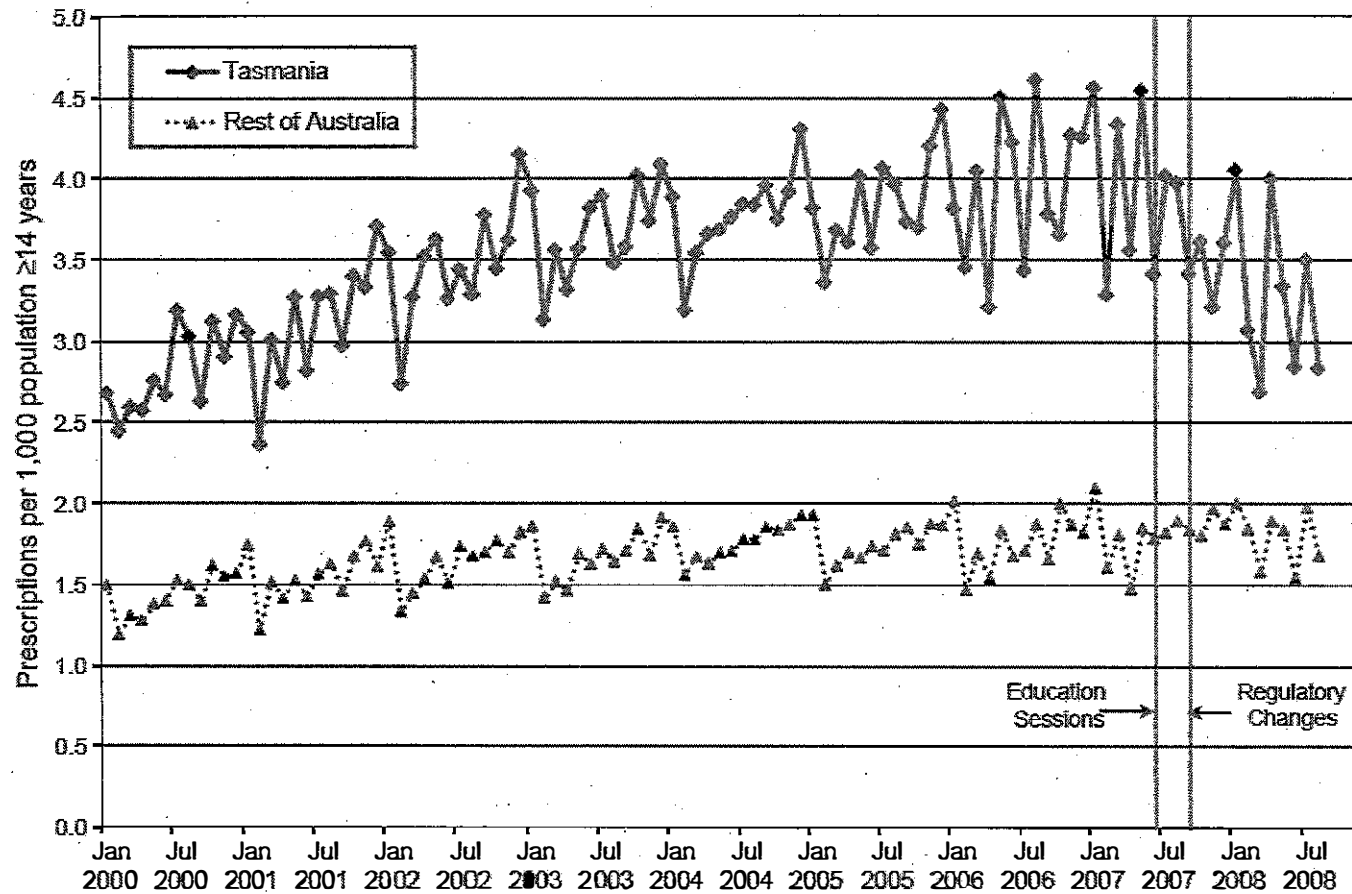


# Australian regulatory and other responses: Tasmania 2007

health



**Figure 1: Population-adjusted PBS and RPBS prescription rates for Tasmania and Australia, 2000–2008.**

Hooper S et al. Alprazolam prescribing in Tasmania: a two-fold intervention designed to reduce inappropriate prescribing and concomitant opiate prescription. *Australasian Psychiatry* 2009;17:

# Australian regulatory and other responses: Victoria 2009

health

Medical Practitioners Board of Victoria

Protecting patients, guiding doctors



## Warning: Alprazolam (Xanax, Kalma, Zamhexsal)

Bulletin  
June 09

Volume 2

→ Alprazolam Abuse

→ National Registration Updates

→ Hearing Summaries

### President's Message

From time to time the Board is required to consider suspending a medical practitioner's registration before any evidence has been tested at a hearing and sometimes before there has been a comprehensive investigation. This is one of the most onerous but important tasks for the Board in terms of balancing its primary responsibility to protect the public with the need to ensure the doctor in question is treated fairly and afforded natural justice.

In these circumstances, the Board can only consider suspending a doctor's registration if it believes, on the basis of the available information, that there is a serious risk to the health and safety of the public if the doctor continues to practice. The perceived risk can be based on concern about the doctor's health, their professional performance or their professional conduct.

Instead of suspending a doctor's registration the Board can, after receiving submissions in person or in writing from the doctor, decide to enter into an agreement with the doctor to alter the way he or she practices medicine. This can only happen if the Board is of the opinion that it is necessary to do so because there is a serious risk to the health and safety of the public if the doctor continues to practice without such restrictions. The Board only takes this action – which is an alternative to suspension – if it is confident that the agreement with the doctor reduces the risk of his or her ongoing practice.

The decision to suspend a doctor's registration or to enter into an agreement is not a "finding of guilt", but is the result of an assessment of risk. After making such a decision, the onus is on the Board to investigate the matter and, when indicated, raise the matter to a hearing at the Victorian Civil and Administrative Tribunal (VCAT) as soon as possible.

The Board's power in relation to suspension is set out in detail in the Health Professions Registration Act 2008. These considerations are completely separate from the powers of formal hearing panels and VCAT to determine to suspend the registration of a medical practitioner after an adverse finding has been made at a hearing.

The Board takes its responsibilities very seriously and works hard to ensure that the public is protected. However, no matter is more carefully considered or subjected to more exhaustive analysis if the available information from when the Board is considering suspending a doctor's registration →

*This item has been prepared by the Department of Human Services.*

Recent evidence suggests that alprazolam is more subject to non-medical use, and causes a disproportionately higher level of serious harm, than other benzodiazepines.

Alprazolam is a drug with particularly high potency and short onset of action, which makes it a preferred drug for recreational abuse. As with other benzodiazepines, inappropriately high doses can cause antegrade amnesia. Anecdotal reports suggest that among the benzodiazepines, non-medical use is particularly associated with harmful experiences such as seizures, traffic accidents and crime-related harm.

Alprazolam is now the most commonly reported benzodiazepine among Australian injecting drug users who report injection of benzodiazepines.

Many witnesses giving evidence to the Victorian Drugs and Crime Prevention Committee's inquiry into Benzodiazepines and other Pharmaceutical Drugs in Victoria expressed concern that alprazolam, when used for recreational purposes, can be particularly dangerous. They commented on its highly addictive qualities. The Senior

Pharmacist at Turning Point Alcohol and Drug Centre commented that for the drug-using population, alprazolam provides the effect they want. Others commented that alprazolam appears to feature more prominently in crime-related activity such as diversion and theft.

The Pharmacy Board of Victoria stated that it was not uncommon for alprazolam (Xanax) tablets (100) to be prescribed and dispensed as private (non-PBS) prescriptions and then on-sold on the street for \$6 per tablet.

The Victorian Inter-hospital Liaison Group expressed concern that alprazolam is one of the most widely abused of the benzodiazepines and that management of withdrawal was particularly difficult.

Most recently, emerging reports from several Needle Syringe Programs (NSPs) describe the effects of high-dose non-medical use of alprazolam by their clients causing problems of anger and aggression, as well as violent and threatening behaviour, which the users do not remember the next day. During these episodes it is not possible to reason with or calm individuals. Alprazolam tablets are also known as 'angry pills'. Some NSPs report that people affected by high doses will commit crimes such as shoplifting but will be unaware of their surroundings.

When they recover in the police cells they do not remember the actions that led to their arrest. When intoxicated they appear to be more at risk of either committing or being the subject of violence, as well as of falls and other injury as a result of intoxication.

There has been particular concern in Tasmania about prescribing and non-medical use of alprazolam. A circular to pharmacists in that state noted that serious injury and death has resulted from the practice of injecting alprazolam alone, or with other drugs, to produce a 'hamster high'.

Alprazolam should only be prescribed when there is a clear indication for its use, after taking into account the risks to the patient and the burden of harm to the community.

The recommendation of the Royal Australian and New Zealand College of Psychiatrists (RANZCP) is that alprazolam has a limited role in the treatment of panic disorder and anxiety. The initial approach should be psychological measures, such as cognitive behavioural therapy. First line drug therapy for panic disorder is stated to be the newer antidepressants, particularly paroxetine and sertraline. Benzodiazepines are listed as second line therapy along with cycloidal anti-epileptics and the MAOIs. This approach is supported by the PBS approval, which is 'for the treatment of panic disorders where other treatments have failed or are inappropriate'.

# Australian regulatory and other responses: Northern Territory 2010

health



DEPARTMENT OF HEALTH AND FAMILIES

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TO ALL NT GENERAL PRACTITIONERS & PSYCHIATRISTS

Dear Doctor,

Re: ALPRAZOLAM AND BENZODIAZEPINE PRESCRIBING

I am writing to you to address a situation of mounting concern in the Northern Territory.

Over the past year, we have seen several people admitted to hospital with severe ischaemic limb damage and disability associated with injecting alprazolam. We are also seeing an increase in other problems associated with inappropriate oral use as well as injecting.

As well, there is growing concern nationally about the escalating harms associated with abuse of benzodiazepines generally, in particular alprazolam, and the need to exercise great care in prescribing.

This is documented in the August edition of the Australian Journal of Family Practice (AJFP) by Monheit *"Currently, alprazolam and oxycodone are the most abused drugs in Australia"*  
<http://www.racgp.org.au/ajfp/201008/201008monheit.pdf>

In June 2009, the Bulletin of the Medical Practitioners Board of Victoria warned doctors that *"Recent evidence suggests that alprazolam is more subject to non-medical use and causes a disproportionately higher level of serious harm, than other benzodiazepines"*. It documents the associated anger and aggression, violent and threatening behaviours, death and serious injury for the user, as well as criminal activity.

I have attached a copy of this Warning, plus a 2007 Tasmanian Health Department advisory ALPRAZOLAM PRESCRIBING GUIDELINES endorsed by RACGP and RANZCP.  
[http://www.dhhs.tas.gov.au/data/assets/pdf\\_file/0020/46514/Alprazolam\\_prescribing\\_guidelines.pdf](http://www.dhhs.tas.gov.au/data/assets/pdf_file/0020/46514/Alprazolam_prescribing_guidelines.pdf)

These Guidelines do NOT support prescribing alprazolam for patients with anxiety other than panic disorder, which is to be distinguished from panic attacks, panic disorder being uncommon.

Alprazolam is NOT considered a first line treatment when patients do suffer from panic disorder. First line pharmacological drugs are newer antidepressants particularly paroxetine and sertraline. An initial approach to panic disorder prophylaxis should include Cognitive Behaviour Therapy (CBT). Some patients who initially cannot use CBT should be commenced on first line pharmacological drugs.

Further, they warn about the particular hazards when there is concurrent use of opiates, including the risk of fatal overdose, and advise that patients with drug abuse should be referred to an Alcohol & Drug specialist/service.

Like the incidents documented in the Victorian document, patients in the NT have presented with acute memory blanks, confused and unable to recall the events of 1 or 2 days, the quantity of alprazolam they have used, their concomitant drug use, and unable to believe that they have "lost a couple of days of my life".

Department of Health

# Australian regulatory and other responses: South Australia 2011

health

## Drugs of Dependence Unit

### Alprazolam prescribing

#### A resource for South Australian prescribers

This resource assists medical practitioners to:

- > Critically examine the need for prescribing alprazolam in their medical practice.
- > Become familiar with current concerns with alprazolam abuse amongst vulnerable populations.
- > Identify risk factors that should trigger patient referral to specialist services.
- > Seek help from regulatory and clinical information sources if requested to prescribe alprazolam.

#### Introduction

Alprazolam is a cold-cold, short-acting benzodiazepine indicated for treatment of anxiety disorders and panic attacks. Ideally alprazolam should be prescribed for short periods, such as two to four weeks. In South Australia alprazolam abuse, especially in drug dependent populations is being reported more frequently. This is similar to other Australian jurisdictions. Large pack sizes and a sought-after pharmacological profile makes alprazolam the benzodiazepine of choice amongst drug dependent populations.

#### Concerns with prescribing alprazolam

Significant consequences for both patient and prescriber may flow from alprazolam abuse. In the worst cases, excessive doses of alprazolam alone or in combination with other benzodiazepines, opioids, or alcohol may result in death. Other concerns include:

- > Initiation or maintenance of benzodiazepine dependence
- > Interference with opioid pharmacotherapy treatment
- > Risk of severe benzodiazepine withdrawal syndrome and seizures
- > Increased risk of motor vehicle accidents (whether as driver or pedestrian).

For prescribers, concerns include the prescriber:

- > becoming known amongst drug-dependent populations as an alprazolam 'script doctor'
- > contributing to the already substantial black trade in pharmaceutical drugs
- > placing themselves at professional, civil, or criminal risk for prescribing to known dependent persons.



Department of Health

# National Pharmaceutical Drug Misuse Strategy

Department of Health

health

## Pharmaceutical drug misuse problems in Australia:

Complex issues, balanced responses

Roger Nicholas  
Nicole Lee  
Ann Roche



Department of Health

## BRIEF COMMUNICATION

## The use of alprazolam by people who inject drugs in Melbourne, Australia

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## Abstract

**Introduction and Aims.** In Australia, people who inject drugs (PWID) commonly report the use of benzodiazepines (BZDs). This paper explores the emerging use of alprazolam among PWID in Melbourne, Australia. **Design and Methods.** This study reports on 3 years of data collected through the Victorian Illicit Drug Reporting System (2008–2010). Structured interviews were conducted with 451 PWID and analysed using odds ratios and  $\chi^2$ -tests for trends over time. **Results.** While the proportion of PWID reporting recent BZD use remained stable over time, the proportion reporting alprazolam to be their most commonly used BZD fluctuated, peaking in 2009. Alprazolam users were significantly more likely to report using illicit BZDs and to report recent BZD injection compared with users of other BZDs. Alprazolam use was associated with the sale of drugs for cash, but not with other criminal activities. **Discussion and Conclusion.** The fluctuations in alprazolam use over time may be reflective of medical practitioners ceasing to prescribe alprazolam in response to reports of associated harms; however, this may in turn be driving the illicit alprazolam market. While the data do not indicate a clear association between alprazolam use and harms, considering the potential severity of associated harms and the association between alprazolam use and anterograde amnesia, patterns of alprazolam use among PWID should be closely monitored. Potential changes to prescribing practice should consider unintended consequences, such as replacement with other BZD types, or illicitly obtained BZDs. [Horyniak D, Reddel S, Quinn B, Dietze P. The use of alprazolam by people who inject drugs in Melbourne, Australia. *Drug Alcohol Rev* 2011]

**Key words:** injecting drug use, benzodiazepine, alprazolam.

## Introduction

Benzodiazepines (BZDs), predominantly used in the treatment of anxiety, are among the most widely used drug classes in the world [1–3]. Use of BZDs by people who inject drugs (PWID) has been reported in Australia [4–7] and elsewhere [8–15], presumably to achieve increased intoxication and manage drug withdrawal [16–18].

Around two-thirds of Australian PWID accessed through the Illicit Drug Reporting System (IDRS) report recent (mostly oral) BZD use, with similar pro-

portions reporting licit and illicit use [19–21]. While diazepam has been the most commonly used BZD among PWID in the IDRS samples [5,6], IDRS data in 2008 and 2009 suggested that the use of alprazolam among PWID in Melbourne may be increasing [22,23].

Alprazolam is a short-acting BZD, indicated for use in the treatment of anxiety (short-term), and panic disorders [24]. In Australia, alprazolam is recommended only for treatment of 'panic disorder where other treatments have failed or are inappropriate', with antidepressants recommended as first-line therapy [25,26]. Under the Pharmaceutical Benefits Scheme,

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authority (approval by Medicare Australia) must be obtained by medical practitioners prior to prescription of alprazolam [25].

Recently, Needle and Syringe Program staff accessed through the IDRS in Melbourne have reported increasing antisocial behaviour, particularly opportunistic criminal activity, believed to be associated with alprazolam use [22]. Clinical studies have shown alprazolam to be associated with drug-induced anterograde amnesia (the inability to create new memories after drug consumption, with no effect on recall of prior events) and aggressive behaviour [27–33], which may be related to reports of antisocial behaviour.

These findings prompted the Medical Practitioner's Board of Victoria (MPBV) to issue a warning in June 2009 to all registered practitioners in the state that 'alprazolam is more subject to non-medical use, and causes a disproportionately high level of serious harm, than other benzodiazepines', recommending that 'alprazolam should only be prescribed where there is a clear indication for its use' [34].

In this study, we examined 3 years of drug user survey data from the IDRS to describe patterns of alprazolam use and associated harms among PWID in Melbourne, Australia, in the context of publicly available prescribing data.

## Methods

### *Illicit Drug Reporting System*

IDRS methodology has been described in detail elsewhere [35]. In this study, we used 3 years of PWID survey data from the Victorian IDRS (2008–2010). Participants were recruited using convenience sampling through Needle and Syringe Programs in five regions of Melbourne between June and August each year. Participants were aged 18 or above, had injected drugs at least monthly in the 6 months preceding interview, and had resided in Melbourne for the past year. They were reimbursed \$40 for their time and out-of-pocket expenses, in accordance with accepted practices. We analysed questions related to the main type of BZD reported as having been recently used in the context of demographic, drug use and harms questions.

Ethics approval for this study was obtained from the Victorian Department of Human Services (2008), Alfred Hospital (2009–2010) and Peninsula Health (2008–2010).

### *Prescriptions data*

Prescriptions data for alprazolam and diazepam were obtained from Medicare Australia [25], and used in

conjunction with population data from the Australian Bureau of Statistics [36] to calculate crude BZD prescription rates for the state of Victoria.

### *Statistical analysis*

Data were analysed using odds ratios (OR) and 95% confidence intervals (95% CI) for categorical variables, Wilcoxon rank sum tests for non-parametric continuous variables, and  $\chi^2$ -tests for trends over time, with a significance level of  $P = 0.05$ . All analyses were conducted in Stata V.11 (Statacorp LP, College Station, TX, USA).

## Results

A total of 451 PWID were interviewed over the 3 years. The median age of participants was 35 years (range: 19–58 years), 71% were male, and 54% were prescribed Opioid Substitution Therapy (OST, predominantly methadone) at the time of interview. The sample characteristics were stable, but in 2009 there were more female participants ( $P < 0.05$ ), and smaller numbers reporting heroin as their drug of choice ( $P < 0.05$ ), compared with other years (Table 1).

Both lifetime and recent (last 6 months) BZD use were common, reported by 91% and 74% of participants respectively. Only 6% of participants reported recent BZD injection. Similar numbers of participants reported using solely illicitly obtained BZDs (35%), solely licit BZDs (26%) and a combination of both licit and illicit (39%). Among those who reported using both licitly and illicitly obtained BZDs, 60% reported using primarily licitly obtained BZDs, with these participants reporting BZD use at a significantly higher frequency compared with illicit BZD users [median: 180 days, interquartile range (IQR): 48–180 days vs. median: 12 days, IQR: 4–48 days] ( $P < 0.05$ ). Patterns and frequency of BZD use remained stable over time.

Ninety-one per cent of all recent BZD users ( $n = 304$ ) reported their main type of BZD used, of whom two-thirds reported most commonly using diazepam. The percentage of participants who most commonly used alprazolam peaked in 2009 (35%), before decreasing significantly in 2010 (22%,  $P = 0.05$ ). Among those who reported mostly using alprazolam ( $n = 81$ ), the percentage who reported predominantly using illicitly obtained alprazolam ranged from 46% (2008) to 71% (2010).

Table 2 displays the main demographic and drug use characteristics of participants who predominantly used alprazolam compared with users of other BZDs. Univariate analysis indicated that alprazolam users were more than three times more likely than other

## Benzodiazepines

**Table 1.** Demographic characteristics and patterns of BZD use among Illicit Drug Reporting System participants, 2008–2010

	2008 <i>n</i> = 150 <i>n</i> (%)	2009 <i>n</i> = 150 <i>n</i> (%)	2010 <i>n</i> = 151 <i>n</i> (%)	Total <i>n</i> = 451 <i>n</i> (%)
Male gender	120 <sup>a</sup> (80.0)	94 (62.7)	106 (70.2)	320 (71.0)
Median age (range)	35 (21–56)	35 (19–56)	35 (20–58)	35 (19–58)
Live in stable accommodation	101 (67.3)	80 (53.3)	52 (34.4)	233 (51.7)
Australian-born	104 (69.3)	132 (88.0)	132 (88.0)	369 (81.8)
Identify as ATSI	5 (3.3)	9 (6.0)	13 (8.6)	27 (6.0)
Median highest grade of school completed (range)	10 (3–12)	10 (3–12)	10 (6–12)	10 (3–12)
Unemployed	129 (86.0)	125 (83.3)	134 (88.7)	388 (86.0)
Currently prescribed OST	84 (56.0)	85 (56.7)	75 (49.7)	244 (54.1)
Ever in prison	78 (52.0)	82 (55.0)	86 (57.3)	246 (54.8)
Median age first injected (range)	17 (7–48)	17 (7–47)	17 (11–38)	17 (7–48)
Drug of choice: heroin	109 (72.7)	84 (56.0)	103 (68.2)	296 (65.6)
Ever used BZDs	132 (88.0)	143 (95.3)	135 (89.4)	410 (90.9)
Recently used BZDs	104 (69.3)	120 (80.0)	111 (73.5)	335 (74.3)
Main form of BZD used	<i>n</i> = 103	<i>n</i> = 116	<i>n</i> = 109	<i>n</i> = 328
Licit	68 (66.0)	69 (59.5)	60 (55.1)	197 (60.1)
Illicit	35 (34.0)	47 (40.5)	49 (45.0)	131 (39.9)
Main brand of BZD used	<i>n</i> = 97	<i>n</i> = 107	<i>n</i> = 100	<i>n</i> = 304
Alprazolam	22 (22.7)	37 (34.6)	22 (22.0)	81 (26.6)
Diazepam	62 (63.9)	63 (58.9)	67 (67.0)	192 (63.2)
Other	13 (13.4)	7 (6.5)	11 (11.0)	31 (10.2)

<sup>a</sup>Includes one participant who identified as transgender. ATSI, Aboriginal or Torres Strait Islander; BZD, benzodiazepine; OST, Opioid Substitution Therapy.

