



Poor practice or malpractice?

The rise and rise of generic substitution

The availability of legal drugs in Australia is largely governed by the Therapeutic Goods Administration [TGA] and the Pharmaceutical Benefits Scheme [PBS]. It's the former that allows the drugs to be accessed by Australians and it's the latter that lists them for government subsidy so that most of us can afford most of them.

In the United States of America, where expenditure on pharmaceuticals is unmatched anywhere in the world, something like 44,000,000 US citizens do not have effective access to the prescription medicines they need. The health insurance industry in the US is competitive, as we seem to get told with particular vigor these days, indeed it is fiercely so. In fact, the US Food and Drug Administration or FDA has approved thousands more drugs and supplements for US citizens than our TGA has approved for us.

But in the US health insurance is something that for most people comes with their job – so if you are in a low paid job you are likely to be in a low benefit fund. A Harris Poll conducted in 2001 of a random sample of 1,010 adult Americans found 39 percent of people with annual incomes of less than \$15,000 per annum had not filled a script in the previous 12 months. And this in a country where in 2003 there were an estimated 3.4 billion prescriptions filled in “drugstores” and through “mail order”. In 2004 prescription drug sales amounted to \$216 billion. [Ukens C. How mail order pharmacy gained in market share in 2003. *Drug Topics* Mar 22, 2004; 148]

The fact is that if you are poorly

paid and poorly insured and cannot afford one of the competitive higher end health insurance schemes, you are in for a hard trot if you need more expensive medications. If you're without employment, you're generally buggered. Current talk of selling Medibank Private invariably brings criticism that we are moving to an Americanised health insurance model, one that puts more and more of the onus on consumers rather than on government. Let's hope we don't end up in that particular ball park. It has been a hot political issue in countless elections and even Bill Clinton couldn't get medicines to all Americans needing them. You may recall he had Hillary Clinton, a contender for his old job and a powerful mover and shaker in her own right, on the job and she simply couldn't turn the system around.

Dr. Sidney M. Wolfe, director of the US based Public Citizen's Health Research Group makes the telling point that the US “fails to provide health insurance for about one-seventh of our population and fails to provide prescription drug coverage for millions of Medicare-covered older Americans who cannot afford to purchase drug coverage on their own.”

We often hear Australian politicians tell us that the Australian system is one of the world's best, making many of the most important drugs available to everyone. By and large it is a good system but it is often slow to introduce new drugs into the marketplace and it seems determined to cut costs – even where spending money on medications will save money on all kinds of other

programs and provide sick people – and those who live with them – with healthier, more productive lives.

It is a good system but not a great one. In fact the scheme only covers around 600 drugs, marketed under something like 2,600 brand names. These PBS listed drugs make up around 90% of all prescription medicines available in Australia. You might be surprised at what is not listed.

Many drugs are not subsidised at all – and for all sorts of reasons. Viagra [Sildenafil], for example, and a range of other drugs that could be helpful for many people who have suffered a reduced capacity for, or even a complete loss of, sexual intimacy because of reduced or lost erectile function [which may be the result of anything from stress, ageing, diabetes, trauma, some kinds of epilepsy, and so on] is, for reasons that most non-sniggering Australians would probably find wrong if not just plain wowserish, excluded from having a PBS listing. You can of course get a prescription for Viagra but it's something like \$10 a tablet. Xenical [Orlistat] is another example. It helps your body reduce its fat absorption if you are needing to lose weight and in a community that is battling obesity and its many costs in terms of lost productivity, increased risks of cardiovascular illnesses and so on, you'd have thought it might just get on the list. But no! You can walk into a chemist and buy a month's supply without a prescription but you'll walk out \$130-\$140 lighter with an improved understanding of what PBS listing means.

In fact there are basically three kinds of prescribing in Australia [with hospitals sometimes having different arrangements]. The most common relates to the many medicines that can be prescribed without any restriction on their therapeutic use.

Next are those that can only be prescribed for specific uses. And so a drug that might help young mothers fight a particular kind of breast cancer may be available for that particular use and only that use – while oncologists who would like to use it for older men with prostate cancer cannot prescribe it with PBS subsidy. They can prescribe it but their patients would need to have very deep pockets or a willingness to sell or re-mortgage their houses, assuming they have managed to pay one off over their probably productive lifetime as a taxpayer.

