

## Letters

Letters, which may not necessarily be published in full, should be restricted to not more than 250 words. When relevant, comment on the letter is sought from the author. Due to production schedules, it is normally not possible to publish letters received in response to material appearing in a particular issue earlier than the second or third subsequent issue.

### Generics – equal or not?

Editor, – I read with interest the article by Professor Birkett on generics (Aust Prescr 2003;26:85–7). However, the recent introduction of a generic form of the immunosuppressive drug cyclosporin confuses one of the key messages.

The abstract of the article states, ‘There are no generic formulations of drugs with a narrow therapeutic index as it would be difficult for them to meet the required standard of bioequivalence’. The body of the article then explains why there are no generic forms for drugs such as digoxin and phenytoin where the dose is critical. It is therefore difficult to understand the reasoning behind the current situation with cyclosporin. This is arguably the most critical dose drug on the market. The fine balancing act between immunosuppressive efficacy and nephrotoxicity (and other dose-dependent adverse effects) is perhaps the most challenging part of practice for transplant clinicians, and requires careful and frequent monitoring of drug concentrations. The use of cyclosporin is further complicated by numerous significant drug interactions.

The generic form of cyclosporin seems to invalidate a key message in Professor Birkett’s article and has left this reader confused. Generic forms of established medications have an important place in the Australian market, however, clinicians and consumers need to be very aware of the need for careful monitoring when a generic form of a ‘difficult’ drug such as cyclosporin becomes available. It is critical to minimise interchange between formulations without clear awareness by all parties involved in the patient’s care.

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Editor, – In the article ‘Generics – equal or not’ (Aust Prescr 2003;26:85–7), Professor Birkett mentions that ‘...there are no generic products in Australia, for example, for digoxin...’ Unfortunately there is! There is a generic of digoxin called Sigmaxin/Sigmaxin PG made by Fawns and McAllan which is available on the Pharmaceutical Benefits Scheme. I have not had a look at the tablets to see how similar they are to Lanoxin/Lanoxin PG and as I have recently come back from overseas, I am not sure how long they have been available.

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Editor, – The recent article by Professor Birkett (Aust Prescr 2003;26:85–7) was an interesting contribution to the debate on generic drugs. However, we wish to point out a serious

flaw in the argument for patients with chronic paroxysmal diseases like epilepsy. Generics are licensed for use if they show acceptable bioequivalence in short-term pharmacokinetic studies. We have no argument with this standard for drugs used to treat short-lived conditions, often using supra-therapeutic doses, such as antibiotics for bacterial infection. Similarly, for chronic conditions like hypertension or diabetes where there is a physiological marker that is a continuous variable, minor dosage adjustments can easily be made using a generic without adverse clinical consequences even if bioequivalence is imperfect.

In contrast, epilepsy is characterised by a state where the patient is apparently physiologically normal with seizures punctuating their lives in an episodic and unpredictable manner. Issues related to antiepileptic drugs are often identified as the cause for unpredictable seizures, including poor absorption associated with intercurrent infection, other drugs, diarrhoea or non-compliance. The type of evaluation done for generics to establish bioequivalence simply does not match what is required for conditions with a narrow therapeutic window such as epilepsy. There are many uncontrolled and anecdotal reports of patients having breakthrough seizures on changing from one form of an antiepileptic drug to another.<sup>1,2</sup> Unfortunately, because of the nature of the problem, it is difficult to plan rigorous clinical trials to test the frequency and severity of such adverse events.<sup>3</sup>

We have no problem with the use of generic antiepileptic drugs, if a patient uses the same formulation continuously. However, the principle that patients requiring chronic therapy can be safely **switched** from one formulation of the drug to another, based on short-term bioequivalence studies, is a view that we cannot endorse. The consequences of a single seizure in an otherwise controlled patient can be devastating in terms of loss of driving licence, loss of job, physical injury or even loss of life. The temptation for the patient to take the cheaper alternative, often without the doctor’s knowledge, needs to be corrected. The importance of this issue should be reinforced by the prescribing doctor and other healthcare professionals, particularly pharmacists.

