



Therapeutic Goods Administration
PO Box 100
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31 August 2018

Dear Sir/Madam

CONSULTATION: BOXED WARNING GUIDANCE

Painaustralia welcomes the opportunity to provide input to the Therapeutic Goods Administration's (TGA) consultation on boxed warning guidance for prescription medicines in Australia.

Painaustralia is the national peak body working to improve the quality of life of people living with pain, their families and carers, and to minimise the social and economic burden of pain. Members include pain and other specialists, health practitioners, health groups, consumers and researchers. Painaustralia works with our network to inform practical and strategic solutions to address this complex and widespread issue. As such, the issue of boxed warning guidance is an important one for us and our members.

Painaustralia and its members have been actively engaged on the issue of quality use of medicines for many years. As the TGA's consultation paper notes, boxed warnings typically concern prominent safety issues with a potential for major impact on public health.

As many people living with chronic pain opt to self-medicate their condition, it is vital that they are able to understand the components of their medication, and the risks associated with them. When it comes to prescribed medications, clear visibility of safety concerns are vital to ensure prescribers are aware of the risks and in aiding consumers to comply with their course of treatment and avoid adverse health outcomes.

As noted in the consultation paper, boxed warnings within the product information document for a medicine can represent one of the most serious types of warnings that can be mandated by a regulatory agency as a risk mitigation strategy. The guidance is intended to assist sponsors to understand their obligations and prescribers to understand the rationale for the warning and the magnitude of risk. This is of particular relevance to the growing concerns around prescribing and misuse of pharmaceutical opioids in Australia.

Understanding Pain:

One in five Australian adults are estimated to live with chronic pain (daily pain for more than three months, experienced in the last three months)¹. This is consistent with global estimates.² Pain in general is prevalent, with 67% of Australians reporting experienced bodily pain in the last four weeks in 2007-08. Around one in ten Australians experience severe or very severe levels of pain.³

The rates of chronic pain are on a par with the prevalence of mental ill-health in Australia,⁴ yet pain remains a neglected and misunderstood as a public health issue.⁵ Pain conditions are widespread,

¹ <https://www.ncbi.nlm.nih.gov/pubmed/11166468>

² <https://www.ncbi.nlm.nih.gov/pubmed/27537761>

³ <http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/4841.0Chapter12011>

⁴ <http://www.health.gov.au/internet/main/publishing.nsf/content/mental-fifth-national-mental-health-plan>

⁵ <https://bmcpublichealth.biomedcentral.com/articles/10.1186/1471-2458-11-770>

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with 30% of the population or 6.9 million Australians reporting arthritis in 2014-15, back pain was the third leading cause of disease burden in 2011 and one in 11 Australians reported osteoarthritis in 2011.⁶

Almost one in five of all GP consultations involved patients who had arthritis, chronic back pain or both conditions, irrespective of whether the condition was managed.⁷ Some pain conditions are more prevalent in rural communities, with people outside the major cities reported to be 23% more likely to have back pain, rising to 30% for residents aged 55 to 64.⁸ This may be due to a greater proportion of the working population undertaking manual labour in these communities, increasing the incidence of workplace injury which can lead to pain conditions.

Children and adolescents are also affected by chronic pain, though it can be overlooked in these age groups due to a range of factors. Between 25 to 35 per cent of children experience chronic pain, with the greatest incidence in adolescents, especially for young girls, and about five per cent of children have moderate to severe pain, with headaches, abdominal pain, limb pain and complex regional pain syndrome the most common forms of pain.⁹

Reliance on medication for pain management:

Since February 2018 medicines containing codeine are no longer available without a prescription from a doctor or other suitably qualified health professional. Codeine upscheduling highlighted low levels of awareness in the community of alternative pain treatment options, including non-pharmacological options. Resources were required to provide greater awareness of these options.¹⁰

Similarly, the use of prescription opioids to manage chronic pain is an issue that is gathering increasing attention. Pharmaceutical opioids are the most commonly misused pharmaceutical (3.6%), followed by sedatives (1.6%).¹¹ Opioids are analgesics — used to treat pain — and include pharmaceutical medicines like codeine, oxycodone and fentanyl, as well as illicit substances like heroin. Opioids can be effectively used to treat acute or cancer pain, but there is increasing evidence that they are being over-prescribed for people experiencing chronic pain of an ongoing nature.

