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Issue Brief

Evidence-Based Decision-Making Within Australia's Pharmaceutical Benefits Scheme

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ABSTRACT: In Australia, most prescription drugs are subsidized through the Pharmaceutical Benefits Scheme (PBS), one of several government programs in which evidence-based decision making is applied to the funding of health technologies. PBS processes are intended to ensure "value for money" for the Australian taxpayer and to support affordable, equitable access to prescription medicines; they are not intended as a mechanism for cost containment. The inclusion of a drug on the national formulary depends on the recommendation of the Pharmaceutical Benefits Advisory Committee (PBAC), which considers not only the comparative effectiveness but also the comparative cost-effectiveness of drugs proposed for listing. While some decisions have been controversial, the PBS retains strong public support. Moreover, evidence does not suggest that the consideration of cost-effectiveness has created a negative environment for the drug industry: Australia has a high penetration of patented medicines, with prices for some recently approved drugs at U.S. levels.

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OVERVIEW

Australia has a comprehensive system of universal health insurance coverage for both outpatient and hospital services called Medicare. Non-hospital services are funded mainly on a fee-for-service basis, while free access to public hospitals is supported by grants to state and territorial governments. Most prescription drugs are subsidized through the Pharmaceutical Benefits Scheme (PBS), one of several government programs in which evidence-based decision making is applied to the funding of health technologies.[1] This paper focuses on the PBS, which nearly 20 years ago became the first of these programs to introduce evidence-based health technology assessment.

Australia's PBS subsidizes most outpatient prescription drugs. The inclusion of a drug on the national formulary is dependent on the recommendation of the Pharmaceutical Benefits Advisory Committee (PBAC). Since the early

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1990s, the PBAC has considered not only the comparative effectiveness, but also the comparative cost-effectiveness of drugs proposed for PBS listing.

The PBAC is an independent statutory committee, appointed by the Health Minister; the cost of running its listing process is about US$10 million per year. The PBAC generally does not set its own work agenda, but reviews applications (usually submitted by manufacturers) for the listing of new drugs or of additional uses of already-listed drugs. Evidence submitted by the applicant is evaluated by staff of the Department of Health, assisted by contracted academic groups. While there is a preference for evidence from randomized controlled trials directly comparing a new drug with the drug or treatment it is mostly likely to replace, other evidence (indirect comparisons, nonrandomized studies) is weighed on a case-by-case basis.

Based on the evidence and the evaluation, the PBAC may recommend an unrestricted listing on the formulary, or listing for specified indications only, and in some cases may require prior authorization to prescribe. There is no specific cost-effectiveness threshold for approval; a higher cost-effectiveness ratio may be considered acceptable in relation to a drug for the treatment of a life-threatening condition for which there is a lack of effective alternative treatments, whereas a drug with a more modest incremental cost relative to its projected improvement in health outcomes may not be recommended if there is significant uncertainty in the estimate of cost-effectiveness. A drug that has not been recommended by the PBAC cannot be added to the PBS formulary, but the Health Minister may choose not to list a recommended drug.

While some PBAC decisions have been controversial—particularly decisions not to recommend the listing of certain oncology medicines—the PBS retains strong public support. Moreover, evidence does not suggest that the "fourth hurdle" of cost-effectiveness in drug approval has created a negative environment for the drug industry: Australia has a high penetration of patented medicines, prices for some recently approved drugs are at U.S. levels, and overall PBS spending rose 11 percent a year during the period 1996–97 to 2004–05.

Importantly, the PBS processes are intended to ensure value for money for the Australian taxpayer and to support affordable, equitable access to prescription medicines for all Australians, and are not intended as a mechanism for cost containment.

BACKGROUND: THE PHARMACEUTICAL BENEFITS SCHEME AND PHARMACEUTICAL BENEFITS ADVISORY COMMITTEE

The PBS has its origins as far back as 1919, when a limited program was established to provide subsidized medicines to World War I veterans and their families. When the PBS was formally established in 1948, it covered all drugs for pensioners and 139 "life saving and disease preventing" drugs for everyone else.[2] Since then it has evolved into a formulary of more than 3,500 different items. The list of benefits is comprehensive, covering most medical conditions for which drug therapy is appropriate.

It is estimated that around 80 percent of all prescriptions dispensed in Australia are subsidized under the PBS. Most PBS prescriptions are dispensed through community pharmacies, but PBS subsidies are also available to patients in private hospitals and people in residential care facilities. The federal government also subsidizes certain high-cost drugs supplied to hospital outpatients. Drugs supplied to public-hospital inpatients are, like other care in these facilities, generally the responsibility of state and territorial governments.