**Table 2.** Characteristics of alprazolam users compared with other BZD users, 2008–2010

	Alprazolam Users <i>n</i> = 81 <i>n</i> (%)	Other BZD Users <i>n</i> = 223 <i>n</i> (%)	Unadjusted OR (95% CI)
Male gender	53 (65.4)	151 (67.4)	0.90 (0.51–1.61)
Median age (range)	33 (20–51)	35 (21–58)	—
Stable accommodation	38 (46.9)	107 (48.0)	0.96 (0.56–1.65)
Australian-born	70 (86.4)	186 (83.4)	1.27 (0.59–2.91)
Unemployed	67 (82.7)	192 (86.1)	0.77 (0.37–1.67)
Currently prescribed OST	54 (66.7)	111 (49.8)	2.02 (1.15–3.60)*
Mainly used illicit BZDs	47 (59.5)	66 (29.6)	3.49 (1.98–6.18)*
Median days used illicit BZDs (IQR)	21 (6–48)	11 (4–35)	—
Recent BZD injection	12 (14.8)	11 (4.9)	3.35 (1.28–8.80)*
Recent heroin overdose	10 (12.4)	21 (9.4)	1.35 (0.54–3.18)
Ever in prison	44 (55.0)	114 (51.4)	1.16 (0.67–2.00)
Arrested in last 12 months	40 (49.4)	110 (49.6)	0.99 (0.58–1.71)
Committed property crime (last month)	22 (27.2)	49 (22.0)	1.32 (0.70–2.45)
Committed violent crime (last month)	6 (7.4)	16 (7.2)	1.04 (0.32–2.91)
Sold drugs for cash profit (last month)	34 (42.0)	60 (26.9)	1.97 (1.11–3.45)*
Committed fraud (last month)	3 (3.7)	8 (3.6)	1.03 (0.17–4.44)
Recent mental health problem	43 (53.1)	144 (64.9)	0.61 (0.35–1.06)

\**P* < 0.05. BZD, benzodiazepine; CI, confidence interval; IQR, interquartile range; OR, odds ratio; OST, Opioid Substitution Therapy.

BZD users to report both recent illicit BZD use (OR: 3.49, 95% CI: 1.98–6.18) and recent BZD injection (OR: 3.35, 95% CI: 1.28–8.80). Among those participants who reported recent illicit BZD use, alprazolam

users used more frequently than other BZD users (median: 21 days, IQR: 6–48 days vs. median: 11 days, IQR: 4–35 days). There were no significant differences across groups in patterns of use of other



## Benzodiazepines

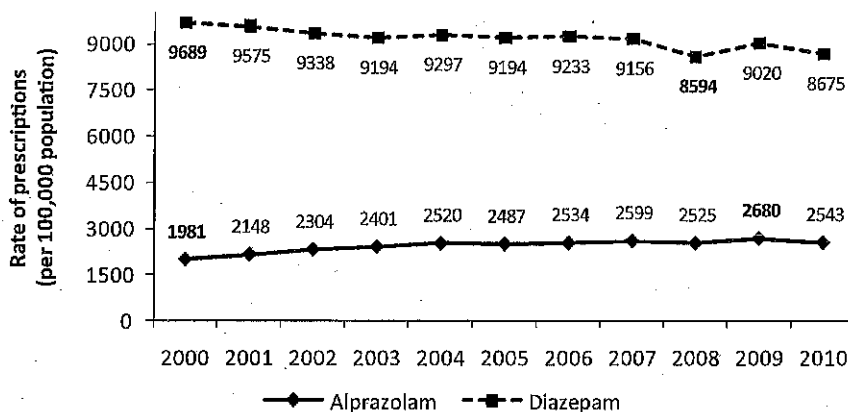


Figure 1. Alprazolam and diazepam prescription rate, Victoria, 2000–2010.

drugs; however, alprazolam users were significantly more likely than other BZD users to report being prescribed OST.

While alprazolam users were no more likely than other BZD users to report lifetime history of incarceration, arrest in the past 12 months, recent property crime or recent violent crime, they were twice as likely as other BZD users to report selling drugs for a cash profit in the past month (OR: 1.97, 95% CI: 1.11–3.45) (Table 2).

Prescriptions data show that the rate of alprazolam prescription in Victoria increased by 28% over the past decade, peaking in 2009 (Figure 1). In contrast, while the rate of diazepam prescriptions remained consistently higher than that of alprazolam, there was an overall 10% decrease in diazepam prescriptions over the same period.

## Discussion

Reports of alprazolam use among PWID fluctuated over time, with use peaking in 2009. This trend is also reflected in the general population, with a decade-long increase in alprazolam prescriptions also peaking in 2009. The decrease in alprazolam use seen in 2010 may reflect the influence of MPBV's warning, which led to the implementation of guidelines within some service providers to limit the prescription of alprazolam to PWID, particularly those receiving OST [22].

While the percentage of BZD users who reported predominantly using illicit BZDs overall remained stable, there was a significant association between alprazolam use and illicit BZD use. This may reflect decreasing access to prescribed alprazolam, potentially as a consequence of changes to prescribing practices within services. A similar effect was observed in Tasmania, where regulatory changes to alprazolam prescribing, including restricting alprazolam prescribing among

patients receiving opioid medications, led to a reduction in prescribed alprazolam use, but had no impact on the use of diverted alprazolam [37]. While a rapid response in policy and practice is integral in preventing escalation of potentially harmful drug practices, it is important that unintended consequences, such as reliance on the illicit market, should be considered prior to implementation.

Alprazolam users were twice as likely as other BZD users to report being prescribed OST at the time of interview. Given that BZDs act as respiratory depressants, the risk of overdose among alprazolam users on OST is of significant concern [38–41]. Recent analysis of forensic data indicated that more than half of all heroin-related deaths in Victoria over the last two decades involved BZDs [42], with a large increase in the involvement of alprazolam since 2000 [43].

We did not observe an association between alprazolam use and antisocial behaviour in our sample. While alprazolam users were significantly more likely than other BZD users to report recent sale of drugs for a cash profit, this may reflect the burgeoning illicit alprazolam market. Alprazolam users, however, were no more likely than other BZD users to report other criminal activities. Clinical trials, however, have shown that alprazolam-treated patients display higher levels of aggression compared with a placebo [28,44], with alprazolam-related aggression tending to be recognised by others, but not by the patients themselves [44]. This raises the possibility that perpetration of crime might be underreported in our sample, as participants may perceive violence committed under the influence of alprazolam differently from other violence committed. Further, given that alprazolam causes anterograde amnesia, perpetration of crime may be underreported because participants did not recall incidents which may have taken place while intoxicated. In the context of Melbourne's illicit drug markets, where demand for

alprazolam continues despite changes in availability, the potential for unrecognised violence remains.

### Conclusion

This study reports on the emergence of alprazolam use among PWID in Melbourne. While our data do not indicate a clear association between alprazolam use and specific harms, given the potential severity of alprazolam-related harms described in the literature, patterns of alprazolam use among PWID should continue to be closely monitored. The addition of detailed questions in drug trends monitoring studies relating to alprazolam use, market characteristics and related harms is recommended, as our study only focused on those reporting alprazolam as the main BZD they had used. Comparison of trends in BZD prescribing and use across jurisdictions will also help to further understand the impact of MPBV's warning on alprazolam use in Victoria. Furthermore, potential changes to prescribing practice should consider unintended consequences, such as replacement with other drug types or illicitly obtained drugs.

### Acknowledgements

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## Benzodiazepines



[REDACTED]

Dear Sir, Madam,

As an academic and an accredited pharmacist who has been involved in providing MMR since 2006, I wish to express my opinion regarding the above proposal.

Benzodiazepines are widely prescribed for elderly for various medical conditions including; anxiety, sleep, epilepsy and pain management. Their misuse could contribute to several problems such as increase risk of falls, tolerance and addiction. Furthermore, these medications are often taken in combination with other drugs that may have additive sedative effects particularly in the elderly. In such patients, alternatives to benzodiazepines may be preferable and may include antidepressants, anticonvulsants, buspirone, antihypertensive agents and the newer neuroleptic medications

From my experience, a significant number of residents are on unnecessary doses of benzodiazepines and are reluctant to change them as they have been on them for a long time. Some of these residents are taking not just one benzodiazepine drug but two in many cases.

Considering to reschedule all benzodiazepines from S4 to S8 will limit their use and will result in prescribers thinking of alternative first line treatments of the various conditions for effective management of their residents. Better residents' managements will lead to quality use of medications, lower cost and less use of health care services because of reduction of falls, etc...

I believe the issue of managers' time, staff workload at the various facilities and the lack of legislations governing the handling of S8 medications in aged care facilities have to be resolved sooner than later and the problems associated with those issues are far less than the benefits that could result in less residents using benzodiazepines as a result of its rescheduling to S8.

I believe that rescheduling benzodiazepines will result in aged care staff better handling of medications in general and increase residents' safety.

Thank you for the opportunity to submit my opinion.

Regards

[REDACTED]



Submission:  
**Proposal to reschedule  
benzodiazepines from  
Schedule 4 to Schedule 8**

**VAADA Vision**

A Victorian community in which the harms associated with drug use are reduced and general health and wellbeing is promoted.

**VAADA Objectives**

To provide leadership, representation, advocacy and information to the alcohol and other drug and related sectors.

January 2013

## The Victorian Alcohol and Drug Association

The Victorian Alcohol and Drug Association (VAADA) is the peak body for alcohol and other drug (AOD) services in Victoria. We provide advocacy, leadership, information and representation on AOD issues both within and beyond the AOD sector.

As a state-wide peak organisation, VAADA has a broad constituency. Our membership and stakeholders include 'drug specific' organisations, consumer advocacy organisations, hospitals, community health centres, primary health organisations, disability services, religious services, general youth services, local government and others, as well as interested individuals.

VAADA's Board is elected from the membership and comprises a range of expertise in the provision and management of alcohol and other drug services and related services.

As a peak organisation, VAADA's purpose is to ensure that the issues for both people experiencing the harms associated with alcohol and other drug use, and the organisations that support them, are well represented in policy, program development, and public discussion.

### Introduction

VAADA welcomes the opportunity to provide feedback on the scheduling proposal for the consideration of the Advisory Committee on Medicines Scheduling (ACMS) to reschedule benzodiazepines (BNZ) from Schedule 4 to Schedule 8. This proposal raises a number of contentious issues which involves a range of stakeholders.

VAADA is of the view that the re-scheduling of any BNZ should be carefully considered and accompanied by robust review which considers a range of issues including overall health outcomes, safety, diversion, morbidity, mortality, cost, feasibility and downstream impacts (for instance, the impact on AOD withdrawal services).

VAADA is also of the view that any proposals to reschedule BNZ should involve comprehensive consultation with consumers and not be limited to professionals, policy makers and medical practitioners.

A recent online survey with the Victorian alcohol and other drug (AOD) treatment sector on BNZ highlighted a range of issues and provides the foundations for VAADA's comments in this submission. The majority of survey respondents indicated that only alprazolam should be rescheduled from Sch. 4 to 8.

### Sector survey on benzodiazepines

VAADA has maintained concerns regarding the harms associated with pharmaceutical misuse and has undertaken a consultation with a range of stakeholders on the harms associated with BNZ in order to better understand the factors that should be taken into consideration and potential implications of this approach.

## Benzodiazepines

This led to the facilitation of an electronic survey throughout October 2012, which requested services to refer to the impact of BNZ on their service users. The survey was conducted via survey monkey and was advertised through VAADA ENEWS, ADCA Update and the Anex NSPForum and raised the question of rescheduling BNZ.

There was significant interest from stakeholders, with 125 responses received over the two week survey period.

### Overview of BNZ

Benzodiazepines are widely prescribed in Australia with over five million prescriptions recorded through the PBS on an annual basis (Jones, Nielsen, Bruno, Frei and Lubman 2011, p 862) and play a key role in the treatment of anxiety related issues including sleep disorders, as well as agitation, movement disorders (Nicholas, Lee and Roche 2011, p 12), withdrawal from alcohol dependence and treatment for epilepsy (Drugs and Crime Prevention Committee 2007, p 17). BNZ play a key role in maintaining the health and wellbeing of a significant portion of the population and therefore appropriate access to this class of medication must be maintained. However, a number of studies, statistics and organisational observations indicate that there are potential harms occurring through the misuse and overprescribing of BNZ, and furthermore that taking these drugs for over four weeks can result in dependency (Nicholas, Lee and Roche 2011a, p 121). It should be noted that GPs are the primary source for most of those who misuse BNZ (Jones et al 2011, p 864).

There are different types of BNZ which can be broadly divided into long-acting, intermediate-acting and short-acting BNZ (Leung 2011, p 282). Research indicates that short-acting BNZ have 'greater abuse potential' (Drugs and Crime Prevention Committee 2007, p 21). Harms associated with the misuse of BNZ can vary depending on a range of reasons; for instance, statistics released by the Coroners Court of Victoria (2012) indicate that diazepam (long-acting) is associated with more drug deaths than alprazolam (short-acting) in 2011 (123 and 56 respectively) making diazepam a more dangerous drug when reflecting on gross mortality. However, 80 per cent of the responses in the VAADA survey (2012) indicated that alprazolam is contributing to the greatest quantum of harms, with only 14 per cent nominating diazepam. Other research, including Jones et al (2011) and Horyniak, Reddel, Quann and Dietze (2012) also highlight significant harms associated with alprazolam misuse.

As Jones et al (2011, p 862) indicate, GPs have been identified as the primary sources of supply of BNZ for people commencing drug treatment who misuse these drugs. This is indicative of the need to ensure that the prescribing practices of GPs for drug using populations are catering for their needs, providing appropriate access to necessary medication and reducing the harms associated with misusing both licit and illicit drugs. To this end, VAADA (2012a) has prepared a position paper on pharmaceuticals which details a range of recommendations including the roll out of a state wide real time prescription monitoring program as well as the need for the Victorian Government to host a summit on pharmaceutical misuse.

The harms associated with BNZ misuse is severe in many cases, however the process of rescheduling must be cognizant of the significant benefits these medications provide for those in need. A careful

## Benzodiazepines

balance must be achieved in ensuring that BNZ are readily accessible with the appropriate safeguards in place to promote best practice prescribing.

### Harms associated with benzodiazepines

The VAADA survey (2012) indicated that 92 per cent of respondents believe that AOD treatment service users experience problems with BNZ with 80 per cent of those respondents reporting that alprazolam as most problematic. From 1999 to 2010, prescriptions for alprazolam has increased from 243,026 to over 400,000 (Jones et al 2011, p 862) with between four to 16 per cent of BNZ prescriptions being made out to identified 'prescription shoppers' (Nicholas, Lee and Roche 2011a, p 125). Regarding prescribing levels, Rintoul, Dobbin, Nielsen, Degenhardt and Drummer (2012) note that there has been a 611 per cent increase in alprazolam prescriptions over the past 21 years. The Pharmacy Guild of Australia (2012, p 3) note that Xanax (alprazolam) and Oxycontin consist of the most commonly forged pharmaceutical scripts.

Some of the harms associated with BNZ use and misuse are as follows:

- Dependence (VAADA 2012);
- Impaired driving skills (Leung 2011, p 282);
- Increased risk of falls and other harms in older people (Coutinho, Fletcher, Bloch and Rodrigues 2008, p 5) including memory loss (Nicholas, Lee and Roche 2011a, p 121);
- In some cases, aggressiveness (Drugs and Crime Prevention Committee 2007, pp 20-21; Jones et al 2011, p 864) and disinhibited behaviour (VAADA 2012);
- Withdrawal symptoms occurring as early as after one week of use (Drugs and Crime Prevention Committee 2007, p 23);
- Diversion and nonmedical use (Horyniak et al 2012, p 588; VAADA 2012);
- Mortality, with BNZ contributing to just over 50 per cent of drug deaths in Victoria in 2011 (179 of 356) with diazepam and alprazolam contributing respectively to 34.6 and 12.1 per cent of all drug deaths in 2011 (Coroners Court 2012);
- Although diazepam contributed to more drug deaths in Victoria than alprazolam in 2011, taking into account the number of prescriptions for both drugs, the mortality rate for alprazolam was higher (1:3057 prescriptions) than diazepam (1:3796 prescriptions)<sup>1</sup>
- High prevalence in polydrug use with half of all heroin related deaths in Victoria in 2007-2008 involving alprazolam (Horyniak et al 2012, p 558) and over half of all heroin deaths in Victoria from 1990 – 2008 involving BNZ ( Rintoul, Dobbin, Nielsen and Drummer 2010); and
- Significant risks regarding the intravenous use of BNZ (VAADA 2012).

The sector survey (VAADA 2012) relayed concerns from a range of stakeholders including the Victorian AOD treatment sector regarding adverse outcomes which could occur through rescheduling BNZ, including:

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<sup>1</sup> This data was sourced from undertaking searches on Medicare Australia Statistics for prescription numbers related to alprazolam and diazepam in Victoria (January 1 – 31 December 2011 and dividing the total number of prescriptions by the 2011 Victorian mortality rate for both drug types.



## Benzodiazepines

- Limiting access to known drug users and the impact this could have on diversion to illicit drugs or doctor shopping;
- That many opioid based pharmaceuticals (Schedule 8) are still regularly misused and highly prevalent on drug death data (Coroners Court 2012);
- Concerns from the sector regarding the impact of rescheduling on rural and regional communities, where access to medications is already a significant problem. Nissen, Kyle, Stowasser, Lim, Jones and McLean (2010, p 34) highlight the disparity in GP access between urban and rural and regional areas, with 90 GPs per 100,000 population in urban areas and 80 per 100,000 population in rural and regional areas.

These challenges require careful consideration and should be accounted in considering rescheduling.

### Populations misusing benzodiazepines

Approximately three per cent of Victorians over the age of 14 reported misusing BNZ at least once (Killian, Matthews and Lloyd 2012, p 90) with approximately 1.5 million PBS/RPBS scripts dispensed in Victoria in 2010 (Killian et al 2012, p 88).

Identified at risk populations include those engaged in the criminal justice system, with research from Australian Institute of Criminology indicating that BNZ were used by 25 per cent of police detainees (most commonly used pharmaceutical by this population (Ng and Macgregor 2012, p 1; McGregor, Gately and Fleming 2011, p 5)) and were viewed by 86 per cent of detainees as being 'easy' or 'very easy' to procure (Ng and Macgregor 2012, p 1). Two out of five of these users obtained BNZ without a prescription in their own name and 12 per cent engaged in 'doctor shopping' (Ng and Macgregor 2012, p 3, 4).

Horyniak et al (2012, p 588) found that individuals on pharmacotherapy are twice as likely to be using alprazolam as any other BNZ and that the risk of mortality amongst alprazolam users on pharmacotherapy is a concern. The Coroners Court of Victoria (2012) found that BNZ were involved in 60 per cent of methadone deaths (278 of 462) between 2000 – 2011 with diazepam contributing to just under half and alprazolam contributing to one eighth of these deaths. The above analysis is indicative of diazepam being of greater risk to pharmacotherapy participants using methadone, however, regrading risk to the general population, the analysis (above) of prescription numbers and mortality is indicative of a higher rate of mortality for alprazolam.

BNZ contributed to two thirds of drug deaths with oxycodone as a contributing substance (175 of 265) between 2000 - 2011, with diazepam contributing to 128 and alprazolam contributing to 41 of these deaths (Coroners Court 2012).

The modest analysis undertaken in this submission is indicative that the risks vary depending on the demographic under scrutiny. It is evident that much more research must be undertaken to establish at risk communities, considering a range of demographics including age, ethnicity and other health and welfare related elements. This data should be used to establish initiatives to reduce the harms associated with pharmaceutical misuse.

## Recommendations

The rescheduling of BNZ is a complex issue and we reiterate the need for robust consultation from a range of stakeholders as well as comprehensive reviews accompanying any modifications. An overriding concern is, however, the ease with which BNZ can be accessed to misuse. With regard to this inquiry, VAADA recommends the following:

1. That alprazolam be rescheduled to Sch. 8, as recommended in the VAADA survey (2012) and that a comprehensive review of the impact of this action be undertaken within three years. Such a review should consider:
  - a. The health and therapeutic outcomes associated with rescheduling;
  - b. Changes in drug usage trends, including diversion to other pharmaceuticals or illicit drugs; and
  - c. Changes in prescribing practices from GPs.
2. That prescribing practices regarding all BNZ be reviewed with a view to ensuring that best practice prescribing is encouraged reflecting on potential harms which can occur from long term BNZ use;
3. That consideration is given to implementing stricter conditions on prescribing diazepam for long term users; and
4. The recommendation proposed by Rintoul et al (2012) being that people who inject drugs are provided 'with information about the risks and harms of concurrent alprazolam and opioid use, particularly injection of alprazolam'.

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16 January 2013

The Secretary  
Scheduling Secretariat  
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**Re: Invitation for public comment - ACMS and ACCS meetings, March 2013  
Notice inviting public submissions under Regulation 42ZCZK of the Therapeutic  
Goods Regulation 1990**

The safe and effective use of medicines is the core business of pharmacists. The Society of Hospital Pharmacists of Australia (SHPA) is the national professional organisation for more than 3,000 pharmacists, pharmacists in training, pharmacy technicians and associates working across Australia's health system. SHPA is the only professional pharmacy organisation with a core base of members practising in public and private hospitals and other health service facilities.

SHPA does not have access to the documentation supporting the proposed changes nor the specific reasons for the proposed changes; therefore SHPA offers the following general comments regarding the scheduling proposal for benzodiazepines.

SHPA fully appreciates the potential for the misuse of benzodiazepines and the adverse effects associated with the long term use of these medicines. We agree that the 'ready' availability of these medicines in the community contributes to the disease burden associated with the misuse and inappropriate use of benzodiazepines. However our members have expressed their concern that a blanket application of Schedule 8 to all benzodiazepines in all dose forms would, in isolation, achieve little change in the use and misuse of these medicines while adding a significant burden to the community and healthcare workers and facilities using and managing these medicines.

SHPA believes that:

- A sole focus on restrictive regulation by introducing a scheduling change of all benzodiazepines to Schedule 8 will not solve the problem of benzodiazepine misuse
- A blanket scheduling change of all benzodiazepines to Schedule 8 may have unintended consequences which may increase patient harm
- There needs to be extensive, widespread consultation, which addresses jurisdictional variation, in formulating and delivering a coordinated national response to the problem of benzodiazepine misuse
- If a determination is made to implement the proposed scheduling change, that a realistic lead-time is established that takes into consideration the need for achieving a national health initiative, as well as the inherent impact of new storage requirements.

SHPA believes that a blanket scheduling change of all benzodiazepines to Schedule 8 is not a panacea – any strategy to address the misuse of benzodiazepines must focus on the

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**The Society of Hospital Pharmacists of Australia**

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## Benzodiazepines

appropriate prescribing of these medicines. Driving changes in prescribing solely through a change in scheduling will have limited success in addressing inappropriate prescribing of these medicines and, as is the experience with other Schedule 8 medicines, a minimal impact on their illicit use.

