Australian Government
Department of Health
Therapeutic Goods Administration

Addressing prescription opioid use and misuse in Australia

Regulatory Impact Self-Assessment Report

Version 1.0, November 2019

TGA Health Safety Regulation

Contents

The problem – increasing use of and harms from prescription opioids

In 2014, almost 3 million people in Australia were prescribed at least one opioid under the Pharmaceutical Benefits Scheme (PBS) or Repatriation PBS (RPBS). Since the end of 2009, there has been a general increase in prescriptions, from about 10 million annually to 14 million annually.

Levels of prescription opioid overdose, including accidental overdose are at record levels in Australia and internationally. One of the contributing factors has been significant 'indication creep' – their use in a range of types of chronic non-cancer pain, despite limited evidence of efficacy or safety for opioids in many of those patients. Use in chronic pain is also driven by the inconsistent efficacy of alternative medicines in chronic pain such as non-steroidal anti-inflammatory drugs (NSAIDs), gabapentoids, antidepressants and muscle relaxants; opioid analgesics are often used when pain is refractory to these other treatments. Judicious prescribing for some patients with chronic non-cancer pain has been described as an appropriate option.

Australia currently ranks eighth internationally on the numbers of defined daily doses of prescription opioids per million population (at about 40% the level of the USA). In the USA, opioid analgesics are now the most commonly prescribed class of medications.

Pharmaceutical opioid deaths in Australia now exceed heroin deaths by a significant margin – by 2-2.5 times – the reverse of what was seen in the 1990s. Between 2011 and 2015 there were 2,145 deaths associated with oxycodone, morphine, codeine, fentanyl, tramadol and/or pethidine compared with 985 due to heroin. Pharmaceutical opioid deaths particularly dominate in the over 30 age group.

Why government action is needed

Opioid use and misuse is having a critical impact on patients, their families and the health system. Every day in Australia, nearly 150 hospitalisations and 14 emergency department admissions involve opioid harm; and three people die from drug-induced deaths involving opioid use.[1]

As such, the Australian Government has asked the Therapeutic Goods Administration (TGA) to play a role in tackling the problem; and in early 2018 a public consultation was conducted on potential actions and activities the TGA could undertake to mitigate the risks of inappropriate use and misuse of prescription opioid products.

It is recognised that use, and misuse, of opioids is affected by a wider range of factors than just TGA's regulation of these products, including, but not limited to, the availability of pain management specialists and services. However, as overseas experience by comparable medicine regulators demonstrates, regulatory actions can influence and lead to changes in prescriber behaviour.

[1] https://www.aihw.gov.au/reports/illicit-use-of-drugs/opioid-harm-in-australia/contents/summary

Proposed policy options

Acknowledging that strong opioids play a critical role in managing severe acute pain following trauma and major surgery, as well as pain experienced in many forms of cancer and some other conditions, it was agreed that any regulatory response must not unduly restrict informed, rational prescribing of these products.

The focus was on the higher-risk Schedule 8 (S8) opioids, although some Schedule 4 (S4) opioids were also considered.

The possible options (which are not mutually exclusive) considered were:

Option 1: Consider the pack sizes for strong (S8) opioids

Require sponsors to register both smaller (such as maximum three-day) pack sizes for treatment of patients with acute pain and suitable pack sizes (14 or 28-day).

Option 2: Consider a review of the indications for strong (S8) opioids

Review indications for the S8 opioids and align them to current clinical guidelines for appropriate prescription of these products.

Option 3: Consider whether the highest dose products should remain on the market, or be restricted to specialist/ authority prescribing

Review the place of the higher dose S8 opioid products in the management of chronic cancer and non-cancer pain and whether certain high dose products should continue to be registered. We would consider if specific controls, such as approval to prescribe through states and territories or the PBS should be introduced.

Option 4: Strengthening of the Risk Management Plans for opioid products

Review current risk management plans for opioids to determine whether they currently reflect best practice in opioid prescribing and management of risks.

Option 5: Review of label warnings and revision to Consumer Medicines Information

Under this option, warnings could be placed on the packaging of opioid products identifying the risk of dependence and overdose and lack of efficacy in the long term treatment of chronic non-cancer pain, noting that the complexity of appropriate management of chronic non-cancer pain needs to be recognised. The CMI would also be reviewed to provide greater emphasis on risks of dependence, especially those associated with high doses.

Option 6: Consider incentives for expedited TGA review of improved products for pain relief and opioid antidotes

Provide priority review to new chemical entities that are viable alternatives to opioids for pain relief and also expedite the review of smaller pack sizes and/or abuse-deterrent formulations and products that can be used to negate the effect of opioids.

Option 7: Potential changes to use of appendices in the Poisons Standard to provide additional regulatory controls for strong S8 opioids (this could potentially include controls of prescribing for particular populations or classes of medical practitioners, additional safety directions or label warning statements, specific dispensing labels).

Powers under medicines scheduling could potentially include controls of prescribing for particular populations or classes of medical practitioners, additional safety directions or label warning statements, specific dispensing labels.

Option 8: Increase health professional awareness of alternatives to opioids (both S4 and S8 opioids) in the management of chronic pain.

Improving health practitioner uptake and awareness of existing clinical guidelines for the management of acute and chronic pain, which further provide advice on the use of non-pharmacological and alternate pharmacological therapies for the management of pain.