Under the PBS, beneficiaries fall into one of two categories that determine the amount patients contribute towards the cost of their medicines. In 2009, general beneficiaries contribute a maximum copayment of AUS$32.90 (about US$24) per item, while concessional beneficiaries—people who receive certain pensions and benefits or who meet certain criteria for being declared to be disadvantaged—pay AUS$5.30 (about US$4) per item, and the PBS pays the balance, up to the listed price. Safety-net (stop-loss) arrangements, which reduce the amount payable when a specified threshold is reached within a calendar year, limit patients' out of pocket expenses.[3]

Copayment amounts are adjusted on January 1 of each year, in line with movement in the consumer price index. Copayments contribute around 15 percent of total government expenditures in the program.[4]

In the early 1990s, amid concern over rising costs, the PBS became the first national pharmaceutical reimbursement program to introduce an explicit consideration of "value for money" as a prerequisite for formulary listing. Before a drug may be added to the PBS formulary, it must first be registered for sale in Australia. As with other nations' regulatory processes for drugs, this involves an assessment of efficacy, safety, and quality. Once it has marketing approval, a drug may be dispensed as a private prescription, with the patient paying the full cost (which may be offset by a contribution from the patient's private health insurance). To be covered under the PBS, however, a drug must meet an additional criterion—the fourth hurdle of cost-effectiveness.

Submissions seeking the listing of new medicines on the PBS (or for making changes to existing listings) are considered by the Pharmaceutical Benefits Advisory Committee. The PBAC is a statutory independent expert committee established under the National Health Act of 1953 (the Act) to make recommendations to the Minister for Health and Ageing on which medicines should be included on the schedule of pharmaceutical benefits and any conditions that should apply. A 1987 amendment to the legislation requires that when considering a proposal for the listing of a new medicine on the PBS formulary, the PBAC must take into account the effectiveness and cost of a medicine compared with other drug (or non-drug) therapies.[5]

A medicine that is more costly than other available treatments is generally only recommended for subsidy if it provides a clinically significant improvement in effectiveness or reduction in toxicity. The evaluation and decision-making process are sometimes referred to as "making a decision at the margin"—assessing the costs and benefits of replacing an existing treatment with the treatment proposed. In essence, the process may be thought of conceptually as one of "purchasing outcomes" rather than drugs, in that unless a new medicine offers an additional clinical benefit (improved outcome) relative to current alternatives, it will not be listed at a higher price (i.e., receive a higher subsidy).

POLICY FRAMEWORK, PRINCIPLES, AND OBJECTIVES

The PBS operates under the umbrella of Australia's National Medicines Policy, which has as its overall aim "to meet medication and related service needs, so that both optimal health outcomes and economic objectives are achieved."[6] The policy has four central pillars:

- medicines meeting appropriate standards of quality, safety, and efficacy;
- timely access to the medicines that Australians need, at a cost individuals and the community can afford;
- the quality use of medicines; and
- the maintenance of a responsible and viable drug industry.

The PBS facilitates access to prescription medicines by subsidizing their costs, reflecting the premise that cost should not constitute a substantial barrier to people's access to medicines they need. Recognizing such subsidies are not costless to society—and the community as a whole must bear them—the National Medicines Policy is premised in part on the understanding that consumers should be encouraged to understand the costs, benefits, and risks of medicines, and that access should be supported by rational use.

While the PBS is a demand-driven program with an uncapped appropriation, the introduction of cost-effectiveness evaluation as a prerequisite for formulary listing was not intended as a cost-containment mechanism per se, but rather as a way of ensuring that drugs added to the national formulary reflect value for money.

Role of the Pharmaceutical Benefits Advisory Committee

- Recommends drugs and medicinal preparations to the Minister for Health for funding under the Pharmaceutical Benefits Scheme (PBS).
- Recommends vaccines for funding under the National Immunisation Program (since 2006).
- Advises the minister and the Pharmaceutical Benefits Pricing Authority about cost-effectiveness ("value for money").
- Recommends maximum quantities and repeats on the basis of community use, and any restrictions on the indications where the PBS subsidy is available.
- Regularly reviews the list of PBS items.
- Advises the minister about any other matters relating to the PBS.

