medicine, and a range of other factors, including the severity of illness, the extent of unmet need, and the views of consumers. The PBAC is particularly interested in recommending a new medicine for listing when it provides an obvious clinical advance for patients, extending survival and/or improving quality of life.

Perception of delays in access to cancer medicines

The PBAC reviews a medicine when an application for the medicine – usually from a pharmaceutical company (sponsor) - is submitted to it. Following a positive PBAC recommendation, the medicine will be listed on the Pharmaceutical Benefits Schedule when the sponsor has agreed to supply the product at an agreed price, and the government has approved the expenditure and the inclusion of the drug on the PBS. The time for the PBAC review process is currently 17 weeks from submission of the application to recommendation.

There is a perception that delays in access to the listing of cancer (and other) medicines are due to PBAC processes. In fact, delays are often due to the failure of pharmaceutical companies to apply for listing, or to reach agreement with government on the conditions of supply. Some cancer medicines are never submitted to the PBAC.

When the PBAC does not recommend the listing of a new drug, this is most often because the benefit of the drug has not been demonstrated or is too small relative to the proposed price. Benefits of cancer drugs are assessed in terms of effects on overall survival, progression free-survival, response to treatment and quality of life and toxicity. Many new cancer drugs produce only very small gains in survival, less than three months, and have very little impact on quality of life, or negative impacts due to side effects.

The PBAC is concerned that there is often a mismatch between the public perception of the value of cancer medicines (often developed through the media) and the data presented by the sponsor on a confidential basis to the PBAC. This confidentiality requirement is at the insistence of the pharmaceutical industry.

In the Committee's opinion, bypassing the PBAC process to "expedite" access to new cancer drugs would greatly increase the cost to the community and diminish the sustainability of the PBS without any commensurate gain in health outcomes. It would also lead to justified resentment among patients with other diseases.

PBAC Recommendations.

1. To improve transparency, patients and clinicians should be given access to sponsor submissions, and to the evaluation of these data by PBAC and its subcommittees,

including the details of the recommendations.
2. Funding of the Secretariat and of independent consumer groups needs to be enhanced to support greater stakeholder consultation.
3. Data on the outcomes of all patients treated with new drugs should be collected nationally, and monitored on a real-time basis.
4. Community consultation should be carried out to ascertain the value placed by society on very small improvements in survival or progression free survival for patients with cancer.
5. Processes should be developed to generate plain language presentations for lay and professional audiences on the benefits, harms and costs of new drugs.

This submission represents the views of the current members of the Pharmaceutical Benefits Advisory Committee. It addresses particularly TOR B of the Senate Inquiry but will also respond to the other TORS. The PBAC welcomes the opportunity to contribute to this important process.

Who are the members of the PBAC?

The PBAC members are listed on the Department of Health website.[1] Currently there are 16 members plus the Chair. The Chair is employed as a full time position; the other members include practising clinicians and pharmacists, a health economist and a consumer representative. At the time of this submission, there are three members who are oncologists or haematologists.

Introduction

The PBAC's duty to provide advice to the Minister of Health is defined by Section 101 of the National Health Act. Section 101 (3) (A) specifies that the '*Committee shall give consideration to the effectiveness and cost of therapy involving the use of the drug, preparation or class, including by comparing the effectiveness and cost of that therapy with that of alternative therapies, whether or not involving the use of other drugs or preparations*.'

Section 101 (3) (B) states that '*where therapy involving the use of a particular drug or medicinal preparation, or a class of drugs and medicinal preparations, is substantially more costly than an alternative therapy or alternative therapies, whether or not involving the use of other drugs or preparations, the Committee:*

(a) shall not recommend to the Minister that the drug, preparation or class be made available as pharmaceutical benefits under this Part unless the Committee is satisfied that the first mentioned therapy, for some patients, provides a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies'

Therefore, the Act explicitly requires the PBAC to consider cost *and* clinical effectiveness *relative to existing therapies* when considering a drug. "Cost" means both cost per patient treated and total cost to the PBS, taking into account the number of patients likely to be given the drug.

