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Submission to Productivity Commission Inquiry

Impact of Advances in Medical Technology on Healthcare Expenditure in Australia

Contents

Recommendations Against Terms of Reference

The costs and benefits for the Australian community of advances in pharmaceuticals as an aspect of medical technology, taking into account recent substantive studies undertaken elsewhere, international experience in ensuring cost effectiveness of health care, the established economic, social, health and environmental objectives of the Government and community expectations of appropriate healthcare provision.

- Retain and strengthen the independent status and scientific expertise of members of the Pharmaceutical Benefits Advisory Committee ("PBAC") and its Economic Sub Committee ("ESC") to evaluate advances ("innovations") in pharmaceuticals for whether they offer overall community benefit when compared against existing products and therapies.
- To this end, recommend against PBAC funding through cost-recovery from industry and instead recommend increased government remuneration of PBAC experts.
- Recommend the creation and support of mechanisms to routinely and effectively calculate the fiscal advantages of PBAC cost-effectiveness pricing
- Recommend that, given the origins of the PBS in a constitutional referendum, that any step towards a shift of the PBS from providing universal access to affordable essential medicines to reward of claims of pharmaceutical innovation, is put to the Australian people at a referendum
- Encourage expansion of PBAC scientific cost minimisation and cost-effectiveness evaluation to cover all medicines used in hospital settings
- Encourage development of a systematic process for scientifically re-assessing the clinical and cost-effectiveness of medicines after listing on the PBS

Identify the key drivers of medical technology demand

- Encourage horizon-scanning research to evaluate whether new pharmaceutical product launchings (applications for marketing approval or PBS listing) are responding to genuine community need and offer clinical and cost-effectiveness advantages over existing therapies
- Encourage health technology assessment research on the drivers behind the marketing, lobbying and intellectual property strategies of multinational pharmaceutical corporations and their Australian subsidiaries, particularly focusing on the "evergreening" strategies of brand name patents nearing expiry.
- Ensure that pharmaceutical company suggestions encouraging "expanding the influence of market signals in consumer choice" do not facilitate direct-to-consumer advertising which bypasses critical scientific product evaluation by learned intermediaries to the detriment of patient safety and cost to the taxpayer

Impact of advances in medical technology on healthcare expenditure and areas of significant potential growth

- Ensure financial sustainability of the PBS continues to be predicated on scientific cost minimisation and clinical and cost-effectiveness bargaining of levels of government reimbursement accorded to manufacturers
- Ensure mechanisms are in place to require that any attempt to shift financial sustainability of the PBS to increases in the consumer co-payments or incentives for private health insurance coverage of medicines, is based on credible scientific data, particualt concerning the flow on costs to health services
- Investigate the incorporation into the PBS system of pharmaceutical price control mechanisms in other OECD countries, such as that in the UK which caps pharmaceutical profits at an agreed rate in any year.

Mechanisms and processes for ensuring cost-effectiveness

- Ensure that applications for PBS listing, should continue to be placed in a comparitor class for the purposes of PBAC evaluations which, if appropriate, includes generic products
- Support the choice of comparitor being made on independent expert scientific pharmaco-economic evaluations as currently performed by the members of the PBAC / ESC.
- Recommend legislation requiring applicant companies for PBS listing to provide information requested by the PBAC as crucial to a cost-effectiveness evaluation
- Recommend legislation allowing price-volume agreements to be enforceable

- Recommend that any applicant for PBS listing seeking a price premium based on "innovation" in terms of Annex 2C of the Australia-United States Free Trade agreement ("AUSFTA") be routinely required to provide scientific data for that claim which demonstrably establishes overall public health benefit as required by the opening words of Annex 2C.
- Recommend that an investigation be performed to establish mechanisms whereby pharmaceutical innovation with scientifically proven community benefit can be recognised, as may be required by Annex 2C of the AUSFTA, outside of the PBS and without any need to adjust (or dismantle) its reference pricing system
- Ensure that pharmaceutical companies applying for a PBS product listing and claiming a price premium based on promised overall benefit to the health system (ie: less hospital admissions or other hospital cost savings) agree to reduce the listed price and level of reimbursement if such benefits are subsequently proven not to have eventuated.
- Ensure that the scientific processes used by the PBAC / ESC in its cost-effectiveness evaluations, including its "hierarchy of evidence" are maintained on the best scientific evidence including randomised clinical trials where the applicant product is compared against an existing therapy.
- Recommend that the PBAC process of "restricted listings" continues as a crucial part of its stated purpose of providing overall community benefit and universal access to affordable essential medicines
- Recommend that TGA indications for marketing approval and indications for PBS reimbursement remain distinct scientific concepts based on quality and safety in the former case and community cost-effectiveness in the latter.

Impact of changes in medical technology on the distribution of costs in the health system

- Ensure that any claims by pharmaceutical companies for price premiums or stand alone status based on off-set savings for the health system generally are made a binding part of any price set, so that if such gains do not eventuate prices may be adjusted down.
- Encourage brand name pharmaceutical companies to appreciate that recent expansions in patent terms and other aspects of intellectual property monopoly protection adequately provide substantial rewards for advances in pharmaceutical technology that are shown to offer genuine community benefit. Emphasise in regulatory documents that it is not the task of the PBS to supplement patent royalties. The PBS has a different role as a fiscal lever at the service of the government in the overall public interest.

Impact of advances in health technologies on economic, social and health outcomes

- Support the existing National Medicines Policy and emphasise the creation of data showing the public health detriment that will arise from increased medicines prices achieved by private insurance based schemes or refashioning the PBS reimbursement to make it a supplement to patent royalties.
- Recommend the creation and support of mechanisms to routinely and effectively calculate the fiscal advantages of PBAC cost-effectiveness pricing
- Recommend that, given the origins of the PBS in a constitutional referendum, that any step towards a shift of the PBS from proving universal access to affordable essential medicines to reward of scientifically unsubstantiated claims of pharmaceutical innovation is put to the Australian people at a referendum.
- Recommend that the Australian Consumer and Competition Commission (ACCC) investigate and prevent anti-competitive practices in the Australian pharmaceutical industry, as required by Annex 2C of the AUSFTA.
- Recommend the establishment of *Qui Tam* legislation in Australia to reward corporate whistleblowers who reveal fraud on the government or other anti-competitive practices that unjustly increase costs to the Australian taxpayer in this area.

Executive Summary

Our Pharmaceutical Benefit Scheme (PBS) monopsony buying power saves Australian taxpayers about $A860 million a year. This submission seeks to make the case that multinational pharmaceutical companies in Australia are seeking to implement a variety of

lobbying and regulatory strategies (including threatening or initiating legal patent actions and trade dispute resolution proceedings) in Australia to raise the PBS reimbursement price for brand name listed pharmaceuticals, to reduce generic competition (including by reducing the incentives for generic producers by reducing generic profits and by breaking the PBS cost-effectiveness nexus between brand name and generic products) and ultimately to "eliminate" science-based cost-effectiveness pricing as currently implemented by the PBAC.

It argues that the success of the pharmaceutical multinationals in this endeavour is by no means assured. It states that with an ageing population and the bulk of medicine prescriptions being taken out by those over 65 years of age, the Australian Federal government has many sound reasons for ensuring that its expenditure in this area continues to provide scientifically proven value for money.