The PBAC has no explicit role in the development or promulgation of clinical guidelines. However, the PBAC often has an important, albeit indirect, influence on clinical practice. When recommending the listing of a medicine on the PBS, the PBAC may limit the indications for which the subsidy applies or may require the use of a "stepped therapy" or prior treatment algorithm, or, rarely, apply a "continuation rule"— a requirement that a patient demonstrate a response to treatment—as a prerequisite for access to ongoing subsidized therapy. This is intended to ensure that the use of the medication is consistent with the context in which it has been shown to be cost-effective.

The PBAC's remit was expanded in 2006 to include responsibility for the evaluation of vaccines for funding under the National Immunisation Program. The principles of evaluation that are applied to vaccines are the same as those applied to drugs proposed for listing on the PBS.

STRUCTURE AND SIZE, POSITIONING, AND OUTPUTS

The PBAC is an independent, statutory committee of up to 18 members, with membership of at least one each of the following: consumer, health economist, practicing community pharmacist, general practitioner, clinical pharmacologist; and medical specialist. The remaining members must have qualifications or experience in a field relevant to the functions of the committee. The PBAC chair is a full-time position, with all other members being part-time. All members are appointed by the Minister of Health and Ageing and serve "at the Minister's pleasure." The PBAC meets up to six times a year, with three three-day-long meetings devoted to the consideration of listing submissions; these occur at 17-week intervals. In between these meetings, other, shorter meetings are held as necessary to consider methodological issues and matters of policy and procedure.

The PBAC is also supported in its work by two technical subcommittees:

- The Drug Utilisation Sub-Committee, which monitors the patterns and trends of drug use and evaluates use and financial forecasts in selected major submissions to PBAC. Its members have a broad range of relevant expertise and mainly come from organizations interested in the evaluation of drug utilization;
- The Economics Sub-Committee, which evaluates the cost-effectiveness of major submissions to PBAC, by reviewing and interpreting economic analyses and assessing their quality, validity, and relevance. Its members include clinicians, clinical epidemiologists, health economists, biostatisticians, and clinical pharmacologists.

Submissions to list new drugs or to make substantial changes to existing listings are considered major submissions. Examples include submissions

that: substantially change the listing of a currently restricted drug (adding a new indication or broadening the eligibility criteria of an existing listing); review the comparative cost-effectiveness of a currently listed drug in order to change a PBAC recommendation on its therapeutic relativity, or support a price premium over a comparator; or list a new form (or strength) of a currently listed drug for which a price advantage is requested. Minor submissions are those that do not require the presentation of an economic evaluation.

In 2007, the PBAC considered a total of 209 submissions—122 minor and 87 major. Of these, 151 (72%) were recommended, 45 (22%) were not recommended, 12 (6%) were deferred, and one was withdrawn. The number of submissions has been growing steadily, with an increase of around 40 percent in both major and minor submissions over the last three years.[7]

The PBS program is administered by the Pharmaceutical Evaluation Branch (PEB), which is one of four branches of the Pharmaceutical Benefits Division of the Department of Health and Ageing. The PEB houses the secretariats of the PBAC and its subcommittees, as well as a section that manages price negotiations and provides secretariat support to the Pharmaceutical Benefits Pricing Authority.[8] The PEB has about 80 staff in total, with the cost of running the PBAC listing process estimated at AUS$14 million per annum (about US$10 million) in 2009–10.[9]

USING COMPARATIVE EFFECTIVENESS RESEARCH TO INFORM POLICY DECISIONS

The recommendations of the PBAC are advisory only, and the final decision to list remains with the Minister for Health and Ageing. However, while the Minister may decline a positive listing recommendation made by the PBAC,[10] she may not add a medicine to the PBS formulary in the absence of a positive recommendation from the committee. Further, if the net cost of the addition of a new medicine to the PBS formulary is expected to exceed a certain threshold (after taking into account projected cost offsets, such as reduction in expenditures on medications likely to be substituted in practice), the decision to list also requires the endorsement of the Cabinet. Failure to list a drug recommended by the PBAC has occurred only rarely.

The PBAC's agenda and workload, and the timing of consideration of particular medicines, are generally determined by the filing of submissions by medicines' sponsors (or other entities). From time to time, however, the PBAC will undertake reviews of particular drugs or classes of drugs to consider specific issues of concern.

Drug Application Process and Timelines

An applicant seeking the listing of a medicine on the PBS is required to submit an application prepared in accordance with detailed guidelines. The PBAC guidelines are revised continuously to maintain their methodological currency and to incorporate feedback from users. The most recent revision was published in December 2008.[11]

The PBAC evaluation cycle is fixed at 17 weeks, and the committee considers submissions three times a year (in March, July, and November). The cutoff for filing of major submissions (i.e., those requiring an economic evaluation) is 17 weeks prior to the meeting. To ensure timeliness of the process and avoid undue delays in facilitating access for patients, all submissions submitted by the cutoff are considered at the PBAC's immediately following meeting.