The PBAC fulfils this requirement to evaluate the "cost-effectiveness" of a drug using well-established principles and methodologies described in detail in its Guidelines.[2] The reason to use this approach is that it enables drugs to be compared directly to existing best treatments, and the additional benefits and costs weighed across all types of diseases and treatments. This means that two drugs can be equitably assessed even if one treats a rare but serious disease and another relieves the symptoms of a common

[1] http://www.pbs.gov.au/info/industry/listing/participants/pbac ; also https://www.ausgovboards.gov.au/boards/pharmaceutical-benefits-advisory-committee
[2] http://www.pbac.pbs.gov.au/

less serious chronic condition, or if one is very expensive but will be used for very few patients and another is low cost but will be used by very large numbers of Australians.

The effects of PBAC assessment of cost-effectiveness on access to new medicines

New cancer drugs provide two major challenges to how PBAC makes the cost-effectiveness judgements required by the Act.

Cancer drugs that have been assessed by the Committee in the recent past have nearly all been, by any standards, "substantially more costly" than 'alternative therapies', as has recently been reported in the media[3] and medical literature. [4] The reason new cancer drugs are so expensive has been the subject of considerable debate but it is not simply related to the cost of development and manufacture. The pharmaceutical industry's expectations in relation to price and profit at international and national levels are also relevant.

Given that the new drugs are more costly, the Act requires the PBAC to decide what is a "significant improvement in efficacy or reduction in toxicity". The PBAC's approach has been to assume that, as a principle, all Australians have the same entitlement to the support of the PBS, and therefore that all treatments should be assessed using a common metric: additional dollars spent per additional quality adjusted year of life gained. This measure takes into account survival gains, in the case of illnesses that shorten life, as well as quality of life and the impact of side effects of treatment. The cost-effectiveness of a new treatment is therefore determined by the price requested and by the relative size of the health benefit it offers. If the cost-effectiveness assessment shows that the cost is high in relation to the benefits, price becomes a barrier to access.

The Committee considers that a major barrier to rapid PBS listing for new cancer drugs is the expectations of pharmaceutical companies with respect to pricing. For many new cancer drugs the price being requested, relative to what the drugs achieve, is much higher than for drugs for other serious life-threatening diseases, or for the evidence of health outcomes provided.

It is important to note that almost all new cancer drugs are *not* dramatically more effective than existing treatments. New drugs that transform a uniformly fatal disease into one that can be cured or easily managed are vanishingly rare, and the benefits of new cancer drugs are often, by any reasonable standards, small. As described in Fojo et al 2014,[5] over the period from 2002 to 2014, all new drugs approved in the USA for

[3] http://www.smh.com.au/national/cost-of-cancer-drugs-rises-sharply-to-586-million-20150123-12wru9.html

[4] Karikios DJ et al. Rising cost of anticancer drugs in Australia. Internal Medicine Journal 2014:44(5);458–463

[5] Fojo T et al. Unintended consequences of expensive cancer therapeutics- the pursuit of marginal indications and a me-too mentality that stifles innovation and creativity. JAMA Otolaryngol Head Neck Surg. doi:10.1001/jamaoto.2014.1570

treatment of solid tumours provided a median gain in the progression free period of 2.5 months, and a median gain of 2.1 months of extra life. These results do not include a measure of the quality of life: many patients in these studies had poor quality of life due to the side effects and toxicity of the drugs. In this study, consensus among oncologists was that for a new treatment to be regarded as useful it should offer at least 3 months more life.

There is good evidence that two months additional survival can be *less* than that associated with even minimal palliative care [6], which also offers better quality of life. This raises a major issue related to the funding of drugs for advanced cancer: the tendency for the role of existing effective services to be neglected, in the absence of advocacy from a well-funded constituency. The PBAC is concerned about the importance of ensuring that new drugs that it approves are most effectively used in combination with existing services and treatment options.

