

## 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.

### Treatment of myasthenia gravis

Editor, –The article on myasthenia gravis (Aust Prescr 2007;30:156–60) made no mention of the role of pseudoephedrine (and perhaps other sympathomimetics), which are most useful in addressing ocular ptosis, when cholinesterase blockers fail.

Although the practice is 'off label', knowing about it can be quite eye-opening, especially for those who rely heavily on the official product information. Non-clinical pharmacists conducting home medication reviews will often query the drug, having no idea why it is being used.

Andrew Montanari  
General practitioner  
Tamworth, NSW

*Dr Stephen Reddel, author of the article, comments:*

Dr Montanari is quite correct that sympathomimetics including pseudoephedrine offer a mild improvement in myasthenic syndromes, just as adrenergic blockers such as beta blockers have a mildly deleterious effect.

The benefit is rarely enough to be used as monotherapy other than for a cosmetic degree of ptosis, and tends to be short-lived due to tachyphylaxis. Additionally later withdrawal of pseudoephedrine is difficult because of 'fatigue' experienced upon withdrawal, which I think is usually habituation to the central stimulant effects of the drugs, but is easily confused by the patient as a myasthenic symptom. Long-term consequences of pseudoephedrine use, including hypertension, are not insignificant. In my personal practice I reserve the short-term benefit of these drugs for severely ill patients admitted in crisis, when combined with a neostigmine infusion in the intensive care unit, while awaiting the patient's response to other treatments.

Editor, – I would like to congratulate Dr Stephen Reddel on such a well written article (Aust Prescr 2007;30:156–60), probably the most useful piece I have seen on this little known and often overlooked condition.

Readers may be interested to know that in addition to the New South Wales patient support group, there is also a group in Western Australia, which has recently produced the pamphlet outlining which drugs can worsen myasthenia gravis. As some of these drugs can cause potentially life-threatening exacerbations, the pamphlet has been designed to be easy to use in a hurry, so that the treating doctor or dentist can quickly gauge which drugs to use in a

particular clinical setting. Copies can be obtained from the association, and the information will soon be available on the website as well (Myasthenia Friends and Support Group, [www.myastheniawa.info](http://www.myastheniawa.info) or telephone (08) 9459 7168).

Another Western Australian publication, 'A Handbook for Myasthenics', is available from the association.

Queensland also has a support group: Myasthenia Gravis Association of Queensland ([www.mg-qlld.gil.com.au](http://www.mg-qlld.gil.com.au)).

Jean Foster  
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### Varenicline

Editor, – A recent comment about the drug varenicline (Aust Prescr 2008;31:25–6) carries the statement that 'although many smokers try to stop, very few succeed without assistance'. This statement is not true.

There are now more ex-smokers than smokers in Australia. About 30% of adults, or about 4.5 million people, once smoked and smoke no longer.<sup>1</sup> Most people who attempt to quit do so.

Self-quitting – quitting without the aid of clinical interventions – has not been well studied. About 20 years ago, it was estimated that 90% of Americans who quit did so on their own.<sup>2</sup>

A recent Australian study showed that things have not changed all that much. Quitting cold turkey was the overwhelming method of choice used in their previous quit attempt by former smokers (88% of attempts) and current smokers (62% of attempts). In contrast, nicotine patches had been used by 7% of former smokers and 28% of current smokers.<sup>3</sup>

Pharmacological aids help some smokers quit. But the great majority of smokers continue to quit on their own.

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### Tumour necrosis factor inhibitors

Editor, – Since the article on tumour necrosis factor inhibitors was published (Aust Prescr 2006;29:67–70), further evidence has emerged about the risk of malignancy associated with these drugs. A meta-analysis of nine published randomised placebo-controlled clinical trials of adalimumab and infliximab in rheumatoid arthritis showed a 3.3-fold (95% CI\* 1.2–9.1) increased risk of malignancy.<sup>1</sup> Patients with prior malignancy were excluded from these trials. Malignancies were significantly more common in those taking high doses compared to low doses of tumour necrosis factor inhibitors. A US observational study of 6597 patients with rheumatoid arthritis treated with tumour necrosis factor inhibitors showed that their use was associated with an increased risk of non-melanotic skin cancer (odds ratio 1.5, 95% CI 1.2–1.8) and melanoma (odds ratio 2.3, 95% CI 0.9–5.4).<sup>2</sup> However, no other malignancy was associated and the overall risk of any cancer was 1.0 (95% CI 0.8–1.2).

There is no current evidence for the safety of tumour necrosis factor inhibitors in patients with a history of malignancy. Hence, both the UK guidelines and the current product information for these products recommend that tumour necrosis factor inhibitors should be used with caution in patients with previous malignancy.<sup>3</sup> We suggest that until more long-term safety data are available, patients with recent malignancy should not be required to 'fail' a tumour necrosis factor inhibitor before being eligible for an alternative biological disease-modifying antirheumatic drug therapy under the Pharmaceutical Benefits Scheme.

