

# The subsidy of pharmaceuticals in Australia: processes and challenges

Lloyd Sansom

## Abstract

The increasing costs of health care, including new technologies and pharmaceuticals, pose challenges for all countries both in the developed and the developing world. It is essential that the increased expenditure on pharmaceuticals represents value for money and is seen as an investment in health care rather than simply the purchase of the latest released agent. The system in Australia uses a cost-effectiveness approach to guide the decisions as to whether a new drug can be recommended for subsidy. The need for a greater understanding and transparency of the processes is essential in order for a well-informed public debate to occur about the challenges to the system and its sustainability. The relevant issues are discussed in this article to assist that debate.

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THE INCREASING COST of new pharmaceuticals is placing pressure on the health system of all countries, and a process to assess the incremental cost effectiveness of the new agents is essential to ensure that limited resources are spent to the best advantage in a way which maintains the equity of access that must be a fundamental principle of any system for subsidy. This article discusses the mechanisms by which drugs are considered for subsidy as part of the Pharmaceutical Benefits Scheme (PBS).

## Background

In recognition of the need for government assistance in the subsidy of pharmaceuticals, Australia

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## What is known about the topic?

The Pharmaceutical Benefits Scheme (PBS) over many years has given rise to an extensive specialised literature.

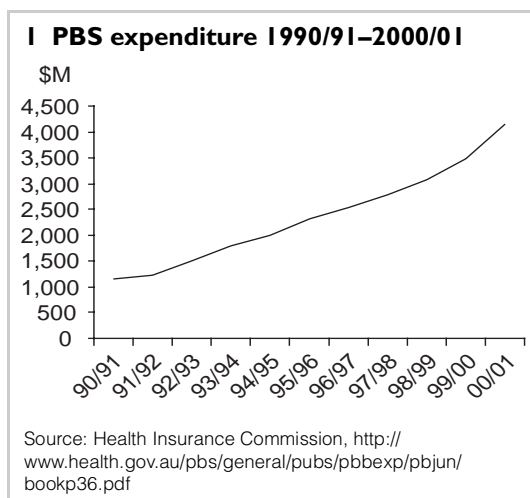
## What does this paper add?

Written by a centrally positioned insider, this article presents an up-to-date account of the mode of operation of the Australia's drug subsidy system and a perspective on the pressures operating on the PBS.

## What are the implications for researchers and policymakers?

Core challenges facing policymakers are identified and explored, including the difficulties and limitations of cost-effectiveness analyses and the imperative of making the PBAC process more transparent.

established a pharmaceutical benefits scheme for war veterans in 1919. A similar scheme for non-veterans was first proposed in 1944 when the *Pharmaceutical Benefits Act* (Cwlth) was passed by the Federal Parliament authorising provision of pharmaceutical benefits free of charge to all residents of Australia. The Medical Society of Victoria issued a writ in the High Court, which subsequently ruled that the 1944 Act went beyond the powers of Australia's constitution. This resulted in a change to the Australian Constitution in 1946 to enable the Federal Government to introduce a national subsidised pharmaceutical scheme. This compares to comparable countries such as Canada, where drug subsidy programs are provided by the individual provinces. About 43% of Australians also have private health insurance, and there is a well established private hospital network conducted by both not-for-profit or for-profit organisations. The involvement of private health in the subsidy of pharmaceuticals is limited, although there is increasing pressure on the health funds to become involved in the subsidy of large cost drugs not currently subsidised under the PBS.



The PBS is primarily a community-based system, although direct Federal Government subsidy via a Highly Specialised Drugs program for use in the public (and private hospital) system is also in place (Highly Specialised Drugs Program, Commonwealth of Australia). In the first year of the PBS the list of subsidised drugs consisted of 139 life-saving drugs costing less than A\$300 000 per annum. In 2004, the Scheme funds about 650 different drugs (in 1600 dosage forms) marketed as nearly 2500 different brands. Over 200 of these drugs have been included on the list as a result of analysis of cost effectiveness, which became a requirement for submissions in 1993 (Mitchell 2002). About 75% of all pharmaceuticals, excluding those provided by state-funded institutions, are funded through the PBS.

### National Medicines Policy (NMP)

The cost of the PBS in 2002–03 was about A\$5.6 billion and over the past decade has been increasing at an annual rate of between 8% and 20%, a rate many believe is unsustainable. Box 1 shows the growth in PBS expenditure in the period 1991–2001. Over the last decade PBS expenditure grew by more than 260%. By contrast, the expenditure on medical benefits grew by 73%, expenditure on public hospitals by the Commonwealth government grew by 73%, and overall Commonwealth expenditure grew by 119%. Reflecting these trends, PBS expenditure increased from 9% to 16.7% of the Commonwealth health budget over

this period. The total health sector spending in Australia as a proportion of GDP is 9.3%, compared with over 16% in the USA.

Access to medicines is an integral component of Australia's National Medicines Policy. The policy consists of four arms or central objectives (Commonwealth of Australia 1999):

- Timely access to the medicines that Australians need, at a cost individuals and the community can afford;
- Medicines meeting appropriate standards of quality, safety and efficacy;
- Quality Use of Medicines; and
- Maintenance of a responsible and viable medicines industry.

