MEDICINES Australia

Better Health through Research and Innovation

Submission to the Australia Senate Community Affairs Reference Committee

Inquiry into Consumer Access to Pharmaceutical Benefits

13 April 2010

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Executive Summary:

Medicines Australia welcomes the opportunity to present its position to the Senate Community Affairs References Committee's inquiry into *Consumer access to pharmaceutical benefits and the creation of new therapeutic groups through the Pharmaceutical Benefits Scheme.*

In particular, Medicines Australia welcomes the wider scrutiny into a number of existing "policy levers" which permit high cost and unpredictable Government interventions into Australia's highly efficient pharmaceuticals market. Medicines Australia believes that these interventions have social and business costs that greatly outweigh the value of any short-term fiscal savings to the Government that they might generate.

The impact on consumers is this, the continued use of Therapeutic Groups as a savings measure after the 2007 PBS Reforms potentially places the health of patients at risk by:

- transferring a proportion of the costs of important medicines from the Government to the patient and therefore increasing the risk of non-compliance;
- assuming without appropriate evidence that an individual patient is able to switch to another medicine within the Therapeutic Group without detriment to the patient's health;
- introducing financial considerations into a doctor's decision to prescribe a medicine most suited to an individual patient's clinical needs.

> *"The continued use of Therapeutic Groups as a savings measure potentially places the health of patients at risk."*

It also creates an unpredictable business environment for companies in Australia. The Therapeutic Group policy permits the Australian Government to intervene in the market at any point in time without consultation. A lack of consultation has been a characteristic of recent Therapeutic Group Premium policy announcements. This in turn puts ongoing investment in Australia at risk.

Further in relation to consumer access to pharmaceutical benefits, and in particular, the impact of the requirement for Cabinet review, Medicines Australia believes a review of existing practices is warranted. The requirement that medicines – already determined by the PBAC to be clinically and cost-effective– undergo further scrutiny by Cabinet before achieving a PBS listing also leads to significant delays in access to consumers and business uncertainty for companies. Recent delays have been up to 12 months for life-saving medicines such as *Avastin* for advanced bowel cancer and *Revlimid* for multiple myeloma. In each case, a number of seriously ill patients missed out on medicines that had been demonstrated to be safe and effective, and already recommended for listing by the independent PBAC.

Medicines Australia does not believe that such measures are required to maintain an efficient and sustainable PBS. Efficiency and sustainability are already hard-wired into the PBS listing process itself. Every single medicine that has been listed on the PBS since 1993 has been rigorously assessed for its relative clinical-effectiveness, safety and cost-effectiveness. This means that it has been demonstrated that the cost of funding a PBS medicine is outweighed by the health and economic benefits that the use of the medicine produces for Australians.

It is in no small part due to the requirement that the price paid for medicines reflects demonstrated value for money that Australia has historically spent, and continues to spend, significantly less on pharmaceuticals than the great majority of OECD countries, both relative to size of economy and as a proportion of total health system expenditure. Recent OECD research also showed that ***Australia pays the fourth lowest prices for innovative or originator medicines relative to economy wide-prices in the whole of the OECD. Furthermore, prices for originator medicines are 81% of the OECD average.***

The efficiency of the PBS was further bolstered in 2007 with the introduction of reforms that permitted the Government to reap the benefits that competition in the off-patent market generated through the Price Disclosure policy. Following independent modelling by PricewaterhouseCoopers, the Australian Government now accepts that PBS Reforms should deliver up to $5.8 billion in savings over 10 years. Already the reforms have seen the effective price paid by the Government for some medicines drop by up to 70%. Even more savings, however, have been foregone through the failure of the Australian Government to administer *Price-Disclosure Policy* in an effective and efficient manner.

It seems incongruous to Medicines Australia that the Australian Government continues to use interventions with such high social and business costs, such as Therapeutic Groups, to generate short-term savings at the very time that it fails to take advantage of efficiencies that the market itself generates with few if any costs to consumers, the taxpayer or to business.

For these reasons, each of which is relevant to consumer access to pharmaceutical benefits and therefore expounded against the relevant Term of Reference in the submission below, Medicines Australia propose the following recommendations.

Recommendations

Medicines Australia recommends that:

1. The Australian Government abolish the Therapeutic Group policy and legislative provisions relating to it because:

    a. the policy potentially places patient interests at risk by:

        i. transferring a proportion of the costs of important medicines from the Government to the patient and therefore increasing the risk of non-compliance;

        ii. assuming without appropriate evidence that an individual patient is able to switch to another medicine within the Therapeutic Group without detriment to the patient's health;

        iii. introducing financial considerations into a doctor's decision to prescribe a medicine most suited to an individual patient's clinical needs

    b. the policy is not required in order to ensure the long-term sustainability of the PBS, the efficiency of which is underpinned by both rigorous cost-effectiveness analysis and growing price competition in the off-patent market.

    c. the policy undermines industry confidence in the Australian business environment by permitting the Government to intervene at any point in time without consultation in the market, putting ongoing investment at risk.

2. The Australian Government provide clear definitions and guidance on all legislation or policy that might compromise Australians' timely access to medicines. In particular, the Government has an obligation to ensure that the term "interchangeability on a patient basis" is clearly defined and guidance provided on the evidence required to establish such a link between medicines.

3. The Australian Government, before intervening in the pharmaceuticals market, conduct appropriate consultations with affected parties and ensure that due process is followed at all times.

4. The Australian Government work with industry to implement a formal price disclosure dispute resolution and audit process to avoid delays in implementing further price disclosure price reductions.

5. The Australian Government increase the threshold at which Cabinet approval is required for the listing of demonstrated cost-effective medicines on the PBS from the current $10 million to $20 million; and index future adjustments to reflect economy-wide prices.

6. The Australian Government commit to reduce the time it currently takes to achieve a PBS listing for those medicines for which Cabinet approval is required.

