the bulk of their revenues are not allocated to research. The lion's share goes to marketing and administration, followed closely by returns to shareholders. The US pharmaceutical industry is consistently ranked by Fortune 500 as the most profitable industry in the US, with a staggering 33% return on shareholders' equity (other Top 10 performers deliver returns of between 14% and 26%); and with profits representing a generous 18% of revenues (other Top 10 performers range from 6% to 13%).[3] Compared to these figures, research and development spending comes a poor third.[4] This is not because industry is uninterested in research, indeed, they are anxious to find the next 'blockbuster' drug. The problem is that breakthrough drugs are increasingly rare. The US Food and Drug Administration estimates that only one third of new drugs submitted to it are truly innovative, the remainder being little or no improvement on existing therapies. In the absence of a real breakthrough, the next best thing is to **make** your drug seem like a breakthrough. This explains the huge marketing budgets, the teams of drug representatives visiting general practice surgeries with glossy folders, and the pressure for direct-to-consumer advertising of new drugs (which assumes that consumers are more easily swayed than physicians).

Drug companies, desperate to maintain growth rates and profits, are increasingly turning to standard business remedies. They are cutting out 'deadwood' (low-profit drugs and research targets), focusing on proven winners (blockbuster drugs and key US, Japanese and European markets) and ensuring that governments legislate in their favour, be this regulatory agencies or trade authorities.

Understanding these corporate practices helps us understand what has gone wrong and what needs to change. We are allowing a private sector industry that has other interests at heart to set the agenda on public health. While industry clearly has a central and important role to play, it is up to health professionals and governments to ensure that issues relating to health, not just wealth, are on the table when decisions affecting drug access are made.

E-mail: mary.moran@london.msf.org

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Conflict of interest: none declared

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.

Splitting tablets

Editor, – The recent article (Aust Prescr 2002;25:133–5) 'Splitting tablets' is very useful, but one point needs clarification.

I refer to the statement: 'Tablets that are scored are usually considered by the manufacturer to be suitable for division... ' and to the reference to azathioprine (Imuran) in Table 1.

It is correct that film-coated tablets should not usually be split, but the more important reason not to split Imuran tablets is that it is a cytotoxic drug. Splitting would be likely to release small particles into the air. Strangely though, Imuran tablets are scored. Apparently, the reason for this is that the tablets which are made in just one location are marketed in many countries, and at least one of them (Germany, I think) requires ALL tablets to be scored.

Jeff Lerner
Pharmacist
Southbank, Vic.

Editor, – The article 'Splitting tablets' (Aust Prescr 2002;25:133–5) outlines practical issues on the splitting of tablets. However, it does contain one deficiency. It fails to mention the potential problem associated with the splitting of tablets containing antineoplastic drugs.

Antineoplastic drugs are potentially toxic medicines and it is essential that patients and other healthcare workers adequately understand their correct use. Many antineoplastic drugs have been found to be mutagenic, teratogenic and carcinogenic on the basis of cell DNA and chromosomal studies, animal models and, to a lesser degree, experience in treated patients. The risk associated with occupational low-level exposure has not been determined. Therefore, without evidence to the contrary, risk is assumed to be present.

Tablets and capsules of antineoplastic drugs must be handled in a manner which minimises exposure to healthy individuals. This includes avoiding skin contact and liberation of powdered drug into the air. Based on this premise, antineoplastic drugs in tablet form should not be split or crushed, and capsules should not be opened. Where required, antineoplastic mixtures should be prepared according to accepted standards.

With the increasing number of oral cytotoxic drugs available on the market, prescribers and consumers must be made aware of the potential dangers, albeit small, in splitting these tablets.

Jim Siderov
Senior Pharmacist, Cancer Services
Pharmacy Department
Austin & Repatriation Medical Centre
Heidelberg, Vic.