The subsidy of pharmaceuticals must be seen as an integral component of the NMP and not separate from it (see Box 2).

The subsidisation of pharmaceuticals should be seen as a part of the process of improved health outcomes rather than an end in itself. One of the greatest challenges for any system of medicines subsidisation, and indeed for the use of cost effectiveness in allocation of resources, is to replicate the results from controlled clinical trials (in which strict control of drug administration and other requirements of the trial is involved) in the practice environment. If a drug is subsidised without any attempt to concurrently put into place those measures which maximise its contribution to health outcomes, then there is a risk that its cost effectiveness in real life will be less favourable than the calculation of cost effectiveness on which the decision to subsidise was made. The integration of the subsidy system and appropriate quality use of medicines initiatives is essential.

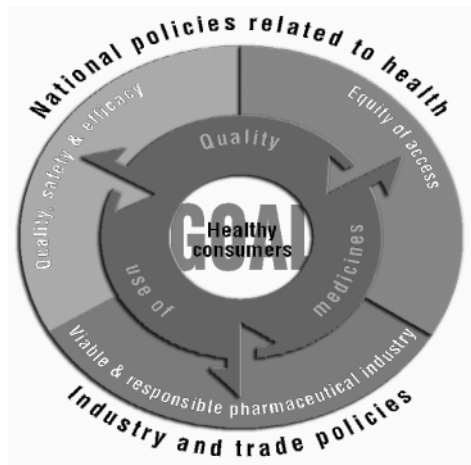
Quality Use of Medicines is defined as:

- Judicious selection of management options;
- Appropriate choice of medicines, where a medicine is considered necessary; and
- Safe and effective use.

### Process for drug registration and subsidy

Before a medicine can be available for use in Australia it must be approved for marketing by the Therapeutic Goods Administration (TGA). The

## 2 Integration of the arms of the National Medicines Policy



Source: Department of Health and Ageing, <http://www.nmp.health.gov.au/pdf/execsumbro.pdf>

medicine is evaluated on the basis of its safety, quality and efficacy. No comparison of the safety or toxicity of the agent with an existing therapy likely to be replaced by the new agent is required as part of this evaluation process. Once a product is approved for marketing and entered onto the Therapeutic Goods Register, it may be prescribed (but not subsidised). Sponsors (usually the manufacturer) can then apply for listing as a pharmaceutical benefit for some or all of the indications approved by the TGA by submitting comparative data and a cost effectiveness analysis. The application for listing is submitted to the Pharmaceutical Benefits Advisory Committee (PBAC) for consideration. If subsidy is recommended, the price is negotiated by the Pharmaceutical Benefit Pricing Authority (PBPA) which makes a recommendation to the Minister for Health and Ageing regarding the price at which the item should be listed. If the total annual expenditure to Government is predicted to exceed A\$10 million, the recommendation must also be approved by the Cabinet before subsidy can occur. The Minister cannot list a drug as a pharmaceutical benefit on the PBS unless a positive recommendation has been received from the PBAC.

## The Pharmaceutical Benefits Advisory Committee (PBAC)

The PBAC was established under national legislation to make recommendation to the Minister for Health and Ageing on which medicinal products should be available for subsidy under the PBS and to provide advice to the Minister on any other matters relating to the PBS as referred by the Minister. On receipt of a submission, the PBAC forwards the material to one of four evaluation groups — one within the Commonwealth Department of Health and Ageing and three external groups — which prepare detailed evaluations on both clinical and economic matters contained in the submission. The PBAC and its sub-committees meet three times a year. There are two expert sub-committees to provide advice to the PBAC.

### Economic sub-committee (ESC)

This sub-committee reviews the clinical and economic evaluations, including cost-effectiveness, prepared from the submission by the evaluation groups and advises PBAC accordingly. The evaluations are also forwarded to the sponsors, who provide responses to the evaluations directly to the ESC.

### Drug utilisation sub-committee (DUSC)

This sub-committee advises PBAC on the estimates of use contained in the submissions and provides data on drug utilisation subsequent to listing as a benefit. The DUSC also conducts regular reviews of the post-listing utilisation data, and significant differences between the actual use and predicted estimates are identified.

The PBAC is required to take into consideration the effectiveness, cost effectiveness and clinical place of the drug relative to existing drug therapies. If no such therapies exist, the drug treatment should be compared with standard medical care. The submissions must address each of these criteria and *Guidelines for the pharmaceutical industry on the preparation of submissions to the pharmaceutical benefits advisory committee* (Commonwealth Department of Health and Ageing 2002) are available to the sponsors (these Guidelines are currently undergoing revision and expansion in consultation with the pharmaceutical industry).

## Requirements of submissions

A submission by a sponsor (usually the manufacturer) must wherever possible contain the following:

### ***Details of the proposed drug and its use on the PBS***

The sponsor is required to submit data which enable an evaluation of the effectiveness and cost-effectiveness of a new product compared with that which the new therapy is most likely to replace in practice (ie, a comparator).