From the accompanying practical perspective, the proposed scheduling change would have smaller impact in the acute hospital setting at the ward level, as many hospitals have already moved to treat many benzodiazepines as recordable medicines, stored in a restricted area (e.g. safe) with regular stock checks. However, this is not the case in all settings where these medicines are stored and used, and our members have raised concerns with this approach.

In the balance of the submission SHPA provides comment on:

1. Other options that could be considered to address the misuse and inappropriate use of these medicines.
2. The impact of the proposed changes to the scheduling of benzodiazepines.

### **1. Other options that could be considered to address the misuse and inappropriate use of these medicines**

If a reduction in the amount and range of benzodiazepines readily available in the community is achieved it is assumed that there would be a corresponding drop in the diversion and misuse of these medicines.

SHPA believes that many medication safety and quality use of medicines principles and strategies should be considered and implemented to reduce the total use and inappropriate use of benzodiazepines rather than a blanket change in scheduling.

Firstly Australia needs national treatment guidelines regarding the instigation and long-term use of benzodiazepines.

The indications for accessing these medicines through the Pharmaceutical Benefits Scheme (PBS) should match any national treatment guidelines and the pack sizes should reflect treatment objectives. The pack sizes provided through the PBS do not encourage short-term use. For example pack sizes of 50 doses should only be available for patient requiring long-term therapy according to the treatment guidelines e.g. treatment of epilepsy, cerebral palsy.

As background we have included relevant sections of SHPA's submission to the *Background discussion paper to support the development of the National Pharmaceutical Drug Misuse Strategy (NPDMS)* made in May 2011 in attachment 1.

SHPA would welcome a national health initiative, including guidelines on the treatment of benzodiazepine withdrawal and a public education campaign, to encourage and support long-term physically dependent therapeutic users of benzodiazepines to cease their medicine. The initiative could seek to reduce the use of benzodiazepines in general, or target specific user groups.

This strategy would require a major education campaign for prescribers (using an educational visiting technique) and a considerable increase in access to drug and alcohol services nationally.

SHPA also believes that the introduction of many e-health initiatives may assist other strategies aimed at reducing the use of benzodiazepines. That is there is potential for features, such as 'real-time' recording of prescriptions and supply of these medicines, to assist to reduce usage.

## 2. The impact of the proposed changes to the scheduling of benzodiazepines

The major risk associated with the proposed change is the potential for a dramatic reduction in access to these medicines to individual patients; either through actions by the prescriber or their inability to maintain a supply of the medicine.

SHPA believes that if all benzodiazepines in all dose forms were to be scheduled from Schedule 4 to Schedule 8 a minimum lead-in time of 18-24 months for implementation would be required.

This time would be required for a national approach to assist the thousand of Australians currently using these medicines (who wish to cease the medicine) to be safely withdrawn from these medicines. As detailed in the *Therapeutic Guidelines (Psychotropic)*, persons with a substance disorder who abuse benzodiazepines require a different approach to the withdrawal of these medicines, as opposed to long-term physically dependent therapeutic users.<sup>1</sup>

Through COAG all state and territory health ministers would need to describe a jurisdictional approach, recruit specialists in the field and fund the services required to support persons wishing to cease the use of their medicines.

A national health initiative would be required which includes guidelines on the treatment of benzodiazepine withdrawal and a public education campaign designed to explain why the changes are occurring and how they will affect people using these medicines. Key national organisations such as the Royal Australian College of General Practitioners (RACGP), National Prescribing Service (NPS), Consumer's Health Forum, Australian National Council on Drugs (ANCD), Alcohol and other Drugs Council of Australia (ADCA), Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT), Australian Nursing Federation (ANF) and other specialist societies including the professional pharmacy organisations would need to be involved in formulating and delivering this national response.

History shows that the removal of a particular sedative(s) from the 'market' (e.g. decreased access to barbiturates and chloral hydrate) results in an alternative medicine(s) being used (e.g. benzodiazepines, opioids). One of the most important aspects of the national initiative would be the description of national clinical guidelines on which therapies should be used to replace benzodiazepines.

There are several groups of consumers that will require ongoing routine access to these medicines and the strategy should address the potential for people in these groups to inappropriately cease the use of their medicines because of the stigma attached to using a 'drug of dependence' e.g. children and adolescents with cerebral palsy (especially after surgical procedures), rehabilitation patients, chronic pain sufferers and people with epilepsy.

If benzodiazepines were Schedule 8 all health services that use or provide these medicines would require a systematic approach to identifying the structural changes required in all medicines storage areas and develop protocols for the use of benzodiazepines in their service.

For example all residential aged care facilities would need to examine any changes required to medicines storage areas, staffing required to supervise medicines use in the facility and treatment guidelines for the prescribing of benzodiazepines. Facilities that use lorazepam injection will need to install dedicated lockable refrigerators. Same day facilities will need to assess their use of benzodiazepines pre, during and post procedure.

## Benzodiazepines

As noted earlier many acute hospitals have already moved to treat many benzodiazepines as recordable medicines at the ward level, stored in a restricted area with regular stock checks. In Victoria, for example, the Royal Melbourne Hospital Inquiry Report by the Health Services Commissioner in 2002 recommended more rigorous storage and audit of medications in wards to address the issue of staff theft and misuse.<sup>2</sup> Most pharmacy departments however, would require significant remodelling to incorporate secure storage facilities for benzodiazepine stock, as well as an increase in staffing required to perform the tasks associated with accountable medicines. Changes in how injectable dose forms will need to be stored will also require structural changes in many medicines storage areas. The use of benzodiazepines in medical emergencies for status epilepticus also needs to be considered e.g. ambulances, doctor's bags, crash trolleys.

Further, we believe a blanket change in scheduling will necessitate a review of all benzodiazepines used and will require the development of treatment guidelines including the management of both long-term physically dependent therapeutic users and benzodiazepine abusers.

The prolonged lead time is also required to allow the state and territory bodies responsible for managing the approval / permit system for Schedule 8 medicines the time to expand and organise systems for the thousands of additional approvals that will be sought and must be managed.

In summary SHPA believes that rather than a blanket change in scheduling, that a national co-ordinated effort based upon medication safety and quality use of medicines principles be supported, and that strategies be implemented that aim to reduce the total use and inappropriate use of benzodiazepines.

[REDACTED]

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## Attachment 1

Extract from SHPA's submission to the *Background discussion paper to support the development of the National Pharmaceutical Drug Misuse Strategy (NPDMS)* made in May 2011.

### **"Q5. How do the current operations of the PBS contribute to, or reduce, the misuse of pharmaceutical drugs?"**

The indications and pack sizes of targeted medicines available through the PBS do not reflect evidence based practice nor support appropriate use of these medicines.

The current PBS restricts prescribers to designated pack sizes that may not be appropriate for many patients. SHPA recommends that a 'starter pack' of 3-5 days of targeted medicines such as benzodiazepines and oxycodone be listed and available through the PBS.

The availability of a starter pack would mean that if targeted medicine was requested by a patient unknown to the prescriber (including prescription shoppers), required for a limited period, or provided on discharge from hospital a small supply could be provided.

The provision of a starter pack would limit the volume of the targeted medicines supplied but would not restrict access to patients with legitimate requirements.

Consideration should also be given to making it harder to prescribe targeted medicines for patients unknown to the prescriber. For example changing the PBS listing and electronic prescribing of targeted medicines to include the need to complete an electronic questionnaire for new patients (decision tree based on Therapeutic Guidelines) re appropriateness of use / indication before electronic prescribing can occur. Large supplies of these medicines could be limited using a similar mechanism.

Finally there is a need to capture data on the supply of targeted medicines irrespective of the schedule, dose, funder or reimbursement / claiming system.

### **Q11. To what extent is there a current evidence / practice gap in Australia concerning the use of benzodiazepines for conditions such as anxiety and insomnia?"**

The gap is in practice rather than evidence. The listed indications and pack sizes of benzodiazepines available through the PBS do not reflect evidence based practice nor support appropriate use of these medicines. The rules governing the PBS do not always support the appropriate use of these medicines.

### **Q14. To what extent is Australia's prescription shopping program able to impact on the misuse of pharmaceuticals?"**

The current program is limited by the data available to be investigated. There is a need to capture data on the supply of targeted medicines irrespective of the schedule, dose, funder or reimbursement / claiming system. .

As noted earlier SHPA recommends that a 'starter pack' of 3-5 days of targeted medicines such as benzodiazepines and oxycodone be listed and available through the PBS. This means that a prescription shopper would need to access a greater number of prescriptions to obtain the same number of tablets.

Rather than limiting access of these medicines to legitimate users the threshold for triggers identifying potential prescription shoppers needs to be lowered and include all prescriptions (PBS and private prescriptions) and the dispensing of these prescriptions. Although this may result in legitimate users being investigated it would improve the ability of bodies such as Medicare Australia, TAC, DVA in identifying rogue practitioners and excessive claims."



Government of **Western Australia**  
Drug and Alcohol Office

The Secretary  
Scheduling Secretariat  
Therapeutic Goods Administration  
GPO Box 9848  
CANBERRA ACT 2601

Dear Sir/Madam

**NOTICE INVITING PUBLIC SUBMISSIONS UNDER REGULATION 42ZCZK OF THE THERAPEUTIC GOODS REGULATIONS 1990**

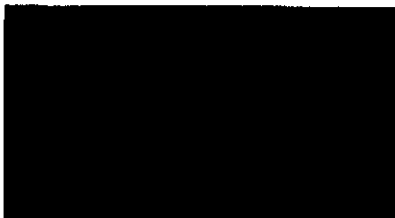
Thank you for the opportunity to comment on this proposal. I write specifically addressing the section titled, Proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8. Problems arising from benzodiazepine dependence and misuse account for a significant proportion of the clinical work of the treatment services funded by the Drug and Alcohol Office (DAO).

Services provided to benzodiazepine dependent clients include inpatient and outpatient withdrawal, counselling and psychotherapy. Polydrug overdose involving benzodiazepines is the most common cause of death in the clients attending our services.

DAO supports changes to the scheduling of benzodiazepines with the objective of reducing people's access to this class of drugs and thereby reducing the morbidity and mortality associated with their use.

I understand that you have also received a submission about this matter from Dr Allan Quigley, the Clinical Director of DAO's specialist treatment service Next Step. DAO supports consideration of the suggestion that as a first step diazepam and temazepam be left in Schedule 4 and all the other benzodiazepines be transferred to Schedule 8. This option would help to minimise any adverse effect of the proposal on those people who are, currently receiving a benefit from their use of prescribed benzodiazepines.

Action by the Therapeutic Goods Administration to reduce the misuse of benzodiazepines should be of high priority and this initiative is supported.



3 January 2013

Benzodiazepines



The Royal Australasian  
College of Physicians

From the President

11 February 2013

Scheduling Secretariat  
Office of Chemical Safety  
Office of Health Protection  
Department of Health and Ageing  
GPO Box 9848  
Canberra ACT 2601

Via email: [SMP@health.gov.au](mailto:SMP@health.gov.au)

Dear Secretariat

**Rescheduling of some medicines including benzodiazepines from Schedule 4 to Schedule 8**

The Royal Australasian College of Physicians (RACP) welcomes the invitation to provide a submission to the Scheduling Secretariat about the rescheduling of some medications to facilitate the quality use of medications. In particular, the RACP wishes to contain our submission solely to the consideration of rescheduling benzodiazepines from Schedule 4 (S4) to Schedule 8 (S8). A detailed response from RACP members to support our recommendations is attached.

The RACP shares the general concern about the misuse of benzodiazepines and recognises that the problem is part of a broad and complex set of circumstances relating to both poor quality use of medicines and illicit use.

The RACP is of the opinion that the rescheduling of all benzodiazepines from S4 to S8 may be an insufficient measure to mitigate their misuse. Moreover, the increase in regulatory control and subsequent paperwork would significantly impact administration costs.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]



The Royal Australasian  
College of Physicians

**Submission to the Therapeutic Goods Administration (TGA) Advisory  
Committee on Medicines Scheduling**

**Executive Summary**

In Australia, approximately seven million prescriptions, both Pharmaceutical Benefits Schedule (PBS) and private prescriptions, for both short and long-acting benzodiazepines are written annually. The RACP shares the general concern about the misuse of benzodiazepines, in particular alprazolam, and recognises that the problem is part of a broad and complex set of circumstances relating to both poor quality use of medicines and illicit use.

On balance of the available evidence, the RACP is of the opinion that the rescheduling of all benzodiazepines from S4 to S8 may be an insufficient measure to mitigate their misuse. No evidence exists that up-scheduling will better align prescribing to properly evaluated and considered patient requirements. Moreover, the increase regulatory control would significantly impact administration costs due to the increased paperwork processing procedures. The RACP proposes the following key recommendations to minimise the misuse of benzodiazepines in Australia:

1. That the Australian Government initially limits the rescheduling of benzodiazepines from S4 to S8, to alprazolam as a first stage in implementation of rescheduling.
2. That all short-acting benzodiazepine prescriptions are time and quantity limited on the basis that there is no evidence for long term efficacy beyond two to three weeks. Prescriptions for durations longer than three weeks should be authorised by an appropriate specialist.
3. That real time data capture and monitoring between prescribers and pharmacists for both PBS and private prescriptions is implemented.
4. That support and development of formal training programs is introduced for all for all prescribers (including general practitioners and specialists), other relevant health care professionals and consumers.
5. That government funding for drug detoxification, residential and rehabilitation services is increased.

## Introduction

The Royal Australasian College of Physicians (RACP) welcomes the invitation to provide a submission to the Scheduling Secretariat on the rescheduling of some medications. The review of the consumption of these medicines is an excellent initiative to facilitate the quality use of medications. In particular, the RACP supports the call for public submissions about consideration of rescheduling of benzodiazepines from Schedule 4 (S4) to Schedule 8 (S8) and wishes to contain its submission solely to this issue.

The prescribing of benzodiazepines for insomnia and anxiety has been the subject of debate for 50 years.

In Australia, approximately seven million prescriptions, both Pharmaceutical Benefits Schedule (PBS) and private prescriptions, for both short and long-acting benzodiazepines are written annually. The RACP shares the general concern about the misuse of benzodiazepines, in particular alprazolam, and recognises that the problem is part of a broad and complex set of circumstances relating to both poor quality use of medicines and illicit use.

On balance of the available evidence, the RACP is of the opinion that the rescheduling of all benzodiazepines from S4 to S8 may be an insufficient measure to mitigate their misuse. No evidence exists that up-scheduling will better align prescribing to properly evaluated and considered patient requirements. Moreover, the increase regulatory control would significantly impact administration costs due to the increased paperwork processing procedures.

The RACP proposes the following key recommendations to minimise the misuse of benzodiazepines in Australia:

## Recommendations

1. *That the Australian Government initially limits the rescheduling of benzodiazepines from S4 to S8, to alprazolam as a first stage in implementation of rescheduling.*
  - 1.1. That the Australian Government initially limits the rescheduling of benzodiazepines from S4 to S8, to alprazolam as a first stage in implementation of rescheduling.
  - 1.2. Consideration could be given to the Tasmanian regulatory model for alprazolam being used as a national prototype. Ongoing vigilant monitoring would be a necessary component of this initiative to identify both intended and unintended consequences, including possible replacement drugs on the 'street/black market'.
2. *That all short-acting benzodiazepine prescriptions are time and quantity limited on the basis that there is no evidence for long term efficacy beyond two to three weeks. Prescriptions for durations longer than three weeks should be authorised by an appropriate specialist.*

## Benzodiazepines

- 2.1. That consideration is given to the frequent clinical review of all ongoing prescribing, in general practice, by an appropriate specialist. For example, a pain medicine specialist, addiction medicine specialist, psychiatrist, neurologist, rehabilitation physician. Moreover; given the high risk of hip fractures in elderly Australians, benzodiazepine usage should be limited in both duration and dose in the elderly, particularly in residential aged care facilities.
- 2.2. That an authority permit is required by prescribers when prescribing benzodiazepines when there is a history of drug dependence. In particular, OST clients requesting clonazepam for seizures should be required to have a neurologist's opinion that no other anticonvulsant is suitable. Such a regulation should exclude the paediatric use of benzodiazepines for control of seizure disorders (clonazepam, clobazam, midazolam and to a very limited extent nitrazepam) and also for managing spasticity (diazepam).
3. *That real time data capture and monitoring between prescribers and pharmacists for both PBS and private prescriptions is implemented.*
  - 3.1. A prototype for consideration is the Drugs and Poisons Information System (DAPIS) Online Remote Access (DORA), a web application that provides GPs and other registered health professionals with information on patients receiving controlled drugs. DORA, used in Tasmania, is a real-time prescription monitoring and reporting tool that assists doctors in their clinical decision-making related to S8 drugs and other identified drugs of concern.
  - 3.2. That consumers prescribed benzodiazepines are encouraged to register for the personally controlled electronic health record; in this way patients receiving concurrent OST could be captured and monitored.
  - 3.3. That all benzodiazepine prescriptions are electronically prescribed. This measure will allow prescribing patterns for benzodiazepines to be monitored and data collected; including expected and unexpected events.
  - 3.4. That the Medicare Prescription Shopping Information Service ("doctor shopping" helpline) Service <sup>1</sup>is upgraded with improved reporting and capture of actual prescribing practices including private prescriptions is increased and monitored to measure any changes in prescribing patterns.
  - 3.5. That the uptake of the Prescription Shopping Information Service is encouraged.
4. *That support and development of formal training programs is introduced for all for all prescribers (including general practitioners and specialists), other relevant health care professionals and consumers.*
  - 4.1. That better education about benzodiazepine prescribing is introduced for all prescribers (including general practitioners and specialists), involved health

## Benzodiazepines

care professionals (HCPs) and consumers. Such education should include continuing education modules for prescribing drugs with abuse potential<sup>1</sup>.

4.2. That a national co-ordinated awareness campaign of the risks of benzodiazepines like alprazolam is raised for prescribers, HCPs and consumers. The National Prescribing Service would be an ideal agency to implement such an educational campaign.

5. *That government funding for drug detoxification, residential and rehabilitation services is increased.*

### Background

#### Benzodiazepine consumption in Australia

Benzodiazepines are widely used in Australia. Approximately seven million prescriptions – both Pharmaceutical Benefits Schedule (PBS) and private - for both short- and long-acting benzodiazepines are written annually<sup>2</sup>. The risk-benefit of benzodiazepines is positive for short term use (two to four weeks). The large number of prescriptions written annually indicates, however, that most prescriptions for benzodiazepines relate to long-term use. For example, up to 20 per cent of elderly Australians who reside in aged care facilities are prescribed benzodiazepines for insomnia for periods ranging from months to years.

The prescribing of benzodiazepines for insomnia and anxiety has been the subject of debate for 50 years. Among the various benzodiazepines large differences exist with regard to their pharmacokinetic properties and metabolism in man. Some benzodiazepines are eliminated from the body at a relatively slow rate (such as diazepam and flunitrazepam ~> 18 hours) and are thus termed long-acting benzodiazepines others are metabolized rather rapidly (such as alprazolam ~< 12 hours) and are termed short-acting benzodiazepines.

Short-acting benzodiazepines are more problematic than long-acting benzodiazepines owing to their fast acting component, which renders their potential to be more addictive and more toxic. Accordingly, a large number of guidelines, both in Australasia and worldwide, recommend against the long-term use of short-acting benzodiazepines as first line treatment for long-term disorders, such as anxiety. Despite this, they are widely prescribed in Australia for long-term disorders<sup>3</sup>. Benzodiazepines are renowned for being a common substance of abuse in Australia<sup>4</sup>. Patients will therefore engage in the practice of prescription shopping to obtain extra supplies of benzodiazepines<sup>4</sup>.

Prescription shopping is when patients unknowingly or deliberately obtain more medicines than is medically needed. This is often done by visiting many doctors, without telling them about their other consultations.

The Prescription Shopping Program (PSP) helps to protect the integrity of the Pharmaceutical Benefits Scheme (PBS) by identifying and reducing the number of patients obtaining PBS subsidised medicine in excess of their medical need. Excessive use of PBS medicines is a health risk as well as a burden to the taxpayer who subsidises both the medicine and the consultation<sup>5</sup>.

## Benzodiazepines

Up to 50 per cent of inmates at Justice Health NSW report illicit benzodiazepine use and up to 66 per cent of clients on concurrent opioid substitution therapy (OST) consume regular doses of benzodiazepines. The benzodiazepine class of medications feature prominently in coroners' reports; most commonly in combination with alcohol, heroin or prescription opioids and psycho stimulant medication such as ecstasy or cocaine. Recognition of the seriousness of substance misuse has led to development of the National Pharmaceutical Drug Misuse Framework to be released later in 2013<sup>6</sup>.

### Risk profile of benzodiazepines

The risk profile of benzodiazepines is often acceptable to patients; however, the medications can have significant adverse effects some of which include: an increased risk of cognitive impairment, confusion, aggression, addiction, withdrawal syndrome falls and accidents (motor vehicle, pedestrian, domestic, recreational and industrial).

The risk of a motor accident is doubled for patients taking benzodiazepines. For example, benzodiazepines have been detected in up to 10 per cent of blood samples in motor vehicle injury cases<sup>7</sup>. Moreover, the risk of a person with detectable blood levels of benzodiazepines involved in a fatal motor vehicle accident has been found to be similar to that for a blood alcohol concentration of 0.10 per cent<sup>8</sup>. Furthermore, motor vehicle accidents are significantly increased for drivers on combinations of alcohol and other psychoactive drugs including opioid substitution therapy (OST<sup>3</sup>);. Benzodiazepines are common drugs implicated in overdose incidents (29 per cent of cases) and in drug-related suicide attempts leading to hospital and emergency department admissions. Furthermore, this class of drugs is associated with significant morbidity and mortality<sup>9 10</sup>.

### Alprazolam

Alprazolam is a short-acting benzodiazepine and its consumption in Australia is more problematic than other short-acting benzodiazepines<sup>11</sup>. When used concurrently with methadone, alprazolam is associated with severe intoxication, paroxysmal aggression and troublesome interactions with potentiation of both drugs<sup>12</sup>. The medication is associated with a higher risk of abuse, dependence and adverse effects: the medication is approximately three times more toxic in overdose and more likely to result in emergency department admission compared to other benzodiazepines<sup>13</sup>. For example, in Victoria during the period 2001 to 2010, alprazolam-related ambulance attendances increased by 132 per cent<sup>14</sup>.

Approximately one million prescriptions annually are written for alprazolam, which is prescribed predominantly as an anxiolytic. In the period 2000 to 2011, the prescribing of alprazolam increased by 87 per cent. The increase is despite little available evidence that alprazolam is superior to other benzodiazepines and despite the medication requiring an authority for PBS reimbursement<sup>15</sup>.

Illicit use of alprazolam is particularly problematic in the Australian community. Anecdotally, workers in substance use treatment facilities report a greater level of harm associated with the use of this medication than from other benzodiazepines. The drug is likely to be sought after by those with substance use disorders, including those who inject drugs, due to its much faster onset of effectiveness, this being a major determinant of the "addictiveness" of a substance<sup>16</sup>.



