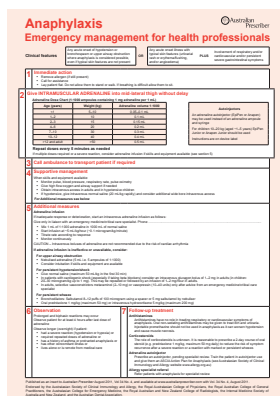


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## Anaphylaxis

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## Letters to the Editor

### Conflict of interest

Editor, – Given what we know about the effects of conflicts with the pharmaceutical industry and medical practice, it is simply no longer acceptable to have significant conflicts of interest and provide meaningful information on the benefits and harms of medicines, especially psychiatric medicines. There is a scholarly review of this issue by the co-founder of the Cochrane Collaboration and co-author of the CONSORT guidelines.<sup>1</sup>

Some articles in *Australian Prescriber* are written by authors who have received payments from the pharmaceutical industry. Your publication – and NPS MedicineWise – risks losing its stature if it continues publishing reviews by extensively conflicted authors.

**Robert Purssey**  
Psychiatrist  
Brisbane

### REFERENCE

1. Gøtzsche P. *Deadly medicines and organised crime: How big pharma has corrupted healthcare*. London: Radcliffe Health; 2013.

*The Editorial Executive Committee of Australian Prescriber comments:*

The Editorial Executive Committee thanks Dr Purssey for raising the topic of conflict of interest. This topic is of particular importance to

organisations that produce independent drug information.<sup>1</sup>

There are several ways that conflict of interest is dealt with in *Australian Prescriber*. All authors and referees are asked to declare any conflicts of interest. The members of the Editorial Committee also have to declare any conflicts of interest and they provide an annual statement of their interests to NPS MedicineWise, the publisher of *Australian Prescriber*.

The Editorial Committee does not automatically reject articles written by authors who declare a conflict of interest. Many clinicians have received support from the pharmaceutical industry to conduct clinical trials. While this may raise the risk of bias, the Editorial Committee believes this can be managed during the editorial process. All articles and editorials are peer-reviewed not only externally, but also by each member of the Editorial Committee. Usually extensive changes are made to articles submitted to *Australian Prescriber*. The Editorial Committee is confident that this process reduces the risk of the published version of a paper being biased by a conflict of interest.

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1. Therapeutic Guidelines. *Independent therapeutic advice: how achievable is it?* *Aust Prescr* 2013;36 Suppl 2.

## A

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. When letters are published, they are usually accompanied in the same issue by their responses or comments. The Committee screens out discourteous, inaccurate or libellous statements. The letters are sub-edited before publication. Authors are required to declare any conflicts of interest. The Committee's decision on publication is final.

## Postoperative pain management

Editor, – I am writing in response to the article by Dr Philip Corke (Aust Prescr 2013;36:202-5) in which he discussed practical issues to consider when prescribing perioperative analgesia. This included planning for longer-term post-discharge pain management in a succinct yet informative manner.

I am disappointed, however, that he did not deal with the disturbing trend of routine prescribing of pregabalin and oxycodone with naloxone controlled-release tablets by acute pain services in certain tertiary hospitals.

Pregabalin is currently listed on the Pharmaceutical Benefits Scheme (PBS) under authority for 'refractory neuropathic pain not controlled by other drugs' and as adjunctive therapy in adults with partial seizures. Dr Corke appears to imply that pregabalin should be used in patients having procedures with a high risk of neuropathic pain, or patients who are predisposed to chronic pain. However, in my personal experience there are many patients who have been started on pregabalin as part of a routine oral analgesic combination after patient-controlled opioid analgesia is stopped. Subsequent management (and cessation) of pregabalin is usually left to the surgical team who do not know why pregabalin was originally prescribed. If the low-risk patient is discharged with pregabalin, then it will perpetuate the myth amongst primary care providers that this drug can be used for chronic pain that is not neuropathic in nature.