*Main comparator:* This is likely to be the therapy that most prescribers will replace with the new agent. However, the selection of the main comparator is often the subject of considerable debate between the PBAC and the sponsor. If the drug is one for which pharmacological analogues exist, then the comparator is likely to be the drug from that class with the greatest market share. If the drug is in a new therapeutic class, then the comparator is likely to be the drug which is used to treat the condition in the largest number of patients. If no currently listed drug is available, then the comparator will be standard medical care (including surgery).

It has become more common for sponsors of new drugs to seek listing for last-line therapy after all appropriate alternative treatments have failed, even though the drug may be registered by the TGA for the first-line setting. This is to maintain a price which cannot be justified on the basis of head-to-head comparison with existing agents. Under such circumstances, the sponsor may recommend placebo (or standard medical care) as the comparator in order to justify a price premium for restricting to last-line therapy. The drug may only be cost effective in patients who have tried and failed other therapy, or where the patient has a contraindication to the first-line drug. If the drug's subsidy is restricted to use after other cheaper and more cost effective agents have been tried (for example as second-line therapy), but is actually prescribed as first line therapy, then the cost effectiveness approach of the PBAC processes is undermined. This use outside subsidised approved indications is commonly referred to as 'leakage'.

A related issue for the PBAC is the use of established drugs for indications for which the original sponsor had not sought marketing

approval even though the drug is now widely used for that indication. Under these circumstances the sponsor may claim that such a drug should not be considered as the main comparator even though it has the highest use in this condition. An example is carbamazepine, which is only approved for epilepsy and trigeminal neuralgia but widely used in the management of neurogenic pain. Its use as comparator for any new drug in this condition could therefore be problematic. The original sponsors of such drugs are generally unwilling to pay the necessary regulatory fees for the evaluation of the drugs in the new indication, particularly as these drugs are commonly out of patent and generic products are available. There is a strong case for the regulatory agency to be able to act affirmatively under such circumstances to include such a new indication if appropriate clinical data of high quality are available.

*Differences between the proposed drug and the main comparator* in respect of, for example, clinical outcomes, toxicity, and contraindications: the drug may have a clinical outcome which is no worse than the comparator but may offer the advantages of a better safety profile. This may result in a more favourable cost effectiveness and may warrant a price premium over the comparator due to a better quality of life outcome, or significant cost offsets due to the better safety.

### ***Data from comparative randomised trials***

The PBAC has strong preference for head-to-head randomised controlled clinical trials, although analyses of trials involving a common reference are acceptable. In some cases head to head studies have not been undertaken and the comparison relies on cross-study comparison between trials which use a common reference. For example, data may be available for the new drug against placebo and for the comparator against placebo. Using the common comparator approach, a comparison between the drug and its comparator is possible. Issues such as the similarity in the inclusion and exclusion criteria of patients in the trials and differences in clinical outcomes measures can, however, make such comparisons difficult to interpret. The PBAC will accept any reasonable evidence but is most influenced by the results of the most rigorous randomised trials.

Issues which must be addressed by the sponsor include whether the subjects included in the trials represent patients for whom subsidy is being requested (in terms of, for example, demographics and disease severity) and whether the doses used in the trial represent those for which TGA approval has been granted. It is common for the PBAC to question the relevance of the requested restriction in view of the clinical data submitted to it.

The results of the trials must be presented as patient-related outcomes of each trial (or meta analysis). The confidence intervals must be presented and whether 'intention to treat' was used for the analysis. Patient-relevant outcomes include primary clinical outcomes, quality of life measures and economic inputs and outcomes. The confidence intervals are necessary for the PBAC to have insight into the extent of uncertainty that exists in the data.

The submission must state, on the basis of the trial evidence, whether:

- The proposed drug has significant clinical advantages over the main comparator
  - more effective and less toxic **or**
  - similar effectiveness but less toxic **or**
  - more effective but more toxic
- The proposed drug is no worse than the comparator in effectiveness and toxicity;
- The proposed drug is less effective but less toxic than the comparator.

If the proposed drug has clinical advantages the importance of this benefit must be discussed as the justification for any increase in price requested in view of the benefit. The use of cost effectiveness analysis (CEA) or cost-utility analysis (CUA) is suitable in these circumstances.

In those situations where it is felt that the clinical trial data do not provide sufficient information on the clinical and economic performance, a modelled economic analysis is provided. This analysis may involve decision tree analysis, Markov Chain process or a Monte Carlo simulation (Bootman, Townsend & McGhan 1991; Drummond et al. 1999).

The sponsor is required to estimate the anticipated usage for at least the first 2 years as well as the reduction of usage of other subsidised drugs. Estimates of the impact of listing on the govern-

ment's health budget must be provided, such as increased use of screening procedures, the additional costs of treating any side effects less the cost offsets of a lower side effect profile, reduction in substituted procedures, etc.