## Benzodiazepines

Anecdotally, alprazolam is reported as relatively inexpensive (the single tablet price varies from \$10 to \$20 depending on the state) easy to get from both the 'street' and/or from multiple and/or compliant General Practitioners (GPs) who are willing to write non-PBS scripts. The combination of compliant GPs and pharmacists render the drug very available outside of the PBS. The low cost of benzodiazepines contributes to this. To illustrate this, it is less expensive for patients who do not have concessional benefits to obtain alprazolam on a private script than to pay PBS prices.

To overcome excessive alprazolam abuse in Tasmania, in 2009, the Tasmanian Government increased regulatory control of the drug to mitigate its use. Regulatory changes included pharmacies being required to report monthly on alprazolam dispensing and prescribers having a permit to prescribe alprazolam for greater than four weeks in situations when opioids are also prescribed such as OST clients. Tasmanian OST clients may not access any benzodiazepines unless the OST prescriber agrees to prescribe them. Restrictions on the prescribing of alprazolam in Tasmania since 2009 have resulted in a reduced number of deaths due to its consumption<sup>17</sup>.

### **Rescheduling of all benzodiazepines from S4 to S8**

The RACP is concerned that rescheduling all benzodiazepines from S4 to S8 will have little effect upon their misuse for several reasons:

First, no strong evidence exists to support this initiative as a satisfactory method of overcoming public health problems associated with their use. Opioid medications are already classified nationwide as Schedule 8 medications. This measure, however, has had little notable effect upon limiting the problems of misuse of drugs, such as oxycodone, in most Australian states and territories. Reduced mortality, as a result of reduced benzodiazepine use, has only been observed in Tasmania where increased prescribing restrictions are in effect<sup>12</sup>.

Second, rescheduling benzodiazepines from S4 to S8 will not control their availability on the black market and there is likelihood that this measure would have the paradoxical effect of increasing their availability on this market. The 'street' value of benzodiazepines is also likely to increase because availability and 'street-talk' influence the cost. For example, in Tasmania the median purchase price has steadily increased from \$5 in 2006 to \$12.50 in 2011 and more recently to \$20 following the 2009 regulatory changes.

Third, because of S8 requirements for storage, paperwork and review of benzodiazepines, there would be significantly increased compliance costs and workloads for regulatory agencies, hospitals, drug and alcohol rehabilitation centres, pharmacies, nursing homes and aged care facilities.

Fourth, given the enormous volume of benzodiazepines that are prescribed annually, if a process of requiring S8 authorisation for long-term use of such drugs is introduced, there may be significant administrative impact related to processing the required paperwork.

Last, the initiative would have a likelihood of unintended consequences amongst prescribers of benzodiazepines including:

- Dilution of the recognition of the particular dangers of alprazolam.
- Changes in prescribing practices such as:

## Benzodiazepines

- Increased prescribing of longer-acting benzodiazepines (that have a half-life greater than although no good therapeutic indications exist for prescribing daily long-term benzodiazepines, particularly in high doses.
- Increased prescribing of another class of Schedule 4 medications, such as atypical antipsychotics and tricyclic antidepressants, for anxiety and insomnia which may be more toxic and expensive.
- Increased availability of replacement drugs becoming available on the 'street' which may be more harmful and result in an increased cost and burden to the community. Those with substance abuse problems are anecdotally reported as having substance preferences for but will readily interchange drugs (including between short and long acting benzodiazepines) according to their availability. Furthermore, in situations where benzodiazepines with similar problematic use to alprazolam have had increased regulation – for example, flunitrazepam and temazepam - another substance has replaced the restricted drug albeit over a period of time <sup>18</sup>.

If rescheduling of benzodiazepines from S4 to S8 is to be introduced, the RACP is of the view that in the first stage this should be limited to alprazolam rather than all benzodiazepines. In situations where benzodiazepines with similar problematic use to alprazolam, such as flunitrazepam and temazepam have had increased regulation, there has been a period of time before misuse of another substance has replaced the restricted drug. If alprazolam is made less accessible by rescheduled to S8, ongoing vigilance would be required to identify any substance used as a replacement.

The RACP's submission highlights the complexity and challenges ahead in working towards more rational and safe prescribing of psychotropic medications in Australia.

**About The Royal Australasian College of Physicians (RACP):** The RACP trains, educates and advocates on behalf of more than 13,500 physicians – often referred to as medical specialists – and 5,000 trainees, across Australia and New Zealand. The College represents more than 32 medical specialties including paediatrics & child health, cardiology, respiratory medicine, neurology, oncology and public health medicine, occupational & environmental medicine, palliative medicine, sexual health medicine, rehabilitation medicine and addiction medicine. Beyond the drive for medical excellence, the RACP is committed to developing health and social policies which bring vital improvements to the wellbeing of patients. [www.racp.edu.au](http://www.racp.edu.au)

<sup>1</sup> <http://www.drugs.vic.gov.au/temazepam/>).




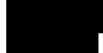
<sup>2</sup> Medicare Statistics website at:  
[https://www.medicareaustralia.gov.au/statistics/pbs\\_item.shtml](https://www.medicareaustralia.gov.au/statistics/pbs_item.shtml)[https://www.medicareaustralia.gov.au/statistics/pbs\\_item.shtml](https://www.medicareaustralia.gov.au/statistics/pbs_item.shtml)

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## Benzodiazepines

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Date	Comment	Author
14 Jan 13	<p>I am not aware of strong evidence that supports rescheduling benzodiazepines from schedule 4 to schedule 8 as a satisfactory method of overcoming any public health problem associated with their use. I understand that such a rescheduling would add considerably to the workload of pharmacy and nursing staff in NSW public hospitals.</p> <p><b>I oppose rescheduling benzodiazepines.</b></p>	
14 Jan 13	<p><b>I oppose rescheduling benzodiazepines.</b></p> <p>It is tricky – I think the benefits might not be worth the cost, especially as we don't have an evidence base that the up-scheduling will better align prescribing to properly evaluated and considered needs. We do have mechanisms to attend to 'excesses' if we only wanted to use them. I'd like to see us spend on upgrading systems of identification and intervention around 'excesses' of benzo prescribing.</p> <p>All good points but no evidence that up scheduling will help. We have plenty of mechanisms to improve the prescribing including surveillance of bad prescribing, education, NPS, consumers, data linkage etc etc.</p> <p>Great work Judy – excellent letter and background document. Be good to get the AMA to endorse – I think they could come at it. I can send the Therapeutics Committee this when everyone is happy</p>	
	<p>Shouldn't we be aligning our approach to opiates and benzos, whatever that may be?</p> <p>I agree scheduling per se is of uncertain value but isn't that an issue equally applicable to opiates?</p> <p>As per the definition - Schedule 8 (S8) drugs and poisons, otherwise known as Controlled Drugs, are substances and preparations for therapeutic use which have high potential for abuse and addiction. Do benzos meet the definition? I suggest that is the test and then how scheduling is regulated and applied is another issue. Classifying them together supports common, rather than separate systems, to address appropriate prescribing.</p>	
14 Jan	<p><b>I agree with the proposal to re-schedule benzodiazepines to S8.</b></p>	

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<p>2013</p>	<p>Problems are</p> <p>(1) almost ubiquitous use of BZs in patients on methadone/buprenorphine, around 66% in most data</p> <p>(2) No good therapeutic indication for prescribing daily long term benzodiazepine, particularly in high doses</p> <p>(3) Seems to me they are often used by community practitioners very early in the management of anxiety/panic.</p> <p>(4) Well described harms of respiratory depression, death, cognitive dysfunction/impaired learning, falls</p> <p>(5) Illicit Benzodiazepines have at some point in their life cycle been sourced from Doctors or pharmacists. People don't manufacture these themselves. I don't know if there is much importation of illicit BZ, but I don't believe so.</p> <p>On the other side of the argument are the practical concerns about how to manage these drugs as an S8. There is no data that schedule change would improve the situation for BZs, but it is there for the rescheduling of ketamine. Most of the psychiatrists I speak to about this don't support it, but I think they don't see the harms. I think the problem is bad prescribing in GPs and some psychiatrists.</p> <p>Occasionally we see patients who have pharmacists willing to distribute them without scripts.</p> <p>I am particularly concerned that use of Benzodiazepines are not indicated for long term management of sleep.</p> <p>If to be used at all, it is for short term use, but are often prescribed long term. This isn't QUM (no evidence of efficacy and significant harm).</p>	
<p>15 Jan 13</p>	<p><b>I agree with the proposal to re-schedule benzodiazepines to S8.</b></p> <p>In addition to Bridin's excellent points, let's explain that people develop physical and psychological dependence to benzodiazepines, making benzodiazepines difficult to stop clinically, so it is important that any decision to start them is made very carefully, with full consideration of the potential harms, similar to other S8 drugs.</p> <p>15-20% of older Australians are prescribed benzodiazepines, predominantly for complaints of poor sleep, and most have taken these medicines for months to years. Tolerance to the hypnotic effects of benzodiazepines develops in weeks-months, but the adverse effects on physical and cognitive function, and the increased risk of falls and hip fracture persist throughout the treatment period.</p>	 

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<p>The benzodiazepines, particularly those of a short acting nature, cause considerable problems with widespread abuse and dependence being seen in the context in which I work.</p> <p>Alprazolam in particular is associated with problematic severe intoxication, paroxysmal aggression, but also troublesome interactions with our methadone clients with potentiation of both drugs when used concurrently</p> <p>Within our withdrawal unit context, we see difficult to control seizure activity in association with alprazolam withdrawal. We fear this condition because it is difficult to treat.</p> <p>In my opinion alprazolam has no place at all in current medical practice, and I strongly support any initiative to reduce its availability. In my opinion a large proportion of the prescribed drug is diverted, injected and/or abused.</p> <p>For that reason I strongly support the rescheduling of alprazolam to a schedule 8 category. I do not see the restriction of all benzodiazepines as being a realistic option as other benzodiazepines are in widespread use and while any can be abused, in a large proportion of cases these are used responsibly.</p>	 
<p><b>Submission on recommendation to make all benzodiazepines Restricted Medicines, S8</b></p> <p>Benzodiazepines remain widely prescribed in Australia (Stephenson et al, 2013), although a large number of guidelines both in Australasia and worldwide, recommend against the long term use of benzodiazepines as first line treatment for anxiety disorders. Despite this, they remain widely used . Of note, the Harvard Brown Anxiety Research Project (Bruce et al 2003) demonstrated that the introduction of the American Psychiatric Association guidelines had little impact on prescribing, although it also demonstrated little difference in outcome for those prescribed SSRIs in accordance with the guidelines compared to those prescribed benzodiazepines, the latter being better tolerated.</p> <p>Despite their acceptability to patients, benzodiazepines have a significant risk profile with addictive potential, increased risk of cognitive impairment, falls and accidents. In a recent study, use of hypnotics (benzodiazepines and benzodiazepine agonist "Z-drugs") was associated excess mortality (Krikpe et al 2012),. For vulnerable populations there is</p>	

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a risk of disinhibition leading to violence and aggression (Jones et al 2011). They are frequently found as contributing substances in overdose deaths. A recent study has demonstrated an excess all cause mortality in chronic users. While often commenced with the intention of use for limited timescale, withdrawal can often be difficult, either due to re-emergence of the anxiety symptoms for which they were originally prescribed, or because withdrawal symptoms can mimic these. They are often sought after by those with substance use disorders, and have significant street value.

In the period 2000 to 2011, prescribing of sedatives in Australia decreased by 26.4%, but that of anxiolytics remained unchanged (Stephenson et al, 2013). Within this category however, there has been a major change with alprazolam prescribing increasing by 87.2%, to the extent that its prescribing now equals that of diazepam, previously the most commonly prescribed anxiolytic. This is despite alprazolam requiring an authority for PBS reimbursement, with this authority only supporting prescription as a second line treatment for Panic Disorder. This escalation in use has occurred despite there being little evidence of its superiority even for this indication, over other benzodiazepines (Moyle et al 2011). A recent publication reviews the role of alprazolam in treatment of Panic Disorder in Australia, raising concerns around associated problems (Moyle et al 2013).

There is widespread anecdotal concern from health workers in services dealing with substance use disorders, that benzodiazepines contribute to problematic behaviour for those dependent upon them, and are associated with worse prognosis in treatment, as well as contributing to overdose deaths. Empirical evidence supports these concerns.

It is therefore considered desirable to attempt to reduce what is seen as inappropriate prescribing of this class of medications. Clearly, the requirement for an authority to prescribe alprazolam and the limitation for this to second line treatment of one specific anxiety disorder, has been ineffective. It has therefore been suggested that all benzodiazepines should be reclassified as restricted medicines, S8.

The large number of benzodiazepine prescriptions written each year, nearly five million (Stephenson et al, 2013), indicates that most will be for long term use. If a process of requiring S8 authorisation for long term use is introduced, unless there is a significant increase in staff numbers in the regulatory agencies throughout Australia, processing these applications will overwhelm the system. Other functions of these agencies will be impeded. It is therefore recommended that only alprazolam be rescheduled as a restricted medicine. With about one million prescriptions annually, this will still provide a large work load, although this may be reduced if the intervention is successful in significantly reducing prescribing.

Why target alprazolam?

Anecdotally, workers in substance use treatment facilities report there being a greater level of harm associated with the use of this medication than from other benzodiazepines. It is likely to be sought after by those

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with substance use disorders due to its much faster onset of effectiveness, this being a major determinant of the "addictiveness" of a substance. The concerns about its specific risks are substantiated by a number of studies demonstrating:

Alprazolam is more toxic than other benzodiazepines in overdose (Isbister et al 2004)

Alprazolam is more sought after by people who inject drugs (Horyniak et al 2012).

While in Melbourne, benzodiazepine ambulance attendances declined in the period 2001 to 2010, alprazolam attendances increased by 132% (Best et al 2013) over the same period.

Alprazolam was implicated in a large number of overdoses and restrictions on its prescribing in Tasmania, has reduced the number of deaths

Thus it is rational to single out this benzodiazepine for restriction of access. It should be noted that benzodiazepines with similar problematic use, again linked to rapidity of onset of effect, have been removed from the market (flunitrazepam and temazepam "gelcaps"). In each case there has been a period of time before misuse of another substance replaced the substance which was no longer available. If alprazolam is made less accessible by being rescheduled as a controlled drug S8, ongoing vigilance will be required to identify any substance being used as a replacement.

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	<p>The Efficacy and Safety of Alprazolam Versus Other Benzodiazepines in the Treatment of Panic Disorder. J Clin Psychopharmacology 31(5) 647-652</p> <p>Moylan S, Giorland G, Nordfjaern T and Berk M (2013). The role of alprazolam for the treatment of panic disorder in Australia. A &amp; NZ J Psychiatry 46(3) 212 - 224</p> <p>Stephensen CP, Karanges E, and McGregor IS (2013) Trends in the utilisation of psychotropic medications in Australia from 2000 to 2011. A &amp; NZ J Psychiatry 47(1) 74-87</p>	
	<p>I suggest some headings and sub-headings such as:</p> <ol style="list-style-type: none"><li>1 Extent of consumption of benzodiazepines in Australia</li><li>2 Nature and extent of problems due to benzodiazepines in Australia</li><li>3 Recommendations</li></ol> <p>In relation to the recommendations I suggest that the recommendations be made much more specific</p> <p>e.g. (1) Benzodiazepine prescriptions should be limited to a maximum of 3 consecutive days with prescriptions for durations longer than 3 days requiring authorisation by a psychiatrist</p> <p>(2) All short acting benzodiazepines be classified as Schedule 8 instead of Schedule 4</p> <p>I think we should argue that it is futile attempting to eradicate benzodiazepines from Australia</p> <p>But the risks of short acting benzodiazepines are much greater than the risks of longer acting benzodiazepines</p> <p>Restricting short acting benzodiazepines is likely to result in an increase in prescribing of longer acting benzodiazepines which is likely to result in less harm</p> <p>We should point out that there is always a risk on unintended negative consequences</p> <p>In particular, more harmful drugs replacing banned or restricted drugs</p> <p><b>30 Jan 2013</b> I support the draft letter</p> <p>In particular I support the idea of restricting alprazolam</p> <p>And all other short acting benzodiazepines</p> <p>But I think we will need to provide some criteria for how to identify short acting benzodiazepines from other sorts of benzodiazepines</p>	




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<p>We are likely to see increasing consumption of longer acting benzodiazepines</p> <p>But I would rather deal with the problems of longer acting benzodiazepines than shorter acting benzodiazepines</p> <p>I like the idea of small changes being evaluated before deciding about any future changes</p> <p><b>30 Jan 13</b></p> <p>(i) I suggest an Executive Summary of the main findings and main recommendations</p> <p>(ii) If alprazolam is restricted, then its place will just be taken by another shorter acting BZD - <b>we should be aiming to make all shorter acting (defined) BZDs harder to get</b> - if they are harder to get legally they may also become harder to get on the black market - but we should realise that consumption of the longer acting BZDs will increase</p> <p>(iii) We should have a strong <b>encouragement that doctors try to reduce or better still slowly wean all elderly patients on BZDs</b> - the relative risk is low but the pool size is so great that the absolute number of casualties is huge - this is mainly a task for GPs but all doctors should be doing this</p>	
<p>I will add some comments to the attached submission, which seems to target Xanax as opposed to all benzos – did I miss some point? And I am never convinced that we can divide benzos into sedatives and hypnotics, given that at various times many have been listed in different countries as one or the other at the same time. They are all benzos.</p> <p>People seem to switch happily from long acting benzos (like flunitrazepam) to short acting ones like Xanax, all the while explaining how each one, along with many others at times, is the best one to use, and I think the issue is more about availability and the street talk and price, rather than any pharmacological logic. With that in mind, there is no point targeting one benzo alone, and it should be all or none. And the Z drugs too.</p> <p>My first major concern with putting all benzos into S8 is that it does not seem to be a mechanism that controls the availability of opioids, noting the current epidemic of OxyContin and transdermal patch injecting, so unless the regulatory bodies get some more teeth and more staff, it will be a symbolic act at best.</p> <p>My second concern is that if benzos are more trouble to prescribe, then all that Doctor Feelgood has to do is prescribe from another class. And voila, we are already seeing Seroquel become the new (far more expensive) Valium, despite it needing an Authority, and drugs like Avanza and the TCAs used as sedatives – with the associated risk of OD and death.</p> <p>My third concern is that many respected doctors, and especially psychiatrists, are very happy to prescribe benzos, teach students to use benzos, feel that chaotic psychotic people can safely use them prn, and generally undermine the view that I believe most members of the Chapter</p>	




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	<p>would have. We need a consistent view on this issue.</p> <p>Fourth, I note that data already exists to help define who these Dr Feelgoods are, but this information does not seem to be well used. I am aware of 3 doctors who have lost their right to prescribe S8s and benzos, and in at least two cases, once it was all over, they admitted that they had created a monster that was consuming them but they could not stop. They were grateful it was over, their practices still function, but it took the authorities over 10 years to act. In the meantime much harm, up to and including incarcerations and deaths, had occurred. It seems foolish to collect potentially useful data and do nothing with it. Using the data to initiate a discussion about behavioural change, and seeing the loss of S8 prescribing rights as a safety device and as a means of protecting a vulnerable practitioner, rather than as a punitive measure, may bring about some real changes.</p> <p>Consequently, any intervention like putting benzos up to S8 must be seen as a trial, and we must monitor the consequences, desired and undesired, expected and unexpected.</p>	
16 Jan 13	<p>Shared Files</p> <p><b>After detailed discussion we do not support this proposal. Instead, we propose that alprazolam alone be transferred to Schedule 8, for the following reasons:</b></p> <ul style="list-style-type: none"><li>• Our clinical experience and our review of the literature support our opinion that not all benzodiazepines are equally problematic. Alprazolam currently stands out among the benzodiazepines, in terms of the risks of abuse, dependence and adverse effects.</li><li>• We believe that reclassifying <b>all</b> benzodiazepines as Schedule 8 medication will dilute recognition of the particular dangers of alprazolam.</li><li>• We note that having all opioid medications classified as Schedule 8 medications has done little to limit the problems with misuse of drugs such as oxycodone (such as Endone and Oxycontin).</li><li>• Unintended consequences are likely if all benzodiazepines are Schedule 8. Doctors will feel less comfortable prescribing benzodiazepines for anxiety and insomnia, and will be more likely to prescribe more toxic and more expensive Schedule 4 medications such as atypical antipsychotics and tricyclic antidepressants. In the addiction field, a number of residential rehabilitation services can operate cheaply as "Schedule 8 free" but still allow for the safe prescription of benzodiazepines. These will no longer be able to provide treatment for a complex and numerous patient group.</li><li>• Compliance costs will be significant for pharmacies, nursing homes and aged care facilities, where there will be new requirements for storage, paperwork and review if all</li></ul>	

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	<p>benzodiazepines are Schedule 8.</p> <p>Of course we share the general concern over abuse of benzodiazepines, but our view is that the most powerful single measure would be to provide real time reporting of prescribing practices to medical practitioners and pharmacists. This approach is professionally accepted and technically feasible. The current Prescription Shopping Information Service ("doctor shopping" helpline) is inadequate, with long delays in reporting and insufficient capture of actual prescribing practices including private prescriptions.</p> <p>In summary, our opinion is that alprazolam should be singled out for Schedule 8 authority only prescribing, rather than all benzodiazepines as a group.</p>	
<p>16 Jan 13</p>	<p>I feel strongly about the availability of BZDs on prescription and the harms I see caused by aberrant use of these medications. I have worked in addiction medicine for over 15 years, both in Tasmania and in WA. I have observed the rapid increase in alprazolam use, and the mitigation of its use in pharmacotherapy clients in Tasmania (where access to alprazolam is virtually nil for patients on pharmacotherapy). In contrast, here in WA there is no restriction on alprazolam and my pharmacotherapy clients report significant use of the drug. (In addition, in Tasmania pharmacotherapy patients may not access any BZDs unless the pharmacotherapy prescriber agrees to prescribe them).</p> <p>I am pleased to see a tightening of access to alprazolam and support the notion completely. However, I believe access to all BZDs should be reduced and feel the position expressed in the attached document does not go far enough. I believe the reclassification of all BZDs would be good medicine and am disturbed at the notion of watering the recommendation down based on the idea of "overburdening" the regulatory system. I feel we could assume that a significant proportion of prescriptions for BZDs would stop due to the inappropriate prescribing - when faced with having to justify use of the BZD many practitioners would be unable to do so rationally. Hence, many prescriptions would not be provided.</p> <p>In addition, if all BZDs with classified S8 then it would be feasible to prevent nearly all instances of co-prescribing in individuals with opiate dependency receiving replacement pharmacotherapy. (There may be the option of prescription under supervision of a specialist addiction physician, in circumstances of limited prescribing for the management of BZD withdrawal).</p>	
<p>16 Jan 2013</p>	<p>Agrees to reschedule from S4 to S8</p>	
<p>17 Jan 2013</p>	<p>My feedback would be that all ongoing prescribing, in General Practice, of potential drugs of dependence ( eg opiates, benzodiazepines) should require clinical review by an appropriate Specialist on an annual basis. Eg Pain Medicine Specialist, Addiction Medicine Specialist, Psychiatrist, Rehabilitation Physician</p>	