Although, as noted above, new drugs for cancer are *not* often dramatically more effective than older drugs, they are routinely dramatically more highly priced. To illustrate this, if the additional gain in survival of 2.1 months noted in the study of FDA approvals comes at an additional cost of $50,000 - $100,000 as is often quoted in the US media, this equates to approximately $300,000 - $500,000 for a year of life in good health gained.

The simplest way to 'improve' the cost effectiveness of a new drug is to decrease the price. If a sponsor is not prepared to reduce the price sufficiently (in the case of vemurafenib for melanoma for example[7]), then it may simply not be possible for PBAC to make a positive recommendation while respecting the requirements of the legislation under which it acts.

Public discussion of new drugs often focuses exclusively on benefits. However, in addition to benefits, PBAC is required to consider the adverse effects of new drugs compared to existing treatments, as well as the effect on quality of life. In the case of regorafenib[8] for example, the PBAC found that the very small gain in life expectancy was outweighed by the significant increase in toxicity as well as substantially higher costs. It was therefore not recommended for listing.

It is of concern to the PBAC that the public discussion of the new cancer medicines rarely appears to include a fair and accurate description of the benefits and harms of products, as well as their cost. It is highly likely that earlier access to cancer drugs will *greatly* increase cost to the community if the mechanism by which earlier access is

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[6] Temel JS, et al. Early palliative care for patients with metastatic non-small cell lung cancer. *New Engl J Med* 2010; 363:733-742.

[7] http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2013-03/vemurafenib

[8] http://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2014-07/regorafenib-psd-07-2014.pdf

granted involves acceptance of prices that result in much higher estimates of cost-effectiveness.

It is essential to note that this is not just a problem for PBAC and the Australian system. In the US in particular, commentators and the US Congress are now investigating the cost of new drugs.[9,10] Similarly, in the UK, there has been much recent debate and review of the clinical benefits of drugs supplied through the Cancer Drugs Fund.[11]

A second challenge for PBAC to manage with new cancer drugs is balancing the urgency of patient need and the quality of data about new drugs.

There is an increasing trend for the clinical evidence documenting the effectiveness and cost-effectiveness of new cancer medicines to be of such poor quality that it does not allow confident assessment of benefit. For example, studies without proper comparison groups are increasingly being used as the basis of proposals for listing. Even when well-designed comparative trials are conducted the data presented are often from early analyses. Decades of research have consistently shown this type of data will over-estimate the benefits of a new medicine or other intervention. Making decisions on the basis of such early data means that the real benefits and harms of new cancer medicines may be unknown or highly uncertain at the time they are proposed for listing. Providing funding for cancer drugs at this very early stage requires acceptance of two major risks: (i) that the benefits hoped for will not be realised and (ii) that additional serious harms will emerge.

These are not simply theoretical risks. Over time we have learnt that the new therapies may be *less* effective than the treatment that it replaced for some patient groups. The net result has been overall reduction in health outcomes (i.e., patients have died sooner than they would have otherwise) at overall higher cost to government. Recent well-documented examples are the withdrawal of the approval of bevacizumab (Avastin) for use in metastatic breast cancer in the US [12]and the "black box" warning and interruption to marketing in the USA arising from major vascular complications of ponatinib.[13]

A further tension that exists in the current system is that compassionate access programs for new products that start before regulatory or reimbursement processes commence increase demand for these products, in the absence of adequate information about benefits and harms. These programs are often limited in number of patients and

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[9] http://www.huffingtonpost.com/jeffrey-sachs/the-drug-that-is-bankrupt_b_6692340.html

[10] Kantarjian H et al. The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts. Blood. 2013;121(22):4439-42. doi: 10.1182/blood-2013-03-490003. Ep

[11] http://www.theguardian.com/society/2015/jan/12/camcer-drugs-fund-financial-boost-but-cut-treatments-nhs

[12] D'Agostino RB. Changing End Points in Breast-Cancer Drug Approval — The Avastin Story. N Engl J Med 2011; 365: DOI: 10.1056/NEJMp1106984

[13] http://www.fda.gov/Drugs/DrugSafety/ucm379554.htm

thus create significant inequity. As a result, there is increased pressure to provide public funding and access to a new product – often in the absence of any plan for ensuring data collection, or review.