### **The PBAC decision-making process**

In essence, the PBAC makes a recommendation regarding the purchase of a health outcome, considers whether the evidence provided supports the request by the sponsor and determines whether the cost per outcome represents 'value for money'. Comparative cost effectiveness forms the basis of that decision. Often there is considerable uncertainty, commonly related to clinical uncertainty, about the estimate of cost effectiveness and that is taken into account in the considerations by the PBAC. The Committee is often asked to state the value of the cost effectiveness ratio that is acceptable in order to get a positive recommendation. However, this does not take into account the confidence interval around the estimate of the incremental cost effectiveness ratio. It is not uncommon for the 90% confidence interval to range five fold or more indicating a high degree of uncertainty around the point estimate. This uncertainty is often related to the clinical data or to the variability seen in the sensitivity analysis of the economic model. Other factors which the PBAC takes into consideration during its deliberations include the severity of the condition being treated, the ability to target therapy to those likely to benefit most, the presence of effective alternatives, and the financial implications for the PBS. The PBAC has on occasions made recommendations that require patients to have met certain criteria of severity of an illness before being allowed subsidised access and to demonstrate a level of response in order to be able to continue to receive the subsidy. Examples include the anticholinesterase drugs in the treatment of mild to moderately severe Alzheimer's disease and the TNF-alpha inhibitors for rheumatoid arthritis. In these cases, the drugs are of acceptable cost effectiveness only in those patients who respond. There is always a concern when patients fail to meet the continuation criteria and need to cease subsidised therapy, and the PBAC would prefer making recommendations for those patients who have a marker of response

before commencing therapy. Unfortunately such markers are not generally available, and the only way 'cost-effective responders' can be identified is to allow eligible patients to commence the drug and then to be evaluated at an appropriate time. While it can be argued that therapy with expensive agents will be ceased by prescribers if the response is unlikely to prolong life or to improve the quality of life of patients, such decisions are more difficult in the absence of an external requirement, particularly in the face of patients' desire to continue therapy.

### Recommendations to the minister

In advising the Minister about a new drug the PBAC may recommend:

- Listing as cost-effective at the price premium requested;
- Listing at a lower price to achieve cost effectiveness;
- Rejection on the basis of unacceptable cost effectiveness;
- Restriction to patient sub group(s) for whom the drug is cost effective.

The Committee can recommend the listing of an agent which would not be considered cost effective under normal circumstances by invoking the 'Rule of Rescue'. This requires that there is no other effective therapy for a severe chronic progressive disease that affects a small number of patients. An example of this approach was the recommendation for funding of Imatinib for accelerated and blast stages of CML.

### Categories of listings

A drug may be recommended for listing without any restrictions and will be subsidised irrespective of the condition for which it is used.

When a drug is deemed to be cost effective only in a limited number of the approved indications then the drug will be listed as a restricted benefit and will only be subsidised for specific indications. For example, fentanyl patches are restricted to "chronic severe disabling pain which is associated with proven malignant neoplasia which is unresponsive to non-narcotic analgesics" (Schedule of Pharmaceutical Benefits 2004) even though the

drug's registration allows use in the management of pain due to non-malignant causes. Another example is azithromycin, for which listing is only approved for the treatment of uncomplicated urethritis and cervicitis due to *Chlamydia trachomatis* and for trachoma, even though the drug has registered indications which include lower and upper respiratory tract infections. The restricted listing of this drug is due to higher cost effectiveness in the other indications and also as an attempt to limit the population exposure to the drug to minimise the risk of the development of resistant common pathogens.

The Government recently established an Expert Advisory Group on Antibiotic Resistance (EAGAR) and the PBAC seeks advice from this group regarding the appropriate listing for any new antibiotic. This is an example of collaboration between committees to improve the Quality Use of Medicines through the listing process.

The difficulty with the restricted benefit approach is that there is no formal audit trail and considerable usage outside subsidy-approved indications can occur. As already mentioned, such usage is commonly referred to as 'leakage' and, while there is no formal study on its extent, some commentators have suggested that it could be quite significant. Currently this matter is dealt with through price/volume arrangements where sales beyond an agreed figure are paid for at a lower price. For the cost-effectiveness approach in decision making to have an impact in practice the extent and reasons for the 'unapproved' use must be examined. In the past there has been no formal communication between the PBAC and prescribers as to the reasons why the PBAC might restrict a listing due to concerns about 'commercial-in-confidence' issues. The PBAC has recently decided that such reasons will now be provided at the time of listing and is negotiating with the National Prescribing Service (NPS) as to the best mechanism to inform prescribers of new listings and of any conditions associated with their subsidy. A recent agreement between the Government and the pharmaceutical industry also attempts to focus attention on the promotion of PBS-approved indications in marketing activities.

The highest category of restriction placed on a PBS approved drug is by an Authority System. For these drugs/indications, approval to prescribe as a benefit must be obtained before commencing therapy. For example, pegylated doxorubicin requires an Authority for “advanced epithelial ovarian cancer in women who have failed a first-line platinum based chemotherapy regimen” (Schedule of Pharmaceutical Benefits 2004).

For some drugs specific biochemical/haematological markers are required and documentary evidence may be required before approval. The Government has recently announced a program to clarify the wording of authority listings to enable better auditing processes. It is envisaged that once this as occurred an on-line approval process will be initiated.