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	<p>This would be an important step in ensuring quality prescribing, addressing the public health risks of diversion and improving health professional education about these potential drugs of dependence.</p> <p>This should be included if all BZs (and Opioid medications) are schedule 8 in to the future.</p>	
<p>16 Jan 2013</p>	<p>Direct Edits on Draft Document</p>	
<p>18 Jan 2013</p>	<p>I read the comments with great interest. The diversity of opinion reflects the complexity of the issue. The most important thing the Commonwealth could achieve would be <b>real-time data sharing between prescribers and pharmacists INCLUDING FOR PRIVATE PRESCRIPTIONS</b>. That way we could identify the rogue patients and the rogues in the professional groups.</p> <p>All benzodiazepines are not equal but the people who have trouble with drug use/abuse will interchange benzodiazepines according to availability. Whilst I am really concerned about the availability of alprazolam, 33 years of providing health care to people in police custody taught me that there is a subset of the population who will readily interchange drugs and use whatever is available. They have preferences, but they are not purists. If we concentrate on a single substance, we may just influence substance preference, as one drug is replaced by another. Earlier in my career, the problem drug in police custody was with clonazepam (because as an anticonvulsant) it came in bottles of 200 tabs rather than the smaller numbers provided in standard packs of other benzodiazepines. Lots of prisoners claimed complex epilepsy only controlled by clonazepam at maximum dose. They quite like the short acting drugs for their rapid onset and ability to have frequent doses.</p> <p>I agree with the sentiment that alprazolam is a particular problem at the moment. It was increasingly evident in my 18 years as Principal Medical Advisor to Victoria Police as alprazolam took over from clonazepam as the benzodiazepine of choice for people in custody. In my unscientific observation alprazolam has special appeal to people with aggressive traits and antisocial personality disorder as they seem genuinely to feel calmer, have a sense of relief and are better able to cope with their lives on low doses. The problem is this group is impulsive and work on the theory that if a little is good, more must be better. They have poor coping ability, low tolerance for discomfort and rapidly develop tolerance to the drug. Consequently they seek increases in dose and start 'doctor shopping'.</p> <p>Prisoners readily talk of obtaining large quantities of alprazolam (200 x 2mg tabs per week) from compliant doctors who write non-PBS scripts. I am currently treating a man who was prescribed 15 x 2 mg tablets/day when I met him. In 2010 I treated a man who was obtaining 25 x 5mg diazepam tablets per day. These people get very sick and have intractable seizures when they are unable to get supplies. By contrast, in another setting I have seen people with genuine panic disorder who do extremely well on alprazolam ½ x 0.25 mg daily</p> <p>Because the benzodiazepines are cheap, <b>the authority system is of little use in controlling availability</b>. For patients who do not have concessional benefits, it is cheaper to obtain alprazolam on a private</p>	

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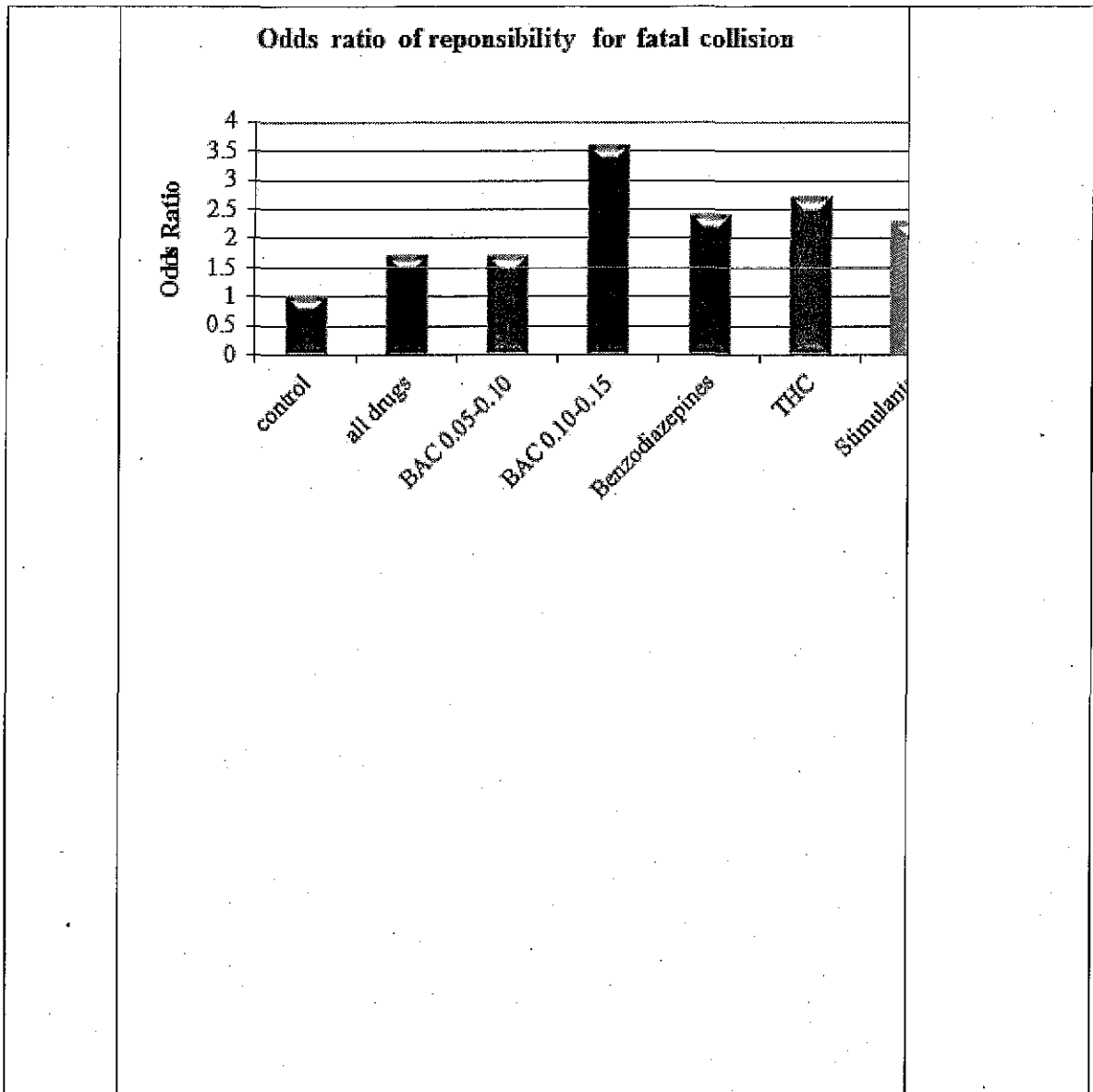
script (~\$20 for a bottle of 50 tablets of 2mg) than pay the PBS pricing. The combination of a compliant pharmacist and doctor make the drug very available outside the PBS. Therefore, from a PBS perspective, it is unregulated. Making the drug a schedule 8 poison would greatly increase the regulatory control.

My particular interest and expertise is the effect of the benzodiazepines on driving. There is an increased risk of personal injury crashes among drivers using anti-anxiety drugs compared with the rest of the population (Skegg, Richards et al. 1979) and this is exacerbated by alcohol and other sedatives. (Seppälä, Korttila et al. 1976) There is a hangover effect and a small dose of any sedative the following day can potentiate the effect. There is a decrement in tasks requiring vigilance at low doses and tolerance is only occasionally noted. The opposite effect, exaggerated impairment, has also been documented. (Kolega 1989) A meta analysis of over 500 studies showed that the serum level of each of the benzodiazepines studied was related to the degree of impairment in the laboratory. (Berghaus 1997)

The benzodiazepine group has been shown to impair driving skills to a similar degree and in similar ways to alcohol. In general terms, the risk of collision is doubled for patients taking benzodiazepines. The impairment and collision risk are greatest in the first two weeks of treatment. (de Gier, Hart et al. 1981) The ICADTS working group concluded that patients should be warned not to drive in the first two weeks of treatment. (Alvarez and de Gier 2002) Although treatment with benzodiazepine tranquillisers will improve clinical anxiety, there is no improvement in their driving ability. (de Gier 1984)

A review of 43,000 hospital outpatients, found that the 53 crash-involved drivers in that sample were 4.9 times more likely than their matched controls to have been using a tranquilliser. (Skegg, Richards et al. 1979) The relative risk of a driver being killed in a traffic crash (assessed by odds ratio analysis) shows a significant increase for drivers consuming alcohol alone, alcohol with other psychoactive drugs, combinations of psychoactive drugs, and cannabis. (Skegg, Richards et al. 1979, Alvarez, Prada et al. 1992, Gerostamoulos, Burke et al. 1996, Alvarez, Sancho et al. 1997, Drummer 2002, Drummer, Gerostamoulos et al. 2003, Drummer 2004, Drummer, Gerostamoulos et al. 2004) The following graph illustrates that the risk of a person with benzodiazepines in their blood being responsible for causing the fatal accident in which he or she dies is similar to that for a blood alcohol concentration of 0.10%

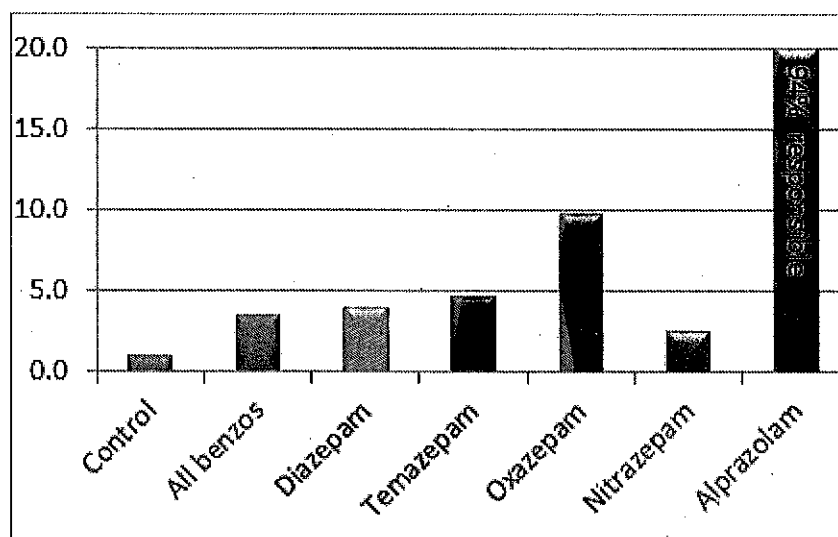
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I am currently conducting research into the presence of drugs and responsibility for collision. (Ogden et. al. 2010, 2011) The following graph illustrates the relative risk that a driver with various benzodiazepines in their blood was responsible for causing the accident in which he or she was injured. The risk with oxazepam is similar to that for a blood alcohol concentration of 0.15%. Only alprazolam was associated with greater responsibility for collision. The early data suggests there is a dose relationship with diazepam.

Of the 44 drivers in who alprazolam was detected, more than half had high or toxic levels of alprazolam. Most had at least one other substance present. Only one had a therapeutic level of alprazolam alone.



### ODDS RATIO OF RESPONSIBILITY FOR COLLISION

Regardless of whether benzodiazepines are added to S8 as a class, whether alprazolam is singled out, or nothing is changed, we MUST do something to bring our concerns to the attention of the profession – psychiatrists and GPs in particular.

#### Evidence of increasing problems with alprazolam include:

- Increasing contribution of alprazolam to illicit opioid (heroin) and prescription opioid combined drug toxicity deaths.
- A disproportionate contribution to non-fatal drug toxicity emergencies presenting to a Victorian emergency department.
- A disproportionate increase in involvement of alprazolam compared to all benzodiazepines in ambulance attendances in Victoria.
- A disproportionate increase in misuse and injection by people who inject drugs
- Identification of a disproportionate level of harm in patients admitted to drug treatment in four States of Australia, including dependence, withdrawal, effects on memory and range of



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injecting-related harms. While diazepam was the main benzodiazepine used by this sample, a large proportion of individuals reporting seizures (55%), traffic accidents (50%), and crime (30%) while under the influence of benzodiazepines, identified that alprazolam was the main benzodiazepine involved.

- The Victorian Parliamentary Drugs and Crime Prevention Committee examining misuse and abuse of benzodiazepines and other pharmaceutical drugs identified from witness submissions and presentations that alprazolam was uniquely problematic.
- A number of sources describe trafficking of alprazolam, with street prices reported to be from \$2 to \$20 in different jurisdictions across Australia while there is no reporting of a street price for other benzodiazepines.
- There is a disproportionate over-representation of alprazolam in data relating to forged prescriptions.
- There are also reports of other crime associated with alprazolam, and concerns from the courts about the contribution of Xanax to crime.
- Evidence from investigation of the role of benzodiazepines in injured drivers in Victoria describes that alprazolam had the most concerning contribution to collisions.

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## Benzodiazepines

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Benzodiazepines

<p>21 Jan 13</p>	<p>Thanks for the opportunity to comment on the proposed RACP submission regarding possible rescheduling of benzodiazepines.</p> <p>I support the intent and content of the circulated draft - currently alprazolam is the benzodiazepine most frequently reported by clinicians in SA as causing problems amongst our client group including those presenting for withdrawal management. Obviously the circulated draft requires editing and proof reading prior to submission.</p>	
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Benzodiazepines

Haven't got much time to comment on the proposal which is a shame as it raises so many issues.


However, just a couple of points on the draft submission. Firstly, flunitrazepam is still available and indeed available on the PBS for phobic, anxiety and terminal conditions. So saying it has been removed from the market might make us look a little silly and detract from our submission.

Secondly, a long bow is being drawn about the decrease in deaths in Tasmania. From my direct observation in Hobart, the death rate from drug overdoses is actually increasing. Officially, it is difficult to be sure because the coroner is several years behind in his findings, so any comment can only be anecdotal, and mine is of an increase.

By the way, are the 5 million scripts PBS ones only? For cost and other reasons a huge number of benzo scripts are now non-PBS - are these included?



Benzodiazepines

<p>17 Jan 13</p>	<p>I agree fully - it will make management much easier</p>	
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30 jan  
2013

Congratulations to everyone. Great Submission. Our incarcerated patients in NSW have very high rates of hazardous alprazolam use and for many it is their benzodiazepine use that leads to their overdoses and reoffending behaviour.

**A couple of questions Judith**

\*Is the submission done and dusted? Should we be including anything about clonazepam misuse. In these days of very effective new generation anticonvulsants, it would be exceedingly rare for pts to genuinely require clonazepam to control epilepsy yet pts very readily can obtain clonazepam by stating they get seizures (which may in fact be benzodiazepine withdrawal seizures). Patients should be required to have neurologists opinion that no other anticonvulsant suitable

\*also are you happy for this submission to be used internally by JH in our multidisciplinary discussions with our primary health and psychiatry colleagues?

I have added a sentence that Specialists should be involved in prescribing > 3 days; would this cover this scenario for clonazepam? I think this would never get approved as too difficult to implement clinically.


Most patients with genuine epilepsy are primarily cared for by general practitioners with only occasional neurologist input. It is already authority listed for "neurologically proven epilepsy" which is very open to interpretation and many doctors prescribe it just because a previous doctor has. Clonazepam is also appropriately used (much less commonly) in palliative care patients and we certainly would not want to hinder that. I don't think your proposal is likely to be adopted, so I think we need to add another

"Patients should not be prescribed clonazepam for epilepsy unless they have well documented neurologist review and assessment that states that seizures have not been controlled by any other anticonvulsant."

Leave it up to you.

**"Patients should be required to have neurologists opinion that no other anticonvulsant suitable"**

## Benzodiazepines

	<p>This submission is both desirable and sensible. The next problematic benzo will be plain old valium. At present the PBS provides 50 tablets on a regular script. This is very good value for a health care card holding addict. The PBS scrips could be reduced to 20 or 25 tabs???</p>	
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## Benzodiazepines

I absolutely agree benzodiazepine misuse is extremely problematic, alprazolam and clonazepam being most problematic.. A large proportion of patients in custody have benzodiazepine dependence /hazardous use, with a significant portion report being "pilled" at the time of their offence with sometimes no recollection of the offence they have committed. Patients undergo withdrawal 'detoxification and many are surprised how well they feel when off BZP. We work with patients re relapse prevention etc however it is exceedingly common for pts to resume BZP use soon after release, as it is so so easy to acquire scripts. Our patients know what to say to the doctor, and who to go to. We have a team of Connections Workers who continue to see patients for the first 4 weeks after release from custody, and they are often involved with managing BZP intoxicated/overdosed patients esp since they have lost their BZP tolerance whilst in custody (and not on BZP) . It is easy for patients to report PTSD" requiring" alprazolam, as many of our patients do have PTSD from traumatic life events. Many of our pts have history of head injury or drug withdrawal seizures thereby "requiring" clonazepam. However these same patients have been seizure free and managed anxiety symptoms in custody without alprazolam or clonazepam.

Her are a few stats that are a few years old. Our clinical experience is that the problem is bigger than these stats indicate.

Information provided by Justice Health on benzodiazepine use by inmates, including data from the Justice Health 2009 Inmate Health Survey.

24% men and 29.1% women reported illicit benzodiazepine use ever.

In the year prior to incarceration of those who had ever used benzodiazepines, 39.6 % were using benzodiazepines but not on a daily basis, and 44.4% were using benzodiazepines on a daily basis.

Regarding illicit benzodiazepine use whilst in custody, 7.5% of men and 11.6% of women self reported use.

Regarding self reported injecting of benzodiazepines, this was 3.4 % for men and 3.2% for women.

61% of all inmates reported being intoxicated at the time of the offence that they are currently incarcerated for. Benzodiazepines were not specifically listed for patients to report on. While most of the intoxications were related to alcohol, cannabis, methamphetamine, heroin and cocaine, there was an "other" category where 11.7% reported intoxication on, which is most likely to be predominantly benzodiazepine as other the substances were listed specifically.

None of the above survey questions looked specifically at benzodiazepine use whilst on OST (though that information could





## Benzodiazepines

potentially be teased out) but given that 25% of the patients were either recently or currently on OST, it can be assumed that there was significant benzodiazepine use in OSP patients, and which we as clinicians are seeing frequently in our patient group.

Also 30% all women and 22% all men reported a history of overdose to the point of unconsciousness, and we know that overdoses frequently involve benzodiazepine use.

Also, a separate survey of young people in custody (juvenile detention) 2009 reported that 1.9% were using benzodiazepines at least weekly prior to their detention.

From our clinical experience benzodiazepine use in the community is very problematic, with patients most commonly reporting using clonazepam and alprazolam, often in excess 20 tablets per day. It is reported as easy and relatively cheap to get from the street or from multiple GPs.

[http://www.justicehealth.nsw.gov.au/publications/2009\\_IHS\\_report.pdf](http://www.justicehealth.nsw.gov.au/publications/2009_IHS_report.pdf)

However I am unsure whether changing to S8 will change the landscape of misuse. Oxycodone misuse is an ever increasing problem which has not been curbed by it being S8. The quantity of number of tablets dispensed per script should be considered. I believe it is also estimated that one third of alprazolam scripts are private and therefore not on PSB radar.

30 Jan 13

Congratulations to everyone. Great Submission. Our incarcerated patients in NSW have very high rates of hazardous alprazolam use and for many it is their benzodiazepine use that leads to their overdoses and reoffending behaviour.

A couple of questions Judith

\*Is the submission done and dusted? Should we be including anything about clonazepam misuse. In these days of very effective new generation anticonvulsants, it would be exceedingly rare for pts to genuinely require clonazepam to control epilepsy yet pts very readily can obtain clonazepam by stating they get seizures (which may in fact be benzodiazepine withdrawal seizures). Patients should be required to have neurologists opinion that no other anticonvulsant suitable

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Most patients with genuine epilepsy are primarily cared for by general practitioners with only occasional neurologist input. It is already authority listed for "neurologically proven epilepsy" which is very open to

## Benzodiazepines

	<p>interpretation and many doctors prescribe it just because a previous doctor has. Clonazepam is also appropriately used (much less commonly) in palliative care patients and we certainly would not want to hinder that. I don't think your proposal is likely to be adopted, so I think we need to add another Perhaps add</p> <p>"Patients should not be prescribed clonazepam for epilepsy unless they have well documented neurologist review and assessment that states that seizures have not been controlled by any other anticonvulsant."</p>	
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Benzodiazepines

**Alprazolam: argument for rescheduling alprazolam to Schedule 8**

**Dr Malcolm Dobbin, PhD MBBS DRANZCOG MPH FAFPHM**

**Senior Medical Advisor (Alcohol and Drugs)**

**Mental Health, Drugs and Regions Division**

**Victorian Department of Health**

**Rescheduling of all benzodiazepines to Schedule 8.**

I support the rescheduling of all benzodiazepines to Schedule 8, because of the problems associated with their misuse, and their contribution to opioid poisoning deaths as a result of combined drug toxicity involving CNS depressant drugs. Benzodiazepines may contribute to combined drug toxicity in many of these deaths involving illicit (heroin) and prescription opioids<sup>1</sup>, often in combination with other CNS depressant substances such as alcohol or other prescription drugs.

Benzodiazepines are recommended for the short-term treatment of anxiety or insomnia, so ideally appropriate prescribing would be limited in duration in most cases. This would obviate the need for practitioners to obtain a permit to prescribe a Schedule 8 drug from State and Territory jurisdictions for chronic prescribing so would not impede appropriate prescribing.

The Australian Statistics on Medicines describes as a Practice Point:

“reserve (benzodiazepines) for short-term use only (eg 2–4 weeks); they should be part of a broader treatment plan, not a first or sole treatment”

**Rescheduling of alprazolam to Schedule 8.**

In the event that rescheduling of all benzodiazepines is not accepted, I

<sup>1</sup> White JM, Irvine RJ. Mechanisms of fatal opioid overdose. *Addiction* 1999;94:961-72.

## Benzodiazepines

believe there is a special case for selective rescheduling of alprazolam to Schedule 8.

Evidence of increasing problems with alprazolam include:

- Increasing contribution of alprazolam to illicit opioid (heroin) and prescription opioid combined drug toxicity deaths.
- A disproportionate contribution to non-fatal drug toxicity emergencies presenting to a Victorian emergency department.
- A disproportionate increase in involvement of alprazolam compared to all benzodiazepines in ambulance attendances in Victoria.
- A disproportionate increase in misuse and injection by people who inject drugs
- Identification of a disproportionate level of harm in patients admitted to drug treatment in four States of Australia, including dependence, withdrawal, effects on memory and range of injecting-related harms. While diazepam was the main benzodiazepine used by this sample, a large proportion of individuals reporting seizures (55%), traffic accidents (50%), and crime (30%) while under the influence of benzodiazepines, identified that alprazolam was the main benzodiazepine involved.
- The Victorian Parliamentary Drugs and Crime Prevention Committee examining misuse and abuse of benzodiazepines and other pharmaceutical drugs identified from witness submissions and presentations that alprazolam was uniquely problematic.
- A number of sources describe trafficking of alprazolam, with street prices reported to be from \$2 to \$20 in different jurisdictions across Australia while there is no reporting of a street price for other benzodiazepines.
- There is a disproportionate over-representation of alprazolam in data relating to forged prescriptions.
- There are also reports of other crime associated with alprazolam, and concerns from the courts about the contribution of Xanax to crime.
- Evidence from investigation of the role of benzodiazepines in injured drivers in Victoria describes that alprazolam had the most concerning contribution to collisions.

