The Pharmacy Guild of Australia

Interim decision & reasons for decisions by delegates of the secretary to the Department of Health

Comments by the Pharmacy Guild of Australia to the proposed amendments referred by the delegate for scheduling advice

Codeine

October 2015

National Secretariat
Level 2, 15 National Circuit, Barton ACT 2600
PO Box 7036, Canberra Business Centre ACT 2610
P: +61 2 6270 1888 • F: +61 2 6270 1800 • E: guild.nat@guild.org.au
www.guild.org.au

Ref: SP1006-18-1188

CONTENTS

Interim Decision 1.1 – Codeine – Amendments to Schedule 2 and 3 entries 3
Overview 3
Guild recommendations 5
Real-time Monitoring System for codeine 6
Current real-time monitoring system – Project STOP 6
Proposed new real-time monitoring system for codeine – prototype 8
System Overview 8
Privacy considerations 8
Storage of information 8
Pharmacy uptake of system 9
Summary 9
Guild responses to specific parts of Interim Decision 10
The risks and benefits of the use of a substance 10
Rescheduling of cold/flu preparations (Schedule 2) 11
Use of alternative OTC analgesics 11
The toxicity of a substance 13
The potential for abuse of a substance 14
Addressing abuse/misuse through rescheduling 14
Scheduling Policy Framework 15
Any other matters that the Secretary considers necessary to protect public health 16
Overseas classifications of codeine 16
Consumer Awareness Campaign 17
Additional impacts of scheduling decision 17

INTERIM DECISION 1.1 – CODEINE – AMENDMENTS TO SCHEDULE 2 AND 3 ENTRIES

Interim Decision: The delegate's Interim Decision is to delete the current Schedule 2 and 3 entries for codeine and amend the current Schedule 4 and 8 entries to reflect this change.

Overview

The Pharmacy Guild of Australia (the Guild) is opposed to the Interim Decision. As stated in our pre-ACMS meeting submission, it is the view of the Guild that the proposed rescheduling changes are a blunt instrument to address misuse and abuse of these medicines. The Guild believes that the proposal would not only be ineffective at addressing concerns of abuse, but could also have unintended consequences such as:

- For the large majority of people who use these products safely and effectively, rescheduling will make pain relief medicines more expensive and more difficult to obtain.

- Rescheduling codeine will result in substantial costs to the Medicare Benefits Schedule (MBS) through an increase in medical practitioner visits. There will be an increase in the workload of medical practitioners and increased waiting times for patients, especially as many medical practices have limited capacity to accept new patients. Patients who reside in regional, rural and remote areas would be most impacted, given the time and cost to visit a medical practitioner is substantially greater compared to metropolitan areas.[1]

- The decision is likely to have cost implications for the Pharmaceutical Benefits Scheme (PBS), particularly if medical practitioners elect to prescribe consumers higher strength codeine products or other opioids listed on the PBS.

- For patients who do not have ready or affordable access to a medical practitioner, their pain management may go untreated and/or lead to an increase of presentations at hospitals.

The Guild acknowledges the concerns relating to patient safety due to misuse of combination codeine analgesics (CCA) and agrees some action needs to be taken. However, the Guild contends that the implementation of a mandatory real-time monitoring system in community pharmacy would be more effective and economical to assist in identifying at-risk consumers, facilitate access to education materials and support appropriate referral when required.

Since the August ACMS meeting, the Guild, in partnership with the Australian Self Medication Industry (ASMI), has developed a prototype real-time monitoring system specifically designed to record and track pharmacy provision of over-the-counter (OTC) products containing codeine. Unlike the current Project STOP system, which is primarily a law enforcement tool to prevent diversion of pseudoephedrine, the prototype system will also be a clinical decision support system, assisting pharmacists in identifying patients who are risk of codeine dependence. The system will also have the capacity for pharmacists to record clinical information and provide guidance regarding suitable referral pathways to support patients better manage their pain and enhance health outcomes.

