will be prevented or delayed in reaching the Australian market. The Australian pharmaceutical market is a competitive one and 'if a company decides not to launch a particular product in Australia, then competitors' products come in'.[4] If there is no competitor then it is possible that a sole manufacturer may decide not to introduce a new product to the Australian market. It is a commercial decision. If cost recovery fees alone swing the manufacturer's net present value calculation of a new drug from a decision to submit (to the Therapeutic Goods Administration (TGA) and subsequently to PBAC) to 'not submit', then the case for registration and PBS listing is likely to have been marginal in the first place.

Another concern is that cost recovery may compromise the independence of the PBAC, because it will be paid by the drug companies. This fear appears to be unfounded because the PBAC has no direct pecuniary interest in the process. All the income from cost recovery fees goes into consolidated revenue rather than to the PBAC itself. Neither the Department of Health and Ageing nor the PBAC would actually see any of the 'cost recovery' funds. Historically the PBAC has shown itself to be strongly independent. Since 1998–99 the TGA has operated on a full cost recovery basis. I have not seen evidence to suggest that the TGA has been compromised by the introduction of cost recovery.

It is fair to say that a lot of effort has gone into making the PBAC process more transparent and responsive to the needs of drug companies and this preceded the introduction of cost recovery. The industry's expectations of the process may increase as a result of the new fees, with an understandable desire for quicker turnaround of PBAC submissions. Time will tell how the PBAC responds to the concurrent demands of meeting their legislative requirements and managing what is the inherently adversarial nature of negotiating drug prices.

Of course there are instances when the imposition of the cost recovery fee is not in the public interest. Under the National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009[2] an exemption may be granted in respect of orphan drugs, the temporary supply of drugs or changes to an existing PBS listing. A fee waiver may be granted if 'the application involves the public interest and payment of the fee would make the application financially unviable'. This may apply when the patient population is not large enough to make the application financially viable, the product is to be used for palliative care or as a paediatric medicine, or for treatment of Aboriginal or Torres Strait Islander people.

For any change in policy it pays to be vigilant and monitor any unintended consequences. If experience is anything to go by, the PBAC process will survive. Numerous reviews and a few detractors have not weakened the inherent strength of a legislated process that supports evidence-based decision making.

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Professor Salkeld has received an honorarium from Pfizer for teaching a short course on 'cost-effectiveness of pharmaceuticals'.

Letters

The Editorial Executive Committee welcomes letters, which should be less than 250 words. Before a decision to publish is made, letters which refer to a published article may be sent to the author for a response. Any letter may be sent to an expert for comment. Letters are usually published together with their responses or comments in the same issue. The Editorial Executive Committee screens out discourteous, inaccurate or libellous statements and sub-edits letters before publication. The Committee's decision on publication is final.

Denosumab

Editor, – We welcome being recognised for transparency in supplying Therapeutic Goods Administration (TGA) evaluation data to *Australian Prescriber* to assist in the preparation of the new drug comment about denosumab (Prolia) (Aust Prescr 2010;33:194).

We were, however, surprised to read a statement, based on a meta-analysis[1] that 'denosumab was not associated with a significant reduction in fracture risk in postmenopausal women', despite your review having previously described a clinical trial which showed statistically significant reductions

in the incidence of vertebral, non-vertebral and hip fracture. This trial recruited 7868 patients and fractures were an independently adjudicated endpoint.[2]

The meta-analysis included three studies (996 patients in total) including a dose-ranging phase 2 study and a study in women with bone loss related to hormone ablative therapy for breast cancer (not an approved indication). Fractures were not a pre-planned outcome in any study analysed and were collected only as adverse events, neither confirmed nor independently adjudicated. Following the peer-reviewed publication of the pivotal fracture trial,[2] any reference to the meta-analysis is profoundly limited.

The omission of these limitations from the new drug comment could leave the reader with the impression that the meta-analysis included data from the trial[2] and that the statistically significant fracture outcomes were negated by the other studies in the meta-analysis.

We feel it important to highlight this so as not to mislead prescribers into believing that the TGA have granted marketing authorisation for a product that is '... not associated with a significant reduction in fracture risk in postmenopausal women'.

Cae Tolman
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Arterial blood gases

Editor, – I read with concern the article on arterial blood gases (Aust Prescr 2010;33:124-9). I believe the emphasis of arterial blood gases over venous blood gases is no longer representative of what is being taught and practised in acute care medicine.

Venous blood gases are easier to obtain, hurt less, are safer and provide extra information about tissue oxygen use that arterial blood gases do not. In combination with a pulse oximeter reading, venous blood gases can be used to guide clinical decision making in the majority of situations where arterial blood gases have previously been thought to be necessary. Venous blood gases are therefore better than arterial blood gases most of the time.

