Hypnosedative access and risk of harm

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Abstract

Aim To review PHARMAC’s decision, effective 1 September 2010, to remove the 1-month restriction on funded prescription of hypnotics and anxiolytics.

Method We consider the evidence for an association between access to these medicines and risk of harm.

Results Prescription volumes and reported harms have both increased over the last decade in New Zealand; available studies and clinical experience suggest a causal link. Preliminary data collected since PHARMAC’s funding change suggest an exacerbation of the problem.

Conclusion The decision to relax funding restrictions on hypnosedatives is expected to increase drug-related harms in a sub-population of users. Improved pharmacovigilance could inform policy regarding these agents.

Based on a recommendation from the Pharmacology and Therapeutics Advisory Committee (PTAC), the New Zealand drugs purchasing agency PHARMAC has decided to lift a longstanding funding restriction on hypnotics and anxiolytics. As of 1 September 2010, the 1-month reimbursement limit per prescription was lifted to 3 months, in accord with most other funded medicines.¹

As is customary for its funding and access decisions, PHARMAC invited submissions on this proposed policy change. The Royal Australian and New Zealand College of Psychiatrists, together with a number of addiction specialists, expressed concern that removal of the monthly funding restriction would likely increase the availability, overuse, and abuse of these compounds. However realistic these concerns might have been, PHARMAC decided to proceed with the change anyway.

PHARMAC’s reasons for lifting the reimbursement restriction include bringing funding policy in line with prescribing regulations, as determined by the New Zealand government’s drugs regulator MedSafe, which has always allowed 3-month prescriptions but required monthly dispensing of the Class C medicines in question.

PHARMAC’s argument is technically correct, but seems to disregard the valuable role that its historical funding restriction has played in prompting regular clinical review and thereby arguably limiting supply and overuse of these drugs. While it is uncertain how much drug-related harm this ‘anomalous’ policy may have prevented over the years, it seems plausible that harms are set to increase with the new, easier access to these medicines.

Overseas evidence indicates that prescribing restrictions can dramatically reduce benzodiazepine supply and related problems² but there is as yet little direct evidence that relaxing restrictions has the opposite effect. Moreover, PTAC and others have
argued that PHARMAC’s historical reimbursement restriction has in some cases compromised the ability of competent prescribers to use these drugs effectively.

Benzodiazepines are class C5 controlled drugs in New Zealand ([www.medsafe.govt.nz/profs/class/classification.asp](http://www.medsafe.govt.nz/profs/class/classification.asp)), with common adverse effects including psychomotor and cognitive impairment and corresponding risk of accidents and falls.3–5

Less common but serious side-effects include mood disorder, disinhibition, suicide and violence, particularly in combination with alcohol or other central nervous system depressants.6–8 Because of a tendency to induce pharmacodynamic tolerance, their effectiveness as hypnotics and anxiolytics wanes with repeated administration and longer-term use is generally contraindicated.9

Tolerance to benzodiazepines, together with a euphoriant effect in many individuals, confers further risks in terms of abuse and dependence.10–13 These problems extend to clonazepam and clobazam, used mainly as anticonvulsants, and to the chemically distinct benzodiazepine agonist zopiclone14,15 but not to buspirone, which is marketed as an anxiolytic but has no street value or abuse potential.16,17

Outcome studies indicate an increased risk of inappropriate benzodiazepine use and of adverse outcomes when prescribing is not regularly reviewed; this appears particularly important during the first 4–6 weeks after initiation.18–21 Prescribing guidelines in many countries, including NZ, recommend short term prescribing wherever possible; the decision to continue beyond 2–4 weeks should be well documented and reviewed at regular intervals.20,22–26

From 2002 to 2010, PHARMAC data indicate that prescriptions for hypnosedatives have increased steadily—an average of 7% annually, with comparable increases in the anxiolytic and hypnotic subgroups (5.5% and 8.0% respectively). The overall growth in prescription volume is driven largely by two agents: zopiclone (13.4% average annual increase) and lorazepam (9.4% increase). Zopiclone is now by far the most frequently prescribed hypnotic in New Zealand with over 560,000 prescriptions during the year ending June 2010. What effect have these increases had on rates of problems and what further effect might be expected from PHARMAC’s reimbursement policy change?