Introduction

Medicines Australia represents the innovative medicines industry in Australia. Our member companies comprise more than 80 per cent of Australia's prescription pharmaceuticals market, and are engaged in the research, development, manufacture, supply and export of prescription medicines.

The pharmaceutical industry is a key industry in Australia which provides benefits to both Australians' health and the health of Australia's economy. Pharmaceutical companies strive to bring to Australians innovative medicines which are both safe and effective; in doing so they also invest around $961 million annually in research and development in Australia.

Our Association represents a high technology, knowledge-intensive industry, contributing significantly to the Australian economy as an employer and exporter. The industry sells over $11 billion worth of medicines domestically and directly employs over 14,000 people in Australia. In 2009, Australian pharmaceutical manufacturing exports totalled more than $4 billion.

As a principal stakeholder, Medicines Australia welcomes the opportunity to present its position to the Senate Community Affairs References Committee's inquiry into *Consumer access to pharmaceutical benefits and the creation of new therapeutic groups through the Pharmaceutical Benefits Scheme.*

Following a brief discussion on the long-term sustainability of the PBS, the remainder of this submission will be devoted to addressing each of the Terms of Reference under consideration by the Senate Committee.

The Pharmaceutical Benefits Scheme – Efficient and Sustainable

Medicines Australia is on record as a strong supporter of the Pharmaceutical Benefits Scheme (PBS). The PBS is an integral part of Australia's tax payer funded, universal healthcare system. It ensures that innovative medicines are available to all Australians regardless of their ability to pay, and it reflects the Australian Government's long-term commitment to achieving equity in access to health services.

The role of the PBS is explicitly recognised in Australia's National Medicines Policy, in particular in its objective to provide "[t]imely access to the medicines that Australians need, at a cost individuals and the community can afford." It is also worthwhile to note that this objective sits alongside another which acknowledges the need to maintain "a responsible and **viable** medicines industry". [1]

[1] The Australian Government, Department of Health and Ageing (2000) *The National Medicines Policy*. Available at www.health.gov.au/internet/main/publishing.nsf/Content/nmp-objectives-policy.htm/$FILE/nmp2000.pdf

The four central objectives of Australia's National Medicines Policy are:

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

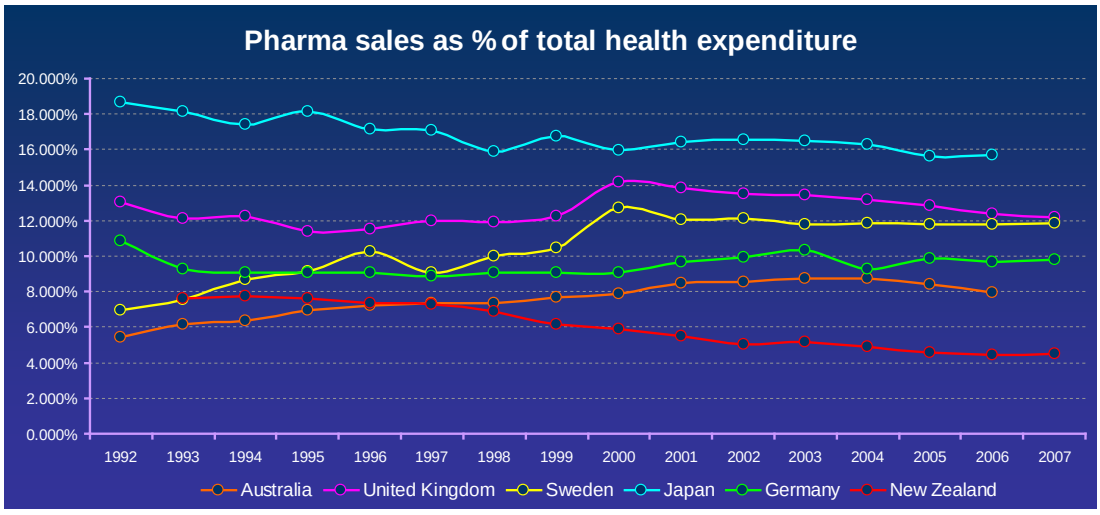
Medicines Australia also strongly supports the policy framework within which the PBS operates, one which guarantees that the Australian Government gets "value-for-money" for every medicine that it decides to subsidise. Every single medicine that has been listed on the PBS since 1993 has been rigorously assessed for its relative clinical-effectiveness, safety and cost-effectiveness. This means that the independent Pharmaceutical Benefits Advisory Committee has analysed the clinical and economic data and concluded that the cost of funding this medicine is outweighed by the health and economic benefits that the use of the medicine produces for Australians. No other part of the health system can claim this. While $8 out of every $100 spent on health in Australia is spent on pharmaceuticals, no other area of health investment can guarantee to deliver more value for money than that invested in the PBS.

> *"Prices for Originator Medicines (in Australia) are 81 per cent of the OECD Average."*

By careful design of the system itself, sustainability and efficiency are hard-wired into the PBS. Australia has historically spent, and continues to spend, significantly less on pharmaceuticals than the great majority of OECD countries, both relative to size of economy and as a proportion of total health system expenditure. No fair-minded, reasonable analysis of the comparative international data can support the claim that PBS expenditure is "out-of-control" as *Figures 1* and *2* demonstrate.