PBS scientific cost minimisation and clinical and cost-effectiveness analysis should be extended to cover all medicines used in public hospitals and should be used to regularly re-evaluate all medicines listed on the PBS. Submissions to the PBAC seeking price premiums or the breaking of therapeutic class, for example, by an allegedly "innovative" medicine should be required (as is indicated by the opening words of Annex 2C of the AUSFTA) to include a scientific justification of the overall community benefit of the proposed changes and to prove they will not foster anti-competitive conduct. The PBAC should not be required to publish cost-effectiveness thresholds. The PBAC is entitled to make continuance of reimbursement price levels conditional on subsequent research establishing that health benefits promised by the applicant, as well as the former two matters, are unequivocally established (an "outcome guarantee").

Background to Federal Expenditure on the PBS

The PBS operates under the National Medicines Policy, a primary aim of which is to provide universal, timely and affordable access to effective medicines of greatest community utility, whilst maintaining a responsible and viable medicines industry.

Australia's PBS was established as a free formulary of essential drugs after the Second World War by the Chifley Government. It was designed to ensure that all Australian citizens gained access to 139 life-saving medicines. Legislation to create the PBS had to survive two High Court challenges and required a successful Constitutional referendum.[1] This is an extremely important point. The PBS is one of the few examples of public health policy in Australia's history that has an unequivocal democratic mandate. The PBS has evolved into a scheme which covers approximately 600 drug substances in at least double that number of forms and strengths (items), and in four times as many drug brands. Restrictions apply to 778 of the items, 290 of which require an authority prescription. The Commonwealth also pays for several high cost drugs which can only be supplied from hospitals to outpatients under the Highly Specialised Drugs Program or Section 100 drugs (under section 100 of the *National Health Act 1953* (Cth)). These include drugs interferon for the treatment of hepatitis C and

medicines for the treatment of HIV/AIDS. The PBS generally does not reimburse drugs dispensed to patients in public hospitals, which are generally the responsibility of State and Territory Governments.

PBS medicines are available to all Australian residents and to visitors from countries with which Australia has Reciprocal Health Care Agreements. People covered by certain temporary visas (refugees) may also be eligible for PBS medicines. Pensioners, Commonwealth Seniors and some low income earners are eligible for health concession cards issued by Centrelink.[2] A safety-net arrangement has operated since 1 November 1986 where no patient co-payment is required (i.e. pharmaceuticals are free) for concessional patients (and/or their families) if they pay more than a set amount per calendar year on pharmaceuticals. Pensioners receive a Pharmaceutical Allowance to offset the patient payment for PBS prescriptions, regardless of how many prescriptions are filled.

The modern PBS revolves around Part VII section 85 of the *National Health Act* 1953 (Cth). This states that the relevant Minister may declare a medicine listed on the PBS and so subject to government subsidy except for a co-payment. This listing is required to only occur, however, after the Australian Drug Evaluation Committee (ADEC) has approved the relevant pharmaceutical's safety and efficacy and, under s101(4), after the Pharmaceutical Benefits Advisory Committee (PBAC) with secretariat support from the Pharmaceutical Benefits Branch of the Department of Health and Ageing, has evaluated and approved its cost effectiveness. The Pharmaceutical Benefits Pricing Authority (PBPA) in certain circumstances may recommend variation based on the cost of manufacture and the estimates of the international reference price.

Central to the PBAC's cost-effectiveness evaluation is section 101(3) of the *National Health Act* 1958 (Cth). This requires the PBAC to base its recommendation on: "the effectiveness and cost of therapy involving the use of the drug, preparation or class, including by ***comparing the effectiveness and cost*** [emphasis added] of that therapy with that of alternative therapies, whether or not involving the use of other drugs or preparations." The section goes on to state that if the product is "substantially more costly" than the selected comparator in its class it shan't be recommended by the PBAC for PBS listing "unless…[it] provides a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies."

The PBS system that has evolved under this section is a variant of pharmaceutical reference pricing. It requires a pharmaceutical manufacturer ("sponsor") seeking to have a drug listed on the PBS (that has been approved by the TGA on quality and safety criteria for marketing) to make a submission to the PBAC. This submission specifies a disease (and relevant subsets involving patient characteristics) and a listing price based on the pharmaceutical company's assessment of the best relevant available data on clinical effect against the comparitor. The comparator is generally the drug most prescribed on the PBS for the same indication, but may be the standard medical (non-drug) treatment. Pharmaceutical

companies tend to prefer comparisons against the most expensive drug with the best "head to head" data, rather than the compound that is most pharmacologically similar.[3]

This sponsor's application is then passed on to expert reviewers who consider the cost and effectiveness of the product proposed for listing against comparative substances in the relevant therapeutic class. They evaluate whether any of the assumptions in the submission are unjustifiable and create simulations to assess the incremental cost effective ratio (the additional cost for an additional beneficial effect, or Quality of Life Years ("QALY") gained). The reports of these experts ("pink pages") are then passed back to be reviewed by the PBAC along with an industry response ("blue pages") to the experts' reports and the summary from the Economic Sub-Committee ("ESC") in the "green pages." The process is designed to take six weeks and follows guidelines set out on the PBS website. [4]

The PBAC may ask the pharmaceutical manufacturer for additional information, but has no legal power to compel its production, even if not covered by commercial-in-confidence protections. The pharmaceutical manufacturer may be claiming a pricing premium because of a claimed additional benefit (ie: improved effectiveness, better adverse event profile or delivery system) conferred by the new product over its therapeutic rivals. Once a decision is made to list the drug, the PBPA then evaluates the requested price against an international benchmark price for drugs in that class. Under the PBS, the members of the PBAC use pharmaco-economic analysis and reference pricing to determine the cost minimisation, clinical and cost-effectiveness or community value of a new drug against an agreed comparator therapy, while the monopsony bargaining power of the PBPA is used to balance in the public fiscal interest, the increasingly prolonged monopoly rents accorded to brand name pharmaceutical patent holders.[5] Under reference pricing the Australian government reimburses a new PBS listed product in (currently four) narrowly defined therapeutic groups (ACE inhibitors, H2 receptor antagonists, HMG CoA reductase inhibitors (statins) and calcium channel blockers). Pharmaceutical companies can charge whatever price above this the market will bare and in that sense the system offers no restraint on the operation of competitive markets but rather fulfils important social justice goals for the community by facilitating universal access to essential medicines.

The *National Health Act* 1958 (Cth) requires the PBAC, as mentioned, to base its recommendation on a pharmaco-economic comparison of the effectiveness and cost of a drug proposed for listing against an alternative from the relevant therapeutic class. If the proposed product is "substantially more costly" than the selected comparator in its class it will not be recommended by the PBAC for PBS listing unless it provides a significant improvement in efficacy or safety over currently available therapies. For non-equivalent drugs the legislation requires that manufacturers demonstrate an acceptable incremental cost effectiveness ratio (the additional cost for an additional beneficial effect) in order to obtain a higher price. For equivalent drugs (equivalence is determined by a test of 'non inferiority') the cost of acquiring and using the new agent should be no higher than existing established treatments. For

Australian governments, pharmaco-economic analysis, reference pricing and monopsony power has ensured value-for-dollar efficiency when buying drugs for the PBS. For manufacturers, the process of bringing a new patented product to the Australian market at a higher price than currently available medicines may be lengthy, expensive and uncertain. However PBS listing provides a secure foothold in a substantial market.

Foreign brand name pharmaceutical manufacturers have long held the position that PBS clinical and cost effectiveness pricing creates difficulties for innovative drugs to enter the Australian market at a price sufficient to recoup the cost of R&D and production. They claim, without providing supportive scientific research that Australia can only achieve the low price it currently commands for innovation by opportunistically 'free-riding' on the research and development spending of nations, such as the US. This is an ideologic position designed to increase the profits of these companies without reference to the social norms on which the PBS is based. It has recently received some, partial, support in the AUSFTA, particularly Annex 2C and Chapter 17.