Unfortunately, existing pharmacovigilance systems in New Zealand are fragmented and do not allow reliable and comprehensive detection of such harms. One opportunity for ‘joined-up’ detection, the Chemical Injury Surveillance System was launched in 2001, but has yet to be developed in this role regarding prescription medicines, and remains limited to certain regions of the country. As a consequence, the best available current indices are indirect, notably notifications to the National Poisons Centre ([www.poisons.co.nz/](http://www.poisons.co.nz/)); these provide a limited index of one set of harms that can result from prescription of hypnosedatives.

Other important categories of harm, notably cases presenting to hospitals, are inconsistently recorded and very few notified to the Poisons Centre or the Centre for Adverse Reactions monitoring ([http://carm.otago.ac.nz/](http://carm.otago.ac.nz/)). Referrals to alcohol and drug services also provide an indication of problems, but because of regional variation in funding and access cannot be used to estimate problem rates, let alone changes in these over time.
Even though an underestimate of overall harms, Poisons Centre notifications thus provide an important index of prescription drug problems across New Zealand. Calls to the Centre are carefully recorded and can be analyzed by drug, intent, age, and other variables. In addition to self-poisoning, these include non-intentional events including the important and frequent category ‘child exploratory’.

With regard to hypnosedatives, the data indicate an upward trend since 2002 for both anxiolytic and hypnotic subgroups, with average annual increases of 8.9% and 7.2% respectively. It is notable that these figures are of the same magnitude and appear to parallel the growth in prescription volumes described above. Over the seven years to 30 June 2009, a total of 2707 calls related to hypnosedative drugs were recorded by the Poisons Centre; during the same period 5,919,693 prescriptions were recorded. The overall crude rate of 45.7 notifications per 100,000 prescriptions is similar for anxiolytics (47.3) and hypnotics (45.1).

More compelling from the standpoint of causality is the observation of a similar rank order of drugs with regard to prescription volume and poisoning notifications (zopiclone followed by lorazepam and diazepam).

In summary, available data indicate a continuing rise in both hypnosedative prescribing and one set of drug-related harms in New Zealand. The parallel growth in these two measures strongly suggests, but does not prove, a causal link between them. Nonetheless, such a link is plausible, in line with available research, and consistent with clinical experience here and overseas.

In light of this, PHARMAC’s decision to lift the 1-month funding restriction for these drugs seems likely to aggravate an already serious set of problems. Funded repeat prescriptions beyond 1 month inevitably means that clinical review is less likely to occur, and ongoing supply correspondingly more likely. Preliminary trends observed since PHARMAC’s policy adjustment include, for example, no change in the continuing 8–10% annual increase in the number of patients prescribed zopiclone (183,000 in the year ending 30 June 2011) but a rather larger 18% jump in the number of subsidised tablets dispensed (20,232,000) [N.B. the latter figure over-estimates actual supply increases since an unknown number of patients had previously paid for repeats that would not be counted in PHARMAC data prior to September 2010]. More worrying is a corresponding 25% increase (from 210 to 263) in Poison Centre notifications regarding zopiclone over 12 months since the change.

A further increase in problems can be expected, especially in the surprisingly large group with mental disorder and a comorbid tendency to substance misuse. These individuals both supply and consume hypnosedatives available ‘on the street’, and it can reasonably be expected that illicit New Zealand supplies—already identified as a problem—will grow as a consequence of PHARMAC’s funding change. Further difficulty is particularly anticipated from patients who obtain prescriptions from more than one doctor.

PHARMAC has made it clear that its reimbursement policy has now been brought into line with Medsafe’s prescribing regulations for hypnosedatives, and it is up to the latter authority to review and amend these as required. The question then becomes: how much evidence of harm will Medsafe require to do this? Unfortunately, available
pharmacovigilance systems are insufficient to fully define the extent of the problem and its expected escalation with the recent change in funding policy.

Should Medsafe develop vigilance systems and await definitive evidence, or act now on the limited signals available? The fact that 3 months’ funded supply of hypnosedatives is now available from a single prescription constitutes, we believe, an unnecessary and avoidable risk to public health.

Competing interests: None.

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