[1] National Health Performance Authority Media Release 01 October 2015 – People 2 to 3 times more likely to avoid seeing a GP due to cost in some areas

The prototype real-time monitoring system is explained further in the next section. The Guild and ASMI are confident that the full system can be developed and operating in community pharmacies by June 2016, which is the current implementation date for Interim Decision to take effect. The introduction of this system should be complemented by a series of additional measures such as:

- Mandatory warning labels advising consumers of the potential for dependence from prolonged use of these products (greater than 3 days);
- Reduction of pack sizes for these products to a maximum of 3 days' supply;
- Ongoing education for pharmacists, and
- A consumer awareness campaign.

In order to allow time for new real-time monitoring system to be developed and deployed as well as its impact on detecting abuse/misuse analysed and evaluated, **the Guild requests the delegate defers the final decision on changes to the Schedule 2 and Schedule 3 entries for codeine for at least 12 months.**

Key points responding to the Interim Decision are as follows:

1. The risks and benefits of the use of a substance

i. There is evidence that indicates that codeine in OTC doses can offer superior analgesic effects compared to other available OTC analgesics.

ii. Therapeutic guidelines and product information for OTC codeine products usually require patients to take at least two tablets every 4-6 hours. Therefore a patient who is taking a product containing 12-15mg of codeine for mild to moderate pain receives a dose of codeine that is roughly equivalent to the amount they would receive taking a prescription codeine product for the same indication.

iii. There is no evidence to suggest cough and flu preparations are subject to abuse/misuse and the Interim Decision to reschedule these products appears to be based primarily on the purported risk and benefits (efficacy). If the evidence indicates that the risk/benefit profile is not favourable, then the matter should be referred to the relevant section of the Therapeutic Goods Administration (TGA) who can assess whether these products should remain on the Register of Therapeutic Goods. The Guild believes the TGA conducting a comprehensive assessment regarding the risk/benefit profile of codeine is more appropriate than rescheduling in this context as the overall risk/benefit profile of cough and cold products containing codeine will not change based purely on rescheduling.

iv. If codeine is completely removed from Schedule 3, a significant proportion of patients who are currently taking paracetamol/codeine combination products would not be able to effectively and safely treat their condition as other OTC products such as a combination product containing a non-steroidal anti-inflammatory drug (NSAID) are unsuitable. Hence they will have little choice but to obtain a prescription medicine analgesic.

2. The toxicity of a substance

i. Given the statement made in the Interim Decision that it is not practical to ascertain a patient's metaboliser status, the Guild queries why this argument is emphasised as a justification for rescheduling. Rescheduling will restrict access to the majority of patients who are not poor/ultra-metabolisers while offering no additional safeguards for patients who are. In this context, the Guild believes that the risks of harm to a very small number of individuals needs to be balanced against of the vast majority of patients who use these products safely and effectively, particularly given the risk of harm cannot be mitigated purely through rescheduling.

ii. A new pharmacy initiative would enable pharmacists and medical practitioners to work together so that a patient's CYP2D6 status can readily be obtained. Further information can be found in **Attachment 2**.

3. The potential for abuse of a substance

i. Codeine in Schedule 3 products are only indicated for the treatment of acute pain and are sold in small packs (maximum 5 days' supply). The evidence suggests taking Schedule 3 codeine medicines when used as directed to treat episodic or acute pain at the maximum daily dose and maximum treatment period has a little risk of producing dependency.

ii. Rescheduling will not address issues of misuse and abuse.

4. Any other matters that the Secretary considers necessary to protect public health

i. The Guild does not believe the full consequences and disadvantages of this scheduling decision have been properly considered.

ii. Given the sheer magnitude and extent of the impact the proposed scheduling amendment will cause to a wide range of stakeholders, the Guild believes it is imperative that a formal Regulatory Impact Statement (RIS) be conducted prior to any final decision on rescheduling.

Guild recommendations

1. The final decision on codeine be deferred for at least 12 months so that a real-time monitoring system can be implemented and deployed and its impact on detecting abuse/misuse analysed and evaluated.

2. State and Territory Governments as a matter of urgency amend their medicines and poisons regulations where applicable to mandate the online real-time recording of codeine in their respective jurisdictions.

3. The introduction of a real-time monitoring system should be complemented with additional measures such as:

    I. Mandatory warning labels advising consumers of the potential for dependence from prolonged use of these products (greater than 3 days);
    II. Consideration to reduce pack sizes for these products to a maximum of 3 days' supply;
    III. Ongoing education for pharmacists, and
    IV. A consumer awareness campaign.