### **The Pharmaceutical Benefits Pricing Authority**

The recommendations of the PBAC are sent to the Pharmaceutical Benefits Pricing Authority (PBPA) for consideration of pricing issues. The PBPA is a non-statutory committee which makes recommendations on prices for new items recommended by the PBAC to the Minister. The Authority, which has an independent Chair, has membership from the pharmaceutical industry, Consumers’ Health Forum and the government departments of Health and Ageing and of Industry, Tourism, and Resources (Pharmaceutical Benefits Pricing Authority 2003). In considering the price of items the PBPA takes into account the following factors:

- PBAC advice on clinical and cost effectiveness issues;
- Price of alternative brands and price of drugs in the same therapeutic class;
- Cost data information;
- Prescription volume, economics of scale, stability considerations (for example expiry date);
- Level of activity being undertaken by the company in Australia (for example research and development activities);
- Overseas price.

There are several mechanisms used by the PBPA to contain the price of products listed on the PBS.

### **Brand premium policy**

The brand premium policy was introduced in 1990 to increase price competition by allowing companies to set their own price for multi-branded items. The Government subsidises to the lowest priced brand with the patient paying the difference between that price and the prescribed brand. Pharmacists are allowed to brand substitute to the lowest priced approved bioequivalent generic product with the permission of the patient and provided the prescriber has not directed otherwise on the prescription. The average brand premium at May 2003 was \$3.06 and the number of prescriptions dispensed at the benchmark price (54 % of prescriptions for which alternative brands are available) now exceeds the number dispensed with a brand premium.

### **Therapeutic group review policy**

Introduced in 1998, this reference pricing policy applies to narrowly defined therapeutic groups where drugs are of similar safety, efficacy and health outcomes.

The Government subsidises only to the lowest priced drug within the defined subgroup. Companies may set prices above the subsidised amount with the patient paying the price difference in addition to the PBS co-payment. Classes of drugs covered by this policy include H<sub>2</sub> receptor antagonists, ACE inhibitors, HMG CoA reductase inhibitors and the dihydropyridine calcium channel blockers.

### **Weighted average monthly treatment costs (WAMTC)**

Based on the latest 12 months’ utilisation data, treatment cost of the drug per month is calculated and compared with the cost of other drugs in a group and weighted by dosage, strength and volume to find the drugs with the lowest weighted monthly treatment cost. This then sets the benchmark price for that group of drugs. The WAMTC is calculated as the total cost of the drug provided over a period divided by the total number of months of treatment provided.

The H<sub>2</sub> antagonists, ACE inhibitors and HMG CoA reductase inhibitors are examples. The aim of WAMTC is to adjust the pricing of drugs which have been accepted by PBAC to be therapeutically

equivalent so that the cost per month is equivalent. Drugs that are included in the WAMTC are usually accepted by the PBAC on a cost minimisation basis.

### **Price/volume arrangements**

This is a risk sharing arrangement where there is likely to be the potential for significant volumes or uncertainty about future usage. This arrangement is also used where the PBAC has concern that the drug may be used outside the approved cost effective restrictions for subsidy. Any usage greater than that agreed for the approved listing is paid at a lower price, often at the price of the drug which the new agent replaces.

Representatives of the pharmaceutical industry have stated strong opposition to this policy, but PBAC believes that it is not an unreasonable approach to the pricing arrangement for selected drugs in order to maintain cost effectiveness. The PBAC is currently negotiating with the industry as to how an improvement in the prediction of usage patterns may occur to ensure that any price/volume arrangement is based on the best prediction of uptake of a new agent taking into account factors which might impact on the extent of uptake, for example patient preference for a dosage form or inappropriate marketing.

### **Drug prices in Australia**

In 2001, the national government asked the Productivity Commission (a Commonwealth agency providing independent advice on microeconomic policy and regulation) to research the differences in prices of pharmaceutical benefits items in Australia compared with the price in other countries (Productivity Commission 2001). The Commission compared prices in Australia with those in the US, Canada, UK, France, Spain, Sweden and New Zealand. The last four countries have a universal subsidy scheme for pharmaceuticals similar to Australia.

The Commission reported that for new innovative pharmaceuticals the price negotiated by the government in Australia was similar in all these countries except the US and the UK, where prices were 104% and 25% higher, respectively, although the US price may not reflect the 'lowest' price available in that country.

The Commission defined 'me-to' pharmaceuticals as entities for which therapeutic alternatives are available and found that for these agents the price in the US is likely to be between 70% and 94% higher than in Australia, and about 60% higher in Canada, the UK and Sweden, but similar to France, Spain and New Zealand. For generic drug products, prices in Australia were lower than in Sweden, Canada, the US, and the UK.

In its summary, the Commission stated that it considered the reason for the generally lower drug prices in Australia to be the strong emphasis on cost containment within Australia's subsidy arrangements, in particular the cost effectiveness requirement and the reference pricing policy. Notwithstanding this conclusion, the Commission did state that it was difficult to compare prices across countries due to a variety of factors, including systemic differences in health systems. Another factor making such comparisons somewhat unreliable is the difficulty of determining the magnitude of rebates paid to third party payers in other countries since such material is considered to be confidential. It is interesting that for some expensive drugs which the PBAC has recently recommended with an initiation or continuation rule, the Australian price is higher than that available from mail-order pharmacies in the US. This difference most probably reflects the restrictions for subsidy in Australia to those patients who are likely to benefit most and in whom the drug is cost effective, thus resulting in a smaller potential market.