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## REFERENCES

1. Crawford P, Hall WW, Chappell B, Collings J, Stewart A. Generic prescribing for epilepsy. Is it safe? *Seizure* 1996;5:1-5.
2. Guberman A, Corman C. Generic substitution for brand name antiepileptic drugs: a survey. *Can J Neurol Sci* 2000;27:37-43.
3. Lesser RP, Krauss G. Buy some today: can generics be safely substituted for brand-name drugs? *Neurology* 2001;57:571-3.

*Professor D. Birkett, the author of the article, comments:*

In reply to the letters from Dr Faull and Ms Hendry, the point I was making was that the regulatory limits might need to be tightened for narrow therapeutic index drugs, but this would make it more difficult (and expensive) to demonstrate bioequivalence between products.

In relation to digoxin, the Schedule of Pharmaceutical Benefits for 1 August 2003 showed Lanoxin is manufactured by Sigma Pharmaceuticals. The 'generic' brand, Sigmaxin, is manufactured by Fawns and McAllan which is identified in the Schedule as 'a member of Sigma group of companies' and has the same address as Sigma Pharmaceuticals.

Three brands of cyclosporin were listed in the August 2003 edition of the Schedule – Cicloral, Cysporin and Neoral. Cysporin was a Faulding Pharmaceuticals product and has been listed since 2002. Cicloral is a product of Hexal Australia and appeared in the August 2003 Schedule. Cysporin and Cicloral are in fact the same product marketed under different names. This product has presumably been accepted as bioequivalent and therefore clinically equivalent to Neoral by the Therapeutics Goods Administration.

Drs Berkovic and Vajda make some sensible points – particularly that patients with conditions such as epilepsy might be better maintained on the same brand of an anticonvulsant drug. The Pharmaceutical Benefits Scheme

makes allowance for this through the 'no substitution' rule. However, they do confuse the issue by using the term 'cheaper alternative'. They imply elsewhere in the letter that it is not the particular brand used, but the switching between brands that may cause problems due to patient confusion or minor differences in bioavailability. These issues apply equally to generic and innovator brands. For patients with a chronic condition cost is an important factor. The establishment and maintenance of treatment with a brand that provides the lowest cost for the patients will be in their interest.

### Insomnia treatment – an update

Editor, – I would like to inform the readers of *Australian Prescriber* about the ongoing technical appraisal of the newer hypnotics by the UK National Institute for Clinical Excellence. The final statement should appear in the very near future.<sup>1</sup> It will offer information which might complement the recent excellent article by Professor Tiller (*Aust Prescr* 2003;26:78–81), particularly in clarifying pharmacoeconomic issues.

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## REFERENCE

1. National Institute for Clinical Excellence. Technology appraisals in progress: Final Scope – Zaleplon, zolpidem and zopiclone for the management of insomnia. <http://www.nice.org.uk/Docref.asp?d=57815>

## Book review

**Therapeutic Guidelines: Cardiovascular. Version 4.**

**Melbourne: Therapeutic Guidelines Limited; 2003. 265 pages.**

**Price \$33, students \$25.30, plus postage.**

*Aniello Iannuzzi, General Practitioner, Coonabarabran, NSW*

This book goes far beyond what its title suggests. Not only does it provide therapeutic guidelines, but it also addresses current diagnostic and epidemiological considerations relevant to the management of cardiovascular disease in Australia. In essence, it is a mini-textbook; it is much more than a guide.

The first chapter is a concise summary of cardiovascular drugs available in Australia. The next two chapters deal with smoking and the prevention of cardiovascular disease. The rest of the book is more like how one would expect the guidelines to be set out, with chapters devoted to each category of cardiovascular disease (for example, dyslipidaemia, hypertension, heart

failure, arrhythmia). There are interesting sections on preoperative considerations for cardiac patients and deep vein thrombosis prophylaxis for airline travellers.

A most noteworthy feature of this book is that non-pharmacological therapies are given just as much emphasis as drug prescribing. It is a salient reminder for clinicians that our roles extend far beyond just selecting medicines for our patients. Current national recommendations on exercise and diet are included in the text.

The information contained in the guidelines is succinct, current and highly relevant to all clinicians. Medical students, junior doctors, pharmacists and general medical practitioners could comfortably use this book as their complete resource for the management of cardiovascular disease. Specialist physicians and cardiologists may find this a useful tool to compare their own individual management regimens against those most commonly used by their colleagues. Hospitals would find this a most useful addition to libraries and ward reference collections.