Paying for access to new drugs before we know what the true balance of their benefits and harms is likely to be –i.e. before large-scale trials are complete – is *not* harm free: it is prioritising the hopes and interests of patients with cancer *now* over the potential risks to those same patients, as well as the interests of the much larger number of patients who will have the same cancer *in future years.* It is important for all to understand that weighing up this balance can lead to different decisions than would be reached by a patient and their doctor trying to decide the best treatment for that individual person.

Misconceptions about the Assessment of Cost-Effectiveness

There are many misconceptions about the process of assessing data for cancer and all other drugs. Three we wish to address directly are:

> *'The current cost effectiveness tests for listing of drugs on the PBS require extensive clinical trial data that is difficult if not impossible to provide in the case of rare cancers'*[14]
> *'In the deliberations of the PBAC, we understand that overall survival (OS) is usually considered to be the most appropriate end-point; as such, drugs deemed to be efficacious must demonstrate an improvement in OS in Phase III clinical trials.'* [15]

> '*The price government puts on a year of your life is $50,000'*[16]

There is in fact no minimum requirement for the data that the PBAC will consider. However, as noted above, the poorer quality the data, the less confident the Committee can be about the likely benefits and harms of any new treatment. This does not preclude the Committee recommending treatments for rare or uncommon cancers or other diseases and there are many examples of positive recommendations in these conditions (e.g. pazopanib for sarcoma, sunitinib for GIST, eculizumab for atypical haemolytic uraemic syndrome, denosumab for giant cell tumour of bone). Recommendations for these and many other recent applications have been based on whatever outcomes are most robust in the trials in the evidence submitted to the Committee – there is *no* requirement that drugs 'must' show an improvement in 'overall survival' although it is much easier to assess potential benefit when such data are available.

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[14] http://medicinesaustralia.com.au/files/2013/07/Rare-Cancers-Australia-Submission.pdf

[15] http://www.aph.gov.au/Parliamentary_Business/Committees/Senate/Community_Affairs/Cancer_Drugs/Submissions. HSANZ Submission

[16] http://www.news.com.au/lifestyle/health/the-price-government-puts-on-a-year-of-your-life-is-50000/story-fneuzlbd-1226906545558

Similarly, the 'government' (or PBAC) does not have a fixed threshold for valuing a life. In fact the Committee has flexibility to consider not only quality of life, but also rarity of a disease, existing options for treatment, likelihood of cure, as well as effectiveness, safety and cost. This is explicit in the PBAC guidelines. However, the requirement to consider cost-effectiveness is imposed by the legislation, and procedural fairness requires that lives be valued equally. For this reason, the Committee uses numerical values for cost-effectiveness as an aid to consistency of decision-making, both over time and for different diseases.

Suggestions to Improve the Assessment of Cost-Effectiveness.

As noted above, a major concern of the PBAC is the very small improvements in survival offered by new cancer drugs. Newspaper reports, community and patient submissions to the PBAC suggest that some of those concerned about access to new cancer drugs over-estimate the benefit these drugs offer. Further, the evidence presented to the PBAC shows that the benefit of new drugs is often conceived in terms of extension of *quantity* of life at the expense of *quality* of the extended life.

It would be informative for the PBAC and others if the Australian community formulated a consensus view of its priorities in the health care of cancer patients. In particular, it is important to understand whether the public would prioritise high expenditures on drugs for small extensions of life in patients with incurable cancer. The PBAC accepts that very small extensions in life may be worthwhile for some patients. However, the PBAC considers that there should be a formal process for community consensus development, such as a citizens' council or jury, to debate and define what is a minimal worthwhile benefit. This would be more equitable than case-by-case appeals formulated on the basis of individual patient stories which are not necessarily broadly representative of those with the disease.

