PBAC Submission to the TGA consultation paper - Prescription strong (Schedule 8) opioid use and misuse in Australia – options for a regulatory response

Option 1: Consider the pack sizes for Schedule 8 (S8) opioids
Require sponsors to register and make available for supply both smaller (such as maximum three-day) pack sizes for treatment of patients with acute pain and suitable pack sizes (14 or 28-day) for treatment of people with chronic pain due to malignancy.

PBAC comments:

- The premise seems logical and may reduce wastage as patients who require opioids for acute pain may only require a short supply.
- Note that there is a risk of dependence after even a short-supply of opioids.
- Item restrictions would have to be split for short-term and long-term use and would require PBAC input.
- The restrictions would become more complicated, including for DHS to administer.
- For patients with acute pain requiring repeats, there could be implications associated with GP accessibility if there were any requirements for the same GP to be accessed for repeat prescriptions.
- If "require" becomes a condition of supply this would be quite new and would require careful construction so as to contain to opioids, otherwise it would be unlikely to be acceptable.
- Are there any options to promote doctors prescribing lower amounts through broken packs – this option is already available.
- If smaller pack sizes are not available internationally, the cost impost of adding pack sizes / presentations from an industry perspective will be higher if the packs are not otherwise available for other markets. In this instance, sponsors may request that the additional costs be passed on and therefore there will be cost, pricing and expenditure considerations – particularly if this is a requirement upon sponsors. A clear departmental view on this would be necessary.
- Time to availability of new pack sizes would include time for manufacturing considerations such as a scale-up if required, manufacturing changes such as labels in addition to registration of the new packs.
- If there will be new and different packs, there will be labelling considerations to improve communications and distinguishing features. This overlaps with option 5.

Option 2: Consider a review of the indications for strong opioids
The TGA will review indications for the S8 opioids and align them to current clinical guidelines for appropriate prescription of these products.

PBAC comments:

- PBS listing for most strong opioids is currently for chronic severe disabling pain which is unresponsive to non-opioid analgesics. PBAC consultation may be required to differentiate between acute post-surgical pain or cancer-related pain.

- This could involve a post-market review of strong opioids, with potential flow-on impacts on PBS restrictions.
- If the TGA restricts opioid indications, the current restrictions on the PBS may need to be reviewed to ensure they are consistent with the TGA approved indications.
- A PBAC Drug Utilisation Sub-Committee (DUSC) review may be beneficial in considering this option. There would need to be time allocated to undertake such a review.
- Based on the eTG (Appendix 1), use of S8 opioids for non-cancer pain is appropriate for patients with moderate pain that is not adequately relieved by paracetamol and/or an NSAID, and the pain is interfering with the patient's quality of life.

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.

Alternatively specialist-only/authority prescribing could be specified for PBS reimbursement, noting that this would not impact on private prescriptions (these could be potentially managed through state and territory regulations).

PBAC comments:

- There may be some merit in this approach, however initial prescribing criteria may be required that allows GPs to commence treatment whilst awaiting specialist consultation.
- This option requires consideration of which specialty prescribers would be included.
- Under authority prescribing, the capacity of DHS to authorise these prescriptions needs consideration.
- Acute pain is not covered under current PBS restrictions on oxycodone, except immediate release oxycodone – (Restricted benefit for chronic severe disabling pain; the condition must be unresponsive to non-opioid analgesics).
- Most jurisdictions have regulation regarding prescription of opioids that takes into account local nuances such as availability of specialists and pain clinics and difficulties around access in rural areas. This may be best left to the jurisdictions.
- Further stakeholder engagement with clinical experts would be recommended in further considering this option.

Option 4: Strengthening 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.

PBAC comments:

- Pharmacovigilance practices also apply under this option.

Option 5: Review of label warnings and revision to the 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.

PBAC comments:

- Some consumers will read the label warnings, but if care is not taken such warnings could deter patients from taking the drug when it may benefit them.
- CMI changes may be more beneficial for patient education and allow for more detail than a single label warning.
- The practicalities of revising CMI and distribution of these can be problematic. Input from the Consumers Health Forum and the Pharmacy Guild would be beneficial to this option.

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.

PBAC comments:

- This may not be consistent with priority review determination rules, though assessment of drugs and application of the determination rules would be best to take consideration of medicines in the pipeline for which there may be a high clinical need.
- An option for expedited review of innovative/improved products in appropriate presentations would be beneficial.
- There may be benefit in undertaking a horizon scan, including asking industry what is coming and what is innovative/new and considering any products/presentations elsewhere that Australia doesn't currently have.
- Is it possible for the ideal fixed dose combination or single agent strengths to be proactively identified and sought and would this be feasible for industry to undertake given the costs involved?
- Improved products, such as fixed dose combinations, may encounter quality use of medicine issues.
- If this approach were further investigated, the PBAC Executive would need to be engaged in the approach from the beginning.