### **ALPRAZOLAM**

**Approved indications.** Alprazolam is registered in Australia for the short-term symptomatic treatment of anxiety including treatment of anxious patients with some symptoms of depression. It is also registered for panic disorder.

**Pharmaceutical Benefits Scheme listing.** Alprazolam is listed as:

## Benzodiazepines

<p><b>Authority required:</b> Panic disorder where other treatments have failed or are inappropriate. It is not approved as a benefit for the treatment of generalised anxiety disorder.</p> <p>Other commonly prescribed anxiolytics diazepam and oxazepam can be prescribed without requiring an Authority to prescribe as a PBS benefit, and with no restrictions for an approved indication.</p> <p>Despite these constraints, and recommendations of guidelines for the management of panic disorder describing alprazolam as a second line treatment, supply of alprazolam has steadily increased since it became a PBS benefit in 1992.</p> <p><b>Recommendations for treatment of panic disorder.</b></p> <p>Guidelines from three countries recommend that when pharmacotherapy is required for the management of panic disorder, treatment with a selective serotonin reuptake inhibitor (SSRI) or tricyclic antidepressants are the agents of choice<sup>2 3 4</sup>. Benzodiazepines are either no longer recommended or recommended only as a secondary treatment strategy.</p> <p><b>Alprazolam pharmacology.</b> Alprazolam is a potent short-acting benzodiazepine with a rapid onset and offset of effect, pharmacokinetic properties that are associated with a greater risk of dependency and withdrawal<sup>5</sup>. There is evidence that benzodiazepines with a short elimination half-life cause a more severe withdrawal syndrome than those with a long elimination half-life, and there is an increasing body of literature suggesting that quickly eliminated, high potency benzodiazepines including alprazolam may be more likely to cause severe withdrawal reactions than slowly eliminated benzodiazepines such as diazepam<sup>6</sup>. The intensity and prevalence of rebound anxiety with alprazolam seems greater than with other benzodiazepines, and interviews with clinicians with experience of detoxifying patients dependent on benzodiazepines overwhelmingly describe that alprazolam is especially problematic with respect to the intensity and/or duration of</p>	
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<sup>2</sup> RANZCP Guideline Team for Panic Disorder and Agoraphobia. Australian and New Zealand clinical practice guidelines for the treatment of panic disorder and agoraphobia. Aust N Z J Psychiatry. 2003;37:641-656

<sup>3</sup> Work Group On Panic Disorder. Practice guideline for the treatment of patients with panic disorder (second edition). American Psychiatric Association 2009. Available at: <http://www.guidelines.gov/content.aspx?id=14230>. Accessed January 2013

<sup>4</sup> National Institute for Health and Clinical Excellence. Anxiety: NICE Guideline (Amended). London, UK: National Institute for Health and Clinical Excellence; 2007

<sup>5</sup> Moylan S et al. The efficacy and safety of alprazolam versus other benzodiazepines in the treatment of panic disorder. J Clin Psychopharmacol 2011;31:647-52.

<sup>6</sup> Tesar GE. High potency benzodiazepines for short-term management of panic disorder: The US experience. J Clin Psychiatry 1990;51 (suppl):4-10

## Benzodiazepines

<p>the withdrawal syndrome<sup>7</sup>. Alprazolam may also be more toxic than other benzodiazepines in overdose<sup>8</sup></p> <p>There is also evidence to suggest that alprazolam produces more subjective euphoria<sup>9</sup> and is subject to greater abuse liability<sup>10</sup>.</p> <p>If the Australian government wishes to restrict benzodiazepine prescribing by rescheduling them to S8 an initial approach, on a trial basis and with monitoring, could be that only alprazolam (the most frequent short acting benzodiazepine that is misused) is rescheduled to S8.</p> <p>Reasons to reschedule alprazolam alone to S8 include that alprazolam:</p> <ol style="list-style-type: none"><li>1. is approximately three times more toxic in overdose and more likely to result in emergency department admission compared to other benzodiazepines (Isbister et al 2004). For example, in Victoria, while benzodiazepine ambulance attendances declined in the period 2001 to 2010, alprazolam related attendances increased by 132% (Best et al 2013).</li><li>2. is associated with problematic severe intoxication, paroxysmal aggression, and it potentiates the effects of methadone and can therefore be problematic in opioid substitution therapy (Horyniak et al 2012).</li><li>3. deaths in Tasmania have reduced after implementation of restrictions on prescribing.</li></ol> <p><b>Benzodiazepine prescriptions: Australia 2008.</b></p> <p>Data from the Australian Statistics on Medicines (ASOM) describes the supply of benzodiazepines to Australia. In 2008 ASOM reported that there were 7,948,000 prescriptions for benzodiazepines dispensed in Australia, and alprazolam prescriptions comprised 9% of all benzodiazepine prescriptions.</p>	
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<sup>7</sup> Wolf B, Griffiths R. Physical dependence on benzodiazepines: differences within the class. *Drug Alcohol Depend* 1991;29:153-6.

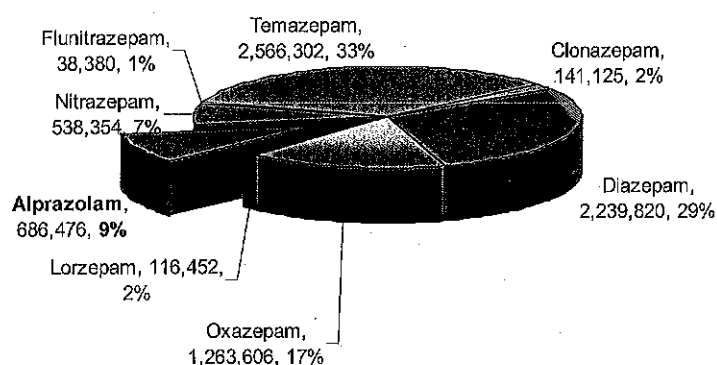
<sup>8</sup> Isbister GK et al. Alprazolam is relatively more toxic than other benzodiazepines in overdose. *Brit J Clin Pharmacol* 2004;58:88-95.

<sup>9</sup> Iguchi MY, Griffiths RR, Bickel WK et al. Relative abuse liability of benzodiazepines in methadone maintained populations in three cities. *NIDA Research Monographs* 1989;95:364-5.

<sup>10</sup> Mumford G, Evans S, Fleishaker J, et al. (1995) Alprazolam absorption kinetics affects abuse liability. *Clinical Pharmacology and Therapeutics* 57: 356-365

## Benzodiazepines

**Benzodiazepine scripts: Australia 2010**



Data from the Australian Statistics on Medicines suggests that a higher proportion of alprazolam prescriptions (37.2%) are privately prescribed than for other commonly prescribed benzodiazepine anxiolytics or hypnotics (see table), possibly as a result of the requirement to obtain an authority to prescribe alprazolam as a PBS benefit.

The cost of standard packs of benzodiazepines is low, and many are available as products from generic pharmaceutical companies, thus making these products available at low cost without the need for PBS subsidy.

Flunitrazepam is available only as an RPBS benefit.

### COMMUNITY PRESCRIPTION DRUG USE in DDD/1000/DAY for high benzodiazepines 2009

	alprazolam	diazepam	oxazepam	flunitrazepam
PBS/RPBS	3.886	4.815	1.878	0.036
SURVEY	2.306	1.516	0.409	0.289
total DDD	6.192	6.331	2.287	0.325
PBS/RPBS (%)	62.8	76.1	82.1	11.1

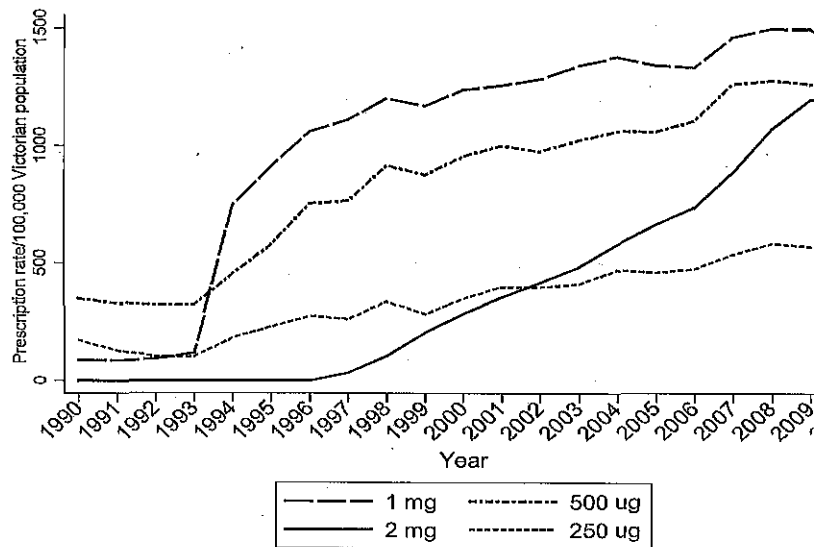
Source: Australian Statistics on Medicines, 2009. Australian Government,

## Benzodiazepines

Department of Health and Ageing.

### Trends in supply of alprazolam.

The following figure describes trends in the rate of supply per 100,000 population of alprazolam to Victoria. The total rate of supply increased shortly after this benzodiazepine was listed as a PBS benefit in 1992. The most remarkable feature of the trends in supply is the markedly disproportionate increase of prescriptions for the high dose 2 mg tablet.



### PROBLEMS WITH BENZODIAZEPINES AND ALPRAZOLAM

#### Contribution to combined drug toxicity deaths.

There is a high prevalence of detection of benzodiazepines in heroin-related deaths. In Victoria, benzodiazepines were found in 55% of all deaths involving heroin reported to the Victorian Coroner in 2004-2008<sup>11</sup>.

A recent examination of detection of different benzodiazepines in heroin-related deaths in Victoria found an increasing trend of detection of

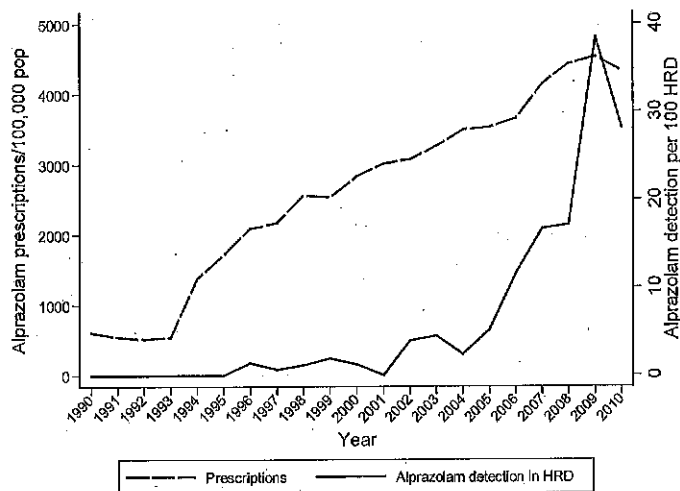
<sup>11</sup> Woods J, Gerostamoulos D, Drummer OH. Heroin deaths in Victoria 2007/2008. Victorian Institute of Forensic Medicine, Department of Forensic Medicine, Monash University. 2009.



## Benzodiazepines

alprazolam in these deaths<sup>12</sup>. Alprazolam detection increased from 5.2% of deaths in 2005 to 35.3% of deaths in 2009. The authors concluded that this increase may be a consequence of increasing misuse of this benzodiazepine, and increased prescribing of the high dose 2mg form.

**Figure: Number of alprazolam prescriptions and detection of alprazolam in heroin-related deaths: Victoria, 1990-2010.**



There is also a high prevalence of detection of benzodiazepines in deaths involving oxycodone and other prescription opioids. Benzodiazepines were detected in 68.6% of oxycodone toxicity deaths in New South Wales in the years 1999-2008<sup>13</sup>.

A US review of poisoning deaths involving oxycodone describes that benzodiazepines were the most frequently detected CNS depressant drugs (56.3%) other than oxycodone in all deaths involving multiple drugs<sup>14</sup>.

**Contribution to non-fatal drug toxicity overdose and emergencies.**

<sup>12</sup> Rintoul A et al. Recent increase in detection of alprazolam in Victorian heroin-related deaths. Med J Aust 2013 (in press).

<sup>13</sup> Darke S et al. Toxicology and characteristics of fatal oxycodone toxicity cases in New South Wales, Australia, 1999-2008. J Forensic Sci 2011;56:690-3.

<sup>14</sup> Cone EJ et al. Oxycodone involvement in drug abuse deaths: A DAWN-based classification scheme applied to an oxycodone post-mortem database containing over 1000 cases. J Analytic Toxicol 2003;27:57-

## Benzodiazepines

<p>Benzodiazepines, and alprazolam are common drugs in overdose incidents leading to hospital and emergency department admissions.</p> <p>A study of of poisoning admissions examined by a regional toxicology service in New South Wales (1997-2002)<sup>15</sup> concluded that:</p> <p style="padding-left: 40px;">"Alprazolam was significantly more toxic than other benzodiazepines. The increased prescription of alprazolam to groups with an increased risk of deliberate self poisoning is concerning and needs review."</p> <p><b>United States.</b> In 2009, slightly over 120 million visits were made to Emergency Departments (EDs) in general-purpose hospitals in the United States, and the Drug Abuse Warning Network (DAWN) estimates that at least 4.5 million of these visits were drug related<sup>16</sup>. Drug-related ED visits have increased by over 80 percent since 2004. This increase primarily reflects greater numbers of medical emergencies associated with adverse reactions, accidental drug ingestions, and misuse or abuse of prescription drugs and over-the-counter medications.</p> <p>About 2.1 million ED visits resulted from medical emergencies involving drug misuse or abuse, the equivalent of 674.4 ED visits per year per 100,000 population. Drugs for insomnia and anxiety were involved in 24.7 percent of visits where drugs and alcohol were taken together, with the largest part of that being benzodiazepines (anti-anxiety drugs; 21.0%).</p> <p>Pain relievers were the most common type of drugs reported in the nonmedical use category of ED visits (47.8%). Drugs used to treat anxiety and insomnia were also seen frequently (33.6%) in visits related to nonmedical use of pharmaceuticals. Benzodiazepines were involved in 29.0 percent of such ED visits, with alprazolam (e.g., Xanax®), indicated in 10.4 percent of such visits.</p> <p>At 38.1 percent, pain relievers were the most commonly involved type of drug in drug-related suicide attempts. Benzodiazepines followed pain relievers at 28.7 percent, with alprazolam and clonazepam (e.g., Klonopin®) accounting for 11.7 percent and 8.1 percent of these visits, respectively.</p> <p>The number of drug-related suicide attempts has remained stable from 2004 to 2009. However, a significant rise was observed in the involvement of two pain relievers—hydrocodone and oxycodone—and</p>	
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<sup>15</sup> Isbister GK et al. Alprazolam is relatively more toxic than other benzodiazepines in overdose. *Brit J Clin Pharmacol* 2004;58:88-95.

<sup>16</sup> Substance Abuse and Mental Health Services Administration, Drug Abuse Warning Network, 2009: National Estimates of Drug-Related Emergency Department Visits. HHS Publication No. (SMA) 11-4659, DAWN Series D-35. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2011. Available from: <http://www.samhsa.gov/data/2k11/DAWN/2k9DAWNED/HTML/DAWN2k9ED.htm>

## Benzodiazepines

three anti-anxiety drugs—alprazolam, clonazepam, and zolpidem (e.g., Ambien®).

Among individuals attending EDs seeking detoxification services, the types of drugs involved, cocaine was observed in 29.2 percent of visits, heroin in 28.4 percent, marijuana in 18.3 percent, and stimulants in 5.4 percent. Among pharmaceuticals, narcotic pain relievers were observed in 38.2 percent of visits, including oxycodone at 22.2 percent. Benzodiazepines were observed in 23.7 percent of visits, with alprazolam at 13.5 percent.

**Victoria, Australia.** A 2004 study of all medication overdose presentations to an inner-city Melbourne hospital found that two benzodiazepines, diazepam and alprazolam, appear to be over-represented in the overdose data relevant to their population levels of prescription<sup>17</sup>.

When the number of overdose events treated involving the different benzodiazepines is related to a more accurate description of the number of prescriptions provided to Victoria in 2004, it can be seen that alprazolam is the most over-represented in terms of the number of presentation per million prescriptions (Victorian data calculated from Australian information supplied by the PBAC Drug Utilisation Subcommittee). See table.

ben zodi aze pine	No. cases	scripts 2004	cases per m scripts
diaz epa m	46	568,787	80.9
alpr azol am	26	174,880	148.7
tem aze pam	20	767,036	26.1

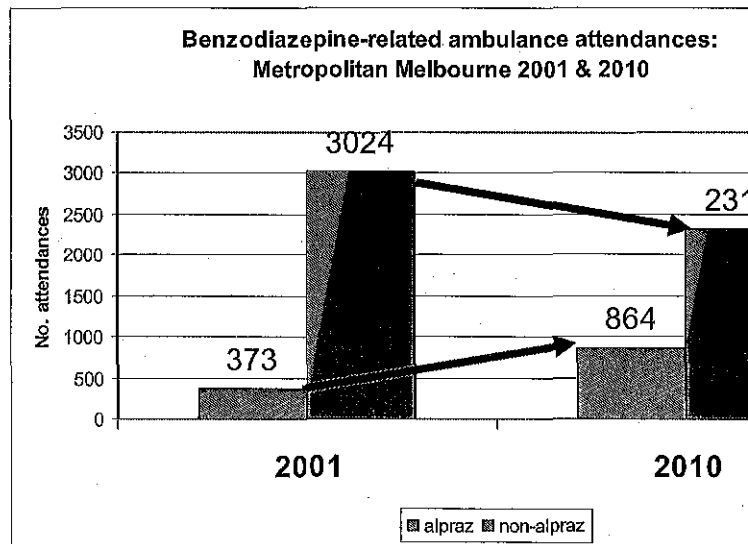
<sup>17</sup> Buykx P et al. Medications used in overdose and how they are acquired – an investigation of cases attending an Inner Melbourne emergency department. Aust NZ J Public Health 2010;34:401-4.

## Benzodiazepines

Another Victorian study examining the antecedent circumstances of non-fatal heroin overdoses found that there was a 28-fold greater risk of overdose if benzodiazepines had been used in the preceding 12 hours<sup>18</sup>.

### Ambulance data from Melbourne.

Best et al reported an analysis of ambulance attendance records in Melbourne to determine trends in involvement of benzodiazepines, and particularly alprazolam in ambulance attendances between 2001 and 2010<sup>19</sup>. They reported a small decline in general number of benzodiazepine attendances, but that alprazolam-related attendances had increased by 132%, and that furthermore taking prescription numbers into account, noted a two-fold increase in rates, and rates for alprazolam arising to double that of diazepam in 2010.



### Misuse by people who inject drugs (PWID).

The National Drug and Alcohol Research Centre auspices the Illicit Drug Reporting System, a continuing study of drug use and harm by people who inject drugs (PWID). The study interviews approximately 100 subjects from each Australian jurisdiction.

<sup>18</sup> Dietze P et al. Transient change in behaviour lead to heroin overdose: results from a case-crossover study of non-fatal overdose. *Addiction* 2005;100:636-42

<sup>19</sup> Best D et al. Alprazolam and wider benzodiazepine misuse in Australia – sources of supply and evidence of harms. *Aust NZ J Psychiatry* 2012;

## Benzodiazepines

In Victoria 71% of the sample reported recent use of benzodiazepines, although a much smaller proportion reported recent injection (2%)<sup>20</sup>. Sixty-nine percent of the sample reported recent use of illicit alprazolam, the highest single report in the Victorian IDRS of illicit use of a prescribed medication.

The 2011 survey focused on the drug or drugs KE perceived to be 'most problematic' at the time of interview. A total of 17 responses were elicited in this area of questioning. The drugs named as most problematic by KE were most commonly prescription opiates (n=8), alprazolam (Xanax, a short-acting benzodiazepine) (n=3) and antipsychotics (n=3).

It can be seen from the table below that for Victorian IDRS subjects:

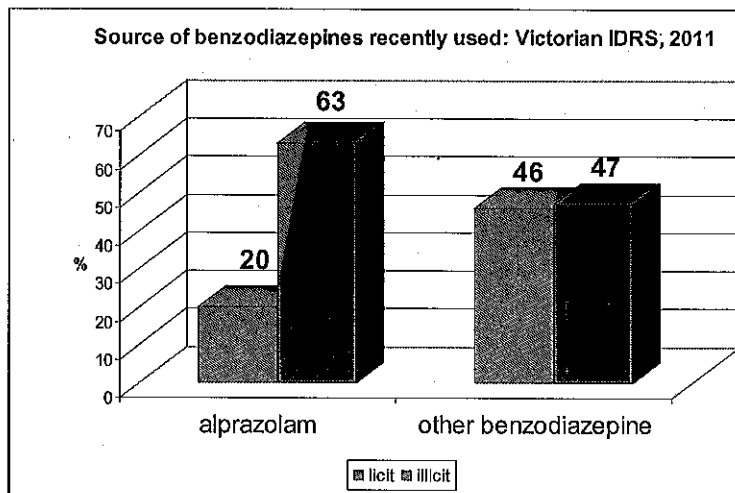
- only 20% of subjects using alprazolam in the last 6 months obtained it on prescription, compared to 46% of other benzodiazepine users
- a higher proportion of subjects using alprazolam in the last 6 months obtained them illicitly without a prescription (63%) than subjects using other benzodiazepines (47%)
- alprazolam injection in the last 6 months was more common (7%) than injection of other benzodiazepines (2%) and alprazolam injected was exclusively obtained illicitly (without prescription).

	Ever used %	Ever injected %	Used last 6 months %	Inje mc
<b>Alprazolam</b>				
Alpraz prescribed	31	3	20	
Alpraz not prescribed	81	11	63	
Any form	88	14	69	
<b>Other benzodiazepines</b>				
Prescribed	75	7	46	
Not prescribed	73	9	47	
Any form	92	12	71	

<sup>20</sup> Kirwan A et al. Drug Trends 2011. Findings from the Illicit Drugs Reporting System. Macfarlane Burnet Institute for Medical Research and Public Health and Turning Point Alcohol and Drug Centre Australian drug Trends Series No 76, Melbourne 2012

## Benzodiazepines

Alprazolam was considerably less likely to be prescribed directly to those using it, and more likely to be obtained through illicit sources (not prescribed to the individual) than other benzodiazepines.



A study of use of alprazolam among Victorian Illicit Drug Reporting System over the 3 years 2008-10 comparing IDRS subjects using alprazolam with those using other benzodiazepines, found that the significant differences were that they were more likely to be currently prescribed opioid substitution treatment (OST) (66.7% vs 49.8%), mainly using illicit benzodiazepines (59.5% vs 29.6%), more likely to have recently injected a benzodiazepine (14.8% vs 4.9%), and more likely to have sold drugs for cash (42.0% vs 26.9%)<sup>21</sup>. The authors also reported that Needle and Syringe Program staff accessed through the IDRS in Melbourne had reported increasing antisocial behaviour, particularly opportunistic criminal activity, believed to be associated with alprazolam use.