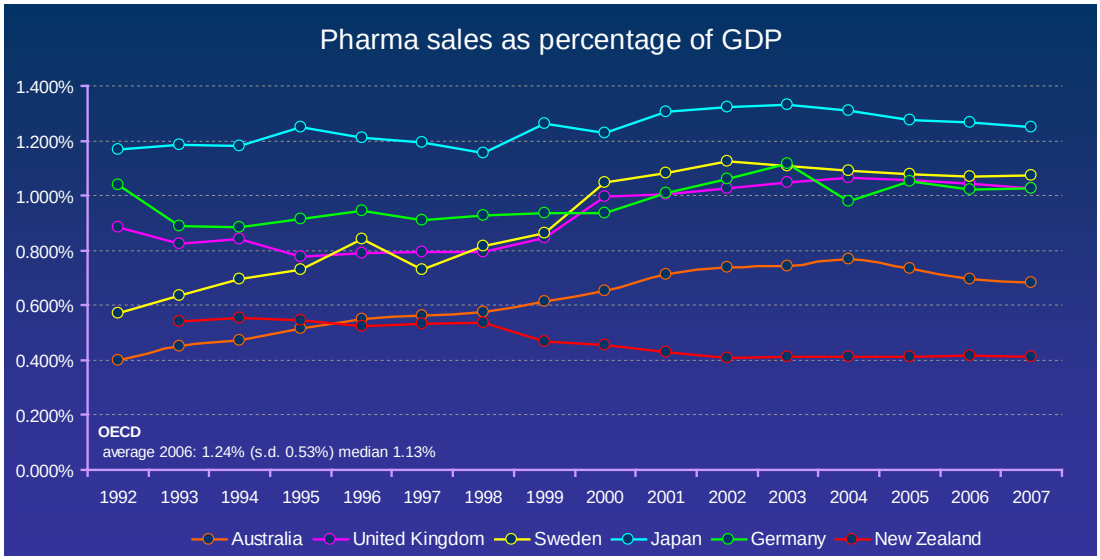
One of the reasons for this is the relatively low prices paid for innovative medicines in Australia. In fact, according to a recent OECD report into global pharmaceutical pricing policies, ***Australia pays the fourth lowest prices for originator medicines relative to economy wide-prices in the OECD. Prices for originator medicines are 81% of the OECD average***. In comparison, the same report suggests that Australia continues to pay significantly over-the-odds for older, off-patent or generic drugs – yet it is the originator medicine prices that measures such as Therapeutic Groups deliberately target.[2]

Figure 1[3]



[2] *OECD, Pharmaceutical Pricing Policies in a Global Market 2008*, pp161-166.
[3] *OECD Health data 2009, Statistics and Indicators for 30 Countries*

Figure 2[4]



PBS Reform

The long-term sustainability and efficiency of the PBS was bolstered by the microeconomic reform of the PBS in 2007. "PBS Reform" split the PBS into two distinct formularies: F1 and F2.

F1 is the market for single brand medicines (i.e. typically patented, originator medicines without competition) where efficient price setting and control is achieved through rigorous cost-effectiveness evaluation and initial prices are set by reference to *different* medicines used to treat the same conditions. The efficient price paid by Government for these medicines is that which can be demonstrated by the clinical trial evidence to be "value-for-money".

F2 is the market for multiple brands of the *same* medicine where competition between *brands* for market share at the pharmacy level sets the price. Before PBS Reform, the Government reimbursed pharmacists for the full listed price of a medicine, regardless of whatever discounting was occurring in the supply chain. After PBS Reform, the Government, through the Price Disclosure Policy, should pay only the price that the product is being sold for in the market. Since 2007, the efficient price for medicines paid by Government for a number of medicines in F2 has already fallen by up to 70%.

> *"Since 2007, the efficient price paid by Government for a number of medicines in the F2 Formulary has already fallen by up to 70 per cent."*

When it was introduced, the Government estimated that PBS Reform would generate up to $3 billion in savings over a 10 year period. Those with a more intimate knowledge of the actual terms of trade in the marketplace believed this to be a significant underestimate. The Pharmacy Guild of Australia commissioned independent modelling of the impact of PBS Reform and concluded that the savings figure is likely to be $7.4 billion over 10 years.

[4] *OECD Health data 2009, Statistics and Indicators for 30 Countries*

Similarly, modelling commissioned by Medicines Australia and undertaken by the Centre for Strategic Economic Studies at Victoria University conservatively estimated the true level to be in the order of $6 billion over the same 10 years, double that which the Government had anticipated.

In February 2010, the Government revised its estimates following independent modelling undertaken by PricewaterhouseCoopers. The Government now accepts that PBS Reforms should deliver up to $5.8 billion in savings over this period. The impact of this on pharmaceutical manufactures, however, is as high as $8.5 billion, with the difference being largely absorbed by a pharmacy compensation package which the Government introduced as part of PBS Reforms.[5]

Given that the originator companies actually account for the majority of the off-patent market in Australia, the innovative pharmaceutical industry has always understood that it would bear the largest cost for the restructuring of the pharmaceuticals market. The industry supported the reforms because it believed that they ensured the long-term sustainability of the PBS *in exchange for* long-term predictability in the pricing market and long-term stability in the policy environment. In short, it exchanged fiscal certainty for government for business certainty for industry.

It is for this reason that Medicines Australia continues to express disappointment at the ongoing intervention by the Government into the pharmaceuticals market. The continued use of the Therapeutic Group policy and the Cabinet review process, in particular, as levers for generating short-term savings is inappropriate as both have significant social and business costs.

Inquiry Terms of Reference:

a. The impact of new therapeutic groups on consumer access to existing PBS drugs, vaccines and future drugs, particularly high cost drugs

Therapeutic Groups are groups of PBS listed medicines that are linked together for pricing reasons regardless of whether the medicines are included in F1 or F2. They comprise different medicines which the Minister for Health and Ageing, on the advice of the PBAC, has determined in accordance to the National Health Act to be "interchangeable on an individual patient basis". It is unclear what this means both at a technical level and in practice.

Since the introduction of PBS Reform in 2007, the Australian Government has announced its intention to form four new Therapeutic Groups. These are: a high potency HMG CoA reductase inhibitor (statin) group for drugs used to treat hypercholesterolemia (i.e. high-cholesterol)[6]: a selective anti-depressants group[7]: an oral bisphosponate group for drugs used to treat osteoporosis[8]: and an oral bisphosponate group for drugs used to treat Paget's disease.[9]

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[5] Commonwealth of Australia (2010)The Impact of PBS Reform Report to Parliament on the *National Health Amendment (Pharmaceutical Benefits Scheme) Act 2007*

[6] Comprising Atorvastatin (F1) and Rosuvastatin (F1)

[7] Comprising Venlafaxine (soon F2) and Desvenlafaxine (F1)

[8] Comprising Alendronic Acid (F2), Alendronic Acid with Colecalciferol (F2), Risedronic Acid (F1), Risedronic Acid with Calcium (F1), Risedronic Acid with Calcium and Colecalciferol (F1)

[9] Comprising Alendronic Acid (F2), Tiludronic Acid (F2), Risedronic Acid (F1)

Only the statin Therapeutic Group, however, has been formed. The three remaining groups have not yet been formed, pending passage of the relevant legislative instruments through the Australian parliament.