The cycle begins with the submission of the application by the sponsor and the preparation of a detailed commentary on the clinical and economic evidence presented in the submission. This is then provided to the sponsor for comment, and the submission, the commentary, and the sponsor's response are provided to the Economics Sub-Committee and Drug Utilisation Sub-Committee, which meet about four weeks before the PBAC meets. The outcomes of the subcommittee meetings are advice to the PBAC; these documents are also sent to sponsors for comment. All these documents—the submission, the commentary, the subcommittees' advice, and the responses from the sponsor—are

considered by PBAC in the 17th week, at which time the PBAC makes a decision to recommend or reject the application, or (uncommonly) to defer the decision pending clarification of a specific issue.

Positive listing recommendations by the PBAC are advisory only, however, with the government making the final decision as to whether and when to list. Broadly, for positive listing recommendations, a recommendation by the PBAC for listing of a product, or the extension of the terms of an existing listing, is referred to the Pharmaceutical Benefits Pricing Authority, which provides advice regarding negotiation of an appropriate price by departmental officers, if required. The PBAC and pricing authority's recommendations are then referred to the Minister for Health and Ageing for decision. Where a proposed listing is expected to add $10 million or more per annum in net cost to the PBS, it must be endorsed by the Cabinet.

If the PBAC rejects an application, the sponsor may resubmit it to a subsequent meeting of the committee (with amendments or new evidence) or, for submissions seeking the listing of a new medicine or new indication, may seek an independent review.

Evidence Synthesis and Evaluation

The PBAC is a user rather than a producer of CER. Formulary listing decisions can be conceptualized as attempting to address the question: What are the costs and benefits of substituting an existing drug (or other treatment modality) most likely to be replaced in practice, with the drug being proposed for listing for the proposed indication? Thus, the analysis is inherently comparative, and the nature and scope of the relevant evidence are critically determined by the use/indication proposed, which then determines the scope of the evidence relevant to answering the key question.

Importantly, the evidence presented to the committee to support an application for listing is identified, collated, and presented by the applicant—usually (but not always) a pharmaceutical company. Detailed reviews of applications are undertaken on behalf of the Department of Health by a network of academic institutions individually contracted to undertake evaluations of submissions for the listing of medicines on the PBS.

The PBAC evaluation processes are evidence-based, scientifically rigorous, and methodologically current. The PBAC does not apply a minimum standard of evidence. Evidence from direct (head-to-head) randomized controlled trials (RCTs) of the proposed drug against the main comparator is generally most persuasive; while there is no minimum standard of evidence—and a submission is not rejected if it fails to present randomized data—the interpretation of the evidence is often more difficult for sponsors, evaluators, and decision-makers alike. Unlike conventional evidentiary hierarchies, the PBAC's preference, in the absence of one or more direct head-to-head RCTs, is to compare two sets of trials where each alternative is randomized with a common reference, such as a placebo (or active common comparator). Overall, the pragmatic position has been not to set a minimum standard, but rather to allow an experienced evaluation and committee process to weigh the acceptability of less-preferred evidence on a case-by-case basis.

Decision-Making

The PBAC does not apply a set of simple decision rules, but rather weighs a range of relevant factors in its considerations. In particular, the PBAC does not apply a fixed threshold when determining acceptable cost-effectiveness. The PBAC chair is on record as saying that PBAC considers that an incremental cost-effectiveness ratio greater than AUS$50,000 per quality-adjusted life year would to be "on the high side." Nevertheless, the committee has declined to recommend the listing of drugs with lower cost-effectiveness ratios and recommended the listing of others with considerably higher ratios. This is because, in addition to acceptable incremental cost-effectiveness, there are several other factors that the PBAC has identified as informing its decision-making. These include:

- Clinical need, particularly for those conditions for which there are no, or few, alternative treatment options, and the extent to which the

proposed treatment reflects a clinically meaningful advance in therapy.