This community discussion on the relative value of quantity and quality of life, and of end-of-life care is urgently needed. All stakeholders need to be aware that a willingness to pay large amounts for drugs which offer only small extensions in life may be creating incentives for pharmaceutical companies to pursue the development of drugs that are only marginally better, rather than concentrating efforts on finding drugs that make a major difference, and at the expense of drugs that improve quality of life.

Timing and affordability of access for patients and PBAC processes

The PBAC currently assesses in excess of 60 applications every four months. The number of applications for new medicines, and thus the workload for the Committee has been increasing over the last three years. Over the last two years, approximately a third of the applications have been for oncology treatments. Currently the PBAC has seventeen out of a possible total of eighteen members. Three of the clinician members are oncologists or haematologists and there is one consumer representative.

The PBS allows access to cancer drugs under the principle of equity and fairness. The cost to the patient of cancer drugs is the same as the cost of all drugs covered on the

PBS. A fundamental principle of the PBS is equity of access irrespective of personal financial means. Published prices for new cancer drugs show that the co-payment of up to $37.39 per script is a tiny fraction of the actual drug price. The great majority of cancer drugs used for the great majority of cancer patients are listed on the PBS and supplied at minimal cost to patients.

The timing of access to new medicines through the PBS depends on three key decision points:
1) submission of an application by a sponsor – the pre-PBAC phase
2) a positive recommendation by the PBAC
3) completion of post-PBAC negotiations and administrative processes, between the sponsor, Department and Government.

Only the second of these decision points is under the control of the PBAC.

1. The pre-PBAC phase

A prerequisite for the PBAC consideration of any new medicine is that the manufacturer is willing and legally able to supply it in Australia. Most of the public data about time to access to medicines is based on data from before parallel submission to the PBAC and TGA was introduced. This includes the widely quoted report, *Access to Cancer Drugs in Australia*. [17] Since 2011, sponsors have been able to submit applications to TGA and PBAC in parallel. Provided the data package is adequate and the price requested by the sponsor is reasonable and found to be cost effective, the PBAC may be of a mind to recommend approval before the final approval by TGA (e.g. dabrafenib for melanoma). However, some sponsors are now choosing to submit applications to the PBAC so far in advance of TGA approval that the PBAC has no option but to reject or defer them, as the TGA-approved indication is critical to determining a PBAC listing. This practice may be distorting the reported time to approval.

Delays in comparison with other countries often relate to when the sponsor decides to submit an application for PBS subsidy (as well as for registration through TGA). Examples of cancer medicines that have been available in the US and/or Europe over the past year and for which applications have not yet (as of February 27th 2015) been considered by the PBAC include ibrutinib (for some leukaemias and lymphomas), nivolumab (melanoma), and olaparib (ovarian cancer) among others. Comparisons of dates of regulatory submissions[18] show that new products are submitted to the TGA a median of 105 days after they are submitted to the European Medicines Agency (EMA), although the TGA accepts the same evidence package as the EMA. This delay will inevitably flow on to the PBAC.[19]

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[17] http://www2.deloitte.com/au/en/pages/economics/articles/access-cancer-medicines-australia.html

[18] http://cirsci.org/node/73 . CIRS R&D Briefing 55 The impact of the changing regulatory environment on the approval of new medicines across six major authorities 2004-2013

[19] Pearce A. et al., 'Delays in access to affordable medicines: Putting policy into perspective. Australian Health Review 2012; 36(4):412-418.

Because the PBAC will not recommend listing a drug that cannot be supplied, the vast majority of applications for new drugs are from manufacturers. However, the PBAC also responds to the changing use of currently listed cancer drugs. Over the past 2 years, there have been a number of changes to broaden listing of currently available cancer (and other) medicines, for example, changes to access conditions for antiretrovirals and taxanes. These changes have been as a result of submissions from specialist medical organisations such as the Medical Oncologists Group of Australia. This clinician-driven process has meant that some listings of cancer products have been brought up to date with sound clinical evidence without having to rely on commercial decisions to submit applications for assessment. Enhancing resources available to specialist medical and other groups to submit applications would be one option to improve access to some products. This is especially relevant for products used to treat relatively uncommon conditions or older off-patent drugs, where there may be no commercial incentive to encourage a sponsor to apply.