4. If the evidence indicates that the risk/benefit profile of a product is not favourable, then the matter should be referred to the relevant section of the TGA who can assess whether these products should remain on the Register of Therapeutic Goods. The Guild does not believe this is a relevant factor in determining scheduling (re)classifications.

5. Given the widespread implications and cost of the rescheduling proposal, it is imperative that a formal Regulatory Impact Statement (RIS) must be conducted prior to any final decision on rescheduling. The RIS should also examine the comparative risk/benefits of implementing a national real-time monitoring system as an alternative strategy.

Real-time Monitoring System for codeine

The Guild, in partnership with Australian Self-Medication Industry (ASMI), have been working with the Guild's IT subsidiary (GuildLink) regarding the development of prototype real-time monitoring system suitable for recording products containing codeine. GuildLink have extensive experience in this area, having operational oversight for Project STOP, a real-time monitoring system currently used in pharmacies to record and track sales of products containing pseudoephedrine. Project STOP has been an effective tool in reducing the diversion of locally sourced pseudoephedrine while maintaining OTC access for patients using the product appropriately for legitimate use. In the absence of such a system, it is highly likely pseudoephedrine would have become a prescription medicine, as is the case in New Zealand where real-time recording of such products does not exist.

The system has the full support of law enforcement agencies in each State/Territory as it provides valuable information that assists in their investigations to identify:

- recidivist purchasers' of products – leading to the commencement of investigations;
- criminal syndicates/networks; and
- Identify 'runner' or 'pseudo runners' who will lead investigations to the drug manufacturers.

State/Territory Health departments have also utilised Project STOP to monitor the compliance of requirements for supplying pseudoephedrine.

Current real-time monitoring system – Project STOP

The Project STOP system was mentioned as part of the Interim Decision which specifically stated:

> *Despite the risks of abuse identified when CCAs were up-scheduled in 2010 there has been no initiative to include CCAs into Project Stop prior to the application to up-schedule codeine to S4.*[2]
>
> *Since OTC CCAs were rescheduled to Schedule 3 in 2010, industry and pharmacy organisations have not been able to fully address concerns regarding codeine dependence.*[3]

The Guild makes the following comments in relation to these points:

- **Technical Constraints** - The Project STOP system was designed solely to record pseudoephedrine sales, in order to prevent these types of products being diverted to the manufacturing of methamphetamines. Project STOP was primarily developed in 2005 and 2006 with moderate changes in 2008 and 2009 hence the technologies, techniques and frameworks utilised in Project STOP are now significantly old in technology terms. Incorporating other products into the Project STOP would pose a significant risk of breaking existing functionality and thus jeopardising the system's existing role of tracking pseudoephedrine.

[2] Interim decisions & reasons for decisions by delegates of the Secretary to the Department of Health – October 2015, 17
[3] IBID, 15

- **Legal Constraints** – As mentioned, the primary purpose of the Project STOP system is to assist in law enforcement (preventing diversion of pseudoephedrine) and information recorded in this system is accessed by law enforcement agencies and health regulators. In contrast, the abuse/misuse of codeine products is a clinical issue rather than a law enforcement issue. Pharmacists would be in breach of the Project STOP User Agreement and privacy laws if they record requests and purchases of non-pseudoephedrine Schedule 3 medicines without explicitly detailing all relevant information to patients. This is not practical for pharmacists to convey this lengthy and complex information to every individual patient.

- **Government inaction** – The Guild has for many years advocated for the implementation of a real-time system to address issues of abuse/misuse. In our submissions in 2009 and 2010 to the then National Drugs and Poisons Scheduling Committee (NDPSC) considering the re-scheduling of OTC CCAs from Schedule 2 to Schedule 3, the Guild advocated for a real-time monitoring system to provide pharmacists with a clinical decision support tool, noting that re-scheduling alone was a blunt instrument.

  The Guild disseminates information to Guild members regarding appropriate supply of these products and reminding pharmacists of their obligations under the relevant Pharmacy Board Guidelines. However, Governments must play a role in determining and implementing effective changes/initiatives to address matters relevant to public health (such as codeine abuse/misuse) in consultation with stakeholders.