The PBS is projected to almost double its proportion of GDP, to 1.29 per cent, by 2014-2015, most of this expenditure being on the expanding category of people aged over 65. In the 2002-03 fiscal year, the Australian government spent $7.2 billion on public hospital services (increasing approx. 6% per year), $8.2 billion on Medicare (increasing approx. 5% per year) and $4.5 billion on the PBS (approx .10% per year). [6] IMS Health, for example, has calculated that the Australian pharmaceutical market is forecast to grow at a compound annual growth rate of over 9.3% in the period 2003-2008.[7] At the same time increased medical awareness of the importance of prevention and early treatment have lead to increased prescriptions in high PBS expenditure areas such as hypertension, high cholesterol diabetes and depression State-funded hospitals are limiting the supply of drugs to discharged patients and privatising outpatient clinics and pharmacies. The effect of this is that the PBS now pays for these drugs.

Australia, however, compares well with other Organisation for Economic Co-operation and Development ("OECD") nations having universal pharmaceutical cover (ie: Sweden, France, Spain, New Zealand and the UK). Much of the credit for this must be given to the cost-effectiveness pricing mechanism of the PBAC.

2005 Budget figures show the government expects to gain over $1 billion from the 12.5% price reduction for new brand listings on the PBS over the next four years: $139 million in 2005-06, rising to over $326 million in 2007-08. It also flagged increasing patient co-payments for prescriptions and improving the quality use of PBS medicines. One area that has no received sufficient attention, it will be argued here, is ensuring that innovative or brand name drugs applying for and having received listing for PBS reimbursement, justify on scientific grounds their overall benefit to public health.

Strategies for PBS Sustainability

Reduction of Payments to Pharmacists

There are three prime components to PBS sustainability are continued cost-effectiveness pricing ensuring vale for money for innovative pharmaceuticals, encouragement for rapid market entry (after brand name compound patent expiry) of multiple cheaper generic products and assistance from pharmacists.

Renegotiation of the pharmacy agreement between the Federal Government and the Pharmacy Guild of Australia has been estimated to save $8 billion over 10 years on PBS expenditure if it reduces chemists 10% mark up for buying PBS-listed medicines. Medicine wholesalers were paid $500 million in 2004 under the pharmacy agreement. The Government's possible alternatives include reducing wholesalers' cut to 5 per cent or replacing it with a flat fee.[8]

The Australian Competition and Consumer Commission is investigating an anti-competitive or price fixing complaint by the Australian Consumers Association that software programs (called WiniFred, part-owned by the Pharmacy Guild and Amfac, which is itself owned by Australian company Cosmos) used by 60% of pharmacists, has inflated prices by including 75% mark-ups on medicines obtained under private prescription, while drugs on the pharmaceutical benefits scheme attracted a patient charge of $3.36 per script. [9] The practice is estimated to add about $80 million each year to the cost drugs obtained under the PBS.

The Federal Government is also concerned that chemists have been pocketing 30% wholesale price discounts from manufacturers. One example is Arrow Pharmaceutical's Simvar, a generic copy of Merck's cholesterol-lowering simvastatin drug Zocor, where pharmacists have been claiming the retail price less the PBS patient co-payment, rather than passing the savings onto consumers or the PBS. Requiring some of these discounts to be passed back to the PBS could reduce costs by tens of millions of dollars a year.

Preventing Evergreening

"Evergreening", the tactical extension of brand name monopoly rights over "innovative" medicines that have large sales, costs millions of dollars each year to the economies of developed nations.[10] As pharmaceutical companies struggles to market new molecular entities with genuine community benefit in terms of reducing the burden of illness, "evergreening" the devising of ever-more-creative ways of prolonging patent rights has become the dominant area of innovation (albeit legal in nature) carried out by pharmaceutical multinationals. "Evergreening" raises PBS expenditure by delaying or inhibiting the rapid market entry of multiple cheap generic substitutes. "Evergreening" can take the form of encrusting brand name products whose compound patent is about to expire with multiple patents covering delivery systems or even packaging. As will be explained later it is a process that may have been facilitated by article 17.10.4 of the AUSFTA. It may also take the form of

illegal activities (as it has in other jurisdictions) where brand name firms delay registering products or devise spurious patents which then become the subject of threats to generic competitors. Preventing evergreening by the creation of a specialist agency with both medicines and patent expertise, by the creation of a single unified register of all pharmaceutical patents, by the creation of incentives for generic market entry will be crucial in ensuring the long term sustainability of the PBS.

Raising CoPayment Level

Increasing co-payments by patients is probably the most direct way the Federal government has of substantially reducing PBS costs. This can take the form of either at a flat rate for everyone, or fee in proportion to a patient's capacity to pay (means testing), or fee proportional to the actual price of the medication purchased. Recent NATSEM modelling (on 1996-97 data) of a flat 25 per cent rise in co-payments for general and concessional patients indicated an annual saving to the PBS of $181 million. However, such an increase will burden the lowest income earners. Increases in co-payments can result in patients not filling their scripts, and the significant risk of deferred general health care costs for the society and the individual patient. Means-testing any increase in co-payments may avoid the burden on low income earners, however, the PBS goal of *universal access to essential medicines* would be compromised.

Proportional co-payments (to the actual price of the drug) might send valuable price-signals to patients to deter over consumption, and to encourage compliance with medication regimes and GPs to prescribe cheaper alternatives. However, chronic users of expensive drugs, are often concessionary patients least able to afford the extra payments.

Co-payments inhibit the use of essential medicines (including those for hypertension, high cholesterol, asthma, depression, heart conditions, diabetes, and thyroid conditions). Reducing the use of such essential medicines may cost the health system much more money than it saves.

In Australia, major co-payment changes were introduced into PBS in November 1990. At that time, the co-payment for general users rose from $11.00 to $15.00, and pensioners faced a co-payment or ‘price signal’ of $2.50 for the first time. However, to minimise adverse outcomes, the pension was increased by $2.50 and a ‘safety net’ was introduced for both groups. The co-payment changes lowered the use of both essential and discretionary drugs by both concessional users and the general community.

The 27% per cent increase in co-payments and safety net thresholds announced in the 2002–2003 Budget were not accompanied by compensatory measures to lessen their impact on financially disadvantaged people with chronic illness.

The number of PBS prescriptions dispensed has dropped by over 5%, with year on year Health Insurance Commission (“HIC”) figures showing two million fewer scripts filled since co-payment increases were imposed on 1 January 2005.[11]

Restriction on Direct-to-Consumer Advertising

Promotion by manufacturers direct-to-consumers has been a major driver of inappropriate and (as the Vioxx debacle shows) unsafe drug use. Tax deductibility for drug company promotional expenses should be removed. The pharmaceutical industry's push for direct to consumer advertising through misleadingly exploiting aspects of Annex 2C of the AUSFTA, must be resisted. Regulation is this area needs to be taken out of the hands of the Australian Pharmaceutical Manufacturers Association (APMA) Code of Conduct and given to the Australian Competition and Consumer Commission. The latter organization should be accorded (as is required by Annex 2C of the AUSFTA) a very broad mandate to protect patients from anti-competitive conduct by pharmaceutical manufacturers.