- The degree of uncertainty in the estimate of incremental cost-effectiveness. This is a particularly difficult area, as it is not uncommon to see a drug with an ICER with a reasonable point estimate but with a very wide confidence interval. This may reflect a weakness in the clinical trial data, difficulty in measuring or valuing the difference in effect, or uncertainty arising (usually) from a modeled economic evaluation, as reflected in modeled sensitivity analyses.
- The potential total cost to the PBS and/or Government health budgets.
- The scope for use of the drug beyond any restriction for subsidy, and the extent to which a restriction can be constructed that satisfactorily distinguishes use that is acceptably cost-effective from use that is not cost-effective.
- The potential for adverse outcomes arising from availability with subsidy (e.g., PBAC may restrict subsidized use of certain antibiotics to limit the development of resistant organisms).
- The affordability of the medicine to the patient in the absence of a subsidy.
- The "rule of rescue"—reserved for drugs for serious or fatal diseases for which no other treatments are available.

These individual factors are not weighted equally by the PBAC in its decision-making process and will be of greater or lesser importance in different situations. For that reason, the importance of any particular factor cannot be quantified.

The PBAC may recommend listing of a medicine on the PBS as an unrestricted benefit, which has no restrictions on its subsidized therapeutic use. Or, it may a recommend a "restricted" benefit, under which the medicine may be prescribed only for specific therapeutic uses, or an "authority required" benefit, under which the medicine requires prior authorization. These requirements may be imposed to:

- limit PBS usage to the approved indications;
- allow the controlled introduction of a drug in a new therapeutic class;
- limit PBS usage to the indications, conditions, or settings seen as being appropriate for clinical, cost-effectiveness, or other reasons; or
- alleviate concerns about adverse reactions, possible misuse, overuse, or abuse.

Transparency

Until relatively recently, both the existence and content of PBAC submissions were treated as confidential and only limited information about PBAC recommendations was released. In October 2005, the first detailed accounts of the PBAC's deliberations, including descriptions of the evidence considered by the committee, were published on the Department of Health and Ageing's Web site in the form of Public Summary Documents.[12] These are developed from the PBAC minutes, presented in a standardized format, with some limited redactions. In September 2008, the PBAC agenda for the forthcoming November 2008 meeting was published for the first time, with an invitation for public comment.[13]

The provision of information to prescribers about comparative effectiveness and cost-effectiveness is critical to rational prescribing and achieving cost-effective use in practice. It also imposes a greater degree of accountability on all parties and is resource intensive. It is hoped that greater transparency will give rise to more informed debate about the PBS and the challenges of maintaining affordable access to medicines for the whole community.

Review and Appeal

PBAC recommendations are not subject to appeal or merits review.[14] Sponsors may make a resubmission to PBAC if a previous application has failed to result in a listing recommendation, or if the sponsor wishes to

broaden the subsidized indications or vary the listing restriction. However, where no new evidence or analysis is available, a sponsor whose application for the listing of a medicine or new indication has been rejected by the PBAC may seek an independent review.[15] A review is based on information which has already been presented to the PBAC, and no new information or evidence beyond that presented to the PBAC may be considered. In seeking an independent review, applicants must identify the issue(s) in dispute on which review is sought, and these must reflect the PBAC's reasons for rejecting the application.

An independent review is generally conducted by a single expert reviewer, whose findings, together with any comments by the sponsor, are presented to the PBAC for consideration. The PBAC is required to consider the findings of the review and determine whether they warrant reconsideration of the application. If the PBAC reconsiders the application, it may set aside, revise, or confirm its previous recommendation. (There have been only two completed independent reviews since this option was made available in 2005.[16])

Conflict of Interest Policies

No conflicts of interests are acceptable in the case of members of the PBAC and its subcommittees, or among staff of external evaluation groups. Committee members are required to lodge annual conflict-of-interest declarations and make such declarations at each meeting. External evaluation groups are also required to be free of potential conflicts of interest arising from other sources of funding.

THE MEDIA AND PUBLIC PERCEPTIONS OF THE PBS AND PBAC

The PBS and PBAC are frequently the subject of public and media attention. Most often controversial are the listing recommendations of the PBAC, both positive and negative, but significant comment is also directed at the time taken for drugs to be listed, the prices of PBS-listed medicines, and the magnitude and affordability of copayments.