Guidelines for using opioids to treat pain have changed markedly, with prescription of opioids now only recommended for acute or cancer pain or palliative care. A recent landmark randomised controlled trial of long-term opioids compared to non-opioid medicines found the use of opioids failed to improve function but caused adverse effects and marginal pain intensity.¹

Governments around the world are looking at ways to minimise access to opioids and ensure the safe and effective use of medications. Without adequate access and knowledge of pain management, there is a greater reliance on pain medications to treat chronic pain despite limited evidence of their efficacy for that purpose or safety considerations.¹² This has seen a 30 per cent increase in opioid prescribing between 2009 and 2014¹³. Subsequently, too many Australians are dying due to overdoses involving prescription opioids and adverse effects of polypharmacy.

⁶ <https://www.aihw.gov.au/reports-statistics/health-conditions-disability-deaths/chronic-musculoskeletal-conditions/overview>

⁷ <https://www.myhealthycommunities.gov.au/our-reports/gp-care-patients-chronic-conditions/december-2014/report/key-findings-gp-care-for-patients-with-arthritis-and-chronic-back-pain>

⁸ <http://www.abs.gov.au/AUSSTATS/abs%40.nsf/Lookup/4102.0Main%2BFeatures30Mar%2B2011>

⁹ <http://www.anzca.edu.au/documents/children-with-chronic-pain-miss-out-on-services-me.pdf>

¹⁰ <https://www.tga.gov.au/codeine-information-hub-how-and-where-get-advice>

¹¹ AIHW 2018, Alcohol, tobacco & other drugs in Australia. Canberra Access online at:

<https://www.aihw.gov.au/reports/alcohol/alcohol-tobacco-other-drugs-australia/contents/impacts/social-impacts>

¹² <http://fpm.anzca.edu.au/documents/pm1-2010.pdf>

¹³ <https://www.tga.gov.au/sites/default/files/consultation-prescription-strong-schedule-8-opioid-use-misuse-in-australia-options-for-regulatory-response.pdf>

This is particularly pertinent in regional areas, where there is less access and availability of pain specialists and services due to geographical and cost barriers. Consumption of prescription opioids in regional areas was much greater than in capital cities as found in a 2017 analysis of 54 wastewater sites by the Australian Criminal Intelligence Commission. Consumption of powerful opioids oxycodone and fentanyl in regional sites was well above capital city levels, with the average use of oxycodone in regional areas almost double that in capital cities.¹⁴ The Australian Commission on Safety and Quality in Health Care revealed opioid medications were being prescribed in some regional areas at 10 times the rate of other areas and they recommend action on pain and opioid management in rural areas.¹⁵

Awareness of pain and pain management is also low amongst health practitioners. For example, clinicians' beliefs and practice behaviours relating to low back pain (LBP) were found to be discordant with contemporary evidence on the most effective treatments.¹⁶

Holistic strategies are required to ensure the safe and effective use of medications in pain management, including increasing understanding of best practice pain management in the community and among health practitioners.

Need to reinforce careful prescribing of opioids.

The non-medical use of pharmaceutical drugs is an increasing public health problem in Australia, with evidence suggesting increasing prevalence of misuse and associated harms, including mortality.

In 2016, an Australian most likely to die from a drug induced death was a middle-aged man misusing multiple prescription medications such as benzodiazepines or oxycodone.¹⁷ Benzodiazepines were also the most common drug present in drug induced deaths in 2016 (663 deaths involved benzodiazepines or 36.7%). In over 96% of these drug deaths, they were taken with other drugs, including alcohol¹⁸

Recent reports from the Australian Institute of Health and Welfare (AIHW) indicate that the rate of dispensed prescriptions for pharmaceutical opioids has been climbing—up 24% between 2010–11 and 2014–15. Between 2006 and 2016, the number of deaths where opioids were present rose by 127%.¹⁹

Most concerning, the misuse of pharmaceuticals is perceived to be acceptable by 28% of Australians, which is higher than for the use of other drugs such as cannabis or methamphetamine.²⁰

Thus, there is a need to reinforce information around opioid prescribing, particularly reminding healthcare professionals and the public of the need for careful prescribing and use of pharmaceutical opioids.