  While the Guild stands ready to assist Governments on such matters, it is ultimately Governments that have to make the necessary legislative changes and create the regulatory environment in order for real-time monitoring system to operate at optimal effectiveness. To date, no Government at any level has initiated discussions with the Guild to discuss concerns regarding codeine dependence and the implementation of a real-time monitoring system. This is in spite of all Governments being aware about this problem.

  The National Pharmaceutical Drug Misuse Action Framework (The Framework), endorsed in 2012 by Commonwealth, State and Territory Health Ministers, stated that painkillers and tranquillisers were causing increasing addiction, overdoses, trafficking and crime. The Framework recommended smaller pack sizes, more support for pharmacists, and the overdue launch of a national electronic recording and reporting of controlled drugs (ERRCD) system, providing real-time alerts about products such as codeine and higher risk script items.

  Despite this Framework, very little has actually been implemented. Even straight forward measures such as State/Territory Governments making legislative amendments to mandate the recording of codeine has not taken place.

  The Guild notes that despite Project STOP's success in preventing diversion of locally sourced pseudoephedrine, no Government currently provides any funding towards the maintenance of this vital system, despite the Guild's repeated requests.[4] Furthermore, there are a number of jurisdictions where the recording of pseudoephedrine in an online real-time system is not mandatory, again in spite of the Guild's repeated advocacy in having national consistency on this matter.

  The Guild is ultimately restricted in its ability to assist in addressing concerns relevant to pharmacy and public health if Governments are unwilling to offer support. The Guild therefore rejects the inference suggested in the Interim Decision that addressing codeine dependence is purely the responsibility of pharmacy and industry organisations with Governments having no role.

[4] The Commonwealth Attorney-General's department provided funding for the initial national roll-out of the system in 2007.

Proposed new real-time monitoring system for codeine – prototype

As mentioned in our pre-meeting submission a consumer survey conducted by the Guild in April 2015 found the majority of respondents (95 per cent) indicated they were prepared to have their details recorded when purchasing codeine combination products if this meant these products would remain available over-the-counter.

In recognition of concerns regarding abuse/misuse and the urgency of the need for such a system, the Guild has elected to develop a prototype of a new real-time monitoring system designed as a clinical decision support tool that when fully operational, will be accessible across pharmacies nationally. The Guild will conduct broader consultation with a range of stakeholders including consumer groups, State/Territory health departments, industry during the development and implementation phase.

System Overview

Attachment 1 details the high level system workflow. Prior to recording a product in this system, a pharmacist will have first determined through an initial discussion with the patient, that a codeine appropriate is suitable. The pharmacist will then enter the patient's identification details into the system to view records of previous use and any clinical notes recorded by other pharmacists. These records will provide the pharmacist with additional information to determine whether a codeine product is therapeutically appropriate. The pharmacist will then record the details of the current transaction (allowed, denied or safety sale) including clinical information in relation to reason(s) for use, recommended duration of use and any follow up referral actions. Detailed screen shots of each individual step in the workflow is also included in the attachment.

Privacy considerations

Recording of patient details is based on patient consent and reflect the Australian Privacy Principles Guidelines.[5]

If a patient does not grant their consent, their details will not be recorded on the system. Equally, a pharmacist can elect not to supply codeine products to these patients and instead recommend an alternative non-codeine product or treatment option (e.g. referral option).

Storage of information

The new system will record similar information that is recorded under the existing Project STOP system. Specifically the system will record:

- The name of the product (including specific pack size);
- Where a product was purchased previously (pharmacy postcode);
- The patient's unique identification number (e.g. driver's licence number); and
- Whether previous purchase requests were allowed, denied or processed as a safety sale.

[5] Privacy Fact sheet 20: Consent and the handling information in your eHealth record

In addition, the new system will also record clinical information such as:

- The reason for use (e.g. neck pain, back pain, post-surgical);
- Recommendations regarding length of use; and
- Whether any follow up actions have been provided to the patient (e.g. referral to medical practitioner, pain management plan).

Pharmacists will be able to view all records associated with the patient's identification number to confirm the therapeutic need for the medicine and that the treatment is or remains appropriate for the specific pain condition and that the patient continues to use the medicine safely and appropriately. If a problem or risk is identified, the pharmacist can record any interventions provided within their scope of practice as well as any referrals to other health care professionals.