The purpose of grouping medicines into Therapeutic Groups is to impose a ceiling on the price that the Government will pay for a medicine. This ceiling is that of the lowest priced medicine in the group. Typically, this is achieved by exposing the group annually to a form of reference pricing called the Weighted Average Monthly Treatment Cost calculation - a complex piece of statistical analysis designed to ensure that the monthly treatment cost for any patient is on average the same across all medicines in the group. This has the effect of rapidly ratcheting prices down as the Government rarely accepts a price increase for a medicine regardless of the outcome of the calculations.

Most importantly, however, should one member of a Therapeutic Group move to F2 following the entry of a generic competitor into the market, all members of the group are moved immediately into F2 regardless of patent status or whether there is market-based brand competition for the medicine. This triggers an automatic 12.5% price reduction for all medicines in the group.

The decision to form a Therapeutic Group does, however, permit a sponsor to put a ***Therapeutic Group Premium*** on an affected medicine. This price premium is applied on top of the existing patient co-payment. The Government permits this because it considers all medicines in the Therapeutic Group to be "interchangeable on an individual patient basis", requiring only that one brand of a medicine within the group is "premium-free".

This implies that a patient unable to pay the additional out-of-pocket cost can switch without any detriment to their health to any other medicine within the group. The policy also permits a doctor to seek an exemption from the premium for a patient who the doctor believes should not switch for clinical reasons. Under such circumstances, the cost of the premium is transferred back to the Government and no savings are achieved.

The actual impact of applying a premium is not possible to quantify, but the following can be logically inferred from what we do know from the research: any increase in out-of-pocket patient costs lead directly to a decrease in medication compliance. It follows that a decrease in compliance, in accordance to all principles of the Quality Use of Medicines, leads to a preventable loss of health.[10]

The addition of a price premium also has the effect of introducing financial concerns into clinical decision making. Instead of making a decision purely on the clinical requirements of the patient, a doctor must also make a prescribing decision that takes into consideration the affordability of a medicine for a patient. This is the case for new patients when commencing treatment, as well as for patients who have been stabilised and responding well on an existing treatment regimes.

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[10] Hynd A, Roughead EE, Preen DB, Glover J, Bulsara M, Semmens J. The impact of co-payment increases on dispensings of government-subsidised medicines in Australia. Pharmacoepidemiol Drug Saf. 2008 Nov;17(11):1091-9.

It is important to note that all of the medicines that have been included in the new Therapeutic Groups are used for chronic conditions. Clinicians are faced with the choice of switching a stabilised patient to a new medicine, with all the associated risk of inferior response or adverse events, or take the risk that a patient for financial reasons might be non-compliant with the current but more expensive regime.[11]

Under such circumstances, Medicines Australia believes that it is absolutely critical that the Government is confident that a patient stabilised on one medicine can switch to another medicine within the group without any risk of detriment to a patient's health. Medicines Australia does not believe that such confidence is warranted given what is accepted knowledge about the inter-personal variability due to genetic or any number of environment variables that influence drug response. It is important to note that as far as Medicines Australia can ascertain, inter-personal variability is not formally assessed by the PBAC when it provides its advice to the Minister.

[This point will be fully discussed under the next Term of Reference dealing with the criteria and clinical evidence used to qualify drugs as interchangeable at a patient level].

At this point, criticism might be levelled at a company for applying a Therapeutic Group premium to a medicine as this is a choice made, not by the Government, but by the company. Medicines Australia believes that such criticism is unwarranted due to the realities of operating a for-profit enterprise in a market subject to unpredictable government intervention that results in large and sudden price-cuts at the hands of a monopsonist.

The ability to apply a premium is essential for a company to smooth over such volatility in the business environment, especially since most local companies need to negotiate with overseas based head-offices before it can adjust any prices in the market. These discussions can take several months.

Medicines Australia has long argued that a predictable and stable pricing market is important for "maintaining a responsible and viable medicines industry in Australia" – the fourth plank of the National Medicines Policy. Decisions about whether to seek listing for new medicines, as well as ongoing investment in clinical trial research and manufacturing in Australia are directly affected by business confidence in the regulatory and pricing environment.

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[11] A clinician may also apply an exemption from a premium for a patient due to:

- adverse effects occurring with all of the base-priced drugs; or
- drug interactions occurring with all of the base-priced drugs; or
- drug interactions expected to occur with all of the base-priced drugs; or
- The transfer to a base-priced drug would cause patient confusion resulting in problems with compliance.

Such an exemption, however, requires an approved PBS Authority prescription from Medicare Australia adding substantially to the administrative burden of the doctor as well as the cost of the medicine to the taxpayer. Medicines Australia is unable to find any official statistics on the number of exemptions granted. Any exemption granted, however, calls into question whether a medicine – from the point of view of the clinician and patient – is truly "interchangeable on an individual patient basis".

Current legislation empowers the Minister to create Therapeutic Groups at any point in time and without consultation with affected parties. Most importantly, as discussed above, decisions to form a Therapeutic Group effectively dissolve the boundary between F1 and F2 as all medicines in the Therapeutic Group will be moved to F2 regardless of patent status once one member of the group is subject to generic competition. This means that "on patent" medicines will be forced to take mandatory price cuts (12.5%) well before a sponsor had anticipated and without notice.

The decision to form all four Therapeutic Groups since the introduction of PBS Reform was taken unilaterally and without warning. This has had serious consequences for affected companies whose revenue streams have been unexpectedly and heavily affected by such government intervention. This in turn serves to undermine confidence in the Australian market.