Then there is the third category where an “authority” is required for PBS subsidy to apply. This means that your doctor has to get prior approval from Medicare Australia before he or she can give you the prescription. The drugs involved here are usually high cost drugs that your doctor has to argue are necessary for you to take, usually because the cheaper ones didn’t do the trick. A high cost drug here means that the Pharmaceutical company has what is usually called an international “floor” price below which they will not supply their drug anywhere – and certainly not to first-world countries with a perceived capacity to pay. Too often they also apply this floor price idea to second and third

world countries and then wonder why some governments have the temerity to override them and ignore their patents in efforts to save the lives of their citizens.

Most of the prescribing information you would ever wish to find is available on the internet at sites such as <http://www.health.gov.au/pbschedule>, so I won’t labor any of this any further except to mention one other requirement in the prescribing regulations.

If there is a generic drug available, that is, a cheaper “copy” of a previously patented “brand” now on the market, doctors are required to indicate if the brand substitution is not permitted on the prescription they write. This is meant as a direction to pharmacists, or their sales assistants, not to ask if you would like a cheaper “identical” drug, but as we know, it is an instruction that is often ignored both in Australia and overseas where similar efforts are made by physicians who want to know exactly what you will be taking for your condition.

There is a note in the regulations that also stipulates that “PBS prescriptions must not be prepared using a computer prescribing program that contains a default which would result in all prescriptions being indicated as Brand Substitution Not Permitted”. The common prescribing software used by Australian general practitioners therefore defaults to allow a generic to be substituted if available. In other words the government wants doctors to have to make an effort if they want you to stay away from a generic medication and on

the specific formulation that they have in mind when they do the prescribing.

The PBS – interestingly enough, originally resisted vigorously by doctors as an intrusion into their prescribing practices – is geared to make drugs available to most of the population most of the time while keeping its costs under control.

The main reason for the introduction of the PBS seems to have been to ensure that antibiotics would be widely accessible by the population. Conditions such as tuberculosis or consumption, had seemingly at last met their match with the introduction of antibiotics like streptomycin, and antibiotics became such a major foil to many of the illnesses that patients presented with that they were arguably over-prescribed. The doctors who were licensed to prescribe them were those who practiced what was called “allopathic” medicine. Ironically, despite their opposition to it, allopathic doctors were major beneficiaries of the scheme which saw a dramatic falling away from naturopathic, homeopathic and osteopathic medical practice, so much so that we now refer to allopaths as doctors or general practitioners while we continue to call naturopaths . . . naturopaths. The PBS or government drug subsidy, was now well and truly funneling big dollars into allopathic practice.

Another group benefiting greatly from this was of course the pharmaceutical industry. Costs [what they charge for their drugs] have risen and risen and some would say have spiralled way out

PHARMACEUTICAL BENEFITS SCHEME

This table briefly shows the kind of subsidies we are talking about that enable consumers to have a very real degree of certainty in what they will be up for with most prescriptions.

	Most consumers	Consumers who are concession card holders
Maximum price for a “listed” drug	\$29.50	\$4.70
A “safety net” applies once you’ve paid . . .	\$960.10 in any year	\$253.80 in any year or you/your family have filled 52 scripts within a calendar year
Cost per script after the “safety net” has been applied . . .	\$4.70	No charge

Believe it or not there is a “safety net” card issue fee of \$7.43
Some drugs – usually ones that are quite expensive in their “branded” form – are given a “special” status so that patients can continue to have them even though much cheaper alternatives are arguably available. These medications attract a special patient contribution but oddly that extra cost does not count towards the PBS Safety Net.

of control, beyond anything that even remotely resembles recovery of research costs or even decent profit margins. While the whole argument that drugs cost too much is debatable, and there are excellent arguments that if everyone got any drug or medical procedure they needed to help them better manage their health, the savings to the community in so many other areas would be astronomical far outweighing the treatment costs. That however is another argument for another time.

The PBS costs the Australian taxpayer billions of dollars each year [\$4,630,000,000 in 2002-2003 and we paid another \$850,000,000 for these same prescription drugs out of our own pockets] so rational savings that do not impact negatively on health outcomes have to be worth a try. We often hear that it is spiralling upwards and out of control. This is too simple an analysis as the costs actually jump up and down. In the early 90's growth was over 25% per annum but a couple of years ago it was down to 10% and falling. More expensive drugs are often seen as a major problem for the PBS's future, but they may also bring cures to illnesses that previously required lifetime drug taking, and other improvements, such as keeping younger people healthier for longer, and older people out of high cost care facilities for longer, and in all kinds of ways drive overall health costs down.