Restriction on Inappropriate Advertising to Doctors and Prescribing

This has been a major area where pharmaceutical companies have sought to increase profits in a manner that is often at odds with cost-effectiveness and patient safety. Pfizer Australia, for example, has recently been fined for breaching the drug industry's own marketing code of conduct over a letter it sent to health professionals defending the safety of celecoxib (Celebrex) after the recall of rofecoxib (Vioxx) stating that "the cardiovascular safety profile of Celebrex has been extensively studied" and that "the data do not indicate significant cardiovascular safety concerns with Celebrex." [12] In January 2005 Medicines Australia's code of conduct appeals committee determined that Pfizer had breached the code's provision requiring promotional material to "be current, accurate, balanced and [that it] must not mislead either directly, by implication, or by omission." The committee imposed a fine of $A25 000 and directed that a corrective letter be sent to all recipients of the original letter. In May 2005 Pfizer's appeal against the decision was dismissed. In its review the committee determined that as the letter could "have had a major effect on prescribing and possible safety implications, it should be considered a severe breach." The fine, however, is insignificant in comparison with the $A100m worth of celecoxib that Pfizer sold in Australia in 2003-4. In 2003 Pfizer Australia was fined a total of $A20 000 for two breaches of the code relating to its promotion of sildenafil (Viagra). In 2004 Pfizer was found to have breached the code on three occasions and was directed to withdraw promotional material.

The anti-arthritis drug Celebrex was expected to cost the PBS $40 million in its first year, but ended up costing $160 million, ostensibly through inappropriate advertising to doctors and resultant inappropriate prescribing. Between $50 million and $1 billion of PBS expenditure in 2003-4 may have been due to inappropriate prescribing.

In 1992, the Commonwealth Pharmaceutical Health and Rational Use of Medicines (PHARM) Committee recommended a quality use of medicines (QUM) policy as the final integrating arm of the National Medicines Policy. Strategies included ensuring doctors received independent information from an independent National Medicines Centre, drug audits, and targeted education aimed at both consumers and health providers. Subsequently a

National Prescribing Service (NPS) was created to focus on educating prescribers by working with Divisions of General Practice. It focused on encouraging GPs to change their prescribing behaviour, particularly with respect to three high cost/high growth drug groups (antibiotics, peptic ulcer drugs, cardiovascular drugs). Half of the savings accruing from the changes were to be allocated to GPs. The 2001 allocated a further $14.6 million (over four years) for 'a consumer education strategy'. Also involved are the National Institute of Clinical Studies (NICS), the Australian Council of Quality and Safety in Health Care (ACQSHC) and the National Health Information Management Council (NHIMAC). These initiatives should be extended and rationalised.

The brand name pharmaceutical industry in Australia currently is currently permitted to underwrite the cost of GP electronic prescribing packages in return for advertising and other rights. Such prescribing software should contain nationally endorsed evidence-based information repositories on the cost-effectiveness of medicines such as the Australian Medicines Handbook and Therapeutic Guidelines, the Pharmaceutical Benefits Schedule, Australian Prescriber and the Adverse Drug Reaction Bulletin

Agreements between generic and brand name manufacturers

Generic firms appear to have decided to form alliances (through licensing, co-marketing or distribution agreements) with big PHRMA, rather than compete. Large brand name manufacturers such as Novartis have been acquiring generic producers. This further restricts genuine competition in the pharmaceutical industry and encourages collusion between brand name and generic manufacturers.

PBAC Cost recovery

The 2005 budget contained a direction to the Department of Health and Ageing to "commence consultation with a view to implementing cost recovery for the administration of the PBAC and the PBS listing process from 2007-08". The Budget figures show that cost recovery of around $11 million per year is expected to result from the measure once it is introduced. This measure is fraught with peril for the scientific reputation and independence of the PBAC. Industry cost recovery has been cited as a mjor factor undermining the effectiveness of the US Food and Drug Administration (FDA) in the face of the recent Vioxx scandal. Instead of cost recovery, the Federal government should ensure increased remuneration and immunity from liability for PBAC officials.

A further threat to the scientific independence of the PBAC is the presence of an industry member. There should be a review of this arrangement with regard to its effect on the reputation and quality of PBAC work.

Fast Track Drug Applications

The 2005 budget also stated that "In 2005-06, the department will trial a fast-track process to streamline the listing procedures for some drug applications. The department will consult on the design and development of new business processes and information technology systems to significantly reduce the time taken for approved drugs to be listed on the PBS and available to the community." The Budget also said measures would be implemented "to improve the value obtained from generic medicines and to further facilitate their use in the community".

Encouraging Generic Usage

New computer software could be installed in doctors' surgeries to automatically select the cheaper (but equally effective) generic medicine, when GPs write prescriptions.[13] In a joint statement, health minister Tony Abbott and industry minister Ian McFarlane have also maintained that dispensing labels will have to display the name of the active ingredient in a medicine more prominently than the brand name. This should mean that consumers are clear they are taking the correct medicine even if they choose a cheaper brand." The Federal government is also considering publishing on the internet a list of interchangeable bioequivalent products and typical prices. All bioequivalent medicines will be shown as interchangeable in the Schedule of Pharmaceutical Benefits.

The ministers also said there would be an information campaign to increase understanding of generic medicines by consumers and health professionals but at the same time, the Budget papers indicated that the community awareness campaign for the PBS itself would cease.

Changes to Cost-Effectiveness Pricing

PhRMA has listed the following reasons why Australia was placed on the US Trade Repesentative "WATCH LIST": 1. Our Pharmaceutical Benefit Scheme (PBS) monopsony buying power saves Australian taxpayers about $A860 million a year. 2. The Australian PBS under therapeutic group premiums (TGP) reference pricing, reimburses drugs in a common class only to the level of the base/benchmark price product. This process achieves PBS savings of approx. A$460 million over four years but inhibits PhRMA’s highly restricted definition of “innovation” where the latter concept practically equates to any product for whom a new PBS listing is sought.

Pharmaceutical “innovation” in this limited sense (not explicitly related to community benefit) is becoming not only more and more expensive, but more scarce and less supported by credible research on its community benefit. Nonetheless it is clear that brand name pharmaceutical companies will be lobbying for various changes to the operation of the PBS cost-effectiveness system based on Annex 2C of the AUSFTA. Annex 2C does not on its terms justify such changes and there was no reasonable expectation accorded either side that they would be made (the Australian government repeatedly stated during negotiations that they

would not be made). Still, in the absence of a definitive WTO or AUSFTA dispute settlement ruling phRMA may continue to lobby for such alterations. They could include demanding price premiums for claims of "innovation" and demands that a new product not be placed in a reference class.

The Australian response to such demands should be to highlight that the recognition of innovation and research and development does not explicitly in Annex 2C require changes to the PBS (unlike transparency under Annex 2C (2). Further, the opening words of Annex 2C also require scientific proof of the public health benefits of an innovative drug.

Preventing PBS "Leakage"

If a drug is listed for subsidy on the basis of acceptable cost-effectiveness for a severe disease, its cost-effectiveness is diluted if there is widespread use or 'leakage' for less severe disease outside the PBS restrictions or for which there are already cheaper effective drug treatments. Celebrex and Losec were examples of "leakage" causing expenditure rises to the PBS. The former was authorised for chronic arthritis but has been prescribed on subsidy for e.g. sports injuries. Losec was authorised for serious ulcer conditions, but was heavily prescribed for more minor reflux problems.

The factors that lead to and sustain leakage include a lack of timely independent information for doctors about effective, and cost-effective clinical application of new drugs, and manufacturers' aggressive promotion of new products for uses beyond those approved by the PBS or scientifically validated as cost-effective. The pharmaceutical industry also attempts to 'medicalises' normal processes and minor ailments, in order to broaden its markets.