It is for these reasons that Medicines Australia has argued that the continued formation of Therapeutic Groups is against the spirit of PBS Reform (and possibly even in breach of the law as will be described below in section e). When it agreed to PBS Reform in 2007, at a cost now independently estimated to be as high as $8.5 billion over 10 years, industry believed that it was providing the Government with fiscal certainty in exchange for long-term predictability in the pricing market and long-term stability in the policy environment. It is clear that this was not the case given the continued formation of Therapeutic Groups.

> *"This [Therapeutic Group] policy is not required for long-term sustainability of the PBS, the efficiency of which is underpinned by both rigorous cost-effectiveness analysis and growing price competition in the off-patent market."*

Recommendation 1:

Medicines Australia recommends that the Australian Government abolish the Therapeutic Group policy and legislative provisions relating to it because:

a. *this policy potentially places patient interests at risk by:*

    i. *Transferring a proportion of the costs of important medicines from the Government to the patient and therefore increasing the risk of non-compliance;*

    ii. *Assuming without appropriate evidence that an individual patient is able to switch to another medicine within the Therapeutic Group without detriment to the patient's health;*

    iii. *Introducing financial considerations into a doctor's decision to prescribe a medicine most suited to an individual patient's clinical needs.*

b. *this policy is not required in order to ensure the long-term sustainability of the PBS, the efficiency of which is underpinned by both rigorous cost-effectiveness analysis and growing price competition in the off-patent market.*

c. *this policy undermines industry confidence in the Australian business environment by permitting the Government to intervene at any point in time without consultation in the market, putting ongoing investment at risk.*

b. The criteria and clinical evidence used to qualify drugs as interchangeable at a patient level

As argued above, it is critically important for patient health that medicines included in Therapeutic Groups are ***genuinely*** "interchangeable on an individual patient basis". In the absence of this confidence, the Government risks the health of many consumers by introducing financial considerations into clinical decision making.

Is such confidence warranted? The relevant legislation covering the formation of Therapeutic Groups states that the Minister for Health and Ageing "***may*** have regard to advice of the Pharmaceutical Benefits Advisory Committee to the effect that a drug or medicinal preparation should, or should not, be treated as interchangeable on an individual patient basis with another drug or medicinal preparation."

Although the term "interchangeable on an individual patient basis" appears in the legislation, Medicines Australia has been unable to extract any advice on what this means in practice. Medicines Australia has on a number of occasions approached both the Department of Health and Ageing and the PBAC for guidance on a workable definition or set of criteria which would give industry some understanding of the policy and predictability about the pricing environment. **Despite repeated attempts, Medicines Australia has still not been provided with this advice**.

The only advice that Medicines Australia has been provided is that the PBAC makes its determinations concerning "intechangeability" based on the evidence provided in PBS listing submissions. These submissions most commonly present detailed clinical trial data alongside economic modelling and analysis to make one of the following cases for a PBS listing:

a. that a new medicine is clinically superior to existing available treatment options and therefore is deserving of a higher price. These are commonly referred to as cost-effectiveness submissions; *or*

b. that a new drug is no worse clinically than existing available treatment options and therefore the price paid should not increase the total cost to Government for providing that treatment. These are commonly referred to as cost-minimisation submissions.

It has been suggested to Medicines Australia that evidence presented in the cost-minimisation submissions are the principal source for determining whether a medicine is interchangeable on an individual patient basis with another medicine. There is good reason, however, to be cautious about using this type of evidence for such a purpose.

Cost-minimisation submissions typically only present data from trials that are specifically designed to establish that a medicine is 'non-inferior.'[12] That is to say, they are designed to test the hypothesis that statistically a drug is no worse clinically than the drug to which it is being compared. It is generally accepted as inappropriate to infer any other conclusion from such trials, including any conclusion that one drug might be superior or even that the drugs are equivalent. Such claims are normally satisfied through superiority or equivalence trials respectively.[13]

If, indeed, the PBAC is using non-inferiority trials as the principal source of evidence to advise that medicines are "interchangeable on an individual patient basis", Medicines Australia believes that the Committee is using evidence that is not suitable for answering the relevant question.[14]

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[12] Alternatively, in the absence of head-to-head trials, indirect comparisons using a common reference (e.g. placebo arms of RCTs) are often used. It is rare for the PBAC to accept a claim of superiority based on evidence from an indirect comparison. Most commonly a claim of non-inferiority is accepted. Again, however, it is not a claim of equivalence that is being demonstrated.

[13] With reference to the International Conference on Harmonisation document on statistical principles for clinical trials (ICH E9), a recent scholarly article on assessing comparative efficacy provided the following definitions for different types of trials:

- **Superiority trial**: A trial with the primary objective of showing that the response to the investigational product is superior to a comparative agent (active or placebo control)
- **Non-inferiority trial**: A trial with the primary objective of showing that the response to the investigational product is not clinically inferior to a comparative agent (active or placebo control)
- **Equivalence trial**: A trial with the primary objective of showing that the response to two or more treatments differs by an amount which is clinically unimportant. This is usually demonstrated by showing that the true treatment difference is likely to lie between a lower and an upper equivalence margin of clinically acceptable differences.