The PBAC has a strong interest in preventative measures and has welcomed and considered applications from Cancer Council Australia, National Heart Foundation of Australia, Australian Council on Smoking and Health and Quit Victoria in consideration of aids to stop smoking.

2. The PBAC phase

Once an application to list a drug is submitted to the PBAC, the committee evaluation and decision process is completed in 17 weeks. Sponsors are advised a week after the meeting and decisions are made public 6 weeks after the meeting. For comparison, the process can take up to 2 years in the UK or 6-12 months in Canada. The most common reason for PBAC not approving a submission is because the sponsor fails to meet the legislative requirement to establish comparative effectiveness and comparative cost-effectiveness. This is typically because the requested price is too high in relation to the benefits provided, compared to existing treatments.

3. The post-PBAC phase

Delays following a positive recommendation by PBAC may be due to inability of the sponsor and Government to agree on the price and other details of financial agreements. For example, there was an 18-month delay between the Committee's recommendation for the listing of abiraterone for metastatic prostate cancer and the sponsor agreeing to supply the drug on the PBS under the recommended circumstances.[20] During this period, there were multiple additional applications for the same product and listing that had to be reviewed by the PBAC.

Problems with PBAC processes

The PBAC considers that one of the major reasons for the current perceptions of delay and 'unfair' and 'inequitable' decision-making about cancer drugs as well as other medicines is lack of transparency.

[20] http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2012-11/abiraterone

As the current processes have gradually evolved over the past two decades, there are some obvious issues that need to be addressed. Consumers and patient groups only find out what is on the agenda two months before a meeting and the publication of the agenda is not widely known. The most emphasis is given to protecting 'commercial-in confidence' information, rather than allowing an effective discussion in the community of the real benefits, harms and cost of the products that are being proposed. Cost and price information is systematically redacted from published documents at the insistence of the pharmaceutical companies and submissions are not published. In an attempt to improve transparency in decision-making, PBAC moved to make the Public Summary Documents describing each application and the PBAC's recommendations and reasons a redacted version of the Committee Minutes. Despite this, currently there is no systematic communication strategy with respect to negative committee recommendations. Consumers and clinicians do not know what data have been provided to the PBAC, compared to what may be available in the public domain.

The solution to some of these problems is first to improve the transparency of the system. Although some information of high commercial value may need to be withheld, the Committee believes that the great majority of the documents submitted to the PBAC can, and should, be made publicly available. This is essential if consumers, patients and clinicians are to make full use of opportunities to present their views about new medicines. Consultation with stakeholders should be a routine part of the process of considering new groups of drugs, but that cannot occur if stakeholders do not have access to the information submitted to the PBAC.

For the most recent meeting (March 2015) the Committee piloted a new process of consumer and patient hearings on selected applications, prior to the meeting. For the first time, these hearings allowed a direct conversation between the PBAC and patient groups about the benefits and harms and costs of some of the medicines on the Committee agenda. Both the PBAC and patient groups found these discussions extremely informative. Equally, the PBAC members were concerned to hear directly that the perceived benefits from some of these new drugs were completely at odds with the evidence that was in the company submissions.

There clearly needs to be a systematic approach to communicating recommendations from the Committee, especially when the listing is not recommended. The communication needs to be appropriately tailored to consumers. All of these activities have been recommended or commenced, but are hampered by lack of resources and appropriate personnel.

A further complexity in relation to information exchange is the technical nature of scientific and clinical research. Robust methodology is the bedrock of legitimate scientific research. Adherence to this methodology is central to the integrity of science and medicine and protects the public from decisions made on the basis of opinions from experts or popular beliefs. The PBAC acknowledges that communicating the rationale for PBAC decisions is particularly difficult where it involves complex technical information. The PBAC is working to improve clarity of communication and has worked

with the Department of Health, with consumer input, to ensure that the fullest possible details of its assessments are published on the website.