To minimise 'leakage' the PBAC has recommended it obtain legislative support for price-volume agreements. These permit an applicant drug's price to be set according to the number of prescriptions estimated necessary to treat a specific condition for which it has been scientifically proven to be cost-effective. If sales exceed the agreed volume then the price is reduced. A single drug with four major uses could thus have four different prices reflecting differing levels of cost-effectiveness, each with its own item number in the Schedule of Pharmaceutical Benefits. If sales exceeded the agreed volumes for each indication then the price paid to the pharmaceutical company would be substantially reduced.

Cost Effectiveness Reviews of Drugs Already on the PBS,

Regular reviews of the cost minimisation and cost-effectiveness of drugs already listed on the PBS list could be an extremely useful means of controlling PBS expenditure. Drugs currently on the PBS that were listed pre-1993 have not been assessed for cost-effectiveness. A drug's price should be changed if its actual patterns of use in the community are different than predicted or if post-marketing evidence shows that a drug worked better or worse in the community that it had in the original clinical trials. A permanent and properly resourced review

process within the PBAC should conduct similar reviews on a large number of listed drugs, with a view to reviewing prices in the light of post-marketing evidence and to control leakage.

Outcome Measures and Restricted Listings

There is insufficient credible scientific research to justify the PBAC cost minimisation and clinical and cost effectiveness evaluation involving surrogate outcome indicators (outside mortality rates, life years saved or quality adjusted life years. The PBAC should not be required to publish cost-effectiveness thresholds. To do so would be to create a false and distorting certainty for subsequent applicants, that will impede scientific evaluation proceedings, as it must, on a case-by-case basis.

It is implicit in the scientific nature of the clinical and cost effectiveness evaluation process that restricted listings, where a new drug is deemed to be cost-effective for only a limited number of indications, continue to create PBS indications for listing that are narrower than the TGA registered indications. The fact that this (and other measures related to clinical and cost effectiveness evaluation) creates less profits for brand name pharmaceutical companies should never be a reason in itself for dismantling a regulatory component. Patent royalties are designed to provide profits and reward for innovation. There is no warrant in either scientific evidence or democratic legitimacy for converting the PBAC reimbursement process into an additional form of patent royalty

De-Listing of Cost-Ineffective Drugs from the PBS

De-listing drugs from the PBS that have been shown to be costing-effective will undoubtedly assist in reducing PBS expenditure. The 1996-97 Budget announced the de-listing of a range of topical anti-fungal medicines at a projected cost-saving of $16 million over four years. The 1997-98 Budget announced the de-listing of some anti-inflammatory pharmaceuticals, medicines for common stomach problems and others for treatment of minor nail infections, for an estimated cost-saving of $112 million over four years. The 2000-2001 Budget announced the de-listing of a range of nasal sprays, saving $61 million over four years.

De-listing may, however, place undue burdens on groups who are least able to bear them (80 per cent of PBS beneficiaries are concessional patients). Cost reductions have sometimes been sought through the de-listing of certain groups of pharmaceuticals from the PBS Schedule.

Brand Premium Policy

Prices paid by the PBS are set at the lowest priced brand of bio-equivalent drugs. If a patient is prescribed a brand which is not the lowest priced among bio-equivalents, the patient will be required to pay the difference (the brand premium), if any, between their level of co-payment and the brand's price. This process is based on scientifically established cost-effectiveness. It should not be disrupted by industry claims for a price premium (based on Annex 2C(1) of the

AUSFTA) simply because of a scientifically unsubstantiated claim that a product is innovative. Any such claim should arrive with data establishing the product's public health benefitand in any event should not be regarded as being required to be directed at PBAC processes (unlike the transparency requirements in Annex 2C(2).

Therapeutic Group Premium Policy

Prices paid by the PBS for drugs in 4 therapeutic groups are set at the lowest priced drug within that group of (not necessarily bio-equivalent) drugs. Again, the patient pays the price difference (the therapeutic group premium) if the least expensive drug within the group is prescribed. Annex 2C (1) of the AUSFTA does not justify brand name producers demanding increased "flexibility" in choice of comparitor, according to the PBAC guidelines, without achieving a requisite level of scientific proof in each individual case. Whether such a comparitor has been in existence for some time, is generic or has a low price should not be disqualifying factors according to the basic principles underpinning the PBS and the Australian Medicines Policy.

Role of private Insurance in Pharmaceutical Policy

Currently in Australia, private health insurance schemes cannot subsidise medications listed on the PBS, but often often cover non-PBS prescription medicines. Greater involvement of private insurance in medicines policy in Australia would undoubtedly make cost containment more difficult and expose Australia's ageing population to US-style elevations in drug prices and reduce the range of choices available to consumers (US Health Insurance Funds usually only cover a formulary of items for which they have negotiated special deals with the manufacturers). This involvement could be either (a) public subsidy for all listed drugs for low-income/concessional patients, with higher-income earners requiring private subsidy, or (b) public subsidy for everyone for a very limited range of drugs (maybe life-saving ones), and private cover required for all other drugs.

Impact of the AUSFTA

The Free Trade Agreement signed by Australia and the United States (AUSFTA) in May 2004 included commitments relating to federal health care programs dealing with the reimbursement of prescription medicines. These were articulated in Annex 2C (Pharmaceuticals) to Chapter 2 National Treatment and Market Access for Goods, an associated Exchange of Letters, between the Australian Trade Minister and the US Trade Representative and Chapter 17 on pharmaceutical intellectual property.

Throughout the negotiation of the AUSFTA the Australian Government openly expressed its reasonable expectations that the fundamental architecture and sustainability of the Pharmaceutical Benefits Scheme (PBS) and the integrity of the Pharmaceutical Benefits Advisory Committee (PBAC) as the pre-eminent advisory body to government on the listing of

medicines on the PBS, would be protected. No changes to the *National Health Act 1953* (Cth) were necessary to implement Australia's AUSFTA commitments.

AUSFTA Articles and the PBS

The 1000 page AUSFTA contains approximately fifty provisions in four areas of concern regarding the PBS. The first is Annex 2-C (Pharmaceuticals). The second is contained in side-letters between the Australian Trade Minister and US Trade Ambassador. The third involves Chapter 17 (Intellectual Property Rights) and the fourth is in Chapter 21 (Dispute Resolution Procedures).[14]

Annex 2C (Pharmaceuticals)

The first source of possible dispute resolution proceedings between the parties are the interpretive principles set out in Annex 2C (1) (dealing with pharmaceuticals). Annex 2C is part of Chapter Two of the AUSFTA. Annex 2C (1) commences with this statement of primary or overarching principle:

> **"The Parties are committed to facilitating high quality health care and continued improvements in public health for their nationals."**

The article then continues to enumerate the following subsidiary principles:

> **"In pursuing these objectives, the Parties are committed to the following principles:**
> **a)the important role played by innovative pharmaceutical products in delivering high quality health care**
> **b)the importance of research and development in the pharmaceutical industry and of appropriate government support, including through intellectual property protection and other policies**
> **c)the need to promote timely and affordable access to innovative pharmaceuticals through transparent, expeditious, and accountable procedures, without impeding a Party's ability to apply appropriate standards of quality, safety, and efficacy; and**
> **d) The need to recognize the value of innovative pharmaceuticals through the operation of competitive markets or by adopting or maintaining procedures that appropriately value the objectively demonstrated therapeutic significance of a pharmaceutical [emphasis added].**

The first thing to note is that these principles (unlike those in Annex 2C(2) on transparency) do not specifically refer to the PBS. The fact that the PBS is not mentioned in Annex 2C(1) suggests there can be no legitimate expectation from either the US or Australia that the only way to implement these principles is to make changes to the PBS.

