| Regulatory options for consideration | For consideration – as outlined in the TGA's consultation paper (attached and available online) | Your feedback/comments |
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| **Option 1:** Consider the pack sizes for strong (S8) opioids | • **The option**: 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.<br>• **Potential implementation**: If agreed, these changes may be able to be implemented using powers through either or both the scheduling and/or the registration process. | Supported.<br><br>Easy to do. Will reduce inadvertent opioid dependence post acute pain. |
| **Option 2:** Consider a review of the indications for strong (S8) opioids | • **The option:** The TGA will review indications for the S8 opioids and align them to current clinical guidelines for appropriate prescription of these products.<br>• **Potential implementation:**This could be done following review of Cochrane and other reviews and meta-analyses of clinical data on opioid efficacy, assessment of therapeutic guidelines for pain treatment and through a standard consultative TGA process. It would require changes to the PI for the products where required (see sections 9D and 25AA of the*Therapeutic Goods Act 1989*). The TGA does have the necessary legal powers to enforce safety-related PI changes. | Strongly supported.<br><br>Opioids are unique as major class of drug which has never been assessed for its main usage – chronic non-cancer pain.<br><br>They should be assessed as a new medication, for efficacy in specific pain indications (i.e. back pain, arthritis, neuropathic pain), as well as safety including the risk of dependence, overdose and the risk of diversion to people for whom they were not prescribed.<br><br>The mechanism should be systematic review of RCTs with meta-anlyses (and if possible network meta-analyses). Existing Cochrane reviews find little benefit for opioids in chronic non cancer pain and it is likely that opioids would not meet the criteria to have maket authorisation for chronic non cancer pain conditions. This could NOT be done through a "standard TGA consultative process".<br><br>There would be enormous commercial interest in this review and the review group should have clear distance from any opioid manufacturers. It should look at long time efficacy, given that most people who take opioids for more than a few weeks are still taking them one year later. It should also look into efficacy and adverse |

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| | | effects of different opioids, i.e. full agonists vs partial agonists, strong opioids vs tramadol and tapentadol, abuse deterrent formulations etc…<br><br>As for other new medications, this review should be followed by a PBAC consideration of the funding of opioids. It used to be a PBAC requirement that for funding, opioids needed to be commenced in a hospital outpatients. This effectively limited use.<br><br>If asd a result of such as review, olpioids did not meet the standard for marketing approval in chronic non-cancer pain – there should be a separate process for deciding what to do with the people who have already been prescribed opioids for chronic non cancer pain. |
| **Option 3:** Consider whether the highest dose products should remain on the market, or be restricted to specialist/ authority prescribing | • **The option:**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.<br><br>• **Potential implementation**: The TGA could undertake a safety review of the benefit/ risk ratio for higher dose S8 opioid products but data is likely to be confounded due to different chronic pain populations (cancer versus non-cancer pain) and opioid tolerance.<br><br>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). | As long as this does not affect the capacity of people receiving high doses for palliative care then this is supported.<br><br>It will reduce overdose deaths if the largest size pill is unlikely to kill an opioid naiive person who takes it either by mistake or deliberately.<br><br>Limiting higher doses by authority or PBS is also a good strategy.<br><br>Dose may also be able to be limited through the authority process i.e. state authorities may give approval to use up to s certain dose without specialist approval. This would also be efective against private prescriptions. |
| **Option 4:** Strengthening of the Risk Management Plans for opioid products | • **The option:**Review current risk management plans for opioids to determine whether they currently reflect best practice in opioid prescribing and management of risks. | While risk management is clearly a good idea when it comes to opioids, putting all the emphasis on doctors to minimise the risk is likely to be ineffective. Clients who are the highest risk often exert |

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| | • **Potential implementation:**Work with sponsors to update their Risk Management Plans (RMPs) to minimise risks associated with overdose, misuse and abuse. | significant pressure on doctors if they know there are no clear rules or guidelines preventing prescribing.<br><br>The risk management approach in the US was ineffective.<br><br>In the current circumstances, where the TGA has NOT reviewed the evidence for the effectiveness of opioids for chronic non cancer pain, it would be inappropriate to give responsibility for training programmes to be developed by the pharmaceutical industry. Only when there are clear guidelines on the types of painful conditions for which specific opioids can be marketed would it be appropriate for the opioid industry to have any role in educating prescribers.<br><br>Having said that, anyone given a potentially lethal dose of opioids to take home should be given naloxone and trained in its use (also family members) as per WHO guidelines. |
| **Option 5:** Review of label warnings and revision to Consumer Medicines Information | • **The option:**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.<br><br>• **Potential implementation:**This may be able to be achieved through modification to the current Therapeutic Goods Order around prescription medicines (TGO 91), although changes to appendices to the Poisons Standard (Scheduling) and to conditions of registration of new strong (S8) opioids could also underpin this requirement. We would need to work with sponsors to obtain CMI changes. It would need to be determined whether S4 opioids such as tramadol would be included in this | Warning labels are clearly indicated given the high risk of death from opioids.<br><br>Returning unused medication to pharmacy also a good idea, although at present pharmacies don't know what to do with them. |