Arterial blood gases are now rarely obtained from patients in emergency departments, especially children, unless there is repeated sampling from an arterial line, usually inserted for haemodynamic monitoring. This is because venous blood gases (along with pulse oximetry) provide adequate information for the majority of acute paediatric and adult clinical scenarios, including sepsis, asthma, chronic lung disease, toxicology, diabetic ketoacidosis, and therapy adjustments for invasive and non-invasive ventilation. Reviews in the literature aim to educate that venous blood gases can replace arterial blood gases in most acute care clinical scenarios.[1,2]

Decisions involving oxygenation can be made with information from a pulse oximeter, unless there is poor waveform. Modern pulse oximeters are accurate +/– 2% down to saturations as low as 70%. Given this accuracy, it is questionable concerning the value of arterial verses venous blood gases and pulse oximetry to assess the need for domiciliary oxygen therapy.

Although local anaesthetic reduces the pain of arterial blood gases sampling without decreasing success rates, a better option is to just not do them at all.

Lindsay Bridgford
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Dr Abhishek Verma and Dr Paul Roach, authors of the article, comment:

We acknowledge that in the acute setting, sampling venous blood is sufficient to obtain information about a patient's acid–base and ventilation status. Combined with pulse oximetry, venous blood gases are useful in a variety of clinical scenarios. However, there are some important caveats. It is essential to obtain a good waveform for pulse oximetry if the result is used for estimating the oxygen saturation and partial pressure. Yet, in several acute situations – for instance, sepsis, trauma or cardiac arrest – peripheral circulation may be inadequate so it is difficult to obtain any information about potential hypoxaemia. Pulse oximetry can also be influenced by other factors, such as if the patient is vasoconstricted due to inotrope use or is excessively moving or shivering. Also when a patient presents with toxic gas exposure or carbon monoxide

poisoning, a falsely high oximetry reading may confound the recognition of severe tissue hypoxaemia. Taking an arterial blood gas sample in these instances ameliorates the problems of estimating the oxygenation entirely.

Pulse oximetry, while being a far less invasive method of determining the state of oxygenation than arterial blood gas analysis, does rely on an understanding of the physiology of the oxygen–haemoglobin disassociation curve. These are concepts that many medical students and junior doctors are not always cognisant of, and so the interpretation of oxygenation status from an arterial blood gas sample remains important.

Current Australian guidelines still require arterial blood gas analysis before domiciliary oxygen can be legally prescribed. Accordingly, the performance and interpretation of arterial blood gases remains a very important skill for a clinician.

Management of delirium in the elderly

Editor, – Thank you to Dr Caplan for the excellent and timely review of the management of delirium in the elderly (Aust Prescr 2011;34:16-8). Benzodiazepines (diazepam in particular) are the treatment of choice for delirium tremens in Australia. I would like to point out that benzodiazepines can at times be the cause of delirium.

Midazolam, diazepam, triazolam, lorazepam and clonazepam have all been reported to cause confusion, agitation, aggression and disinhibition in the very young and elderly. This is the so-called 'paradoxical reaction' from benzodiazepines.

Paradoxical reaction has been reported as a rare condition in the normal population. However, past reports suggest that its incidence is significant in certain populations such as intensive care patients and postoperative elderly patients, particularly elderly people with risk factors for delirium, as pointed out by Dr Caplan.

I have encountered a number of elderly patients given diazepam for alcohol withdrawal who have developed confusion, agitation and on rare occasions hallucination. The most severe cases are those managed by inexperienced resident medical officers who have mistaken the presentations with delirium tremens. The patients were given cumulatively large doses of diazepam as a result and their condition deteriorated further. It is a reminder to us all that the elderly can be more at risk of adverse reactions to medications, and often conservative measures as listed by Dr Caplan should be the treatment of choice.

Raymond Chan
Addiction medicine physician
Dandenong Hospital, Vic.

Dr G Caplan, author of the article, comments:

I thank Dr Chan for his kind words. There is no doubt that cumulatively large doses of benzodiazepines, as well as antipsychotics, will frequently exacerbate delirium in older patients. Dosing schedules for young patients with psychosis or delirium may act as a recipe for disaster in older patients. There is also evidence from a small randomised controlled trial in young AIDS patients that lorazepam is not an effective treatment for delirium and perhaps makes things worse. However the comparators, haloperidol and chlorpromazine, were effective,[1] as antipsychotics have been in other trials.

Because of the hazards of drug interactions and adverse effects, initial management should always focus on stopping drugs that may be aetiological.