More interestingly though, the principles clearly indicate that any submission by US companies that the PBS should reward "innovation" to a greater extent should also contain research showing how facilitating high quality health care and continued improvements in public health for their nationals.

Annex 2C(1)(c) makes clear that the parties are committed to promoting "affordable" access to innovative pharmaceuticals. Similarly, Annex 2C(1)(d) creates a commitment by the

parties that recognition of innovative pharmaceuticals may involve either "competitive markets" or "procedures that appropriately value the objectively demonstrated therapeutic significance" of a pharmaceutical. These provisions could justify the PBAC asking the any submission seeking greater regard for "innovative" pharmaceuticals must include supporting data showing that the changes will not lead to anti-competitive conduct and that they are justifiable on the basis of objectively demonstrated therapeutic significance.

As a principle of construction it must be assumed that "objectively demonstrated therapeutic significance" in Annex 2C(1)(d) is not a mere repetition of "quality, safety and efficacy," as appears in subparagraph 2C(1)(c). Annex 2C(1)(d) thus confirms a legitimate expectation of continuance of PBS reference pricing by the Australian government. It also suggests, however, that a claim for pharmaceutical innovation intrinsically involves an evaluation of the products "affordability" and "objectively demonstrated therapeutic significance."

The word "innovative" in relation to pharmaceuticals is not defined in the AUSFTA. Annex 2C.(1)(a) links "innovation" with "high quality health care," Annex 2C.1(c) to "affordability" and "accountability" and Annex 2C.1 (d) to "objectively demonstrated therapeutic significance." This suggests that pharmaceutical "innovation" under the AUSFTA must be seen in the context of the products proven social or comparative therapeutic value.

Articles 31 and 32 of the *Vienna Convention on the Law of Treaties* are incorporated in the AUSFTA by article 21.9.2. Referable contextual documents important in interpreting "innovation" and the "legitimate expectations" of the Parties concerning pharmaceutical regulation, (by virtue of article 32 of the *Vienna Convention on the Law of Treaties*) include the Australian AUSFTA implementing amendments adding a new 26D to the *Therapeutic Goods Act* 1989 (Cth). These permit the Attorney-General of the Commonwealth to join an application by the manufacturer of a brand name pharmaceutical for an interlocutory injunction against a generic seeking to enter the market and claim compensation for any damage the Commonwealth has suffered by delayed entry of the cheaper generic. That provision in particular indicates that the Australian public health expectations regarding "innovative" pharmaceuticals were that their intellectual property protection would not inhibit the rapid entry of cheap generic pharmaceuticals onto the PBS which is crucial for low medicines prices under its cost-effectiveness system. The US reserved its rights over these amendments in the final exchange of letters but the Australian government did not contradict the other argument which is consistent with its public pronouncements on the issue.

Subparagraph (f) of Annex 2C(2) allows US pharmaceutical applicants to ask for an "independent review process" of a PBAC recommendation or determination. The Australian government position on this is that such process will not involve any overturning of PBAC decisions. A detailed mechanism for this independent review process has been established.

Annex 2C(3) establishes a "Medicines Working Group" between health officials from each country. US officials appear to have a different expectations of the likely impact of this

working group than do Australian officials.[9] The Medicines Working Group is prohibited from promoting discussion and mutual understanding on the issues mentioned in Annex2C(4). These relate to "making innovative medical products more quickly available to their nationals." As such, the Medicines Working Group is excluded from discussing any of the issues related to "innovative" pharmaceuticals in Annex 2C(1). This is because all the principles related to "innovative" pharmaceuticals in Annex 2C.1 relate directly or indirectly to nationals having more expeditious access to them. The agenda of the Medicines Working Group is thus restricted to Annex 2C(2).

The Medicines Working Group is also not authorised under the AUSFTA (Annex 2C(3)(b)) to discuss any aspect of the PBS, whether legislative in nature or otherwise that is not mentioned in Annex 2C(2). It, for example, cannot explore elements of the cost-effectiveness system, such as the "leakage" of official to unauthorised usage.[15] Similarly, it should not be able to discuss comparison of the product prosed for marketing approval against non-pharmaceutical alternatives.[16]

Finally, Annex 2C(5) permits a pharmaceutical manufacturer to disseminate pharmaceutical information via the Internet (for example via links on sites frequently used by Australian patients). This appears to be a PhRMA strategy to facilitate Direct to Consumer Advertising ("DTCA") in Australia. DTCA is legal in the USA but not in Australia. It has been associated with a substantial and expensive increase in usage of the products which are often not in accord with clinical best-practice.[17]

Exchange of Letters and Price Adjustment

An exchange of letters between Trade Minister Vaile and US Ambassador Zoellick dated 18 May 2004 notes that Australia shall provide opportunities for pharmaceutical manufacturers to apply for an adjustment to PBS prices. This provision assumes the continuance of the mechanisms of the Pharmaceutical Benefits Pricing Tribunal. Attempts by PhRMA to seek price rises for already listed products might run up against the argument that this is not a process supporting "innovation" in accordance with the principles at the beginning of Annex 2C.

Chapter 17: Intellectual Property Protection,

Chapter 17 of the AUSFTA includes a variety of provisions apparently designed to protect the interests of US pharmaceutical multinationals. Compulsory licensing of pharmaceuticals is restricted to a standard more stringent than that applying in TRIPS (17.9.7). Production of drugs to assist a public health crisis in a neighbouring country that has issues a compulsory license but lacks its own medicines manufacturing capacity, is prevented (17.9.6). This, however, cannot truly be considered a "benefit" that must be passed on to other TRIPS

members. The process of "evergreening" brand name pharmaceutical patents, so as to exclude cost-lowering generic competition is facilitated (17.10.4).[18]

Article 17.9.4 preventing parallel importation sits uneasily with the *Doha Declaration on TRIPS and Public Health* which had confirmed that each WTO member may establish its own regime of exhaustion of intellectual property rights, and thus that such parallel importation could not be considered a violation of TRIPS.[19]

Having failed in multilateral fora to restrict this exemption to specific diseases like HIV/AIDS or malaria, PhRMA in 17.9.7 achieved a restriction on compulsory licensing to "TRIPS-Plus" standard of "national emergency, or other circumstances of extreme urgency."[20]

Article 17.9.8 of the AUSFTA locks the parties into the enhanced protectionist patent terms where there have been delays in issuing patent approval. By this article PhRMA appears to have sought to get around the tactic of some countries to inhibit its socially inappropriate patent protectionism by adopting delayed administrative approaches to initial registration.

Article 17.10.4 is the now notorious "evergreening provision. It pursues PhRMAs global agenda (repeatedly stated on the USTR "Trade Watch" list) of ensuring pharmaceutical marketing approval is linked with patent validity. Canada was made to implement a similar provision in its *Patented Medicines (Notice of Compliance) Regulations* in 1993 after entering the North American Free Trade Agreement ("NAFTA"). Ever since, the Canadian Office of Patented Medicines and Liason has been fighting the inhibition of rapid entry of cheap generic medicines to the market with strategies worthy of emulation in Australia.

Independent analysis has demonstrated that delayed entry of generic drugs as result of intellectual property changes in the FTA could have a significant impact on the cost of the PBS and its future viability as well as over-the-counter and hospital provided medicines.[21]

The new 26C and 26D in the *Therapeutic Goods Act 1989* (Cth) will assist to prevent the problem of brand name pharmaceutical patent "evergreening" under article 17.10.4. Of crucial importance might be the capacity of the Commonwealth Attorney-General under these amendmens to join an application for an injunction by a brand name patent holder against a generic medicines manufacturer and to claim damages where the injunction has caused a price rise under the PBS. This mechanism allows Australia under article 32 of the *Vienna Convention on the Law of Treaties* to claim that its actionable legitimate expectation was that article 17.10.4 would not increase medicines prices under the PBS.