\*CI = confidence interval

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### Relationships between health professionals and industry

Editor, – In a recent article (Aust Prescr 2007;30:150–3), Professor Paul Komesaroff mentions the Pharmaceutical Society of Australia's policy on gifts from pharmaceutical companies. The Society (PSA) also has a more comprehensive document entitled 'Guidelines for pharmacists' relationship with the pharmaceutical industry' which covers a broad range of issues including the promotion of healthcare products, conduct of meetings with medical representatives, gifts and inducements, loyalty schemes and support of educational activities.

While access to the guidelines is restricted to members of the PSA, we would be very happy to share the document with the author or other potential writers and researchers in this field.

Kerry Deans  
Chief Executive Officer  
Pharmaceutical Society of Australia  
Canberra

(Editorial note: Ms Deans is no longer with the PSA)

Editor, – I refer to Professor Komesaroff's article (Aust Prescr 2007;30:150–3) whereby he understandably expresses concern about the influence that the pharmaceutical industry potentially exerts over prescribing clinicians. It must however be stated that few practising clinicians owe their livelihood to any one pharmaceutical company or product. This is in stark contrast to the involvement of other third party providers that exist within the healthcare system. The obvious example that comes to mind is medical practitioners whose work is predominately or entirely devoted to providing medicolegal reports for insurance companies. In this situation, there is more than a pharmaceutical company notepad, biro, or dinner on the line. Despite all this, it would seem evident that the majority of medical practitioners do practise ethically and appropriately.

Other circumstances involving third party healthcare stakeholders may have the potential to compromise a doctor's livelihood while raising considerable concern about the possible adverse impact on medical ethics and patient care. Recently, I heard of a situation where a young medical specialist who has a rather large practice and hires consulting rooms from a well-known private hospital, was told by hospital management that if he did not admit more inpatients, he would be told to vacate the consulting rooms

on short notice, and this would be 'a pure business decision'. Seemingly, the conduct of pharmaceutical companies would appear to be just one dimension of potentially scurrilous interference in medical management.

Ian Katz  
Consultant psychiatrist  
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*Professor Komesaroff, author of the article, comments:*

This letter makes a single, but important, point that the influence of the 'for profit' sector is not limited to the pharmaceutical industry. While this does not reflect on any of the specific content of my article, it is nonetheless worth drawing attention to the fact that many of the arguments and concerns do apply more widely to include other influences such as those from the biotechnology industry, the private healthcare industry and the contract research organisation sector.

### **New drugs – sitagliptin**

Editor, –The monograph about sitagliptin (Aust Prescr 2008;31:49–55) states that 'while patients with liver disease may be able to take sitagliptin, it is not recommended for patients with renal impairment'. This is presumably because just over 70% of the drug is excreted unchanged in the urine. There are, however, facts – both in the monograph itself and elsewhere – to refute the quoted statement.

First, as noted in the monograph, the drug is presented in three strengths, 25, 50 and 100 mg tablets; this is solely due to the fact that sitagliptin can be safely given to patients with renal impairment (in doses commensurate with the severity of the renal impairment). Second, both the Australian<sup>1</sup> and US<sup>2</sup> product information for sitagliptin state that, 'for patients with moderate renal insufficiency, the recommended dose is 50 mg daily, while 25 mg daily is recommended and safe for patients with severe or end-stage renal disease (including those on renal replacement therapy)'.

Use of the general phrase 'patients with renal impairment' suggests that this is a distinct and perhaps minor group of patients. It is therefore not only misleading, but clearly inaccurate. Patients with type 2 diabetes who were enrolled in the UK Prospective Diabetes Study were followed for a median of 15 years as part of one of its many sub-studies (UKPDS 74).<sup>3</sup> At the end of this period, about 40% developed albuminuria and 30% developed 'renal impairment' (with some overlap between the two groups).

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### *The Editor comments:*

The safety of using sitagliptin in patients with renal insufficiency was no doubt considered in the evaluation of the drug by the Therapeutic Goods Administration (TGA). Unfortunately, the TGA does not publish these evaluations and sometimes there can be delays in finalising the Australian product information.

It is therefore necessary to consider overseas evaluations when preparing a comment about a new drug.

Dr Lowy is correct that the product information in the USA includes doses for use in renal insufficiency, however the European Medicines Agency (EMA) took a more cautious approach. Its evaluation found that the data were too limited to confirm the safety of sitagliptin in patients with moderate to severe renal insufficiency.<sup>1</sup>

Clearly, the European, USA and Australian regulatory agencies have assessed the data in different ways. Without more transparency in the Australian system we will not know how the TGA interpreted the evidence.

To try and overcome this problem the Editor wrote to the manufacturer seeking more information about sitagliptin, before the new drug comment was published. There was no reply.

### **Reference**

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