Specific decisions by the PBAC to reject and, at times, to recommend the listing of specific therapies can engender strong public, prescriber, industry, and media responses.[17] Frequently cited examples include the PBAC's 1998 decision to reject the listing of Viagra, in part due to concerns over the likely extent of use and potential cost to the program, which led to litigation in the Federal Court. The sponsor claimed that the PBAC had overstepped its authority in not limiting its consideration to evidence of comparative safety, efficacy, and cost-effectiveness. The Court rejected this argument, a decision that was subsequently upheld on appeal.[18]

Equally controversial was the PBAC's decision in 2000 to reject the listing of trastuzumab (Herceptin) for women with HER-2 positive advanced metastatic breast cancer, on the basis of inadequate cost-effectiveness. The government of the day, facing intense public pressure but unable to list the drug on the PBS in the absence of a positive recommendation, chose to sidestep the PBAC by establishing a separate "Herceptin Program" to fund the drug. Recommendations by the PBAC concerning the human papillomavirus vaccine Gardasil, Alimta (pemetrexed) for mesothelioma, and Velcade (bortezomib) for multiple myeloma, are other examples of decisions that have attracted significant comment.

Australia's pursuit of a free-trade agreement with the United States in 2003–04 led to a period of significant public debate around the PBS. Throughout the negotiations, there was speculation in the media, and among academics and NGOs in particular, that the PBS would be targeted as a non-tariff barrier in the negotiations and was at risk of being compromised in exchange for better market access for Australian commodities. The public release of the agreed text in May 2004 was met with allegations that the provisions of the Pharmaceuticals Annex of the agreement would undermine the fundamental listing and pricing processes of the PBS and drive increases in the prices paid for PBS medicines. In fact, the specific obligations of the text refer only to timeliness, transparency,

and consultation in formulary listing processes and make no reference to pricing.[19]

As the PBAC grapples with expensive biologicals and end-of-life drugs, listing recommendations are not infrequently accompanied by closely specified PBS restrictions and, at times, stepped-therapy requirements. These often arise because drugs either lack robust evidence of a clinically important additional benefit over existing therapies (some because they have been studied only in placebo-controlled trials), or the incremental costs of obtaining those benefits are such that the drugs are cost-effective in only narrowly defined groups of patients. The PBAC, in attempting to facilitate access while at the same time ensuring value for money for the taxpayer, may thus recommend that subsidized access be limited to last-line therapy, or be highly targeted, or in a small number of cases will require patients to demonstrate a response to treatment as a prerequisite for ongoing subsidized access. This highlights a key policy challenge: finding ways to continue expanding access to important new therapies, while at the same time maintaining cost-effectiveness as a key criterion for listing and safeguarding the affordability and sustainability of the program into the future.

IMPACT ON POLICY AND PRACTICE

As the PBS enters its seventh decade, economic analysis as a prerequisite for PBS formulary listing has been in use for more than 15 years, and the "Australian approach" has been applied to more than 1,200 submissions. About half of the drugs currently on the PBS formulary have been listed on the basis of a pharmacoeconomic evaluation, and the proportion increases each year with the listing of new medicines. As noted above, the evidence-based economic evaluation framework was not intended as a cost-containment mechanism per se, but rather as a means of ensuring efficiency and value for money. Indeed, average nominal growth in PBS expenditures was more than 11 percent per year in the period 1996–97 to 2004–05.[20]

While there has been no formal evaluation of this fourth-hurdle system, the use of evidence and the assessment of comparative effectiveness and cost-effectiveness are well accepted. This has been facilitated by a number of factors: the general availability of clinical trial evidence, in part reflecting the longstanding regulatory requirements applied to pharmaceuticals; a strong legislative basis for the role of the PBAC; and the availability, albeit limited, of relevant technical skills within the bureaucracy and Australian academic institutions.[21] On the other hand, the process has sometimes been hampered by limited understanding on the part of patients and prescribers, and occasionally by opposition from sectors of industry. This lack of understanding may reflect in part the low levels of transparency that prevailed until relatively recently.

The PBS has been found to perform well in terms of the criteria of equity, efficiency, quality, and acceptability.[22] In terms of acceptability, while many PBAC recommendations are considered controversial, the PBS itself has strong public support. Equity is supported by reducing financial barriers to access; efficiency, by ensuring that all new drugs demonstrate cost-effectiveness prior to listing.[23] This implies that, even where net program costs are increased through the listing of a new drug, the increased expenditure theoretically represents good value for money for the taxpayer, because the drug has first been established as cost-effective—through improvements in quality and/or quantity of life, or by way of offsets in other areas of the heath sector or other government programs.