However, much discussion of these issues occurs outside the formal channels over which the Department and the PBAC have control. The Committee believes the information presented to the public – both lay and professional – is often in a form that is difficult to interpret and often misunderstood. In the Committee's view, a useful reform would be standards for presenting information in newspapers, in communicating with patient groups, and in advertising to doctors, such as recommending the consistent use of metrics such as "numbers needed to treat or harm" to present benefits and harms, and that costs be revealed when new drugs are discussed.

Options to promote early access

Over the last three years the PBAC has worked with the Department, clinicians and some sponsors to develop processes for 'managed entry' or 'coverage with evidence development'. The principle underpinning these arrangements is that the risks associated with early access to (unproven) products are shared between sponsor and funder and made clear to patients and clinicians.

In managed entry, a provisional price for the drug is set on the basis of the sponsor's estimate of effectiveness and toxicity, while data on outcomes are systematically collected from patients and prescribing doctors. In this way the clinical risk of lack of benefit and potential for harm are countered, because those outcomes are detected early because national data are collected. The financial risks associated with PBS-listing a drug whose effectiveness is uncertain, but which the PBAC believes is *not* likely to be cost-effective at the sponsors' preferred price, are shared between sponsor and government because the sponsor agrees to repay money if the drug is less effective in actual use than was predicted. Two recent examples are the recommendations for listing crizotinib (for lung cancer) and trametinib (for melanoma).[21]

The Committee believes that this is an approach that meets current patients' needs for rapid access to possibly useful drugs without compromising other important values. There are several issues that need to be considered, however, in formulating these types of recommendations.

Firstly, the PBAC must have confidence that the clinical data provided at the initial application show evidence of likely benefit of treatment to patients. Secondly the sponsor should have additional studies in progress that will potentially confirm this benefit and allow accurate assessment of the size of the benefit over existing treatments. Alternatively, the sponsor needs to be prepared to collect data from Australian patients to establish the benefits, harms and costs of treatment. Clinicians and patients therefore need to agree to have such data collected; the Committee notes that this raises issues of privacy that are beyond its remit, but that optimal

[21] http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/pbac-outcomes/2014-11

implementation of managed entry may require legislative change. Thirdly, the sponsor needs to propose a price that is potentially cost-effective, on the basis of the data available at the time of PBAC consideration. Finally, the sponsor and Department need to execute a contract to ensure all of these issues are agreed, as well as a strategy for delisting the product and/or recovering excess payments if the hoped-for benefits are not confirmed. This process, including the fact the drug may be delisted, needs to be very clearly communicated to patients.

Although such arrangements may be one solution to the perceived need for early access to promising new medicines, it cannot be the only approach. There needs to be a frank and complete discussion between the community and pharmaceutical manufacturers about what the Australian community expects in terms of benefits and harms of new medicines, balancing early access with uncertainty, and understanding opportunity cost compared to other use of the same health care resources and the community's willingness to pay. The PBAC could then reflect these values and preferences accurately in its assessment and recommendations.

Proposals to improve PBAC processes and enhance early access

The PBAC would like to propose the following changes to the current system.

1.Full transparency of information about applications across the TGA and PBAC processes. Consumers, patients and clinicians would then know when an application is actually under evaluation, as well as expected dates for outcomes.

2. Increased resources to the PBAC and Secretariat (in the Department of Health) to allow additional stakeholder consultation during evaluation. Currently, stakeholder meetings are generally held only after an initial consideration by PBAC, simply due to lack of time and resources. Early consultation on defining the clinical place of new treatments as well as defining patient relevant outcomes would assist both the PBAC in its deliberations, and the sponsors in preparing appropriate submissions.

3. Develop effective mechanisms for data collection about new medicines - including managed entry type programs. Linking data is critically important if early access is to be made available.