Dispute Resolution, Cross-Retaliation and Non-Violation Nullification of Benefits

Finally, under the dispute resolution chapter 21, an unelected panel of three nominated trade lawyers (article 21.7) will have the power to interpret compliance with obligations in the AUSFTA. Perhaps of greatest concern for the PBS, in this chapter, is article 21.2 (c). This is what is known in international trade law as a "non-violation nullification of benefits" clause.

"NVNB" articles in many ways are a supercharged mechanism of commercially-focused treaty interpretation. They allow dispute resolution proceedings to be commenced where only the "spirit" of the treaty had been broken, or more technically, the "legitimate expectations" of US corporations had been nullified, particularly for present purposes, in key areas of the agreement related to pharmaceutical intellectual property.3

Article 21.2(c) allows a damages claim by either Australia or the US where a "benefit" that either could reasonably have expected to accrue under articles including chapter 2 (including Annex 2C on pharmaceuticals) and chapter 17 (intellectual property)the FTA is not realised even though no specific provision has been breached.[22] Australia for example coulod clearly claim that one of its legitimate expectations was the continuance of cost-effectiveness pricing under the PBS. Any move by US corporations supported by the US government through the USTR to undermine this could entitle dispute resolution proceedings that may best be brought in the WTO rather than under the AUSFTA.

Independent Review Mechanism[23]

Following the conclusion of the FTA concerns were raised in Australia over the potential impact on the PBS of the commitment to establish an independent review of recommendations made to Government by PBAC. This was one of a range of measures agreed to enhance the transparency and accountability of the operation of the PBS. The Australian Government has openly expressed its legitimate expectations that the commitments it has made in this area will have no adverse impact on the sustainability of the PBS. What follows is taken from the official Federal government description of the process. It highlights the reasonable expectation of the Australian government that scientific cost-effectiveness pricing evaluations would remains central to PBAC processes after the AUSFTA is in place.

The relevant AUSFTA text is Annex 2-C which requires the Parties to: "...make available an independent review process that may be invoked at the request of an applicant directly affected by a recommendation or determination."

This is clarified in the associated Exchange of Letters that states that: Australia shall provide an opportunity for independent review of PBAC determinations, where an application has not resulted in a PBAC recommendation to list.

The independent review process established by the Australian Government will be independent of the applicant, the PBAC and of the staff of, or staff employed under contract to, the Department of Health and Ageing involved in any prior evaluations of the drug for the indication(s) requested. An independent review may only be sought by an applicant - that is the sponsor of the application to the PBAC. Independent review will only be made available where an application to the PBAC has not resulted in a recommendation to list. A convenor will be appointed to manage the independent review function. The convenor will not conduct reviews but, for each review, will appoint a reviewer from a panel of identified experts. The reviewer may seek clarification of the information available by discussion with the applicant or the

PBAC or the Department, as arranged through the convenor. Following consultation with the convenor the reviewer may also consult, as appropriate, with other relevant experts.

In the first round of PBAC applications in 2005, the new independent review mechanism was not invoked in relation to some rejections that took place. It may be that data on the cost of such rejections is being stored to justify subsequent dispute resolution proceedings under the AUSFTA that may have the effect of clarifying the changes to the PBS required by the AUSFTA. If this is the case, then Australia similarly needs to be preparing data able to justify its own reasonable expectations in this area (particularly the continuance of PBS clinical and cost effectiveness evaluations).

The Fiscal and Social Benefits of PBAC Cost-Effectiveness Pricing

As mentioned previously the federal government has announced it expects to save $740 if the price of each new generic medicine entering the market creates a 12.5% price drop (calculated for example on the Weighted Average Monthly Treatment Cost ("WAMTC")) for all products in that therapeutic class from the next PBS Schedule publication. Part of the justification for such a policy may be claims that Australian generic prices are high relative to nations such as the US. Yet, what should not be forgotten in considering such arguments is that little good evidence exists of these comparisons when exchange rates and relative purchasing power, as well as the relative cost of brand name pharmaceuticals are taken into account. A crucial factor has been Australian reference pricing which keeps brand name prices at levels that accurately reflect their scientifically proven cost effectiveness.

Arguments have been raised by the pharmaceutical industry that its brand name companies are entitled, in addition to increased royalties from expanded patent terms, to potentially unlimited profits (to the extent that the international and national market is manipulated by cartelism and collusion) to sustain their research and development levels. Assertions that such research and development will bring benefits to the health system (for example though less frequent and lengthy hospital admissions) should not be accepted as requiring regulatory changes without two factors being in place: 1) that credible scientific research justifies the proposed health benefits 2) that research programs are established to monitor whether such newly listed medications deliver the proposed benefits 3) that binding agreements are made that price premiums may be reduced or the PBS reimbursement level reduced if subsequently such benefits do not eventuate within a reasonable time.

Our group currently have an ARC funded project to examine the impacts of international trade agreements, in particular the AUSFTA on access to medicines in Australia. It is hoped that our research may be able to investigate ways in which to model at least four scenarios likely to involve PBS expenditure in the immediate future.

12.5% Cost Reduction with Increased Number of Generic Market Entrants

Under this model, the Federal government's policy of 12.5% reduction applies to the usually expected number of additional generic market entrants after brand name patent expiry on high sales volume PBS-listed medications. In 1999 the Federal government accorded an additional 5 years of patent life to brand name pharmaceuticals to become fully compliant with the World Trade Organisation ("WTO") Trade Related Intellectual Property Rights ("TRIPS") agreement. This meant that only a small number of generic medicines were listed on the PBS between 1999 and 2004. Over 100 compound patents for brand name patents, however, are due to expire in Australia between 2006 and 2010. Research commissioned by the Australian Generic Industry Manufacturers Association has calculated that on the basis of expected patent expiries in classes such as Angiotensin Converting Enzyme Inhibitors, HMG Coenzyme A Reductase Inhibitors, Calcium Channel Blocking Agents, Selective Serotonin Reuptake Inhibitors, Angiotensin II receptor Antagonists and H2-Receptor Antagonists (approx. 40% of PBS expenditure) $1,343 million will be saved between April 2005 and March 2009. If 15 new generic products enter the market between April 2005 and March 2009, the saving to the PBS will approach an additional $1 billion.[24]

Substantially Reduced Number of Generic Market Entrants

One scenario our group has previously raised, is that regulatory changes in the AUSFTA, may facilitate "evergreening" of brand name patents and delayed generic drug entry. If the usual number of generic drug products related to 5 high expenditure PBS medicines (simvastatin, atarvastatin, pravastatin, sertraline and flixotide) experience delayed market entry of 24 months, PBS expenditure may increase by $1.2 billion. Such changes may also be used by brand name pharmaceutical companies to lobbying for increased intellectual property protection related to over-the-counter medicines with resultant price rises.[25]

Threat to Cost-Effectiveness PBS Pricing

This model would present a case in which US plans to "eliminate" pharmaceutical price controls were completely realised in Australia. There can be no question that the US has designs in this direction and hopes to use Australia as an example with which to commence dismantling pharmaceutical price controls, regardless of their social utility and equity or scientific validity, in OECD countries.[26] Whether they will achieve this object will depend on the extent to which Australian regulatory authorities are prepared to use in such negotiations the terms of Annex 2C which support cost minimisation and clinical and cost-effectiveness pricing under the PBS.

