EDITORIAL

# Off-label prescribing

**Richard Day**
Professor of Clinical Pharmacology
St Vincent's Hospital Clinical School and Pharmacology
School of Medical Sciences
Faculty of Medicine
University of New South Wales

Director
Clinical Pharmacology and Toxicology
St Vincent's Hospital
Sydney

**Key words**
Pharmaceutical Benefits Scheme, Therapeutic Goods Administration

*Aust Prescr 2013;36:182–3*

'Off-label' prescribing occurs when a drug is prescribed for an indication, a route of administration, or a patient group that is not included in the approved product information document for that drug.

Prescribing off label is unavoidable and very common, especially if your practice includes children, pregnant women or palliative care. Off-label prescribing means that the Therapeutic Goods Administration (TGA) has not approved the indication, route of administration or patient group. It does not mean that the TGA has rejected the indication. Commonly the TGA has not been asked to evaluate the indication.

There are many scenarios of off-label prescribing. Examples include meloxicam, a non-steroidal anti-inflammatory drug (NSAID), when used to treat rheumatoid arthritis in children under 18 years, or rosuvastatin, an HMGCoA reductase inhibitor (statin), for the primary prevention of cardiovascular events in a 45-year-old male with a plasma cholesterol of 6 mmol/L and without other risk factors. In the product information meloxicam is contraindicated for children, and rosuvastatin is not indicated for primary prevention in men below the age of 50 years with moderate hypercholesterolaemia and no other risk factors. In the case of meloxicam, studies have probably not been undertaken with the aim of applying to extend the indication to children. In contrast to the product information, the Australian Medicines Handbook does not list treating children with any NSAID as a contraindication or even a 'precaution'. This acknowledges that as a class NSAIDs may be used in children if attention is paid to the dose and the risk factors for adverse effects. Some NSAIDs, for example naproxen, have an indication in the product information for use in children older than two years, and ibuprofen is available over the counter, illustrating the confusion if product information alone is relied upon.

Another reason an indication is not registered is that it is uncommon. Sulfasalazine is used for peripheral joint involvement in ankylosing spondylitis, but there is no such indication or guidance in the product information. This 'current use' is listed in Therapeutic Guidelines.[1] If a drug is 'off patent' and there are a number of generic versions available, there is little motivation for the originator company or any of the generic companies to undertake studies for registering an uncommon indication. The economics simply do not warrant this course of action.

Despite the considerable use of medicines for off-label indications there is little guidance for prescribers. The product information will not include advice about unapproved indications and the drug companies are unable to promote these indications. The older the drug is, the less reliable the product information is for accepted uses of the drug. While a prescriber can ask a drug company for information about using a drug for an unapproved indication, the company needs to tread a fine line to avoid being accused of 'promoting' the indication.

Off-label prescribing does not refer to those indications that are registered by the TGA but not subsidised by the Pharmaceutical Benefits Scheme (PBS). A reasonably common reason for the indication not to be subsidised by the PBS is that the company might not have applied for a subsidy or not reached agreement about the price of the drug. A recent example was gabapentin, a second-line antiepileptic drug with some effect in neuropathic pain. That indication was never subsidised on the PBS, so patients with neuropathic pain had to pay a high price for a month's supply on private prescription unless it was provided through a public hospital. Similarly, disulfiram, prescribed to support abstinence from alcohol in selected patients, is registered by the TGA for this indication. It can only be prescribed

## From the Editor

Information about new drugs is an important part of *Australian Prescriber*. We aim to publish this information on the internet as soon as the drug is marketed, and subsequently in print. Although there are five new drugs in this issue, you can find information about other drugs scheduled for release this month at australianprescriber.com.

The internet can provide therapy as well as information. Lisa Lampe includes some of the available online resources in her review of the treatment of anxiety.

Patients are likely to be anxious about having surgery. Anxiety can increase postoperative pain and Philip Corke explains the importance of effective analgesic management. This is an example of the patient-centred prescribing discussed by Andrew Knight. Vasi Naganathan would agree that tailoring therapy to the individual is important when using cardiovascular drugs in older people.

Individualised therapy may be facilitated by increased understanding of a patient's genetics. Aidan McElduff describes some of the genetic changes which contribute to diabetes.

The number of genetically engineered drugs is increasing. Biological therapies are expensive so they are starting to appear in our annual list of Top 10 drugs.

privately in the community as it is not listed on the PBS. This makes it difficult for many patients with alcohol dependency to afford the treatment. Other drugs with a similar indication, such as naltrexone and acamprosate, are listed on the PBS but are very much more expensive to the taxpayer. Some patients are disadvantaged by not having access to a cheaper alternative treatment for alcohol dependency.[2]

If the drug is listed on the PBS with a 'restriction' or a requirement to gain an 'authority', the drug cannot be prescribed or subsidised for a non-PBS listed indication.

There is no legal impediment to prescribing off label, however the onus is on the prescriber to defend their prescription for an indication that is not listed in the product information. If, in the opinion of the prescriber, the off-label prescription can be supported by reasonable quality evidence, for example the indication is identified in the Australian Medicines Handbook, the prescriber should proceed if this is in the patient's best interests.

It is best if your patient knows that their prescription is off label, and why you are recommending the drug. Making a note of this 'conversation' in the patient's records and possibly even recording that the patient 'consented' would be good practice (guidance on approaches to gaining consent for off-label prescribing has recently become available).[3,4] The more uncommon the indication for prescribing the drug, the more important it is that the patient understands and accepts the rationale for your prescription. This approach is not different from what should ideally be done for the prescription of any drug. However, the rationale for an off-label prescription might be subject to more scrutiny in the case of a serious adverse event. This conversation with the patient also helps when the patient cannot find information about the indication in the Consumer Medicines Information (CMI), which is the approved drug information for consumers. You can warn the patient about its absence as many patients will be concerned that 'their' indication is not in the CMI.

**the onus is on the prescriber to defend an off-label prescription**

It is important to know when you are prescribing off label and it is good that your patients know and understand why. Having evidence or information from the Australian Medicines Handbook, Therapeutic Guidelines or NPS MedicineWise that supports your prescribing decision is very desirable. ◀

*Conflict of interest: none declared*

## REFERENCES

1. eTG complete [internet]. Melbourne: Therapeutic Guidelines Limited; 2013 Mar. www.tg.org.au/index.php?sectionid=71 [cited 2013 Nov 7]
2. Lipworth WL, Wodak AD, Haber PS, Day RO. Why is disulfiram not on the PBS? Med J Aust 2011;195:371-2.
3. Gazarian M, Kelly M, McPhee JR, Graudins LV, Ward RL, Campbell TJ. Off-label use of medicines: consensus recommendations for evaluating appropriateness. Med J Aust 2006;185:544-8.
4. The Council of Australian Therapeutic Advisory Groups. Rethinking medicines decision-making in Australian hospitals: Guiding principles for the quality use of off-label medicines. www.catag.org.au [cited 2013 Nov 20]

## Online first – publishing between issues of *Australian Prescriber*

*Australian Prescriber* is published every two months, in print and online. However, new drugs can become available at any time. We aim to publish information about these drugs as soon as possible at **australianprescriber.com**. We may also publish topical articles here. Online first content will then be incorporated into the next issue of the journal.

From this month, we will send additional e-alerts with links to Online First content. To receive these updates, make sure you are subscribed to an e-alert by visiting **australianprescriber.com/contact_us/mailing_list#email_alert**

You can also follow @AustPrescriber on Twitter.