### **The PBS and the Australian-American free trade agreement**

The pharmaceutical Annex to the Free Trade Agreement does not alter the basic structure or mechanisms of the PBAC processes. The PBAC will remain the only body that can make recommendations to the Minister regarding listing on the PBS. The Minister cannot list a drug on the PBS unless a positive recommendation has been received from the PBAC. The Free Trade Agreement does not alter this process and the PBAC remains the gatekeeper of the system. Many of the commitments of Australia in the Free Trade Agreement regarding the PBAC processes are already in place and no further action is required. (eg, the pre-submission



consultations with officers of the Department of Health and Ageing, the ability of sponsors to respond to the evaluations prepared by the Pharmaceutical Benefits Branch Evaluation section and the sub-committees of the PBAC, and the current availability of comprehensive guidelines for preparations of submissions.) The commitment to provide a review process has been accepted by the PBAC as appropriate, provided it occurs in a transparent framework. The currently agreed position of the PBAC and Medicines Australia is that the sponsor may seek a review of a PBAC decision not to recommend listing. The specific issues which form the basis of the review must be from the list of reasons given by the PBAC for rejection. A convenor, appointed by the Minister to be responsible for the oversight of the review process, will appoint a person with the required expertise in the matters under review from a panel of experts. No new material will be submitted and only that material considered by the PBAC will be the subject of the review. The reviewer may seek clarification of any matter from the evaluators, the sponsor or the PBAC but no formal hearings before the reviewer will be allowed. The report of the reviewer will be forwarded to the PBAC, which will consider the report and determine if any matter raised in the report justifies the reversal of the original decision. The sponsor will not be allowed to resubmit an application for the drug if a review is being conducted. The sponsor will have to decide either to seek a review or to prepare a resubmission addressing the reasons given by the PBAC for the rejection. The PBAC believes that there should be a continuum of transparency for the entire process — the reasons for the rejection, the reasons for the review, the report of the reviewer and the PBAC's response should all be available in the public domain. In the event that the PBAC reaffirms its original decision to reject the application, the sponsor will be entitled to prepare a resubmission at any future time. The matter of hearing before the PBAC is another issue currently being discussed. The PBAC has no issues around this requirement other than the practicalities of the process. At recent meetings, the PBAC has considered over 30 applications and the meeting times have been extended to three days to allow adequate consideration of all applications. If

each of the sponsors to these applications were allowed to have a 20 minute hearing with the PBAC this would add a further 2 days to the meeting time which would make the conduct of meetings almost impossible. Medicines Australia have agreed with the PBAC on the need to limit these hearings, and the parties are currently discussing options which would allow compliance with the requirements of the Free Trade Agreement, but at the same time allow a pragmatic process to be developed.

There is nothing in the Free Trade Agreement which would limit the timeliness of the availability of generic products onto the Australian market. Generic products are essential to the sustainability of the PBS and any issue which inappropriately delays the introduction of generics is to be opposed. However, the matter of 'evergreening' is an issue, but this would be a concern even without the Free Trade Agreement. 'Evergreening' is the circumstance in which the originator adds further matters to the original patent, or applies for new patents in relation to the same product, in an attempt to extend the period of protection from generic competition for a particular drug. This may be appropriate if the addition is truly innovative, but examples exist overseas where the material added is simply to delay the introduction of a generic competitor and force the generic company to the courts for resolution. Generic companies have to address all patents which have been granted on a product. The matters in dispute in the past have been settled by due judicial process, and that will continue. The amendments passed by the Australian Parliament about frivolous or vexatious patents purely for the purpose of delaying the introduction of a generic will allow the courts to impose fines if it finds the extension of the patent was not appropriate. It has been debated as to whether this legislation was required or whether the existing laws of Australia would allow these matters to be resolved.

Some commentators believe that the Free Trade Agreement will undermine the authority of the PBAC and its processes and place increasing pressure on its members. The members of the PBAC see the Free Trade Agreement as an opportunity to obtain greater transparency of the entire process. Transparency will bring with it greater accountabil-

ity on all parties and a higher level of informed debate about the PBS and its sustainability.

### **Transparency of the PBAC process**

One of the difficulties confronting the PBAC is the limitations on the full and open disclosure of reasons for its decisions. Concerns around 'commercial in confidence' issues have restricted the ability of the Committee to release reasons for its decisions. The PBAC has affirmed that consumers and health professionals have a right to that information and that it has a responsibility to ensure that full disclosure is made. Negotiations with the pharmaceutical industry as to the mechanism by which this will occur are under way, taking into account the confidential issues which need to be addressed. The role of the media as a responsible component in the dissemination of information on new drugs also needs to be addressed since much of the material in the lay press tends to be sensational and elevate false hopes in many patients suffering from serious and life threatening diseases.