Eichler HG, Bloechl-Daum B, Abadie E, Barnett D, König F, Pearson S.
Relative efficacy of drugs: an emerging issue between regulatory agencies and third-party payers.
Nature Review Drug Discovery 2010 Feb 26

[14] Relevant examples from the PBAC Public Summary Documents are:

From 2007 PBAC Recommendation to list Risedronate for osteoporoses (now grouped with Alendronate)

"The PBAC considered that this resubmission had addressed the Committee's previous concerns and the sponsor's claim that risedronate is no worse than alendronate in terms of effectiveness and toxicity to be reasonable. The PBAC recommended extending the current listing as an authority required benefit to allow subsidised use in the primary treatment of osteoporosis on a cost-minimisation basis as compared to alendronate. The equi-effective doses are risedronate 35 mg weekly being equivalent to alendronate 70 mg weekly.

http://www.health.gov.au/internet/main/publishing.nsf/Content/8C3E03770F8B75E4CA2572FA00138722/$File/Risedronate.pdf

From 2006 PBAC Recommendation to list Rosuvastatin (now grouped with Atorvastatin):

"The submission claimed that rosuvastatin is no worse, in terms of LDL-C lowering efficacy and safety, than Atorvastatin..... The PBAC recommended listing on a cost-minimisation basis with atorvastatin, with the ratio of equi-effective doses being rosuvastatin to atorvastatin1:3."

http://www.health.gov.au/internet/main/publishing.nsf/Content/pbac-psd-rosuvastatin-july06

Furthermore, the evidence presented to the PBAC is directed at establishing the relative clinical and cost-effectiveness of a medicine **at a population level**. It is not designed to assess the extent that any given individual will respond equivalently to **different** medicines used to treat the same conditions. (i.e. interchangeable on an individual patient basis) As this is the practical clinical implication of forming Therapeutic Groups for patients (i.e. that an individual can switch to another medicine in the group without any detrimental impact on his/her health), then Medicines Australia believes that this is, in fact, the relevant frame of reference within which the evidence should be assessed for the purposes of providing advice on "interchangeability".

In the absence of any definition of the term "interchangeable on an individual patient basis" or any guidance on how such decisions are made or the evidence used to make such a case, Medicines Australia is not confident that all medicines in any Therapeutic Group are truly "interchangeable". Without such confidence, Medicines Australia is concerned an individual patient will not always be able to switch from one medicine to another without it being detrimental to his or her health; yet this is the key policy assumption underpinning the creation of Therapeutic Groups, and the reason the Government requires that at least one brand of medicine within a Therapeutic Group be available "premium-free".

Recommendation 2:

Medicines Australia recommends that the Australian Government provide clear definitions and guidance on all legislation or policy that might compromise Australians' timely access to medicines. In particular, the Government has an obligation to ensure that the term "interchangeability on a patient basis" is clearly defined and guidance is provided on the evidence required to establish such a link between medicines.

From 2008 PBAC Recommendation to list Desvenlafaxine (now grouped with Venlafaxine)

"The submission claimed that desvenlafaxine is non-inferior to venlafaxine in treatment effect for the indication of MDD and non-inferior to venlafaxine in terms of safety.
The PBAC accepted that the data presented supported the claim of non-inferiority of desvenlafaxine to venlafaxine in the treatment of MDD and in terms of safety..... The PBAC recommended the listing of desvenlafaxine on the PBS for major depressive disorders on a cost minimisation basis with the parent drug venlafaxine. The equi-effective doses are desvenlafaxine 50 mg and venlafaxine 75 mg.
The PBAC considered that desvenlafaxine would provide a further treatment option for major depressive disorders, however, no evidence was presented to suggest that desvenlafaxine would offer an advantage for any particular patient group over the parent drug venlafaxine.
The PBAC agreed that the indirect comparison presented in the submission supported the claim of non-inferiority of desvenlafaxine to venlafaxine in the treatment of major depressive disorders."

http://www.health.gov.au/internet/main/publishing.nsf/Content/EFD65A5C1CB2F874CA25756E0009CDF3/$File/pbac-psd-desvenlafaxine-nov08.pdf

c. The effect of new therapeutic groups on the number and size of patient contributions.

The Therapeutic Group policy permits companies to apply a patient premium on a medicine. These premiums help companies to mitigate the negative fiscal impacts of unpredictable government interventions in the market; however, they also increase the out-of-pocket costs for consumers when filling a prescription.

For most PBS listed products, patient co-payments are currently set at $5.40 per script for concessional patients (with a safety net threshold of $324); and $33.30 per script for general patients (with a safety net threshold of $1,281.30).

Historically, the size of patient premiums has been modest. A review of Annual Reports of the PBPA available from the Department of Health and Ageing website reveals premiums ranging from as low as $1.07 to as high as $7.00. As at 30 June 2009, four of the six Therapeutic Groups were affected by the Therapeutic Groups Premium Policy.

It is difficult to use past practice, however, to predict the impact of new therapeutic groups on the number and size of patient contributions. It has been historically unusual for Therapeutic Groups to comprise drugs that are not subject to generic competition on a molecule basis. Where generic competition exists, this tends to place downward pressure on any premium that a company might otherwise charge. In the case of the Therapeutic Groups announced since the introduction of PBS Reform, their membership contains a number of on-patent medicines without brand competition. It would be reasonable to expect that for such medicines, it is possible that companies will seek to smooth out the effect of the unexpected revenue loss by applying a premium the size of which is at least the equivalent of the price reduction it took due to its unexpected and early entry into F2. (i.e. at least 12.5%).

The potential size of these premiums puts greater pressure on the Government to ensure that the medicines that comprise the Therapeutic Groups are truly “interchangeable on an individual patient basis”.

d. Consultation undertaken in the development of new therapeutic groups

The Government announced its intention to form all four of the new Therapeutic Groups without any prior consultation with the affected parties. It is assumed that the Minister for Health and Ageing made her determination based on advice received by the PBAC that the relevant medicines should be regarded as “interchangeable on an individual patient basis”.

Medicines Australia has been assured by each of its affected member companies that they were not invited to submit any comment or additional information to the PBAC concerning the question of the potential “interchangeability” of a medicine with other PBS listed medicines prior to the announcement.

According to Section 101 3BA of the National Health Act, if the PBAC recommends a medicine for listing on the PBS, it "**must**.....specify whether the drug or medicinal preparation and another drug or medicinal preparation should be treated as interchangeable on an individual patient basis".

Medicines Australia has interpreted this clause as an obligation of the PBAC to advise the Minister on whether a medicine should be deemed interchangeable at the point of its initial recommendation to list. It is therefore reasonable to assume that such advice should appear in copies of the Short Minutes provided to sponsors as well as in the Public Summary Documents of decisions that are placed in the public domain.

