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.

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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.

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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.*

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    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.*

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 [1]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

care professionals (HCPs) and consumers. Such education should include continuing education modules for prescribing drugs with abuse potential[1].

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[2]. 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[3]. Benzodiazepines are renowned for being a common substance of abuse in Australia[4]. Patients will therefore engage in the practice of prescription shopping to obtain extra supplies of benzodiazepines[4].

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[5].

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[6].

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 [7]. 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 [8]. Furthermore, motor vehicle accidents are significantly increased for drivers on combinations of alcohol and other psychoactive drugs including opioid substitution therapy (OST[3];). 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 [9] [10] .

Alprazolam

Alprazolam is a short-acting benzodiazepine and its consumption in Australia is more problematic than other short-acting benzodiazepines[11]. When used concurrently with methadone, alprazolam is associated with severe intoxication, paroxysmal aggression and troublesome interactions with potentiation of both drugs[12]. 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[13]. For example, in Victoria during the period 2001 to 2010, alprazolam-related ambulance attendances increased by 132 per cent [14].

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 [15].

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 [16].

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[17].

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 supports 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 [12].

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:

- 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 [18].

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

[1] http://www.drugs.vic.gov.au/temazepam/).

[2] Medicare Statistics website at: https://www.medicareaustralia.gov.au/statistics/pbs_item.shtmlhttps://www.medicareaustralia.gov.au/statistics/pbs_item.shtml

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[4] (see http://ndarc.med.unsw.edu.au/project/illicit-drug-reporting-system-idrs).

[5] http://www.medicareaustralia.gov.au/provider/pbs/prescription-shopping/index.jsp

[6].(http://nceta.flinders.edu.au/nceta/research_and_projects/current_projects_and_research#id59).

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