### **Cost effectiveness estimates — in trials and in practice**

The PBAC considers estimates of cost effectiveness based on the results from clinical trials together with costs of the drug and any cost offsets identified in the trial or predicted within economic models. Thus the assessment of cost effectiveness in a submission is generally based on a controlled management of the drug in a population which has been clearly defined by inclusion and exclusion criteria for the trials. Further, the cost effectiveness may be significantly influenced by cost offsets including impacts on other parts of the health care system (reduced hospitalisations, less medical visits, less costly interventions, etc). For some drugs the cost effectiveness is based on surrogate measures of patient-relevant outcomes, and the relationship is often uncertain. It is essential that the cost effectiveness upon which the decision to list depends reflects the cost effectiveness in practice. This problem can be addressed in a number of ways. As mentioned previously the Quality Use of Medicines (QUM) needs to be integrated with the subsidy of a drug. However, one of the issues

which needs to be addressed is the lack of a complete dataset on drug utilisation and the ability to link (using de-identified data) patient data on drug use with health outcomes and the utilisation of other health care resources. The PBS database held by the Health Insurance Commission only contains drugs which are higher priced than the patient co-payment, and the PBAC has available only a sample of the drugs which fall below the co-payment for a given patient through an arrangement with the Pharmacy Guild of Australia. It is essential that complete utilisation of all drugs dispensed through pharmacies be available. Australia has one of the best collections of datasets in the world through the PBS and Medicare Benefits Schedule systems as well as disease registers including cancer registers in each state. The vast majority of doctors and pharmacists use computer records, and it would not be difficult to address many questions such as compliance, adverse events etc. using these records. While it is essential that privacy remains paramount and must in no way be diminished, the evaluation and development of health policy can only occur with adequate and appropriate data. A way forward which addresses the privacy issues must be found in order to be responsive to the need for better post-marketing surveillance.

### **Future challenges to drug subsidy**

Every country in the world is becoming concerned at the influence which the rising cost of pharmaceuticals is having on their health budgets (Taylor 2001). The potential benefits that new drug discoveries can provide in the management and treatment of disease is unquestioned but there is doubt as to the capacity of many countries to provide these agents. The future holds enormous challenges in this area and some are discussed below.

#### ***Small incremental benefits of some newer agents***

An increasing number of newer agents offer statistically significant but small (incremental) clinical advantages at considerable cost. For example, many of the new oncology agents offer a prolongation of life of a few months but at generally unacceptable cost-effectiveness. A recent editorial

in the *New England Journal of Medicine* (Schrug 2004) indicated that in the past decade the survival gain in cancer of the colon has doubled but the cost of the therapy had increased by 320-fold. In an environment of limited resources and subsequent opportunity costs, the dilemma is whether to spend considerable amounts of money for such end-of-life drugs at the expense of some other pharmaceuticals or other components of the health system. These are decisions which the society as a whole through its government must decide. This is likely to be the most important aspect of the whole question of the sustainability of pharmaceutical subsidy systems.

### **Uncertainty of predicted benefits**

A number of newer agents have been trialled for relatively short periods of time, for example 12 months, but the projection is for significant health gains into the future. The sponsors are anxious to market these new technologies as soon as possible due to the rapidity of new information and technology and due to generated consumer expectation for new 'exciting' agents. With an increasing number of drugs there is considerable uncertainty as to the validity of the projections and there is a high uncertainty in the estimation of the cost effectiveness. Under such circumstances, new ways of funding commensurate with the degree of uncertainty need to be found or it will be increasingly difficult to recommend listing because of the high uncertainty in the estimates of cost-effectiveness. One method may be the use of risk-sharing (or shared responsibility) arrangements where a lower price is paid in the early stage of subsidy and is increased when, and if, further data suggest that predicted benefits have been realised. One difficulty with this approach is that it is probable that the 'effective' patent life of some products will be less than the current 20 years due to the rate of development in the knowledge of molecular biology and molecular pathogenesis. This 'shortened' effective patent life will pressure companies to make profits in a shorter period, thereby forcing higher initial prices. Notwithstanding these pressures, an appropriate funding mechanism must be found for these agents as the current arrangements are not sustainable. The requirement for companies to monitor the realisation of any predicted

benefits and any cost-offsets should also be considered, as companies will then need to focus on promoting Quality Use of Medicines relevant to their drugs in an attempt to maximise positive health outcomes. Such measures will require the establishment of databanks of information which enable the monitoring of individuals throughout the progress of their disease. While safeguards can be developed to handle the information in a de-identified manner, issues of privacy are of significant concern.

### **Ageing population**

The ageing population must be considered in any future planning from both an economic, social and health perspective. In a recent report prepared for the Commonwealth Government (Commonwealth of Australia 2002), the projected growth in the PBS expenditure in the period 2001–41 was from 0.4 % to about 3.5 % of gross domestic product, far above expenditure on medical benefits or hospital and other health services. Such a rapid rate of rise must be considered in any forward economic and social plan in regard to demands on taxpayer funds.