Dr J.L. Marriott and Professor R.L. Nation, the authors of the article, comment:

We thank the correspondents for their useful comments on our article. They are correct in suggesting that tablets containing antineoplastic drugs should not be split. To the best of our knowledge, all but one of the antineoplastic drugs available as tablets are marketed as unscored tablets; the one exception is the 50 mg strength of azathioprine tablet available under three brand names (Azuman, Imuran and Thioprine). In this case, it should not be necessary to even contemplate splitting a tablet as a 25 mg strength tablet is available from one of the manufacturers (Imuran). The 25 mg tablet is unscored and, as with other tablets of this type, should not be split.

Editor, – 'Splitting tablets' (Aust Prescr 2002;25:133–5) was a thought-provoking article on a subject that is not usually given much consideration by either practitioners or patients. I would like to add the following few comments on this topic.

1. In circumstances where the splitting of tablets is permissible, cost benefit improves the patient's compliance. A tablet of double strength may offer a 5–15% cost saving compared to half its strength (although this will vary between countries and products). This not only gives a psychological boost to the cost-conscious patient, but also gives a cumulative benefit for chronic diseases like hypertension and diabetes mellitus because of the increased compliance. Further, a patient when asked to take half of a tablet sometimes feels more secure than with a full tablet.
2. Digoxin has been cited as one of the examples for uneven breaking of a tablet that may lead to clinically significant fluctuations. Any fluctuation in the steady state plasma concentration usually requires nearly five half-lives. Digoxin, despite being a drug with a narrow therapeutic index, is far less likely to fluctuate in a significant manner even if the splitting of the tablet is uneven (even if it happens on a daily basis), because of its long half-life.
3. The article could also have suggested that patients should be warned not to consume split tablets which are altered in colour, consistency and contour because of the risk of adverse effects or ineffectiveness.

G. Sivagnanam
Additional Professor of Pharmacology
Chengalpattu Medical College
Chengalpattu
Tamilnadu
India

Off-label promotion and prescribing of gabapentin

Editor, – We write to take issue with the article 'Gabapentin documents raise concerns about off-label promotion and prescribing' (Aust Prescr 2003;26:18–9) and the associated editorial comment. Statements in the article are unfounded and are not relevant to the promotion of gabapentin by Pfizer in Australia, which has always been in accordance with the terms of its registration and the Medicines Australia Code of Conduct.

The use of gabapentin for the treatment of neuropathic pain was approved by the Therapeutic Goods Administration (TGA) in 2000. It is therefore not surprising, as the author notes, that there is an 'increasing use' of this drug for this purpose. Use of a simple comparison of sales trends for gabapentin, lamotrigine and vigabatrin to argue that gabapentin is being promoted inappropriately is misleading. Lamotrigine is subject to a boxed safety warning, and concerns about well-documented adverse effects on visual fields may have directed prescribers away from vigabatrin.

The Cochrane Collaboration[1] may have found 'surprisingly few trials' supporting anticonvulsant use in the treatment of chronic pain. However, the two studies involving gabapentin[2,3] were pivotal in nature and provided the basis for the TGA's approval after evaluation. Three subsequent randomised controlled studies[4,5,6] – the last an independent study not sponsored by the manufacturer – have confirmed the effectiveness of gabapentin in the treatment of neuropathic pain in a wide range of diseases. In light of this, it would be more accurate to say that there is scant evidence of anticonvulsants, **other than** gabapentin (i.e. conventional anticonvulsants), being effective in chronic pain.

In summary, gabapentin has now been shown in five well-designed and published studies of 1095 patients to be effective and acceptably safe for the treatment of neuropathic pain.

While not promoting the use of gabapentin in unapproved indications, Pfizer maintains the right to respond in a professional and balanced manner to doctors' questions about unregistered uses of gabapentin or any other product, allowing doctors to observe the 'extra imperative to carefully weigh the potential benefits and harms involved, and to ensure these are openly canvassed, where possible and appropriate, with patients and their families'.[7] It is then the doctor's prerogative to decide whether gabapentin should be used in such conditions.