If this model were to eventuate not only would PBS expenditure rise as Australia was forced to pay equivalent prices to those in the US for pharmaceuticals. This may have the effect of making the PBS unworkable. The Australian government and people would then lose a powerful fiscal lever to ensure that this community achieves value for money in this area.

Under such a model, access to medicines in Australia would then become a process chiefly of private health insurance, with a "second tier" for those who reached thresholds of poverty or special needs. Given the dominance of concessional card holders in existing PBS usage this would be a radical alteration not only in the basic values underpinning the PBS, but because of the importance of the PBS, to those of an ageing Australian society in general. Such a change would be of such a magnitude and given the origins of the PBS in a constitutional referendum, would itself require a constitutional referendum to achieve legitimacy.

Annex 1 Independent Review Process

Any consultations relating to the conduct of the independent review will be conducted in closed session.The outcomes of the independent review will be made publicly available in a similar timeframe to the publication of outcomes from PBAC meetings. The timeline for the conduct of the independent review will be such that it involves no additional delay in the PBS processes. There will be no time incentive, or disincentive, for applicants to seek a review in preference to making a resubmission to the PBAC. The findings of the independent review will be reported to the PBAC.

After consideration by the PBAC, the review findings and the outcome of the PBAC's reconsideration of the submission in light of the findings of the review will be reported to the Minister for Health and Ageing within 15 days of the PBAC's consideration. Applicants will retain the option to resubmit to the PBAC if additional data or information subsequently become available, but a resubmission will not be accepted while a review is in process. Operation of the Independent Review

Management of the independent review process will be undertaken by a convenor. The convenor's role will be to ensure the integrity and efficient operation of the review process. Individual reviews will be conducted by a reviewer, selected from a panel of experts in relevant disciplines including, but not limited to, clinical pharmacology, epidemiology, pharmaco-epidemiology, health economics, biostatistics, and internal medicine subspecialties.The applicant seeking a review will identify those issues that are in dispute and the review will focus on these issues. The issues must reflect the PBAC's reasons for not recommending listing. The convenor will consider the issues in dispute in appointing an appropriate reviewer. The reviewer must not be an employee or member of the evaluation group that undertook the initial evaluation of the application to the PBAC.

The reviewer will be an individual whose qualifications and expertise are relevant to the key issue(s) under review. When there are disparate issues in contention, the reviewer may seek advice as required after consultation with the convenor. Any person consulted would be identified in the reviewer's report. The reviewer and all people consulted during a review will be required to lodge conflict of interest statements with the convenor. The review will have

access to all the information placed before the PBAC by the applicant, as well as details of the recommendations of the PBAC together with the reports to the PBAC of its sub-committees on the application. No new information is to be provided to the reviewer. Conduct of the review
The applicant will put a request for a review to the convenor in writing, and provide a statement outlining the issues about which the review is sought. The convenor will notify the applicant and the PBAC of the name of the reviewer selected to conduct the review.

The appointed reviewer must declare to the convenor any real or potential conflicts of interest. The convenor will ensure that the reviewer has the credentials to be fair and impartial in conducting the review. The reviewer shall take into consideration all available documents, information and other written material available to the PBAC, including documents, information and material relating to the issues in dispute and to arguments and submissions upon the matters under consideration.

However no new information will be considered, beyond that previously made available to the PBAC.A review will be completed in a timeframe that allows the reporting back to the PBAC meeting in the same timeframe as a resubmission. The convenor will lodge the reviewer's report to the PBAC with the PBAC secretariat no later than 4 weeks before the PBAC meeting at which the matter will be considered, and at the same time provide copies to the applicant.

The applicant will be invited by the PBAC Secretariat to provide a pre-PBAC response to the reviewer's report. Confidential information will be afforded the same level of protection as information put to the PBAC.

Hearings before the PBAC will be confined to specific issues and limited in scope, duration and frequency. Medicines Australia will develop a code of practice to guide applicants in the most appropriate circumstances for seeking a hearing; In view of the need for a pragmatic implementation of this recommendation in the Free Trade Agreement, the PBAC and Medicines Australia will, by mid-2005, consider the alternative option of a hearing before the sub-committees of the PBAC.

Consistent with National Medicines Policy, which states that consumers and health practitioners should be encouraged to understand the costs, benefits and risks of medicines, the working group acknowledges that all stakeholders in the PBS have a need to be informed about PBAC recommendations. Limited information is currently published on the Department of Health and Ageing website, providing only the outcome of each application and a brief summary of the PBAC's reasons.

Details of PBAC recommendations will be available to the public in a timely manner following each PBAC meeting. A Public Summary Document (PSD) will be generated to provide to the public information pertaining to PBAC recommendations. The information will include sufficient relevant clinical, economic and utilisation data to enable stakeholders to understand submissions to the PBAC and the PBAC's view of those submissions. The PSD

will provide information on all aspects of PBAC recommendations, where relevant covering the following:

1. Purpose of the submission - request made to the PBAC, 2. Background, 3. Registration status, 4. Listing requested and PBAC's view, 5. Clinical place for the proposed therapy, 6. Comparator, 7. Clinical trials, 8. Results of trials, 9. Clinical claim, 10. Economic analysis, 11. Estimated PBS usage and financial implications, 12. Recommendation and reasons, 13. Context for decision, 14. Sponsor's comments

The information contained in the PSD will be consistent with that included in the PBAC minutes pertaining to a particular recommendation.

In consultation the PBAC and the sponsor will prepare a draft of the PSD which will be reviewed by both parties taking into account the Commonwealth's duty of confidence to sponsors, where such a duty exists. Both parties will work cooperatively and constructively and negotiate in good faith to provide a PSD which meets the needs of all stakeholders.

Where circumstances warrant the disclosure of information for which the Commonwealth has a duty of confidence, the PBAC and the sponsor will negotiate in good faith to seek a solution which, while protecting confidential information, will enable stakeholders to have adequate information to understand PBAC recommendations.

A sponsor may provide on its website comments additional to those contained in the PSD. Any information or opinion which is published, including that in the PSD should be balanced, fair, and avoid subjectivity/bias. Specific issues relating to content, associated with proposals from sponsors for listing of drugs that are not recommended for listing after a first consideration by the PBAC, will be taken into account in developing the PSD. Further, a delay in the release of a PSD for those drugs, beyond the cut-off date for the following PBAC meeting, will be considered by the PBAC with a view to minimising any adverse impact on those sponsors. If, however, a sponsor of an application which is not recommended for listing after a first consideration by the PBAC seeks an independent review of that recommendation, a PSD will be made available prior to the commencement of the review process.

A Standard Operating Procedure (SOP) will be developed to cover the preparation of the PSD. The Agreed Guiding Principles for Publication of PBAC Recommendations annexed to the working group report will also guide the preparation of the PSD.

To facilitate its implementation the release of PSDs will be phased in during the first half of 2005. Companies seeking an independent review as a result of outcomes from the PBAC's March meeting will be required to have the relevant PSD published.

The PBAC will convene a consultation forum with sponsors early in 2005.The parties (PBAC and sponsors) will monitor the phasing in of the PSD with a view to advising on the need, or otherwise, of a mechanism for resolving disputes between the PBAC and sponsors in regard to the content of a PSD. Twelve months after the implementation of these processes a

review will be undertaken to ensure that the provisions set out in the text of the FTA, as well as the objectives of accountability and transparency for all stakeholders, are being met.

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