Public consultation

The TGA undertook extensive public consultation to reach an informed decision of which regulatory options to pursue. The public consultation was undertaken through a written submission process, which received a total of 98 submissions from a range of stakeholders including health professionals, medical institutions and medical professional bodies; government bodies; consumers and consumer organisations; medicine industry organisations; and industry suppliers/sponsors/manufacturers.

Further consultation on prescription opioid use and misuse in Australia was conducted at a targeted stakeholder workshop on 1 June 2018. Senior staff members from the TGA also have taken part in workshops in Brisbane, Melbourne and Canberra that were organised by peak clinical and pharmacy groups in June and July 2018 on options to manage prescription opioid use and misuse.

Consultation outcomes summary

There was strong and consistent support from these stakeholder engagements for four of the proposed options in the consultation paper. The supported options were:

- reviewing available product pack sizes for opioids commonly used to treat acute pain;
- reviewing the indications for the opioid products used to treat pain;
- reviewing the label warnings and content of Consumer Medicines Information (CMI) documents for opioids; and
- working with stakeholders to raise health professional and consumer awareness about pain management guidelines, including the use of non-opioid alternatives for the management of chronic pain; and safe disposal of opioid products.

The consultation response and stakeholder workshops also raised a number of broader initiatives to address issues associated with opioid abuse and misuse that did not fall within the regulatory remit of the TGA.

Some respondents expressed concern that any regulatory actions should not impair clinically-appropriate access to opioid medications for the treatment of chronic pain, including cancer-related pain. It is recognised that opioids are essential medicines that play a critical role in pain management. In implementing the above options, Australian patients will be able to continue to access opioids appropriately and safely.

Following the initial consultation, the TGA established the Opioid Regulatory Advisory Group (ORAG), which includes representatives from a range of health professional and consumer organisations, to provide independent, expert advice, as TGA has undertaken the three reviews above. ORAG has strongly supported the proposed options and provided advice on how best to implement them.

Reforms being implemented

The TGA has undertaken the above reviews and, as a result, is implementing the following:

- registration of smaller pack sizes for oral immediate-release prescription opioid products;
- requiring boxed warnings and class statements in the Product Information (PI) documents for all prescription opioids in relation to their potential for harmful and hazardous use;
- ensuring that safety information, including the relevant warnings, is prominently displayed in the Consumer Medicines Information (CMI) to provide consistency of language and information across all classes of prescription opioids;
- restricting the indications (the appropriate circumstances for use of a medicine) within the PI documents for prescription opioids where appropriate to reinforce that opioids should only be used when other analgesics have proven not to be effective;
- restricting the indication for fentanyl patches to state they should only be prescribed to treat pain in patients with cancer, patients in palliative care and those with exceptional circumstances in recognition of the increased potential for harmful and hazardous use; and
- education and communication activities using a range of channels to ensure health professionals follow best prescribing practice and consumers are fully informed on how best to use opioids.

Implementation of these actions is consistent with actions other medicines regulators, such as the Food and Drug Administration (FDA) and Health Canada, have taken to reduce prescription opioid misuse.

Smaller pack sizes

Registration of smaller pack sizes will require impacted sponsors to submit a Self-Assessable Request (SAR) to TGA to vary their product's entry on the Australian Register of Therapeutic Goods (ARTG).

Smaller pack sizes reduce unused opioids circulating in the community may be used in harmful or hazardous ways, either inadvertently or deliberately, or become targets for theft. TGA will not de-register existing larger pack sizes, so they continue to be available where they are clinically necessary for a patient's treatment.

Changes to indications, inclusion of boxed warning, inclusion of precautions and warning information and updating CMI

Sponsors will be required to submit a Safety-Related Request (SRR) to TGA to change their product's indication, to include the boxed warning and precautions and warnings class statement. They will also have to make consequential changes to update their products' CMIs.

The indications (the appropriate circumstances for use of a medicine) in the PI documents for prescription opioids will reinforce that opioids should only be used when other analgesics have proven not to be effective.

The updated fentanyl indication will help reduce the inappropriate use of this powerful opioid in patient groups where the risks outweigh the benefits. Fentanyl is a very powerful opioid and therefore overdose is more likely to occur in those patients that have not been prescribed an

opioid before being prescribed fentanyl. Fentanyl is also a major target for diversion and harmful and hazardous use, and the changes will help reduce these undesirable outcomes.

The additional boxed warnings and class statements will remind prescribers of the appropriate circumstances for opioid use and discourage inappropriate prescribing.

The various improvements to information for prescribers and patients will encourage best-practice prescribing and help consumers to be better informed about the potential risks and how to mitigate them.

Regulatory burden costing

A quantification of the regulatory impact of the above actions has been undertaken; and is as follows:

Average annual regulatory costs (from business as usual) ($million)

Change in costs	Business - $	Community Organisation - $	Individual - $	Total change in costs
Option A				
Status quo: current regulatory framework is appropriate – no change is required				
Option B				
Amended the regulatory framework for prescription opioids in accordance with the 5 proposed regulatory changes	$0.108			$0.108

Implementation and evaluation

These actions, with the exception of education activities, will be implemented as per the existing regulatory and business processes TGA has for safety-related changes to a product's registration, with medicine sponsors needing to submit the necessary requests to TGA for review and approval.

Following the introduction of these actions, the prescribing of opioids in Australia is expected to change significantly. The outcomes of these regulatory actions will be evaluated periodically through analysis of key data sources including: PBS prescription volume data and total volume of supply data which is currently procured by the TGA.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Technical and Safety Improvement Section	November 2019

Therapeutic Goods Administration

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