Reports by Australian IDRS subjects of trends in their recent use of alprazolam and of the most common benzodiazepine injected show increasing trends of use and injection of alprazolam in the period 2003 to 2011.

<sup>21</sup> Horyniak D et al. The use of alprazolam by people who inject drugs in Melbourne, Australia. Drug and Alcohol Rev 2011;

## Benzodiazepines

Year	% recent use alprazolam	Most common injected
2003	3	diazepam
2004	4	diazepam
2005	5	diazepam
2006	6	diazepam
2007	11	alprazolam
2008	14	alprazolam
2009	17	alprazolam
2010	21	alprazolam
2011	46	alprazolam

**Benzodiazepine use causes particular problems for opioid dependent people.**

A number of papers describe that benzodiazepine use by injecting drugs users is associated with poorer social functioning, greater levels of polydrug use, and increased risk of HIV risk-taking behaviour such as needle sharing, borrowing or sharing injection equipment, increased frequency of injection, increased injection of heroin and methamphetamines than other PWID<sup>22 23</sup>. Benzodiazepine users in methadone treatment also exhibited higher levels of psychopathology and social dysfunction than other methadone maintenance clients.

Another study examined the health service utilisation and benzodiazepine use among heroin users recruited through the Australian Treatment Outcome Study (ATOS)<sup>24</sup>. Benzodiazepine users had more GP and psychiatrist visits, were more likely to have had an ambulance attendance and had significantly more dispensed prescriptions.

<sup>22</sup> Darke S et al. Benzodiazepine use and HIV risk-taking behaviour among injecting drug users. *Drug Alcohol Depend* 1992;31:31-6.

<sup>23</sup> Darke S et al. Drug use, HIV risk-taking and psychosocial correlates of benzodiazepine use among methadone maintenance clients. *Drug Alcohol Depend* 1993;34:67-70.

<sup>24</sup> Darke S, Ross J et al. Health service utilization and benzodiazepine use among heroin users: findings from the Australian Treatment Outcome Study (ATOS). *Addiction* 2003;98:1129-35.

## Benzodiazepines

<p>Benzodiazepine co-dependence with opioid dependence exacerbates the opiate withdrawal syndrome. In one study, Co-dependent patients had significantly more severe opiate withdrawal symptoms<sup>25</sup></p> <p>Benzodiazepine use by patients in methadone treatment causes significant problems for many patients. Those who used benzodiazepines experienced more polydrug use, and higher self-rated psychopathology and psychological distress scores<sup>26</sup>.</p> <p>Co-ingestion of benzodiazepines with methadone augments the physiological and subjective opioid effects of methadone<sup>27</sup>. Use by methadone patients increased some subjective opioid effects, and this may be related to the relatively greater use and abuse of benzodiazepines in this population.</p> <p><b>Misuse of benzodiazepines amongst drug treatment clients.</b></p> <p><b>Australia.</b> Nielsen et al examined the pharmaceutical drug misuse of clients admitted to drug treatment in four States in Australia (Victoria, Western Australia, Tasmania and Queensland)<sup>28</sup>.</p> <p>Pharmaceutical opioids and benzodiazepines were identified as the most commonly misused prescription drugs, with a broad range of treatment presentations, such as dependence developing from medical use and pharmaceutical drugs being used as a substitute for illicit drugs. Key Experts also reported a group of pharmaceutical misusers who did not present for treatment at traditional alcohol and drug treatment services, with these primary pharmaceutical misusers being thought to be a "hidden population".</p>	
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<sup>25</sup> De Wit C et al. Benzodiazepine co-dependence exacerbates the opiate withdrawal syndrome. *Drug Alcohol Depend* 2004;756:31-5.

<sup>26</sup> Bleich A et al. Benzodiazepine abuse in a methadone maintenance treatment clinic in Israel: characteristics and a pharmacotherapeutic approach. *Isr J Psychiatry Relat Sci* 2002;39:104-12.

<sup>27</sup> Preston KL, Griffiths RR et al. Diazepam and methadone interactions in methadone maintenance. *Clin Pharmacol Ther* 1984;36:534-41

<sup>28</sup> Nielsen S, Bruno R, Carruthers S, Fischer J, Lintzeris N, Stooë M. INVESTIGATION OF PHARMACEUTICAL



## Benzodiazepines

<p>Diazepam and alprazolam were the most common benzodiazepines reported. A range of harms (including dependence, withdrawal, effects on memory and a range of injecting related harms) were reported, although only a minority of these harms resulted in a medical intervention. Among the benzodiazepines, alprazolam was particularly associated with the experience of harmful outcomes.</p> <p>Alprazolam appeared to be more problematic than other benzodiazepines with disproportionate harms associated with alprazolam use.</p> <p>While data indicates that diazepam was the main benzodiazepine used by the sample, a large proportion of individuals reporting seizures (55%), traffic accidents (50%), and crime (30%), while under the influence of benzodiazepines, identified that alprazolam was the main benzodiazepine involved (ahead of diazepam and other benzodiazepines). As such, there was a disproportionately high level of harm associated with alprazolam use.</p> <p>It appears that rates of harms are broadly comparable with pharmaceutical opioids and benzodiazepines, though effects on memory and being arrested while intoxicated appeared more common with benzodiazepines. A disproportionate amount of harm was reported with the benzodiazepine alprazolam.</p> <p>The findings of this study, in agreement with the recommendation in the DCPC report (Drugs and Crime Prevention Committee, 2007) was that alprazolam was more problematic than other benzodiazepines. The finding of disproportionate harms associated with alprazolam use is significant. Monitoring to establish the extent of alprazolam misuse and related harms is warranted to inform consideration of whether a regulatory response is required.</p> <p>The authors referred to a number of journal articles describing problems with alprazolam<sup>29 30 31 32</sup>.</p>	
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<sup>29</sup> French AP (1989) Dangerously aggressive behavior as a side effect of alprazolam. *The American Journal of Psychiatry* 146:276.

<sup>30</sup> Rudorfer MV, Osman OT and Potter WZ (1989) Alprazolam and aggression. *The American Journal of Psychiatry* 146:949-950.

<sup>31</sup> Verster JC and Volkerts ER (2004) Clinical Pharmacology, Clinical Efficacy, and Behavioral Toxicity of Alprazolam: A Review of the Literature. *CNS Drug Reviews* 10:45-76.

## Benzodiazepines

### United States.

A recent paper from the United States reported on the number of substance abuse treatment admissions reporting both benzodiazepines and narcotic pain reliever abuse in the period 2000-2010, and noted that there was a 569.7% increase in these admissions over this period, while the number of other admissions had decreased by 9.6%<sup>33</sup>. The average age of benzodiazepine and narcotic pain reliever combination admissions was 31.2 years, and 66.9% were aged 18-34 years, whereas 43.7% of other admissions were in this age bracket, and a higher proportion of other admissions were older. A higher proportion of these admissions were female than for other admissions.

In 2010, 48.2% reported primary narcotic pain reliever abuse and secondary benzodiazepine abuse, while 9.9% reported primary benzodiazepine abuse and secondary narcotic pain reliever abuse. The remaining 41.7% reported some other primary substance abuse with benzodiazepines and narcotic pain reliever as secondary or tertiary drugs of abuse.

More than one-third of the admissions reported initiating narcotic pain relievers first (34.1%); more than one quarter reported initiating benzodiazepines first (27.1%), and the remainder (38.7%) reported that the two drugs were initiated in the same year.

In the month prior to treatment admission for combination benzodiazepine and narcotic pain reliever abuse, 61.2% reported daily use of any substance compared with 34.6% of other admissions.

Treatment admissions differed in this group, with benzodiazepine and narcotic pain reliever combination admissions were more likely than other admissions to self-refer to treatment (35.7% vs 30.5%), and less likely to be referred through the criminal justice system (20.3% vs 39.8%), suggesting that they were a different cohort.

<sup>32</sup> Verster JC, Volkerts ER and Verbaten MN (2002) Effects of alprazolam on driving ability, memory functioning and psychomotor performance: a randomized, placebo-controlled study. *Neuropsychopharmacology* 27:260-269.

<sup>33</sup> Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. (December 13, 2012). *The TEDS Report: Admissions Reporting Benzodiazepine and Narcotic Pain Reliever Abuse at Treatment Entry*. Rockville, MD.

## Benzodiazepines

<p>Benzodiazepine and narcotic pain reliever combination admissions were more likely to report a co-occurring psychiatric disorder than other admissions (45.7% vs 27.8%).</p> <p>The high proportion of benzodiazepine and narcotic pain reliever admissions reporting daily use suggests behavioural patterns that may be difficult to change, and the individuals involved need to be prepared for the severe withdrawal effects from both drugs, particularly since benzodiazepines may worsen the withdrawal effects of narcotic pain relievers.</p> <p><b>Misuse, diversion and trafficking.</b></p> <p>A US study examining how drug dealers acquire their inventory of prescription drugs, and which types they most commonly sell, found that the type of medication most commonly sold by dealers was prescription opioid analgesics, and to a lesser extent benzodiazepines such as alprazolam.</p> <p>"Xanax pills (2 mg), known as 'zanny bars' or 'footballs', were also a fairly common medication that dealers reported selling, but this comprised a much lower proportion of their overall sales in comparison to opioids."</p> <p>The Drugs and Crime Prevention Committee of the Victorian Parliament recently conducted an <i>Inquiry into The Misuse/Abuse Of Benzodiazepines And Other Forms Of Pharmaceutical Drugs in Victoria Melbourne</i><sup>34</sup>.</p> <p>Because of the evidence they received about the particular concern about alprazolam relative to other benzodiazepines, the committee included a special note on alprazolam (See Appendix 1).</p> <p>Witnesses reported evidence that alprazolam can be particularly dangerous when used for recreational purposes or administered the wrong way. Experts reported the highly addictive qualities and difficulties</p>	
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<sup>34</sup> Drugs and Crime Prevention Committee. Inquiry into the misuse/abuse of benzodiazepines and other forms of pharmaceutical drugs in Victoria Melbourne: Parliament of Victoria 2007.

## Benzodiazepines

<p>associated with withdrawing from the drug. Also that it was becoming favoured as a drug for misuse. There was also concern that alprazolam featured more prominently in crime-related activity. Others reported that alprazolam tablets were being trafficked on the street, used as a 'date rape' drug, or used to facilitate robberies.</p> <p>The note included reference to a submission from the Victorian Interhospital Addiction Liaison Association (VAILA) that alprazolam was one of the most widely abused benzodiazepines, and that management of withdrawal was particularly difficult. VAILA recommended that this benzodiazepine be rescheduled to Schedule 8.</p> <p>The note went on to describe action taken in Tasmania to misuse of alprazolam.</p> <p>Another report by the Drugs and Crime Prevention Committee of the Victorian Parliament<sup>35</sup> <i>Inquiry into the Impact of Drug-related Offending on Female Prisoner Numbers - Interim Report</i>. noted a submission from support organisations for women released from prison reporting that misuse of prescription medications contributed to offending and imprisonment. Women who had been in 'the system' felt that 'pills' presented a greater risk for offending than heroin. The Committee was told that the legal and illegal use of Xanax and benzodiazepines was an issue. Moreover, anecdotal reports alleged there are certain health professionals allegedly well known to prescribe high doses of these and other highly addictive prescription drugs to dependent women on request. The Committee was also told that many clients who had been in prison or police custody in the past six months reported that their offences had not been pre-planned and that they could not recollect their actions as a result of 'Xanax misuse blackouts'</p> <p><b>Trafficking: Street price of alprazolam tablets in Melbourne.</b></p> <p>Submissions to the two Drugs and Crime Prevention Committees inquiries described above report black market prices of alprazolam:</p> <p>A submission to the <i>Inquiry into The Misuse/Abuse Of Benzodiazepines</i></p>	
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<sup>35</sup> Drugs and Crime Prevention Committee. *Inquiry into the Impact of Drug-related Offending on Female Prisoner Numbers - Interim Report*. Melbourne: Parliament of Victoria, 2010

Benzodiazepines

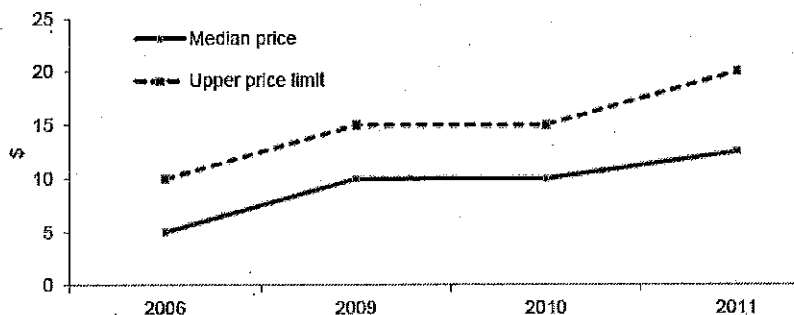
And Other Forms Of Pharmaceutical Drugs in Victoria Melbourne from the Pharmacy Board of Victoria reported that it was not uncommon for Xanax tablets (100) to be prescribed and dispensed as private prescriptions and then on-sold on the street at \$5.00 per tablet.

A submission to the *Inquiry into the Impact of Drug-related Offending on Female Prisoner Numbers - Interim Report* described that "It was further reported that specific areas of Melbourne are well known for the sale and distribution of illegal benzodiazepines, including Richmond and Footscray where it is allegedly possible to purchase three Xanax off the street for \$10."

The Tasmania IDRS has followed prices paid for alprazolam on the street in that State for several years<sup>36</sup>.

In the 2011 study, the median last purchase price for a 2mg alprazolam tablet was \$12.50 (range \$8-20, n=26). The median purchase price has steadily increased from \$5 in 2006 following the regulatory changes in that State. Similarly, the range of prices paid by participants has increased: in 2006, \$10 was the maximum price paid for a 2mg tablet, in 2011 this increased to \$20,

Figure 65: Median and upper limit of prices paid for 2mg alprazolam, 2006-2011



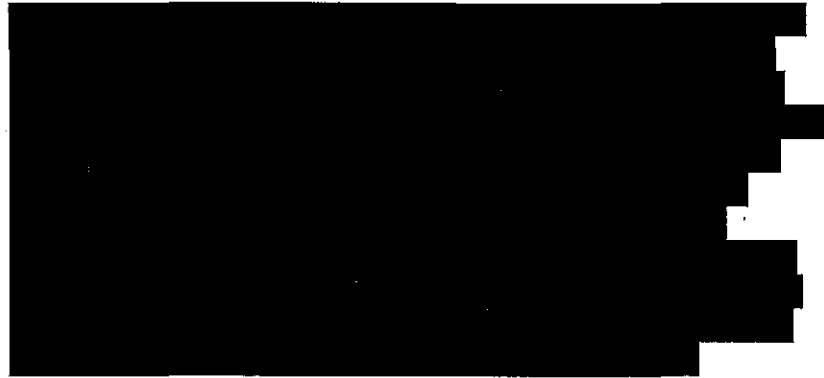
Source: IDRS PWID interviews  
 \*This data was not collected in the 2007-2008 surveys

In 2010 the Chief Health Officer of the Northern Territory informed general practitioners and psychiatrists in the Territory about problems of limb ischaemia from the injection of alprazolam, and other problems (See Appendix 4). The letter included a reference to street price in the Northern Territory and Adelaide: the lucrative street price of a single 2

<sup>36</sup> De Graaf B et al. Tasmanian Drug Trends 2011. Findings from the Illicit Drug reporting System. Australian Drug Trends Series No 77. School of Psychology, University of Tasmania. 2012.

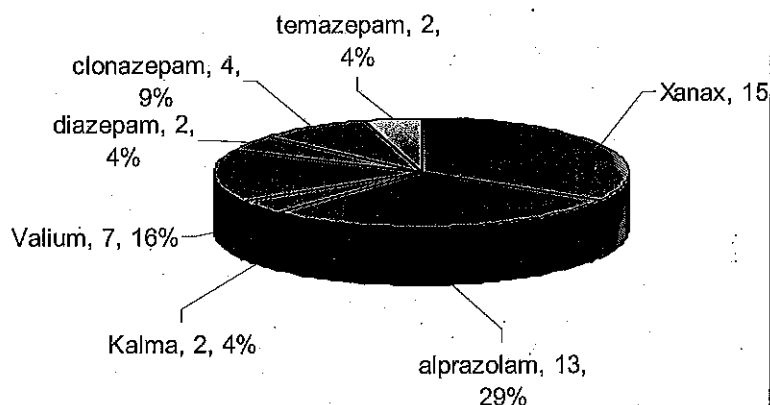
## Benzodiazepines

mg tablet of alprazolam in Darwin and Alice Springs was described as around \$15, and up to \$20, and that it was around \$10 in Adelaide.



A review of a series of consecutive reports of forged or altered prescriptions to Drugs and Poisons Regulation of the Victorian Department of Health in 2012 found that reports of prescriptions forged to obtain benzodiazepines was prevalent. When 96 consecutive reports of all forged prescriptions were examined to identify those where a benzodiazepine was sought and determine the particular benzodiazepine reported to be sought by forgery, alprazolam and the brand names Xanax® and Kalma® comprised 65.4% of all benzodiazepine reports.

**Forged and altered benzodiazepine prescription reports: Victoria, 96 consecutive reports 2012.**



**Other crime associated with alprazolam.**

Best et al report a study of the relationship of benzodiazepine use and crime among substance using offenders recruited through the criminal justice system in Melbourne<sup>37</sup>. These offenders reported high rates of diazepam (84% in the month prior to the index offence) and alprazolam (75% for the prior month) use. There were multiple diversion points involved in acquiring benzodiazepines. There was widespread access to prescriptions for 'fake' as well as 'real' symptoms, as well as high levels of street purchasing – particularly for alprazolam. Additionally, there was considerable trading and sharing of benzodiazepines among substance-using networks. They concluded that alprazolam use is associated with both drug-related offending and increased utilisation of emergency medical resources in Victoria.

Margaret Harding, who presided as magistrate of Victoria's Drug Court for nearly a decade, described her experience of observing the worst outcomes of the criminal justice system because of Xanax<sup>38</sup>. The court's purpose is to divert drug offenders from prison and into treatment provided they comply with certain conditions including drug treatment orders including undergoing regular drug screening. She was reported as believing that without a doubt Xanax was responsible for her revoking more drug orders than any other substance, including heroin, methamphetamines and alcohol

She describes: "Time after time I heard the same story. People who had

<sup>37</sup> Best D, Wilson A, Reed M, et al. (2012) Understanding the role of benzodiazepine use in crime. Melbourne: Victorian Department of Health

<sup>38</sup> Julie-Ann Davies. Daily Life. High anxiety. 25 July 2012. <http://www.dailylife.com.au/health-and-fitness/dl-wellbeing/high-anxiety-20120716-225gd.html> (accessed 17 January 2013).

## Benzodiazepines

<p>struggled really hard to get off heroin and methadone start to get their lives back on track, see their kids again, and then one night on Xanax and it was all gone. They'd go out and commit a string of burglaries and not even remember they'd done it.</p> <p>"And when they came before me - and these were people whose lives I came to know a lot about - and I asked, 'What went wrong?', they would tell me it was much easier to say no to heroin than to Xanax."</p> <p><b>Pharmacy robbery in US.</b></p> <p>The New York Times reported in 2011 that there were 1,800 robberies of U.S. pharmacies in preceding 3 years, and the most common drugs targeted were hydrocodone, oxycodone and Xanax<sup>39</sup>.</p> <p><b>Driving.</b></p> <p>Benzodiazepines are commonly found in blood samples taken from drivers involved in major trauma accidents in Australia<sup>40</sup>. Ogden et al reported on benzodiazepines and the risk of collision in Victoria, Australia<sup>41</sup>. They studied 184 injured drivers and report that while diazepam accounted for 51% of detected benzodiazepines, alprazolam at 11% had the most concerning contribution to collisions with 94% of those detected culpable. The contribution of alcohol in combination with benzodiazepines was significant, particularly in excess of the therapeutic range. They recommended the rescheduling of alprazolam to Schedule 8 should be discussed given that only one of 44 alprazolam drivers had no other drugs in their system or blood levels were within the therapeutic dose range. They also reported that these results probably indicated that this group of drivers were using alprazolam outside normal prescribing patterns possibly indicative of an abuse pattern.</p> <p><b>Responses of Australian regulatory authorities to problems with alprazolam.</b></p> <p>As a result of evidence and reports of particular problems with alprazolam, a number of State and Territory regulatory authorities have communicated concerns to medical practitioners either through leaflets, web pages, or articles in medical registration boards.</p> <p>See attachments 2-5.</p> <p><b>Tasmania. (See Appendix 2).</b> Concern about problems with alprazolam in Tasmania emerged in the mid-2000s, because of concern as follows</p> <ul style="list-style-type: none"><li>• the per capita prescription rate was double that of national rate</li><li>• there were repeated reports of cases of morbidity and mortality involving alprazolam</li><li>• A Working party involving the RANZCP, RACGP, and State government representatives was formed in 2006 to develop a response.</li><li>• Education sessions to regions began in 2007</li><li>• Regulatory changes were enacted in 2007:</li></ul>	
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<sup>39</sup> Goodnough A. Pharmacies besieged by addicted thieves. New York Times, 6 February 2011.

[http://www.nytimes.com/2011/02/07/us/07pharmacies.html?pagewanted=all&\\_r=0](http://www.nytimes.com/2011/02/07/us/07pharmacies.html?pagewanted=all&_r=0) (accessed 15 January 2013).

<sup>40</sup> Ch'ng CW et al. Drug use in motor vehicle drivers presenting to an Australian, adult major trauma centre. Emerg Med Australas 2007;19:359-65.

<sup>41</sup> Ogden EJD et al. Benzodiazepines and risk of collision Presentation to the Australasian Professional Society on Alcohol and Drugs 2012 Annual Conference. 2012.



## Benzodiazepines

- Pharmacy were required to report monthly on alprazolam dispensing
- a permit was required when prescribing alprazolam for more than >4 weeks where opioids also prescribed
- approval was required for patients receiving opioid substitution therapy for opioid dependence (OST)

**Victoria. (See Appendix 3).** Needle and Syringe Program staff in Melbourne had reported increasing antisocial behaviour, particularly opportunistic criminal activity, believed to be associated with alprazolam use, and problems with violent and aggressive behaviour within the program shop fronts, for which they had no memory the next day when they returned. This behaviour was linked to the use of alprazolam, which NSPs described as "angry pills". These findings prompted the Medical Practitioner's Board of Victoria (MPBV) to issue a warning in June 2009 to all registered practitioners in the state that 'alprazolam is more subject to non-medical use, and causes a disproportionately high level of serious harm, than other benzodiazepines', recommending that 'alprazolam should only be prescribed where there is a clear indication for its use'<sup>42</sup>.