Of course, the extent of cost-effectiveness anticipated at the time of listing may not be achieved in practice, for a variety of reasons. The benefits of treatment may be more difficult to realize outside the clinical trial context, particularly in older, younger, or sicker patients. The estimate of cost-effectiveness may be subject to uncertainty because of limitations in the clinical trial evidence, or prescribing may occur outside the PBS restriction (which will generally reflect the limits of cost-effectiveness). Sometimes, this can be mitigated through risk-sharing mechanisms, such as price-volume agreements[24] negotiated at the time a drug is listed, as well as through initiatives to promote

appropriate use of medicines once they are on the formulary.

While the pharmaceutical industry has at times argued that the fourth-hurdle mechanism and its impact on prices is a disincentive to register and market new medicines in Australia, to date there has been no evidence to support this. It is widely believed that PBS drug prices are invariably significantly lower than those in the U.S., an observation that has been supported by a number of analyses over the years.[25] Yet for many new medicines, particularly biologicals, this is no longer the case.[26] In fact, there is evidence to suggest that, for drugs that represent significant advances in therapy—true therapeutic innovations—the prices paid in Australia are as high as in the U.S., and sometimes even higher, for biologics in particular.[27]

A 2005 study comparing the Australian pharmaceuticals industry and commercial environment with those of the U.S., the U.K., Germany, Japan, India, and Singapore ranked Australia second overall behind Singapore, with Australia scoring highly on many indicators related to the industry skills pool, practices, and regulatory processes. The study found that, although the demand for pharmaceutical products in Australia is not strongly price elastic, the subsidization of pharmaceutical prices paid by consumers "almost certainly gives rise to higher sales volumes than would occur in the absence of the subsidy." It also found that the establishment of the PBS has led to a higher penetration of patented pharmaceuticals than in other developed markets.[28]

NOTES

1 Other bodies include the Medical Services Advisory Committee (MSAC), established in 1998 to ensure that new and existing medical procedures funded by Medicare are supported by evidence of safety, clinical effectiveness, and cost-effectiveness. Evidence-based decision making is also applied to the coverage of prostheses under private health insurance arrangements, and most recently to national supply planning and purchase of blood and blood products.

2 C. Sloan, *A History of the Pharmaceutical Benefits Scheme, 1947–1992* (Canberra: Australian Government Publishing Service, 1995).

3 In 2008, the safety-net thresholds are AUS$290.00 (for concessional beneficiaries) and AUS$1141.80 (for general beneficiaries). After reaching the safety-net threshold, general beneficiaries may obtain PBS prescriptions at the concessional copayment rate, and concession beneficiaries are dispensed PBS prescriptions free of charge for the remainder of the calendar year.

4 Department of Health and Ageing, *Expenditure and Prescriptions Twelve Months to June 30, 2007* (Canberra: Department of Health and Ageing, 2008). Available at http://www.health.gov.au/internet/main/publishing.nsf/Content/pbs-stats-pbexp-jun07. These figures do not capture those patient contributions where the cost of the drug is less than the general copayment amount.

5 National Health Act 1953, S101. Available at http://www.austlii.edu.au/au/legis/cth/consol_act/nha1953147/s101.html.

6 Department of Health and Ageing, *National Medicines Policy, 2000* (Canberra: Commonwealth Department of Health and Ageing, 1999).

7 See http://www.health.gov.au/internet/main/publishing.nsf/Content/health-pbs-activity-indicators.

[8] The Pharmaceutical Benefits Pricing Authority (PBPA) is a non-statutory body, established by the Minister for Health and Ageing, to provide advice on the pricing of pharmaceutical benefits supplied under the PBS. The objective of the PBPA is to secure a reliable supply of drugs supplied under the PBS at the most reasonable cost to Australian taxpayers and consumers. The authority fulfills its objective by recommending prices for new drugs recommended for listing by the PBAC and reviewing the prices of drugs listed in the PBS schedule at least annually. See http://www.health.gov.au/internet/main/publishing.nsf/Content/pbs-pbpa-policies-contents

[9] The estimate of operating costs is taken from documents pertaining to a current proposal to introduce cost-recovery for PBAC processes. The explanatory memo to the proposed legislation notes that fees are expected to be approximately AUS$14 million in the second year of operation and will comprise staff costs of AUS$4.1 million, direct costs of AUS$7.3 million (e.g., committee costs, external evaluations, legal fees, information technology (IT) systems, and direct administrative costs), and overheads AUS$2.6 million (e.g., IT infrastructure, property operating expenses, and business support).

[10] There are few examples of the Minister for Health declining a listing recommendation of the PBAC. The most recent example was in 2001, when then-Minister Senator Kay Patterson declined the PBAC's recommendation for a limited listing of sildenafil citrate (Viagra) on the PBS, and at the same time decided to delist all other drugs for erectile dysfunction (two forms of alprostadil).