Reference

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Therapeutic Guidelines: Oral and Dental

Editor, – Associate Professor Michael McCullough says that Therapeutic Guidelines: Oral and Dental is now available to every member of the Australian Dental Association and dental students (Aust Prescr 2010;33:167-70). Does this also apply to the foreign trained dentists who are now practising in Australia? Many of them are working in rural and remote areas with very little peer support and do not appear to be receiving education on accepted Australian therapeutic practices.

As a pharmacist involved in remote and rural and indigenous health issues, I have had many discussions with dentists who have been trained in different treatment protocols from what is accepted as best therapeutic practice in Australia. What is the Australian Dental Association doing to assist this growing number of foreign trained dentists? The professional isolation for these practitioners is of concern to both them and the pharmacists who dispense their prescriptions.

Karalyn J Huxhagen
Professional programs manager
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Associate Professor Michael McCullough comments:

The Australian Dental Association supplies the Therapeutic Guidelines: Oral and Dental to its members for free. Overseas trained dentists are strongly encouraged to join the Australian Dental Association and are treated as student members

before they are registered with the Dental Board of Australia. Overseas trained dentists must pass the Australian Dental Council exams before registration and there is a strong expectation that candidates for these exams will have thorough knowledge of the accepted best therapeutic practice for dentistry as outlined in Therapeutic Guidelines. Without full knowledge of these guidelines it would be extremely unlikely that candidates would pass these very difficult exams.

The Australian Dental Association is very concerned about all rural and remote practising dentists and in particular those trained overseas. It runs an excellent professional development program targeting remote dentists. The program is delivered via the internet as 'webinars' which are generally held in the early evening to have least disturbance to clinical practice. The most recent webinars were extremely well attended (over 70 participants). This service is free and all dentists, particularly overseas trained dentists working in remote regions of Australia where professional interaction is more difficult, should be encouraged to join the Australian Dental Association and access these services.

Book reviews

Nursing Spectrum Drug Handbook

Schull PD. New York: McGraw-Hill; 2010. 1376 pages. $48.

Nurse's Pocket Drug Guide

Barberio JA. New York: McGraw-Hill; 2010. 409 pages. $20.

***Di Crellin**, Nurse practitioner, Royal Children's Hospital, Melbourne, and Lecturer, University of Melbourne*

These books aim to provide comprehensive detail for nurses about a wide range of medications to ensure safe prescription and administration. They contain a lot of information, but it has a North American focus.

The Handbook has comprehensive details, and as a resource intended for nurses the included sections titled 'Administration', 'Patient monitoring' and 'Patient education' focus heavily on the nursing responsibilities of medication management and are a strength of the text.

The content has a section on 'Safe drug administration', which includes a range of useful resources, the majority of which will serve as a quick reference guide before administering a drug. This includes lists of drug compatibilities (for the purposes of administration), conversions and calculations, similar sounding drug names that are easily confused, tablets and capsules that should not be crushed, and the management of poisonings. Other resources included in this section may serve as an education tool rather than a quick reference, such as 'Identifying injection sites' and 'Preventing and treating extravasation'.

There are, however, some omissions in the Handbook, most notably paediatric indications and doses for a number of medications. No pharmacokinetic data are offered, which is a significant limitation of the book.

The Pocket guide presents the 'most frequently used' and 'clinically important' medications. It includes over 1000 medications so there are few significant oversights. There is also a brief section detailing some commonly used herbal medicines. There are some useful summary tables of varying preparations of the same drug (for example paracetamol), similar drugs frequently interchanged or of escalating potency or duration of action (for example steroids, insulins, local anaesthetics) and sound-alike drug names.

The value of the books is limited for Australian nurses by differing drug names, dosing schedules and different treatment practices between Australia and the USA. For example, adrenaline is referred to as epinephrine and is recommended as a treatment for asthma while salbutamol is not included in the book.

As with many pocket books the Guide is slightly larger than some handheld devices, while the content is more limited and is missing the functionality of an electronic resource. The conservation of space has resulted in some sections being difficult to follow because of the extensive use of abbreviations, symbols and brief point form. Furthermore, use of a very small font with few spaces has resulted in a very crowded looking text where detailed entries can be difficult to read. Other than price, the pocket guide is not likely to compare favourably with a handheld device.

The Handbook is supplemented with online resources which include software to download a full-text version for use on a handheld device. With increasing use of smartphones and other handheld devices, textbooks which make a version available for these media have a distinct advantage over texts which are only available in hard copy. The availability of a handheld device version may sway nurses to purchase this text over others. However, these features may not persuade those looking for an Australian reference or for more comprehensive pharmacokinetics.