Pharmacy uptake of system

Currently, over 80 per cent of pharmacies across Australia are registered to use Project STOP to record pseudoephedrine supply. Even in states where the recording of pseudoephedrine is not mandatory (such as Victoria and Tasmania), take up of the system in those jurisdictions is still high with 79 per cent and 90 per cent registration rates respectively. Pharmacists are already familiar with the real-time recording of medicines containing pseudoephedrine through Project STOP, hence they will be able to adapt quickly to the new system. Therefore the Guild is confident of the high uptake of the proposed new system as soon as it becomes available.

However, it is still imperative that State/Territory amend their medicines and poisons regulations to mandate the real-time online recording of OTC codeine products. This will ensure universal coverage of the system in pharmacies throughout the country.

Summary

The Guild is confident that the full system can be developed and operating in community pharmacies by June 2016, which is the current implementation date for Interim Decision to take effect. In order to allow time for new real-time monitoring system to be developed and deployed as well as collection and analysis of data from the system, the Guild requests the scheduling delegate defers the final decision on changes to the Schedule 2 and Schedule 3 entries for codeine for at least 12 months.

In order to maximise the effectiveness of a real-time monitoring system, the Guild advocates as a matter of urgency for the States and Territories to amend their medicines and poisons regulations to mandate the real-time online recording of codeine in their respective jurisdictions.

Recommendation

The final decision on codeine be deferred for at least 12 months so that a real-time monitoring system can be implemented and deployed and its impact on detecting abuse/misuse analysed and evaluated.

State and Territory Governments as a matter of priority amend their medicines and poisons regulations where applicable to mandate the electronic recording of codeine in their respective jurisdictions.

Guild responses to specific parts of Interim Decision

Responses are categorised according to the relevant sections under 52E (1) of the Therapeutic Goods Act.

The risks and benefits of the use of a substance[6]

The following statements are made in the Interim Decision:

> *There is no evidence that low dose codeine combination analgesics provide any additional analgesia over optimal dosing of paracetamol, aspirin or ibuprofen*[7]
>
> *Central consideration in allowing OTC supply of codeine combinations was that the benefits outweighed the risks and therefore asserted that the insufficient data on efficacy may mean that the benefits no longer outweighed the risks. While agreeing that efficacy remains important to any case justifying OTC supply of codeine, the Committee noted the Codeine Working Party advice that there was not sufficient information available to the Members at this time to resolve the question of codeine efficacy at ≤ 30mg.*[8]

The Guild questions the veracity of these statements given there are studies that indicate that while the analgesic effect between paracetamol-codeine combinations and paracetamol alone is small, it has been found to be statistically significant in dosages ranging between 10 to 60mg codeine and 400 to 1000mg paracetamol.[9] [10] Other studies have indicated paracetamol (350mg) in combination codeine (20mg) has a superior analgesic effect to aspirin (500mg).[11]

The vast majority of studies do not examine the efficacy of codeine in doses below 30mg. The Guild believes this is due to the fact that for the treatment of mild to moderate pain, patients will generally be advised by pharmacists to take at least two tablets (in accordance with the therapeutic guidelines and product information) and thus will in fact receive a dose of codeine that is roughly equivalent to the amount they would receive taking a prescription codeine product for the same indication. For example, the product information (PI) for Panadeine Extra ® (Schedule 3) and Panadeine Forte ® (Schedule 4) recommend the same dosage of codeine for mild to moderate pain (two tablets every 4-6 hours for Panedeine Extra ®, 1 tablet over the same period for Panadeine Forte ®, with the Panadeine Forte ® PI only recommending taking 2 tablets for severe pain.[12] [13] Therefore if the guidelines are followed for the treatment of mild to moderate pain, patients will receive the same amount of codeine and double the amount of paracetamol taking Panadeine Extra ® compared to taking Panadeine Forte ®.

Furthermore, the introduction of a real-time monitoring system for OTC CCAs combined with reducing individual Schedule 3 product packs to 3 days' supply, the likelihood of excessive and/or long-term use without intervention and review will be significantly reduced.