[11] Pharmaceutical Benefits Advisory Committee, *Guidelines for Preparing Submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3) December 2008* (Canberra: Commonwealth Department of Health and Ageing, 2007). Available at http://www.health.gov.au/internet/main/publishing.nsf/Content/pbacguidelines-index.

[12] http://www.health.gov.au/internet/wcms/publishing.nsf/content/pbac-psd-psds_explained

[13] http://www.health.gov.au/internet/minister/spublishing.nsf/Content/mr-yr08-nr-nr125.htm

[14] The Australian Administrative Review Council (ARC) has examined the issue of merits review of PBAC recommendations and concluded that it is not appropriate. See http://www.ag.gov.au/agd/WWW/arcHome.nsf/Page/Publications_Reports_Downloads_What_decisions_should_be_subject_to_merit_review. However, judicial review may be sought under Administrative Decisions (Judicial Review) Act 1977 on issues of process and/or procedural fairness.

[15] The Independent Review (PBS) was established as part of Australia's commitments under the Australia–United States Free Trade Agreement (AUSFTA).

[16] See http://www.independentreviewpbs.gov.au. To date, only two independent reviews have been sought and completed.

[17] See, for example, L. Mitchell, "Time in a Bottle," *The Age*, April 6, 2004:http://www.theage.com.au/articles/2004/04/05/1081017097958.html; P. Heinrichs, "Cancer Drug Shame," *The Age*, April 23, 2006: http://www.theage.com.au/articles/2006/04/22/1145344320228.html? page=fullpage# contentSwap2; M. Wilkinson, "Bitter Pill," *Sydney Morning Herald*, Dec. 4, 1999: http://www.smh.com.au/news/9912/04/review/ review3.html.

[18] See Pfizer Pty Ltd. v. Birkett. Federal Court of Australia, March 20, 2000; available at http://www.austlii.edu.au/au/cases/cth/federal_ct/2000/303.html.

[19] Department of Foreign Affairs and Trade, Australia–U.S. Free Trade Agreement, Annex 2C to Chapter 2, "National Treatment and Market Access for Goods," available at: http://www.dfat.gov.au/trade/negotiations/us_fta/final-text/chapter_2.html. In addition to issues arising from the Pharmaceuticals Annex, concern that certain intellectual property provisions would lead to delays in generic market entry in Australia and indirectly to increased PBS costs stalled the passage of the AUSFTA implementing legislation through the Parliament, pending the adoption of key amendments.

[20] *Pharmaceutical Benefits Scheme—History, 1948–49 to 2005–06*. Available at http://www.health.gov.au/internet/main/publishing.nsf/Content/A58720844CBFCB47CA257218000D91C7/$File/Bookp36_39%20-%20table%2016b.pdf.

[21] S. R. Hill, A. Stevens, and D. A. Henry, "A Review of the Use of Evidence in the PBS," in D.M. Fox and A.D. Oxman (eds.), *Informing Judgement: Case Studies of Health Policy and Research in Six Countries* (New York: Milbank Memorial Fund, 2001).

[22] S. J. Duckett, "Drug Policy Down Under: Australia's Pharmaceutical Benefits Scheme," *Health Care Financing Review,* Spring 2004 25(3):55–67.

[23] Ibid.

[24] Under a price-volume agreement, the initial listing price of a drug may be reduced, often to the price of the drug that the new agent replaces, when the volume of use exceeds a predetermined threshold thought to reflect the size of the population in whom use is acceptably cost-effective.

[25] Productivity Commission 2001, *International Pharmaceutical Price Differences, Research Report* (Canberra; AusInfo, 2001).

[26] P. M. Danzon, M. F. Furukawa, "Prices and Availability of Biopharmaceuticals: An International Comparison, *Health Affairs,* Sept./Oct. 2006 25(5):1353–62.

[27] E. E. Roughead, R. Lopert, and L. N. Sansom, "Prices for Innovative Pharmaceutical Products That Provide Health Gain: A Comparison Between Australia and USA," *Value in Health,* Nov.–Dec. 2007 10(6):514–20.

[28] Economist Intelligence Unit, *Benchmarking Study of the Characteristics of the Australian and International Pharmaceuticals Industries: Final Report,* (Economist Intelligence Unit, Sept. 2005). Available at http://www.innovation.gov.au/General/Innov-PS/Documents/Exec_Summary_Pharma_Benchmarking20051123144751.pdf.

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