**Northern Territory. (See Appendix 4).** The Chief Health Officer of the Northern Territory informed general practitioners and psychiatrists in the Territory that over the past year several people had been admitted to hospital with severe ischaemic limb damage and disability associated with injecting of alprazolam. Also that increasing other problems associated with inappropriate oral use as well as injecting. In addition, the letter reported growing concern nationally about the escalating harms associated with abuse of benzodiazepine generally, in particular alprazolam, and the need to exercise great care in prescribing.

The letter described that benzodiazepines, in particular alprazolam, are often sought to enhance the 'high' of injected opioids.

The letter also described the lucrative street price of a single 2 mg tablet of alprazolam in Darwin and Alice Springs at around \$15, and up to \$20, and that it was around \$10 in Adelaide.

**South Australia. (See Appendix 5).** The Drugs of Dependence Unit of South Australian Department of Health provide a resource for prescribers in that State. It described that alprazolam abuse was being more frequently reported. It warned prescribers about the risk of being identified as a 'script doctor'.

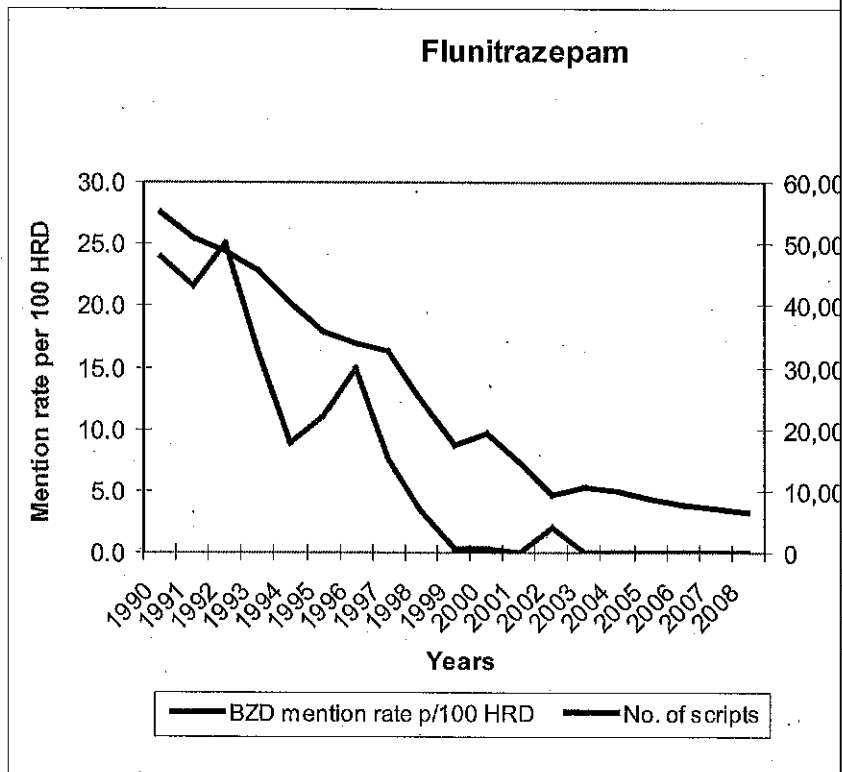
<sup>42</sup> Medical Practitioners Board of Victoria. Warning: Alprazolam (Xanax, Kalma, Zamhexsal), Bulletin. June 2009,

## Benzodiazepines

**Will selective rescheduling of alprazolam to Schedule 8 merely shift the choice of benzodiazepine for misuse to another equally harmful benzodiazepine?**

In recent years particular problems with individual high-risk benzodiazepines resulted in regulatory responses that resulted in considerable public health benefits, and concerns that those misusing them would merely shift to another benzodiazepine for misuse proved unfounded.

**Flunitrazepam (Rohypnol).** When flunitrazepam was rescheduled to Schedule 8 in 1993 because of concerns about its abuse liability, preference for it by people who inject drugs, and association with drug facilitated sexual assault, there was no shift to misuse of other benzodiazepines, but there was a favourable result in a decrease of detection of this drug in heroin-related deaths in Victoria (See figure). Roche pharmaceutical company removed their 2 mg product Rohypnol from the market, and it was replaced with a 1 mg tablet.



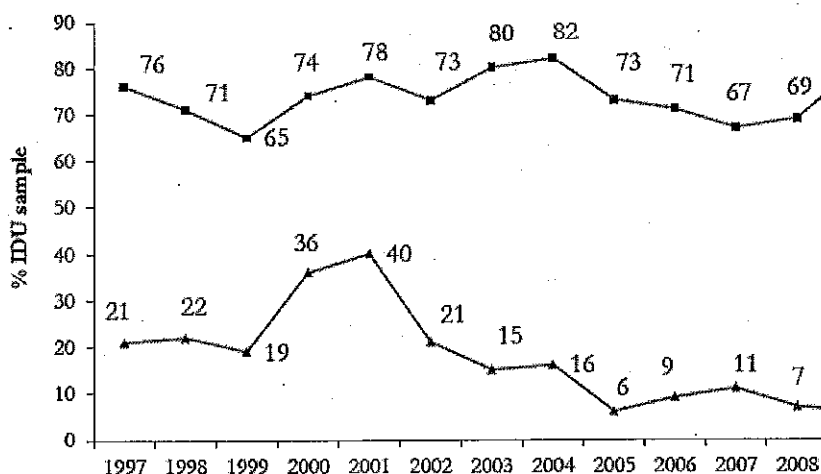
## Benzodiazepines

**Temazepam gelcaps.** When injection of the liquid contents of temazepam gelcaps became prevalent among PWID, and was causing considerable problems with ischaemic limb injury and gangrene, and other vascular and associated problems at the time of the heroin shortage in 2000, the response was first to limit access to the capsules as a PBS subsidised drug while continuing to leave temazepam tablets available as a subsidised drug. The gelcaps were subsequently removed from the market in 2002. There was concern then that PWIDs would merely shift to misusing and injecting other benzodiazepines.

History reveals that injection of temazepam by PWIDs, and benzodiazepine injection generally, has plummeted and remained at very low levels subsequent to the PBS changes and removal of the readily injectable gelcaps from the market.

This graph (the lower curve) describes trends in injecting of benzodiazepines by IDRS subjects in Victoria<sup>43</sup>.

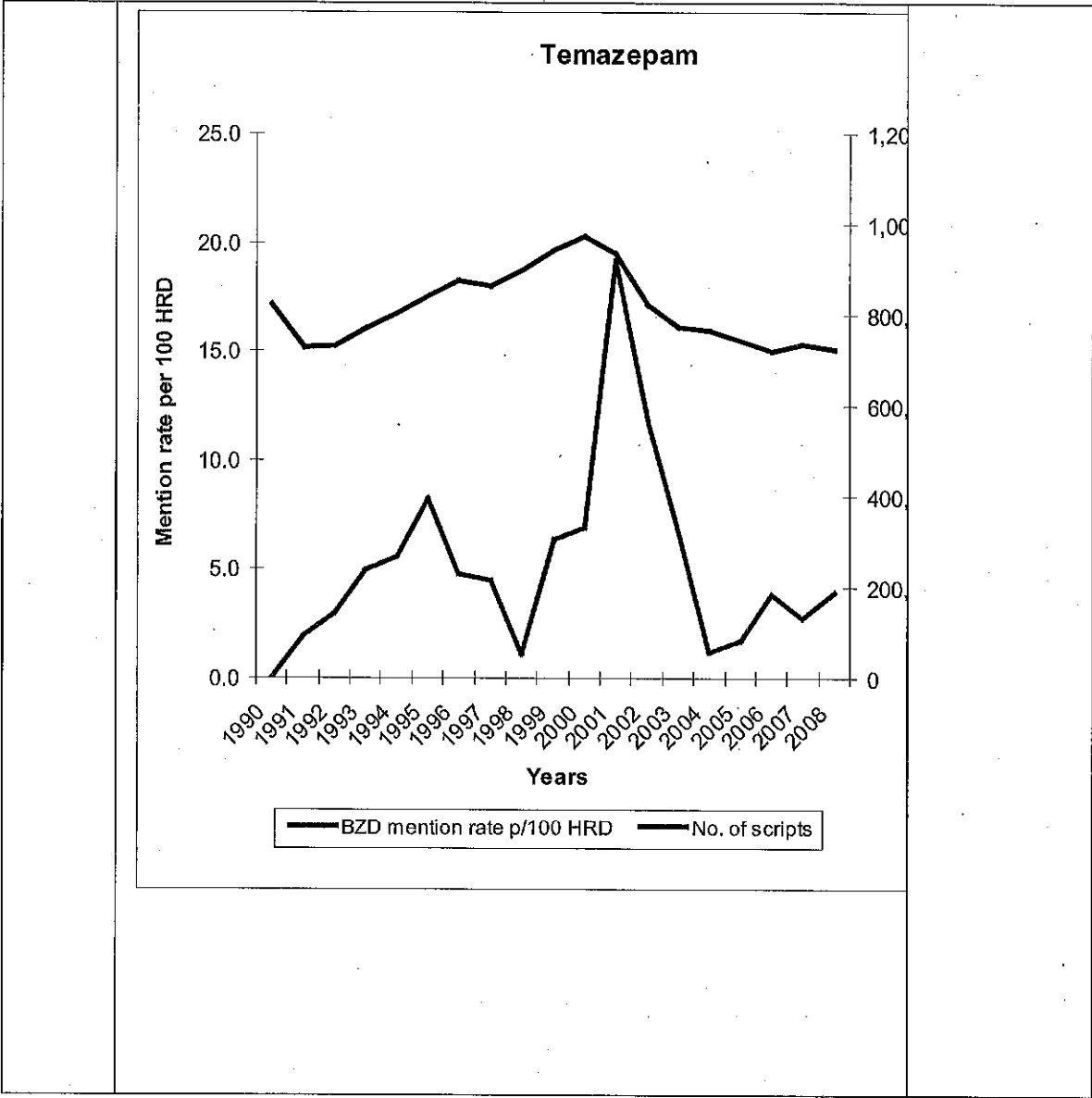
**Figure 7: Percentage of PWID reporting recent benzodiazepine use and injecting of benzodiazepines by IDRS subjects in Victoria 1997-2011**



Detection of temazepam in heroin-related deaths in Victoria, which peaked at the height of the heroin shortage, plummeted subsequent to the removal of the gelcaps from the market.

<sup>43</sup> Kirwan A et al. Drug Trends 2011. Findings from the Illicit Drugs Reporting System. Macfarlane Burnet Institute for Medical Research and Public Health and Turning Point Alcohol and Drug Centre Australian drug Trends Series No 76, Melbourne 2012

Benzodiazepines



## Benzodiazepines

I respond to endorse the chapters statement , recommending alprazolam be rescheduled to s8 In my role on WAs Community opioid pharmacotherapy Mortality review comity and in clinical practice ,I have seen Alprazolam become the most problematic benzodiazepine Seeing it with increasing frequency in abuse situations with anxiety disorders ,poly substance abuse ,behaviour problems and in fatal and non-fatal overdose .

Clearly authorization for panic disorder hasn't limited it's use ,particularly as little provokes panic as readily as alprazolam withdrawal . I would not be in favour of making all benzodiazepines s8 at this time , mainly for practical reasons . Considerable thought regarding implementation and perhaps review of pack size and other means allowing a staged process would be needed to manage a general change of all benzodiazepines to s8 .

## Benzodiazepines

Thank you for your email of 17 January 2013 in which you seek feedback on proposals put forward by the RACP in relation to the possible re-scheduling of the benzodiazepine class of medications or more specifically, alprazolam due to the large number of prescriptions for the entire class. I note in particular and concur with the observations made by the AChAM Policy and Advocacy Committee.

While I applaud the central thrust of this proposal and indeed, agree that we need to look at how we can significantly reduce the often less than clinically appropriate or helpful prescribing of benzodiazepine medications in Australia, I'm not so sure this is the way to achieve this end, at least not in isolation. I would note that a range of other current schedule 8 drugs and in particular, the strong opioids and psychostimulants, are a source of significant clinical and public health concern. Of course, their schedule 8 status has not in itself prevented their inappropriate prescribing and use in the community, though one might quite fairly argue that the regulatory, monitoring and response mechanisms that are in place in most states and territories have served to limit inappropriate prescribing and related harm.

In most but not all states, doctors must have a permit to prescribe schedule 8 medications after 2 months or immediately if there is a history of drug dependence. I understand there are variations in the doses and other aspects of prescribing which determines what different states require and what they do in response. It would be possible to make all benzodiazepine medications recordable and to put in place electronic flags when these medications are prescribed inappropriately, at least in those states that maintain regulatory capacity to respond in such a manner. The DORA system which has been developed in Tasmania and which is now being made available to all states and territories could form the basis of this electronic monitoring and response. However, few states and territories have sufficient regulatory capacity to respond in a meaningful and timely way to breaches. It would be my position that they should develop this capacity but no doubt, others wishing to find every avenue to save health expenditure would not agree.


As an aside, the Commonwealth has an authority system for the prescribing of clonazepam but it is not really working very well because Commonwealth government officers have no clinical knowledge and unfortunately, doctors prescribe this medication in the absence of careful assessment and the establishment of a genuine diagnosis of epilepsy. Of course the authority system relates to payment rather than regulatory authority to prescribe and this distinction is often not well understood. This demonstrates the often disconnect between regulation and clinical acumen and capacity to respond in a meaningful way.

Benzodiazepines

Placing alprazolam on schedule 8 will open up a range of challenges for states and territories including the requirements for recording and safe storage and the administration of these requirements. Once again, it will also raise the challenges of responding in a meaningful and timely way to breaches and defining upfront what those breaches should be. These things need to be carefully worked through. In talking to colleagues, I perceive they also recognise that a broader ranging strategy is required to take this matter forward and this proposal is unlikely to be supported in its current format; even though the overarching objective is sound. While I often lament delays in progressing sound public policy, in these circumstances I would politely suggest that it might be prudent to delay putting this proposal up until there has been further opportunity to work through the detail. I would note that a *National Pharmaceutical Misuse Framework* is pending release and that Tasmania released its *Report - A review of opioid prescribing in Tasmania. Blueprint for the future*. Both of these documents highlight the complexity and challenges ahead in working to ensure more rational and safe prescribing of analgesic and psychotropic medications in Australia.

These are just my brief comments given the short time available to respond. I would be very pleased to work with colleagues in taking this matter forward because I do agree it is important for a range of clinical, public safety and population health reasons.

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<p>29 Jan 13.</p>	<p>In my practice in chronic pain, where polypharmacy occurs , the co prescription of benzodiazepenes with opioids in high doses/ or misused has been associated with significant morbidity and mortality (as reported by the Victorian Coroner)</p> <p>I would consider voting YES , but would take time to read more concerning the motivation for the change and consider implication in variety of practice areas</p>	
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## Benzodiazepines

31 Jan  
13

I respond to endorse the chapters statement , recommending alprazolam be rescheduled to s8 In my role on WAs Community opioid pharmacotherapy Mortality review comity and in clinical practice , I have seen Alprazolam become the most problematic benzodiazepine Seeing it with increasing frequency in abuse situations with anxiety disorders ,poly substance abuse ,behavior problems and in fatal and non fatal overdose

Clearly authorization for panic disorder hasn't limited it's use ,particularly as little provokes panic as readily as alprazolam withdrawal . I would not be in favor of making all benzodiazepines s8 at this time , mainly for practical reasons . Considerable thought regarding implementation and perhaps review of pack size and other means allowing a staged process would be needed to manage a general change of all benzodiazepines to s8 .

**I provide this input on behalf of the Australia and New Zealand Child Neurology Society.**

The major issue that is not discussed in the paper you have forwarded is the use of benzodiazepines for control of seizure disorders (clonazepam, clobazam, midazolam and to a very limited extent nitrazepam) and also for managing spasticity (diazepam). Benzodiazepines are very effective and clobazam is probably one of the most commonly prescribed paediatric anti-epileptic drugs. In these circumstances long term prescription of benzodiazepines is entirely appropriate.

Our concerns are that:

1. Classifying all benzodiazepines as S8 drugs stigmatises patients with epilepsy as taking drugs off addiction which may have adverse impacts on compliance/acceptance of benzodiazepines for seizure control
2. That classifying benzodiazepines as S8 will further complicate the already difficult process of prescribing anti-convulsants (a lot of prescriptions are already authority)

While it is clear there are major community problems associated with benzodiazepines, there does not appear to be evidence that appropriate paediatric prescribing of benzodiazepines has adverse consequences.

I would hope that drugs legitimately used as anti-convulsants/ anti-spasticity medications might be excluded from this process.

I am happy with this we do need to consider one other use of benzos, that required for status at home or school. We may need to add a section regarding this use??

The problem with restricting all use to time cause issues with the use of Midazolam/ Diazepam for acute seizure control in Children (not sure if this is a problem also with adults). The practice is to use nasal or buccal midazolam for acute status, they require a supply at home at all times. Usually we only prescribe limited quantities however some children with intractable seizure require a significant amount of treatment at various

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	<p>times in their life.</p> <p>I am not sure if a streamline authority for this may be a way around it? They do require to be prescribed in multiples of 5 as they are foil protected in packs of 5</p>	
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<p>5 Feb 13</p>	<p>The revised recommendations are much better. The graph I sent you helps explain my concern and might be included in the document: alprazolam is not the only problematic bdz and if up-scheduled, will lead to a shift to other drugs. I doubt the committee wants to be rescheduling various bdz's on an annual basis.</p> <p>The issue here is that S8 scheduling has very limited capacity to protect the public. Other measures, including those listed below are needed.</p>	<p>Paul Haber</p>
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## Benzodiazepines

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Benzodiazepines



[Redacted]

To whom it concerns, (which is all of us)

Having been a registered nurse division 1 for over 30years I am strongly in favour of this amendment. If it stops just one part of the downfall of a safe system then this can only be good for everyone in the community and all health professionals. Why did we ever stop counting it in the registers in the first place? Whose dumb idea was that? Yes it will take a lot longer now to count the S8's but the health department can just pay for more handover time through the Aged care funding instrument if necessary. This will surely cut down the ease of access to S4 benzodiazepines and make the safety of staff and residents alike a lot more stringent. Please go ahead with this amendment as soon as possible.

[Redacted]

[Redacted]

Benzodiazepines



[REDACTED]

Dear Sirs,

This is going to cause chaos;

1. There will be a significant impost on doctors attending aged care facilities who will have to manually write the wording on the scripts. Already script production is a major issue with ACFs and we are desperately short of doctors willing to undertake this work. This rescheduling will be very unhelpful.

2. There will be major problems with chemists and the need for extra secure storage and an excessive amount of accountability.

I am unsure as to the reason for this rescheduling; if it is intended to reduce the usage of benzodiazepines this should be managed by education, not by creating more red tape.

If it is because of concerns that benzodiazepines are being misappropriated / abused, other ways to target how this is happening should be looked at; a blunderbuss approach like this will cause excessive work in an already overloaded system.

[REDACTED]

[REDACTED]

**Benzodiazepines: Proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8.**

Dear Sir/Madam,

I read the proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8 with some interest as I recently completed a doctorate promoting quality psychotropic use in Australian aged care homes. As you may be aware, benzodiazepines are used extensively in this setting. In fact, a recent large national prevalence study found that 41% of all residents were prescribed benzodiazepines, with 26% of residents taking these medications on a regular daily basis, contrary to numerous practice guidelines.<sup>1</sup>

As the public have been provided with limited information we can only speculate why this rescheduling has been mooted. If the proposed rescheduling is intended to reduce the use of benzodiazepines by making them more difficult to obtain, I believe such a move is misguided.

As an example where S8 restrictions have not impacted medication use, the use of transdermal buprenorphine and oxycodone, both S8, and, like benzodiazepines, medications associated with a high rate of dependency, has increased unabated over the past ten years. The S8 restriction does not appear to have impacted the use of either medication.

Research evidence has shown that legislative change may initially result in a slight decrease in the use of medications; however, this strategy is not sustainable. In the United States, regulation was used as a strategy to decrease the use of psychotropic drugs in nursing homes (OBRA-87).<sup>2</sup> After a few years though, rates of use started to creep up to pre-regulation levels and now use is at an all-time high<sup>2</sup>. Many experts theorised that the principle reason for this is that prescribers and administrators simply find a way to get round restrictions. They don't know the reasons why these drugs are inappropriate and therefore are not motivated to promote/ensure quality use of the medication. This is the true root of the problem.

**The most effective way to change prescribing behaviour is through the use of quality, evidence-based education and by highlighting and benchmarking individual prescribing behaviour through the use of audits; followed by targeted patient case-by-case review.**

In a project conducted by the Unit for Medication Outcomes, Research and Education at the University of Tasmania, regular benzodiazepine use in 13 nursing homes was reduced from 38% to 23% over an 18-month period through the use of nurse education, audit feedback and individual resident review. The reduction in use was sustained after the education was completed.<sup>3,4</sup>

An important issue to highlight is that several PBS-subsidised benzodiazepines, specifically oxazepam, nitrazepam, diazepam and temazepam are available in double quantities, with multiple repeats, to aged care home residents who are deemed dependent on benzodiazepines. I can't think of a more effective way to actually promote long-term extended use of these agents. To actually subsidise this inappropriate prescribing practice defies logic. It would make little sense if this subsidisation of double quantity benzodiazepines for extended periods was continued and an S8 restriction applied.

In conclusion, I believe that benzodiazepines should not be rescheduled but that resources are made available to provide coordinated quality education, audit and review to ensure an awareness of the risks associated with benzodiazepine use. This strategy would be more likely to impact use than rescheduling.

Yours sincerely,



## Benzodiazepines

### References:

1. Westbury J, Schotel F, Brown D, Curtain C, Veal F. Psychotropic Use in a large sample of Australian Aged Care Homes: 2011-2012. 2013.
2. Hughes C, Lapane K, Mor V, et.al. The impact of legislation on psychotropic drug use in nursing homes: a cross-national perspective. *J Am Geriatr Soc* 2000;48:931-7
3. Westbury J, Jackson S, Gee P, Peterson G. An effective approach to decrease antipsychotic and benzodiazepine use in nursing homes. *International Psychogeriatrics* 2010;22:26-36.
4. Westbury J, Beld K, Jackson S, Peterson G. Review of psychotropic medication in Tasmanian residential aged care facilities. *Australasian Journal of Ageing* 2010;29:72-9.



## Benzodiazepines

We just got this in our email today for a response that is due tomorrow.

This rescheduling of Benzodiazepines is an absolute joke. It will put more strain on our workload in terms of entering stock coming in and out in the drug register, costs involved in paying pharmacists to stay back to enter in stock, costs of drug register books. If the Guild put forward this submission, they are certainly not looking after their members.

At the end of it all, the pharmacist suffers. We should be targeting doctors prescribing habits.

The more administrative jobs placed on the pharmacist, the less time we have with patients, the higher risk of errors, especially drug register entries, the greater the risk of coming before the state health departments for disciplinary issues.

Please call me on [REDACTED]. I would like to get my point across verbally rather than by email. I would also like to find out who put this request for the rescheduling forward so I can personally give them my point of view.

Sincerely

[REDACTED]

[REDACTED]