Option 7: Potential changes to use of appendices in the Poisons Standard to provide additional regulatory controls for strong opioids

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 care professional awareness of alternatives to opioids (both Schedule 4 and Schedule 8) in the management of chronic pain

Existing clinical guidelines for the management of acute and chronic pain provide advice on the use of non-pharmacological and alternate pharmacological therapies for the management of pain. While these are available there may be limited health practitioner awareness and uptake.

- There is a role for the TGA in terms of prescribing controls, however the scope is limited given that changes will require a whole of system approach. Buy-in is required from all stakeholders in this process, particularly in the education space for pharmacists and clinical prescribers, through the NPS and the colleges.

Possible role of PBAC prescribing controls

- Requiring specialist review prior to prescription of certain medicines
- Narrowing the group of approved prescribers (the paper notes that while many S8 medicines fall below co-payment level for non-concessional patients, concessional patients are prescribed a disproportionate amount of S8 opioids)

PBAC comments:

- The jurisdictions are already seeking to manage prescriber controls, as per comment at option 3.
- Narrowing the group of approved prescribers would be difficult to implement effectively.
- See comments under option 3

The PBAC, or relevant oncologist members at minimum, would welcome any further clinical discussions on these matters as sought by the TGA, and would be particularly keen to be involved in further discussion around option 3.

Appendix 1

Additional relevant information

eTG Guidelines excerpt

(https://tgldcdp-tg-org-au.ez.library.latrobe.edu.au/viewTopic?topicfile=chronic-pain-pharmacological-management#toc_d1e75)

If a patient presents with moderate pain that is not adequately relieved by paracetamol and/or an NSAID, and the pain is interfering with the patient's quality of life, consider **adding** an oral opioid. The most appropriate regimen depends on the patient's response to previous therapy.

Role in chronic nonmalignant pain

Opioids work well in acute pain, but their role in chronic nonmalignant pain is limited. Randomised controlled studies of opioid treatment in chronic nonmalignant pain have been of short duration, so evidence for long-term benefit is lacking.

Experience suggests that opioids work in only one in three patients and that they reduce pain intensity by 30% to 50% at best. In patients taking opioids for chronic nonmalignant pain, about 80% have at least one adverse effect and only 44% remain on opioids long term.

Opioids may help patients by improving their function and quality of life, without necessarily reducing their pain.

Before starting an opioid in patients with chronic nonmalignant pain:

- explore all other treatment options, both physical and psychological
- assess the patient using a multidisciplinary approach
- discuss the adverse effects and possible harms and benefits of long-term opioid therapy
- obtain agreement/acceptance from the patient about the expected outcome of therapy (ie pain reduction rather than complete abolition of pain, reduced suffering, improved function and quality of life)
- explain that the opioid is being used as a trial and treatment will cease if there has not been significant progress towards achieving treatment goals over 4 weeks
- assess the potential for opioid abuse or misuse
- obtain agreement about monitoring, treatment adherence (compliance), and the consequences of nonadherence
- define strategies (open and transparent) to monitor adherence
- consider the use of an 'opioid contract'.

Trialling an opioid

If a decision is made to trial an opioid, always observe the rules outlined in. When assessing response:

- check for improvement in quality of life (sleep, mood, libido) and function (activities)
- record pain scores (for severity and duration of pain).

The opioid should be ceased if there is any evidence of misuse or abuse, if there is no improvement in the patient's wellbeing after 4 weeks, or if the opioids are having a detrimental effect.

Rules for use of opioids in chronic pain

Once a decision has been made to prescribe an opioid for chronic pain, observe the following rules:

- One clinician or team should be responsible for prescribing the opioid.
- Do not introduce an opioid at the same time as another drug.
- To minimise adverse effects, start with a low dose and adjust slowly according to response, ie 'start low and go slow'.
- Use lower doses in older people and monitor carefully.
- Avoid the use of immediate-release or parenteral opioids.
- Advise all patients to take laxatives at the commencement of treatment and then regularly, as needed.
- Remember all opioids have adverse effects.
- Review all prescription drugs and complementary and alternative medicines the patient is taking and check for potential interactions.
- Avoid the use of concurrent benzodiazepines as the combination can cause severe sedation and impair cognition and driving ability.
- Check what other agents the patient is taking that could potentially interact (eg alcohol, cannabis).
- Avoid the use of opioids for breakthrough pain.
- Regularly review the patient to monitor progress and to assess if ongoing opioid treatment is needed.
- If a decision is made to discontinue an opioid, it should be weaned slowly and under supervision. Seek specialist advice if uncertain about the weaning procedure.