¹⁴ <https://www.acic.gov.au/publications/intelligence-products/national-wastewater-drug-monitoring-program-report>

¹⁵ https://www.safetyandquality.gov.au/wp-content/uploads/2015/11/SAQ201_01_FrontSection_v10_FILM_TAGGED-3-Key-findings-and-recommendations.pdf

¹⁶ <https://www.ncbi.nlm.nih.gov/pubmed/23139051>

¹⁷ Australian Bureau of Statistics (2016). Drug Induced Deaths in Australia: A changing story. Access online.

¹⁸ Op.cit ABS 2016

¹⁹ AIHW 2018, Alcohol, tobacco & other drugs in Australia. Canberra Access online at: <https://www.aihw.gov.au/reports/alcohol/alcohol-tobacco-other-drugs-australia/contents/impacts/social-impacts>

²⁰ AIHW 2018, Alcohol, tobacco & other drugs in Australia. Canberra Access online at: <https://www.aihw.gov.au/reports/alcohol/alcohol-tobacco-other-drugs-australia/contents/impacts/social-impact>

The case for Boxed Warnings

Australian and international guidelines support the avoidance of prescribing a combination of opioid and benzodiazepine medications^{21,22}

It is well-established that concomitant use of opioids with central nervous system depressants such as benzodiazepines or alcohol is associated with increased risk of profound sedation, respiratory depression, coma and death²³

These facts combined with the prescribing and accidental overdose data highlight the need for boxed warnings to be implemented for opioid medications in Australia.

Responses to questions raised in Consultations Paper

The following points cover our responses to the specific questions raised in the TGA consultation paper:

1. Required evidence to support a Boxed Warning

Painaustralia is supportive of an evidence-based approach to implementing boxed warnings. We also support the statement that a boxed warning may also be required where causality is not fully demonstrated, if the safety issue is of sufficient concern.

2. When a Boxed Warning is proposed

Painaustralia is supportive of the list of scenarios detailed in the consultation paper which may necessitate an action on boxed warnings.

3. Content of the Boxed Warning

Painaustralia supports 'the intention for the Boxed Warnings to provide a succinct warning statement and draws the attention of the prescriber to more detailed information within the main body of the product information'.

4. Content and Format of the Boxed Warning in the CMI

Painaustralia supports that if a Boxed Warning is required in the Product Information then a similar prominent Boxed Warning should generally also be placed at the beginning of the Consumer Medicines Information in a manner that provides sufficient information for a lay consumer to understand the risks or to prompt a conversation with a healthcare professional.

5. Format of the Boxed Warning in the PI

21 . FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. Updated 05/2017. (accessed online 17/7/2018) (<https://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM515636.pdf>)

22 Webster L. President's Message Eight Principles for Safer Opioid Prescribing. Pain Medicine 2013; 14:959- 961. (accessed online 23/7/18) (<http://onlinelibrary.wiley.com/doi/10.1111/pme.12194/pdf>)

²³ Op.cit. Webster.

Painaustralia is supportive of the formatting options outlined in the consultation paper.

6. Process requirements

Painaustralia is supportive of the process requirements outlined in the consultation paper.

7. Changing or removing a Boxed Warning

Painaustralia is supportive of the provisions outlined in the consultation paper that specify that sponsors must lodge an application with the TGA for a Boxed Warning to be reviewed if new data on the issue or adverse drug reaction becomes available, and/or if other risk management tools are proposed.

8. Timelines and implementation

Painaustralia is supportive of the intent for the guidance to apply prospectively where a Boxed Warning statement is required from the date of registration, and not retrospectively to current marketed products with (or without) existing Boxed Warnings, unless new safety information becomes available that would warrant such a statement.

We are also supportive of the timelines around the planned implementation of finalised guidance to be published later in 2018 and that they will take effect immediately.

Conclusion:

We need to ensure better awareness and provide more effective support to people living with pain if we are to reduce misuse of opioid and other medication in Australia. Dependence and unwanted side-effects can have a devastating impact on people's lives.

While we need to create greater awareness of appropriate use of opioids and other medications and risks associated with misuse, we also need proactive strategies that address current prescribing issues and Painaustralia believes that the TGA's development of guidance such as Boxed Warnings will aid in reducing the misuse of pharmaceutical opioids in Australia.

We trust that the matters raised through our submission will be useful in helping the TGA finalise guidance around Boxed Warnings and welcome the opportunity to discuss our submission with you further.

Yours sincerely

Carol Bennett
Chief Executive Officer