### **Pharmacogenomics**

As the understanding of the molecular pathogenesis of disease and the genetic determinants of drug response increases, so will the use of targeting to identify those patients in whom a response to therapy is optimised and in whom the drug may be cost effective at the price requested. The recent identification of the mutation(s) which identify patients with non-small cell lung cancer who will respond to the drug Gefitinib demonstrates this issue (Lynch et al. 2004). The question is whether the society is ready for this development and how parliaments will address the ethical issues. However it must also be borne in mind that it is unethical to administer a drug to a patient in whom it can be determined the drug will have no response and/or where there is a high risk of serious toxicity.

### **Summary**

Increasing concern about the sustainability of future expenditure on pharmaceuticals is a world-

wide phenomenon (Lopert et al. 2002). The tension between health, social, economic and industry policy is no more apparent than in the area of pharmaceuticals. The rapid development of new drug entities resulting from a greater understanding of molecular pathogenesis is inevitable, as is the increasing demand resulting from an ageing population. Many of the newer agents will not be breakthrough discoveries but will provide small, but significant, incremental improvements in health outcomes which are not likely to be considered cost-effective against current criteria.

The equity of access to health care, including pharmaceuticals, is a central platform of a caring society and must be preserved (Dalton 2001; Harvey 2001). Health expenditure must continue to be focused on outcomes and based on open and transparent decision-making processes. A partnership approach between all stakeholders is essential if we are to benefit from the potential advantages that new drug discoveries offer. All stakeholders must accept a shared responsibility for the maintenance and sustainability of the system. It is essential that the society as a whole be engendered with a sense of ownership and responsibility in health and in health care. The subsidy of pharmaceuticals should always be considered as a component of an integrated, efficient and cost effective health care delivery system focused on health outcomes and the factors which impact on the attainment of those outcomes. Subsidy is an important, but not isolated, component and should not be considered outside the broader framework.

## References

- Bootman JL, Townsend RJ & McGhan WF 1991, *Principles of pharmacoeconomics*, Harvey Whitney Books, Cincinnati.
- Commonwealth Department of Health and Ageing 2002, *Guidelines for the pharmaceutical industry on preparation of submissions to the pharmaceutical benefits advisory committee*, viewed 16 September 2004, <<http://www.health.gov.au/pbs/pharm/pubs/guidelines/pdfs/guidelines.pdf>>.
- Commonwealth of Australia 1999, *National medicines policy*, viewed August 2004, <[www.nmp.health.gov.au](http://www.nmp.health.gov.au)>.
- Commonwealth of Australia 2002, *Intergenerational report 2002-03*, 2002-03 Budget Paper No 5, viewed 16 September 2004, <<http://www.budget.gov.au/2002-03/bp5/html/>>.
- Dalton A 2001, Australia's pharmaceutical benefits system: flawed but improving, and better than anywhere else, *Australian Health Review*, vol. 24, no. 2, pp. 7-14, viewed 16 September 2004, <<http://www.aushealthreview.com.au/documents/publications/30/issues/198/articles/385/24.2-3.pdf>>.
- Drummond M, O'Brien B, Stoddart G & Torrance G 1999, *Methods for the economic evaluation of health care programs*, 2<sup>nd</sup> edition, Oxford University Press, Oxford.
- Harvey R 2001, And on the cover of the guide were two words in red — don't panic, *Australian Health Review*, vol. 24, no. 2, pp. 15-20, viewed 16 September 2004, <<http://www.aushealthreview.com.au/documents/publications/30/issues/198/articles/386/24.2-4.pdf>>.
- Highly specialised drugs program, Commonwealth of Australia, viewed 19 September 2004, <<http://www.health.gov.au/pbs/general/pubs/pbbexp/pbjun03/pdf/book46.pdf>>.
- Lopert R, Lang DL, Hill SR & Henry DA 2002, Differential pricing of drugs: a role for cost-effectiveness analysis? *The Lancet*, vol. 359, pp. 2105-8.
- Lynch TJ, Bell DW, Sordella R, Gurubhagavatula S, Okimoto RA, Brannigan BW, Harris PL, Haserlat SM, Supko JG, Haluska FG, Louis DN, Christiani DC, Settleman J & Haber DA 2004, Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to Gefitinib, *New England Journal of Medicine*, vol. 350, pp. 2129-39.
- Mitchell A 2002, Antipodean assessment: activities, actions and achievements, *International Journal of Technical Assessment in Health Care*, vol. 18, pp. 203-12.
- Pharmaceutical Benefits Pricing Authority 2003, *Annual report*, viewed 16 September 2004, <[www.health.gov.au/pbs/general/pricing/pbparpt.htm](http://www.health.gov.au/pbs/general/pricing/pbparpt.htm)>.
- Productivity Commission 2001, *International pharmaceutical price differences: research report*, The Productivity Commission, Canberra.
- Schedule of Pharmaceutical Benefits for Approved Pharmacists and Medical Practitioners, May 2004, Commonwealth of Australia.
- Schrag D 2004, The price of progress: chemotherapy for colorectal cancer, *New England Journal of Medicine*, vol. 351, pp. 317-19.
- Taylor R 2001, Using health outcomes data to inform decision-making: government agency perspective, *PharmacoEconomics*, vol. 19, pp. 33-8. □