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| | scheme. | |
| **Option 6:** Consider incentives for expedited TGA review of improved products for pain relief and opioid antidotes | • **The option:**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.<br>• **Potential implementation:**This would be responsive to submissions received from sponsors of products and utilise the current regulatory framework. | There is one medication that could reduce the risk of overdose in those people currently prescribed opioids for chronic non cancer pain : the partial opioid agonist buprenrophine. Buprenorphine is typically the treatment of choice for people who become dependent on their strong opioid analgaesics. When transferred to buprenorphine, people do not experience any increase in pain. Their dose can be supervised, if necessary. There is a once a month depot formulation that has been approved by the FDA and another in the pipeline. There are also patches. It is very rare for anyone to die from a buprenorphine overdose, usually high doses of other sedatives are required in combination. This is not to say that buprenorphine has been deonstrated to be mnore effective than placebo in the treatment of chronic pain (nor have other opioids), but it is vertainly safer than other opioids which are currently being prescribed.<br><br>If an opioid is to be used in the management of chronic non cancer pain, it should be buprenorphine as the default position.<br><br>Buprenorphine is currently only available under section 100 for the treatment of opioid dependence. It should be considered for the indication of “opioid tolerance” where the outcome is reduced risk of opioid overdose. One issue is that under section 100 pharmacies are provided the medication but not given a fee for the dispensing costs, which they pass on to the client. These dispensing costs, typically in the order of five dolalrs per day (regardless fo whether the buprenorphine dose is supervised once or seven times per week). This fee structure is inequitable, undermines treatment efficacy, and should be reviewed. The Section 100 schedule should include a payment for dispensing / dosing. |

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| | | RCT studies of buprenorphine in opioid naiive people for pain management should also be considered.<br><br>Abuse deterrent formulations are also important, but most deaths are in people who swallow the tablets. |
| **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). | • **The option:**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.<br><br>• **Potential implementation:**Delegate decision, following public consultation and advice from the Advisory Committee on Medicines Scheduling on additional controls. | Limiting prescribing to specific doctors for NEW patients is workable, as long as there are exemptions for rural GPs or capacity for telemedicine consultations etc for palliative care. |
| **Option 8:** Increase health professional awareness of alternatives to opioids (both S4 and S8 opioids) in the management of chronic pain. | • **The option:**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.<br><br>• **Potential implementation:**The TGA will work with the NPS MedicinesWise and clinical colleges to increase awareness of health practitioners and the uptake of appropriate pain management guidelines in their practices. This could include developing a comprehensive repository of information about the appropriate use of both S4 and S8 opioids. This could use the active networks established | The Nationally Coordinated Codeine Implementation Working Group, (NCCIWG), was a useful group for overseeing the transition to the post-OTC codeine era. The industry representatives and industry linked groups had an important role to play in that. Such a group should have NO role in the determining of prescription opioid policy or opioid clinical guidelines as the conflict of interest is too strong.<br><br>The opioid industry has a commercial interest that conflicts with public health, it has an addictive product, similar to industries like the tobacco and alcohol industries, and substantially different from other pharmaceutical industries where |

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| | under the Nationally Coordinated Codeine Implementation Working Group. | there is a profit motive but where the product is less harmful. The opioid industry has a history of trying to influence clinical guidelines and policy and a high degree of vigilance is required to prevent their influence.<br><br>While guidelines are certainly needed, there should be developed by NHMRC, and not by any group with industry links (including patient advocacy organizations). |

Review of the PBAC subsidy is highly recommended. Limiting of PBS subsidy to people who had been commenced on opioids prior to in a hospital significantly reduced excess prescribing.

In addition to the recommendations above, I would like to emphasize the need to consider new prescriptions for opioids in chronic non-cancer pain as a different clinical situation to people with tolerance to opioids due to past prescribing. If there is a change in policy which significantly limits availability, those patients who are tolerant to opioid need to be continued on opioids until they are transferred to a safer opioid or supported to withdraw safely so that no people seek illicit opioids as a replacement.