As it is we spend a smaller percentage of our GDP on medicines than many comparable OECD countries – and not just because we have such a smart system. The individual out-of-pocket expenses paid by Australians are the highest of the 10 OECD countries with which we are most comparable economically. [Just so you know . . . these are Canada, the United States, New Zealand, Japan, France, Germany, the Netherlands, Sweden and the United Kingdom.]

We have less options than in some comparable countries. And some might say that we are working hard to keep our pharmaceutical options limited – or at least to make sure we save wherever we can. According to the federal Government's *Charter of Budget Honesty* the move towards generics prescribing and dispensing will save around \$740,000,000 over the 4 financial

years 2004-2005 to 2007-2008. Not a bad effort. But is there a hidden cost and if so who is paying it?

The savings with generics come when a generic or copy drug comes onto the market. The government immediately drops its subsidy by 12.5% for all the drugs in that particular group of drugs – that is in the class of drugs that perform the same kind of function. Regardless of what any pharmaceutical company then charges for its version of the drug, the subsidy is paid against the cheapest form of drug in any given class so that if your doctor wants you to have a more expensive drug you will have to pay what is called a “therapeutic premium” or a “brand premium” which is generally somewhere between \$2.50 and \$3.00, though it can be over \$60.

Antiepileptic drugs or AED's generally cost no more than \$29.50 or \$4.70 concession. Some are even cheaper than this. The saving to the consumer each month on a number of commonly used AED's is often quite large and depending on the strength of the drugs supplied, can be up to \$157.20 for Trileptal [oxcarbazepine], up to \$166.09 for Gabatril [tiagabine hydrochloride], and up to \$113.49 for Lamictal [lamotrogine]. Those AED's that are not front line or first use treatments require “authority” to prescribe, and two are scheduled as Special Pharmaceutical Benefits where a therapeutic premium can be asked for as well as the usual patient contribution. For example, for 200mg Topamax [topiramate] the premium is currently \$2.62 on top of the usual \$29.50 or \$4.70 concession, but the cost of the drug to the PBS is \$163.34.

Keppra [levetiracetam] is something of a special case, in that it requires an authority [because treatment with other PBS listed drugs hasn't worked] and it also attracts a therapeutic premium [which the customer has to pay] of up to \$19.84 for a month's supply of the 1 gram [1,000 mg] tablet. However, if your doctor also asks for an exemption from the therapeutic premium at the time he or she seeks the authority to prescribe, the drug will be dispensed for the usual patient contribution. The reasons for the exemption are pretty straightforward, such as adverse reactions to other suitable PBS drugs, adverse interactions with other PBS drugs have occurred

or can be expected to occur, transfer to another AED would cause confusion or compliance issues or result in clinically adverse consequences. The drug costs the PBS up to \$163.90 a month.

In the USA generic drugs account for around 54% of all prescription drugs and consumers and many physicians are greatly pleased that this is the case. They accuse pharmaceutical companies who own the original patented drugs of scaring people about generics in order to protect their market share and they cite research that shows all kinds of health benefits from generics. In a country where drugs can be so hard to access for the less affluent, impossible to access for many, it is no wonder they are received with such enthusiasm by many in the medical community. In Australia where around 25% of prescription drugs are now available as generic drugs, the approach seems to be somewhat more cautious – but only somewhat.

Drugs are clearly big business with pharmaceutical companies now arguably outperforming [making greater profits than] the world's leading banks. A PBS listed drug may cost the scheme tens, hundreds, or even thousands of dollars a year but it will be sold to Australians at the prices given in the table above. All in all the PBS picks up around 80% of the costs of the drugs it has listed.

In the US by comparison [I don't want to labor the “benefits” of competitive health insurance, but I think you need to know] a packet of 50 5mg Valium tablets cost a consumer something like \$110 a packet, a packet of 30 20mg or 40 mg Lipitor around \$130 for a month's supply – that's over \$1500 a year just to control your cholesterol. These same two tablets would cost somewhere between \$29.50 and nothing in Australia. At most the Lipitor would cost \$354 a year, less for a concession card holder and less again if the safety net kicked in. The safety net itself is set lower than the cost of a year's supply of Lipitor in the United States.

The changing regulatory regime in Australia has caught the earnest attention of a good many companies, both here and overseas. The Indian pharmaceutical company Ranbaxy, with global sales of \$1.43 billion in 125 countries brought in 4 new generics in August – and says it is looking to bring in many more. We now have a burgeoning generics industry

in Australia, which by and large is good news – though not quite all round.