[6] Section 52E(1a)- *Therapeutic Goods Act 1989*
[7] Interim decisions & reasons for decisions by delegates of the Secretary to the Department of Health – October 2015, 14
[8] IBID, 14-15
[9] De Craen, A. J., Di Giulio, G., Lampe-Schoenmaeckers, A. J., Kessels, A. G., & Kleijnen, J. (1996). Analgesic efficacy and safety of paracetamol-codeine combinations versus paracetamol alone: a systematic review. *BMJ*, *313*(7053), 321-325.
[10] Macleod, A. G., Ashford, B., Voltz, M., Williams, B., Cramond, T., Gorta, L., & Simpson, J. M. (2002). Paracetamol Versus Paracetamol-Codeine in the Treatment of Post-Operative Dental Pain: A Randomized, Double-Blind, Prospective Trial. *Australian dental journal*, *47*(2), 147-151.
[11] Sveen, K., & Gilhuus-Moe, O. (1975). Paracetamol/codeine in relieving pain following removal of impacted mandibular third molars. *International journal of oral surgery*, *4*(6), 258-266.
[12] MIMs online – Panadeine Extra
[13] MIMs online – Panedeine Forte

Rescheduling of cold/flu preparations (Schedule 2)

As indicated in our pre-meeting submission, the Guild is not aware of any evidence that indicates Schedule 2 phenylephrine products and Schedule 3 pseudoephedrine products containing codeine are subject to abuse/misuse.

As noted in the Interim Decision, the scheduling of codeine for cough and cold preparations was reviewed by the NDPSC in 2009 and the Scheduling delegate in 2011 as part of the cold and cold preparation review. On both occasions the Schedule 2 entry for codeine was deemed as appropriate.[14]

In spite of these previous findings, the decision to delete the Schedule 2 entry for codeine appears to be based primarily on the following statement:

> *The risk/benefit profile for codeine in doses of 8mg – 15mg per dosing unit in combination with other analgesics is unfavourable. There is also a lack of evidence of any benefit of codeine over placebo in the relief of cough, making the risk/benefit profile for this indication unfavourable also.*[15]

The Interim Decision to reschedule these products appears to be based primarily on the purported risk and benefits (efficacy). The Guild queries why this is presented as a key justification for changing the Schedule 2 entry of codeine. The risk/benefit profile will not change based on rescheduling to Schedule 4. If the evidence indicates that the risk/benefit profile is not favourable, then the matter should be referred to the relevant section of the TGA who can assess whether these products should remain on the Register of Therapeutic Goods. The Guild notes this occurred previously with dextropropoxyphene in 2011. This eventually led to more stringent oversight regarding the supply of this medicine.[16] The Guild believes this is the appropriate course of action in this context, rather than rescheduling.

In the interim, if there are immediate concerns regarding the abuse/misuse of these particular codeine products, the Guild suggests they are moved to Schedule 3 in order to be encapsulated in the real-time recording system.

Recommendation

If the evidence indicates that the risk/benefit profile of a product is not favourable, then the matter should be referred to the relevant section of the TGA who can assess whether these products should remain on the register of therapeutic goods. The Guild does not believe this is a relevant factor in determining scheduling (re)classifications.

Use of alternative OTC analgesics

The Interim Decision raised several points in relation to alternative options for patients who are currently taking OTC codeine products:

> *Codeine in the unit doses present in OTC products provides very little additional analgesic effect over and above that provided by the accompanying drug in the combination. It is also noted that there are new combination products with paracetamol and ibuprofen which are more efficacious than low dose CCAs.* [17]

> *A number of the pre-meeting submissions considered it unduly burdensome to require consumers to obtain a prescription for supply of codeine combination analgesics. However,*

[14] Interim decisions & reasons for decisions by delegates of the Secretary to the Department of Health – October 2015, 10
[15] IBID, 12
[16] https://www.tga.gov.au/media-release/update-tga-decision-cancel-prescription-pain-killers-19-september-2013
[17] Interim decisions & reasons for decisions by delegates of the Secretary to the Department of Health – October 2015, 15

pharmacists can recommend alternate pain relief products, such as a paracetamol-ibuprofen combination, or consumers could obtain a prescription (to have on hand when needed for acute pain) if they visit a general practitioner for any reason.[18]

Of the current products supplied without prescription for the treatment of mild to moderate pain, if CCAs are up-scheduled, the remaining options for use by patients or recommendation by pharmacists are aspirin, ibuprofen or paracetamol as single ingredients (all with unrestricted availability from supermarkets and service stations in small pack sizes), combination ibuprofen/paracetamol or paracetamol/caffeine products, and some other NSAIDs such as diclofenac, naproxen and mefanamic acid.