Whilst initial decisions to list the affected high potency statins and the oral bisphosponates predated the legislation, the decision to list Desvenlafaxine came well after this. The Public Summary Document for Desvenlafaxine, however, contains no mention of any PBAC view that Desvenlafaxine should be considered as "interchangeable" with Venlafaxine "on an individual patient basis".[15]

Furthermore, Medicines Australia does not believe that such advice was provided in the Short Minutes of the relevant meeting. As such any advice provided to the Minister on this matter was done so without the knowledge of the affected company.

> *"Medicines Australia believes that the lack of consultation undertaken by the Government prior to announcing its intention to form Therapeutic Groups amounts to a serious breach of proper process and natural justice."*

Given the potentially large financial impacts that such decisions have on affected companies, the unpredictable and non-transparent nature of any determination by the PBAC that any of the medicines might be deemed "interchangeable", and the potential negative flow-on effects for consumers, Medicines Australia believes that the lack of consultation undertaken by the Government prior to announcing its intention to form Therapeutic Groups amounts to a serious breach of proper process and natural justice.

Recommendation 3:

Medicines Australia recommends that the Australian Government, before intervening in the pharmaceuticals market, always conduct appropriate consultations with affected parties and ensure at all times that due process is followed.

[15] Public summary document for **Desvenlafaxine** succinate, tablet, (extended release), 50 mg and 100 mg (base), Pristiq® www.health.gov.au/internet/main/publishing.nsf/Content/EFD65A5C1CB2F874CA25756E0009CDF3/$File/pbac-psd-desvenlafaxine-nov08.pdf

e. The impact of new therapeutic groups on the classification of medicines in F1 and F2 formularies

Medicines Australia has been informed that affected medicines currently listed in F1 will be moved to F2 as soon as any single member of a Therapeutic Group is exposed to generic competition. This permits the Government to enforce a 12.5% price reduction on on-patent medicines well before this was anticipated by the affected company.

When it agreed to PBS Reform in 2007, at a cost to industry now independently estimated to be as high as $8.5 billion over 10 years, industry believed that it was providing the Government with fiscal certainty in exchange for long-term predictability in the pricing market and long-term stability in the policy environment.

It is instructive in this sense that the Revised Explanatory Memorandum for the PBS Reform legislation contains the following statement:

> "*The grandfathering of existing drugs listed on the PBS to formularies through the regulations will provide certainty for industry. The placement of these drugs was largely based on factors applying in late 2006 and has been subject to extensive consultation with industry.*"

More recently Medicines Australia has received legal advice that casts doubt on the powers of the Minister to move medicines from F1 to F2 in circumstances other than the entry of a new bioequivalent (i.e. generic) brand of the medicine in question.

> *"It was not the legislative intention to move a drug from F1 to F2 by means of a Ministerial determination after it was classified on F1 by the regulations at the commencement of the PBS Reform Act unless and until it fails to satisfy any of the F1 criteria at a later time."*

Referencing the Revised Explanatory Memorandum and the Second Reading Speech for the PBS Reform Act, the legal advice provided to Medicines Australia notes that:

- The legislative intention at the commencement of the PBS Reform Act was to "grandfather" existing listed drugs to the F1 and F2 formularies by regulation.
- The focus of the PBS Reform Act was not on the prices of drugs on F1; the focus was to remove any price link between drugs on F1 and drugs on F2 and to reduce prices of multiple brand medicines that are in competition (drugs on F2).
- It was not the legislative intention to move a drug from F1 to F2 by means of a Ministerial determination after it was classified on F1 by the regulations at the commencement of the PBS Reform Act unless and until it fails to satisfy any of the F1 criteria at a later time.

- A failure to satisfy the relevant F1 criteria should occur only if:
    - a ***new*** listed brand of a pharmaceutical item is introduced ***after*** the commencement of the PBS Reform Act that contains the same drug or a different drug that is in the same therapeutic group; and
    - the two listed brands of pharmaceutical items are bioequivalent or biosimilar.

  That is, a drug should only move from F1 to F2 when a new brand of pharmaceutical item is listed and the drug on F1 becomes subject to competition.
- The test of whether two drugs are "interchangeable on an individual patient basis" is different from the test of whether two pharmaceutical items each containing one of those drugs are bioequivalent or biosimilar.
- As a result, a determination by the Minister that two listed drugs are in the same therapeutic group (that is, the two drugs are interchangeable on an individual patient basis) does not mean, of itself, that a drug that is on F1 fails to satisfy any of the F1 criteria and moves to F2. The two brands of pharmaceutical items each containing one of the drugs must be also bioequivalent or biosimilar.
- If a new drug is listed and it is to be in a therapeutic group with an existing drug on F1, it should follow that the determination will be made only if, in addition to the second drugs being interchangeable on an individual patient basis, the two brands of pharmaceutical items contain the drug in F1 and the new listed drug (respectively) are also bioequivalent or biosimilar.

It is appropriate that the Australian Government consider such advice in the context of the application of the Therapeutic Group policy.

f. The delay to price reductions associated with the price disclosure provisions due to take effect on 1 August 2009 and the reasons for the delay

The long-term savings estimated to be delivered through PBS Reform are due to Government aligning its reimbursable price in F2 with the price set by the highly competitive off-patent market. Before PBS Reform, the Government reimbursed pharmacists for the full listed price of a medicine, regardless of whatever discounting was occurring in the supply chain. After PBS Reform, the Government, through the Price Disclosure Policy, should pay only the price that the product is being sold for in the market. Since 2007, the efficient price for medicines paid by Government for a number of medicines in F2 has already fallen by up to 70%.

Medicines Australia has been open in its support of the Price Disclosure Policy because it allows the Government to benefit from efficiencies that the marketplace itself is producing. Any savings generated from it reflect prices for which companies are themselves setting.

It thus minimises the risk of market failure where Government-driven "across the board" price cuts lead to companies removing medicines from the PBS due to commercial non-viability.