We've all read those product information leaflets in small print found inside the packaging of prescription drugs. This is a typical extract – taken from an anti epileptic medication – and is one of a number of warnings that leave you with no doubt that you have a personal responsibility as a consumer to do the right thing – to be a responsible user.

Do not stop using "this medication" unless your doctor tells you to. Do not stop taking it, or change the dose, without checking with your doctor. Do not let yourself run out over the weekend or on holidays. Stopping suddenly may cause unwanted effects or make your condition worse. Your doctor may want you to gradually reduce the amount you are taking before stopping completely.

What you are not likely to read is a warning about generic substitution such as . . .

If you have a prescription written for this medication in the future, make sure that your doctor does not allow for substitution to a generic or brand name drug claiming the same active ingredients. Once you have ensured you have the right prescription, make sure that you do not allow your pharmacist to substitute "this medication" for any other form of this same drug. Changing the formulation that was originally prescribed for you may cause extremely serious side effects and/or make your condition drastically worse.

If you ever do read this I'd love to hear from you because it would mean that there had been a seismic shift in the way the national prescribing authorities take their responsibilities for ensuring that people with epilepsy get the drugs they need and not the drugs that save the PBS money in the short term, or which increase profits to chemists.

Chemists receive a number of fees from the PBS, including dispensing fees for ready-prepared drugs of \$5.15 per script, a dangerous drug fee of \$2.71 per script, and a number of other fees depending on how the drug is prepared. The chemist can also get huge discounts on some drugs when they buy them in bulk – up to 40% has been reported. Of course you may save a dollar or even

two or three, but the bulk of the money being pocketed here is pocketed by the pharmacist and their supplier. In the early years of generic supply in Australia the government was making extra payments to pharmacists for moving people off brand drugs and onto generics.

It remains the case of course that if a drug is sourced by the pharmacist for less than the "brand" drug, or for that matter less than the other generics, the pharmacist may well have a stronger motivation to move it off his or her shelves if they have "stocked up" at the lower price.

Hospital pharmacies and those larger pharmacies that typically handle the business of nursing homes and the like in their districts, typically buy in bulk. What is insidious is that when they dispense using blister packs to the hospitals, nursing homes and hostels that use their services slip in generic drugs in place of the particular formulations prescribed. You can bet that generic drugs bulk purchased by the pharmacy are what will be going into the blister pack wherever possible. We have had repeated experience of this in the state and territory associations that make up our national coalition, Epilepsy Australia. I have even experienced it first hand when a member of my family went into respite care for a month. The effect of this kind of substitution can range from mildly discomforting to totally catastrophic.

According to the Australian Government's MediConnect program being conducted by the Department of Health and Ageing to improve prescribing practice, 140,000 hospital admissions are associated with adverse drug events at a cost of \$380,000,000 annually. Now this is certainly not just a result of generic substitution but the role of generics in adverse outcomes needs to be tracked – and this is clearly not happening with any systematic precision at all.

But to step outside Australia for a moment, let me tell you about a survey of almost 2,800 German, Austrian, and Swiss neurologists (German speaking) contacted via email between December 2005 and January 2006 with a response rate of 21.2% with 594 evaluable responses. I learned of this at a conference on Epilepsy and Society

in Copenhagen [a heck of a long way to go for a meeting but it was a truly useful thing to do] and I had the privilege of hearing Günter Krämer from the Swiss Epilepsy Centre in Zurich talk about the difficulty that generics present to people with epilepsy and their doctors.

Only 24% of the physicians who responded were of the opinion that regulatory criteria to demonstrate bioequivalence of generic drugs are appropriate (German: 25%, Austrian: 35%, Swiss 15%). In other words 76% of the neurologists surveyed thought the bioequivalence criteria for anti epilepsy drugs were unsatisfactory.

92% consider it unacceptable that pharmacists may give a different preparation than the prescribed one to the patient without also providing full information and gaining the consent of the prescribing physician. Many physicians report that they advise their patients on the risks associated with switching from brand to generic anti epilepsy drugs (G: 58%, A: 72%, S: 85%).