The NPS MedicineWise[19] indicates aspirin may not be suitable for people who:

- are pregnant;
- have or have a history of stomach ulcers;
- have a condition causing them to bleed easily;
- have liver problems;
- have asthma;
- have heart failure; or
- high blood pressure.

Apart from being allergic to paracatamol, the NPS MedicineWise[20] advises people with kidney or liver problems, or those with an alcohol dependency to talk to their medical practitioner or pharmacist before taking paracetamol.

The NPSMedicineWise[21] indicates **ibuprofen and other NSAIDs** may not be suitable for:

- people with stomach problems such as ulcers or bleeding;
- people with heart or kidney problems; and
- people with high blood pressure.

Ibuprofen is also not recommended for patients aged over 65 years (unless on the advice of a medical practitioner) and this is a required advisory statement that must appear on all products. [22]

Ibuprofen (and all NSAIDs) can also interact with other classes of medicines including[23]:

- medicines that can increase the risk of bleeding (e.g. warfarin);
- medicines for high blood pressure (anti-hypertensives) and heart failure; ibuprofen and other NSAIDs can cause fluid retention and raise a patient's blood pressure;
- medicines that may affect kidney function (this may increase the chance of kidney problems with ibuprofen);
- medicines that are removed from the body via the kidney; NSAIDs can affect kidney function and so the amount of these other medicines in the body may rise more than it should, increasing a patient's chance of side effects; and
- medicines that can raise potassium levels in the blood (e.g. ACE inhibitors, used to treat high blood pressure); NSAIDs such as ibuprofen can also raise a patient's potassium levels, requiring monitoring by a medical practitioner.

[18] IBID, 17
[19] http://www.nps.org.au/medicines/pain-relief/simple-pain-reliever-and-fever-medicines/aspirin/for-individuals/who-can-take-aspirin
[20] http://www.nps.org.au/medicines/pain-relief/simple-pain-reliever-and-fever-medicines/paracetamol/for-individuals/who-can-take-paracetamol
[21] http://www.nps.org.au/medicines/muscles-bones-and-joints/anti-inflammatory-medicines-nsaids/ibuprofen/for-individuals/who-can-take-ibuprofen
[22] Medicines Advisory Statements Specification 2014 – Ibuprofen https://www.comlaw.gov.au/Details/F2014L00693
[23] http://www.nps.org.au/medicines/muscles-bones-and-joints/anti-inflammatory-medicines-nsaids/ibuprofen/for-individuals/interactions-with-ibuprofen

In addition, a TGA safety review of NSAIDs conducted in 2014 found while use of NSAIDs at prescription-only dosages was already known to increase the risk of high blood pressure, heart failure, heart attack and stroke, the TGA NSAIDs review found that these risks also applied to OTC forms of diclofenac, naproxen and ibuprofen. This led to the mandating of additional warning labels on OTC products.[24]

Combination ibuprofen/paracetamol is not suitable for all patients as some patients cannot use either paracetamol or ibuprofen. A study conducted in Australia indicated the proportion of patients who had some form of contraindication, warning or precaution was close to 25 per cent for ibuprofen and 2 per cent for paracetamol.[25] It is interesting to note that this is a higher proportion than those at risk of codeine related adverse effects as per the combined maximum estimation of poor/ultra-metabolisers of codeine cited in the Interim Decision.[26]

If codeine is completely removed from Schedule 3, a significant proportion of patients who are currently taking paracetamol/codeine combination products would not be able to treat their condition with a combination product containing an NSAID, hence they will have little choice but to obtain a prescription medicine analgesic. A Guild consumer survey conducted in April 2015 mentioned in the pre-meeting submission, found 59 per cent of respondents were taking some form of paracetamol/codeine combination.