William Lam
Medical Director, Neurosciences
Medical Department
Pfizer Australia
West Ryde, NSW

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Complementary medicine interactions

Editor, – I refer to the articles 'It's natural so it must be safe' and 'Interactions between complementary medicines and warfarin' (Aust Prescr 2002;25:50–1, 54–6). I would like to draw your attention to the finding that patients may be using complementary medicine while they are in hospital.

A three-week study in a Sydney hospital found that 61 (12%) of the 511 patients, who had their medication history recorded by a clinical pharmacist, were taking a total of 156 complementary medicines (including vitamins). A high proportion (47%) of the complementary medicines had been self prescribed and 25 (41%) patients were taking complementary medicines without the knowledge of their general practitioner. After admission to hospital 22 (36%) patients continued taking 47 different complementary medicines, but only half of these complementary medicines were recorded in the patients' charts.[1]

Eleven (18%) patients were taking drugs which could potentially interact with the complementary medicines they were taking. Six patients were taking more than one potentially interacting complementary medicine. The use of complementary medicines is significant and warrants routine inclusion in the patient medication histories. Information about potential interactions can be obtained from clinical pharmacists, drug information centres and the Therapeutic Advice and Information Service of the National Prescribing Service.

Susan Welch
Clinical Pharmacist
St Vincent's Public Hospital
Sydney

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Compliance in urban Aboriginal children

Editor, – Australian Aboriginal children experience the highest rates of bacterial respiratory diseases reported in the literature and often have poor treatment outcomes.[1]

Many tribal Aborigines are now sending their children to schools in capital cities. The children are set up in accommodation, often without adult supervision. Volunteers assist in everyday activities including attempting to oversee nutritional and medication needs.

These children are at risk of being unable to take their medications. In their home environment, they are used to having any medications given to them directly by bush health professionals.

In the urban situation, a child from a tribal environment who is prescribed an antibiotic to be taken three times daily for a number of days is just not going to do it. It has been the experience of volunteers who visit these children that unless they are there to give the medication, it is not going to be taken. Taking medicines themselves is just not part of the children's culture.

My plea would be to all prescribers to attempt to think of **once-daily** alternatives to multiple daily doses. Additionally, pharmacists dispensing for these children should be aware of limitations under which the volunteers operate and a discreet telephone call to the prescriber might be in order.

Associate Professor Louis Roller
Department of Pharmacy Practice
Monash University
Melbourne

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Recommendations for warfarin in Victorian public hospitals

Editor, – There are currently two brands of warfarin available in Australia (Marevan and Coumadin), both manufactured by the Boots Company. These brands have not been demonstrated to be bioequivalent.[1] There is no clinical justification for both products, and availability contributes to potential medication errors and confusion for patients and carers.[2,3,4]

The problem has been considered by the Melbourne Teaching Hospitals' Drug Usage Group (MTHDUG). This consists of 11 member hospitals and 19 associate member hospitals and is an affiliate of the Victorian Drug Usage Advisory Committee.

MTHDUG approached the manufacturer in early 2001 suggesting that consideration be given to phasing out one of the brands, however it has been reluctant to do so. Consequently, MTHDUG after communication and feedback from key stakeholders with an interest in the monitoring and prescribing of warfarin has made the following recommendations:

1. that Coumadin, the more widely used brand, be the primary brand of warfarin to be stocked and prescribed in Victorian hospitals;
2. that Marevan will be supplied only if specifically requested for a particular patient.

The impact of this strategy will be limited initially to patients commencing warfarin therapy in public hospitals. It is hoped that other institutions and individual doctors who also start warfarin therapy will also consider only prescribing Coumadin. Substitution of Coumadin in patients whose INR is stable on Marevan will require close monitoring.

MTHDUG is notifying community pharmacists and general practitioners about the recommendations through a range of professional forums and publications. Assessment of the impact of these recommendations will be ongoing.

Michael Dooley
Chairman
Melbourne Teaching Hospitals' Drug Usage Group
Carlton, Vic.

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