There are real problems in the ways generics are tested in the first place. Gillian Shenfield who is a professor of clinical pharmacology at the University of Sydney at the Royal North Shore Hospital made what I thought were two very telling observations on a recent edition of *Health Matters*, a widely respected ABC radio program. She found herself agreeing with the Public Citizen's Health Research Group's Sidney M. Wolfe: "I totally agree with him. He talked about clinical trials being done in healthy people and if we're talking say a drug for arthritis, people will be chosen who haven't got too much else wrong with them. They won't have diabetes, they won't have a lot of heart disease, they won't have high blood pressure. But for the average doctor with a patient sitting across from them with arthritis, they will have one or all of those things and they'll often be over 65 and very few trials are done on people over 65. So I totally agree."

Dr Krämer's approach as a physician was to try to guarantee his patients a continuity of supply once he had their seizures stabilised. His frustration and that of his colleagues was palpable and reminded me of that expressed by a number of Australian neurologists. He

quoted two US surveys [Wilner 2002 and 2004] of neurologists that came off a smaller base than the one he and his colleagues in the German section of the International League Against Epilepsy had pulled together, but it nonetheless provides some important insights into what can go wrong with generic prescribing to people living with epilepsy.

67.8% of the US neurologists participating in the survey reported breakthrough seizures for their patients after switching from a brand drug to a generic one. 56% reported increased side effects after a switch from brand to generic and 81.6% stated that the FDA standards for the demonstration of AED bioavailability are not sufficiently narrow.

Dr Krämer made the point that both the doctor and the patient should hold the view that the risks are reasonably low before making any switch to generic medication. Patients need to be fully informed and in his view their consent should be sought given that the risks involve seizure recurrence and/or reduced tolerability. Failure to gain this consent arguably could lead to the physician being liable to damage claims.

Australian Medical Association President, Dr Mukesh Haikerwal, stated last February in a press release that “A decision to prescribe a generic or change to a generic – disregarding relevant clinical considerations – can be dangerous and is irresponsible.”

So what should occur if a person is given generic antiepileptic medication and has breakthrough seizures or worse? In my view there are several logical outcomes. We will be looking at these at our national meeting in October with a view to taking the campaign further.

1. If informed consent was not obtained from both the doctor and the person living with epilepsy, then a regulatory regime should be in place to ensure that the person or business dispensing the substituted drugs is stopped from doing this a second time.

I suggest that a person proven to have dispensed a substitute drug without the informed consent, whether it's over the counter at the pharmacy or in blister packs to people in nursing homes and so on, should face an appropriate tribunal of peers and face losing their right to

dispense drugs without supervision for a period specified by the review group. If they continue to offend they should be suspended, and even eventually removed, from professional practice.

2. A medical practitioner who writes a script should take the time to ensure that the person for whom the script is being written is fully aware of what is to happen in terms of generic substitution. If they have allowed a generic substitution to occur, and an adverse

outcome follows, the script should be admissible as evidence of malpractice. In this event it is reasonable for a patient or their family to seek redress of some sort and at the very least a tribunal should be asked to consider an appropriate penalty for the prescriber. If they continue to offend they should be suspended or even removed from professional practice.

3. In a system where we cannot take legal action against the health bureaucrats whose decision making adversely affects us or puts our well being at unreasonable and unnecessary risk, we are left with the notion of Ministerial Responsibility. This needs to be restated by all political parties because as it stands few modern day Australian politicians ever step up to the plate and take Ministerial Responsibility for the things that happen on their watch – let alone demonstrate any understanding of this important convention of Westminster Parliamentary Democracy. Perhaps we just need to ask Tony Abbott and Julia Gillard what they will do when adverse outcomes resulting from unreasonable substitution of medicines are reported.

4. Epilepsy Australia is currently looking at how we can best work with politicians who are prepared to listen and to understand the devastation that generics can bring to people living with epilepsy, to bring about a comprehensive ban on substitution for all antiepileptic drugs.

5. We also need to get the message out that 40% of people on antiepileptic

drugs do not yet have full seizure control and we need to be bringing more formulations of anticonvulsants on line rather than less.

6. The disgrace that vagal nerve stimulation is still not listed as a Medicare item number needs to be rectified. If people needing them

can have pace makers why can't children wracked with uncontrolled seizures have a similar device called a vagal nerve stimulator. And then there are a range of other devices that could come online if

the Australian government gave greater support to the Australian researchers who are working on them.

Finally, Epilepsy Australia is interested in hearing from anyone who has experienced an adverse outcome because of drug substitution whether generic or not. We are prepared to work with you to obtain senior legal counsel and possibly to find a way to take the matter to court.

“So what should occur if a person is given generic antiepileptic medication and has breakthrough seizures or worse?”

Russell Pollard