There is only one brand of oxycodone in combination with naloxone in Australia. It is PBS-listed for moderate-severe chronic pain unresponsive to non-opioid analgesia. This drug is not considered in recent guidelines.<sup>1</sup> The main incentive to prescribe this drug is to avoid opioid-induced adverse effects, particularly constipation through naloxone as a competitive opioid antagonist at mu receptors in the gut wall. While the oxycodone component is believed to have bioequivalence with other single-drug sustained-release oxycodone, the naloxone component is reported to have less than 3% oral bioavailability due to significant first-pass metabolism, although naloxone, more than oxycodone, appears to be affected more in patients with renal or hepatic impairment.

NPS MedicineWise says that oxycodone with naloxone is 'not indicated for acute pain'.<sup>2</sup> However,

the product information suggests otherwise as reproduced here:

Targin tablets are not recommended for immediate pre-operative use and post-operative use for the first 24 hours after surgery. Depending on the type and extent of surgery, the anaesthetic procedure selected, other co-medication and the individual health status of the patient, the exact timing for initiating treatment with Targin tablets depends on a careful risk-benefit assessment for each individual patient.

I have also noticed an increasing trend by several hospital-based acute pain services to prescribe oxycodone with naloxone after patient-controlled analgesia is stopped, even to patients with no history of constipation. Similar to pregabalin, this off-label use is a source of dilemma for surgical teams.

The first submission of oxycodone with naloxone to the Pharmaceutical Benefits Advisory Committee was rejected on the basis of an uncertain and high cost-effectiveness ratio. Subsequent approval was only granted after revised economic modelling comparative with long-term use of oxycodone plus an over-the-counter laxative.<sup>3</sup> Therefore it is uncertain if decision making to prescribe oxycodone with naloxone for postoperative patients with low risk of constipation is based on similarly vigorous harm-benefit assessment.

**Shyan Goh**  
Locum orthopaedic surgeon  
Sydney

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## *Dr Corke, the author of the article, comments:*



Thank you for your observations on the postoperative use of pregabalin and oxycodone with naloxone.

Two recent meta-analyses of acute postoperative pain management concluded that pain intensity is not reduced by pregabalin.<sup>1,2</sup> There is a small reduction in 24-hour opioid consumption (10–15 mg). Postoperative vomiting is reduced, but this is only evident if prophylactic antiemetics are omitted.

Patients receiving pregabalin have a greater risk of developing adverse effects (visual disturbance, dizziness, sedation and headache). These effects are predictable given the relatively large doses of pregabalin required (225–300 mg) to achieve an opioid-sparing effect.

On current evidence the routine use of pregabalin for acute pain is not supported. There may however be a role for pregabalin in patients who are receiving high doses of opioids preoperatively or are at risk of severe and prolonged postoperative pain where a neuropathic component is likely, such as post-thoracotomy.<sup>3</sup>

Oxycodone with naloxone may be useful in patients with chronic pain who develop opioid-induced constipation. It is not authorised for use in the management of acute pain. Constipation associated with opioid use in acute postoperative pain is usually managed with concurrent administration of laxatives. Unlike chronic pain, the dynamic nature of acute pain often necessitates breakthrough opioid analgesia, for example during periods of mobilisation and physiotherapy. This is usually managed with the immediate-release oxycodone as needed. In patients receiving oxycodone with naloxone, this additional opioid load may overwhelm the capacity of the naloxone to reduce opioid-induced constipation. Also, patients prescribed oxycodone with naloxone may not receive prophylactic laxatives or may think they are

unnecessary and paradoxically may be at a greater risk of developing constipation.

It is likely that the increased use of oxycodone with naloxone by 'certain tertiary hospital' acute pain services relates to its reduced potential for abuse and diversion compared with slow-release oxycodone alone. The naloxone component of the combination will cause withdrawal symptoms when injected and is not favoured by intravenous drug users.<sup>4</sup>

On discharge from hospital, patients and their GPs should receive a written summary of the postoperative pain medications and the planned weaning process. Patients who are discharged on complex analgesics (high-dose opioids and/or gabapentinoids) require review within 4–6 weeks in an acute-on-chronic pain clinic. The surgical team should not be responsible for the postoperative management of complex analgesic pain medications.

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