Medicines Australia also supported the introduction of the Price Disclosure Policy because of an a assurance by Government that savings generated through such microeconomic reform in the commodity market would provide "headroom" for the funding of new innovative medicines in the cost-effectiveness based F1 market. As such, for Medicines Australia, it is vital that Price Disclosure is administered in an efficient and competent manner.

As a concept, it appears that the Price Disclosure Policy has significant potential for driving ongoing efficiencies in the pharmaceutical market. Since 2007, the efficient price for medicines paid by Government for some "disclosed" medicines in F2 has already fallen by up to 70%. Nonetheless the implementation of price disclosure has so far been characterised by a number of administrative errors that have led to significant delays in the realisation of savings.

Medicines Australia has long been concerned about the absence of a formal price disclosure dispute resolution and audit process. As the price disclosure policy is designed to extract savings facilitated by companies' discounting practices, it is vital that the calculations and data used by the Government to determine price alterations can be verified, and that any resultant disputes can be resolved in a transparent and fair manner.

At present, the only recourse that a sponsor has to resolve questions of fact or process is the judicial system, a route already taken by one company following the very first round of price disclosure related price reductions. The court not only found in favour of the company, but also highlighted a number of administrative anomalies that demonstrated standard operating procedures were not followed. It has been estimated that these delays have resulted in an estimated loss of $11 million of savings.[16]

Medicines Australia maintains that this outcome could have been avoided had the Government introduced a formal dispute resolution and audit system. More than 12 months ago, KPMG provided the Government with an options paper for the introduction of such a scheme. Whilst Medicines Australia provided feedback on the paper, no further work has been forthcoming on the matter.

Medicines Australia has repeatedly urged the Government to work with the industry to ensure that administration of the Price Disclosure policy is efficient and accurate. In particular, it is imperative that a formal dispute resolution and audit process is introduced to validate, and ensure confidence in the administration of the policy.

[16] Australia, SENATE ESTIMATES COMMITTEE: COMMUNITY AFFAIRS LEGISLATION COMMITTEE: *Health And Ageing Portfolio: Outcome 2 - Access to Pharmaceutical Services - Pharmaceutical Benefits Division*, p CA52, 10 February 2010

Recommendation 4:

Medicines Australia recommends that the Australian Government work with industry to implement a formal price disclosure dispute resolution and audit process to avoid delays in implementing further price disclosure price reductions.

g. The process and timing of consideration by Cabinet of high cost drugs and vaccines

The requirement that Cabinet approve the listing of any medicine costing more than $10 million per annum can add more than 12 months to the time it takes for some medicines to be available to the Australian public. During this period, Australians are denied access to life-saving drugs which the PBAC has deemed to be clinically and cost-effective.

> "[Cabinet] delays mean longer periods of debilitating illness for patients, time off work and increased use of other health services. In some cases, such delays can literally be life-threatening."

Such delays mean longer periods of debilitating illness for patients, time off work and increased use of other health services. In some cases, such delays can literally be life-threatening. Medicines that have been recently delayed by the Cabinet review process before achieving PBS listing include: *Sutent* for renal cell carcinoma (kidney cancer) – 10 months; *Avastin* for advanced bowel cancer – 12 months; and *Revlimid* for multiple myeloma – 13 months.

Internal analysis by Medicines Australia suggests that the average time between a positive PBAC recommendation and an actual PBS listing for those medicines requiring Cabinet approval is increasing. From 2006 until late 2007, Cabinet considered eight medicines. The average time from PBAC recommendation to PBS listing was just short of 200 days. For the six medicines considered since then the average time to listing has increased by 94 days.

Importantly, no medicine has been rejected by Cabinet, calling into question the need for such oversight.

The $10 million threshold at which Cabinet approval is required was established in 2001 and has remained at this level ever since. It has not been adjusted to reflect changes in the economy or even indexed to inflation.

By failing to adjust the threshold to accommodate economy-wide price changes over time the listing of an increasing number of new medicines is likely to be delayed in the future.

This was recently recognised by the Productivity Commission, when in its *2008 Annual Review of Regulatory Burden on Business: Manufacturing and Distributive Trades,* it commented that:

"The Government should consider the merits of increasing the threshold to account for price changes over the past six years and implementing an automatic annual indexation adjustment."[17]

Medicines Australia has been provided with data by the Department of Health and Ageing that show that even a small rise in the value of threshold would significantly reduce delays to the listing process for many medicines. For example, these data show that doubling the threshold to $20 million would have reduced the number of medicines requiring Cabinet consideration from 2002-03 to 2007-08 by 54%.

Figure 3: Number of Cabinet submissions if the threshold was increased

Threshold	2002-03	2003-04	2004-05	2005-06	2006-07	2007-08	Total	Percentage Reduction
$10m (current)	2	5	3	5	13	11	39	0%
$15m	2	3	2	4	8	4	23	41%
$20m	1	3	2	4	6	2	18	54%
$50m	0	3	0	0	2	1	6	85%

Source: Department of Health and Ageing

In addition to improving patient access to new medicines, relieving Cabinet time pressures and removing a regulatory burden for some medicines that companies are seeking to have listed, Medicines Australia believes that increasing the threshold will not cost the Government any additional money. For example, Medicines Australia is not aware of any medicines in the $10 million to $20 million cost range where Cabinet has rejected listing a medicine on the PBS. It is therefore unlikely that increasing the threshold to $20 million would lead to increased Government spending.

Recommendation 5:

Medicines Australia recommends that the Australian Government increase the threshold at which Cabinet approval is required for the listing of demonstrated cost-effective medicines on the PBS from the current $10 million to $20 million; and index future adjustments to reflect economy-wide prices.

Recommendation 6:

Medicines Australia recommends the Australian Government commit to reduce the time it currently takes to achieve a PBS listing for those medicines for which Cabinet approval is required.

[17] Productivity Commission (2008) *Annual Review of Regulatory Burden: Manufacturing and Distributive Trades* p80.