The toxicity of a substance[27]

The Interim Decision makes several references to risk of ultra-rapid and poor metabolisers of codeine. The decision states:

> *The major impact on public health of the proposed amendment would be a reduction in the risk to those individuals who, unbeknownst to themselves, have a rapid metaboliser phenotype of CYP4502D6 and are therefore at significant risk of excessive morphine concentrations following ingestion of usually recommended doses of codeine for any indication.[28]*

In this context, the Guild believes that the risks of harm to a very small number of individuals (some studies have put the number of ultra-metabolisers at 3 per cent of the population[29]) needs to be balanced against of the vast majority of patients who use these products safely and effectively, particularly given the risk of harm cannot be mitigated purely through rescheduling as noted in the Interim Decision:

> *If codeine is to remain in use as an analgesic, then the patient's metaboliser status needs to be ascertained prior to prescription or dispensing, however this is not practical. [30]*

Taking into account the statement above that it is **not practical** to ascertain a patient's metaboliser status, the Guild queries why this argument is emphasised as a justification for rescheduling, as it will restrict access to the majority of patients who are **not** poor/ultra-metabolisers while offering no additional safeguards for patients who are.

The Guild argues that low dose codeine products should remain in Schedule 3 for the following reasons:

- For patients who are poor metabolisers, the introduction of the real-time monitoring system could enable pharmacists to readily identify patients who may be poor metabolisers based on previous usage contained in the system.

[24] https://www.tga.gov.au/alert/non-steroidal-anti-inflammatory-drugs-and-diclofenac-reviews
[25] Clarke, G. D., Adams, I. M., & Dunagan, F. M. (2008). Using suitability profiles to better inform consumers' choice of commonly used over-the-counter analgesics. *International Journal of Pharmacy Practice*, *16*(5), 333-336.
[26] Interim decisions & reasons for decisions by delegates of the Secretary to the Department of Health – October 2015, 16
[27] Section 52E(1b)- *Therapeutic Goods Act 1989*
[28] Interim decisions & reasons for decisions by delegates of the Secretary to the Department of Health – October 2015, 13-14
[29] See Attachment 2, 4
[30] Interim decisions & reasons for decisions by delegates of the Secretary to the Department of Health – October 2015, 17

- The Guild wishes to draw attention to a new pharmacy initiative whereby pharmacists and medical practitioners work together so that a patient's CYP2D6 status can readily be obtained. Further information can be found in **Attachment 2**.

- For ultra-metabolisers who are unavoidably exposed to codeine, the Guild considers that it would be worse in terms of adverse events if these patients used a prescription medicine with a higher dose of codeine rather than a low dose product.

The potential for abuse of a substance[31]

Addressing abuse/misuse through rescheduling

There has been ongoing discussion regarding the potential and actual rate of misuse/abuse of codeine. OTC codeine medicine abuse is a recognised problem internationally but is not completely understood. Studies have indicated research is needed to quantify the scale of abuse, evaluate interventions and capture individual experiences, to inform policy, regulation and interventions.[32]

The Guild believes it is often difficult to draw meaningful conclusions from reports due to factors such as:

- The dates that are covered as part of the study. Many studies assess abuse/misuse of codeine prior to 2010, when OTC codeine was rescheduled from Schedule 2 to Schedule 3 and the maximum available pack size was greatly reduced. Therefore, any conclusions made on OTC codeine based on data pre-2010 are not factoring in critical changes to the scheduling of these medicines.

- Lack of specificity of misuse/abuse for OTC codeine compared to prescription codeine products. Several studies suggest that abuse/misuse of prescription codeine products is similar or worse than OTC codeine.[33] Therefore the effectiveness of rescheduling codeine to prescription to address abuse/misuse must be questioned.

- Additional factors involved in abuse/misuse such as multiple drug toxicity and high rates of comorbid health problems such as mental illness illicit substance use and chronic pain.[34]

Accurately estimating the associated risk for the general population is difficult, which the NDPSC noted when it considered the scheduling of codeine in 2009. As noted in the Interim Decision, while the NDPSC stated it was not possible to accurately estimate the associated risk of harm, it was reasonably assumed:

- The proportion of all users abuse OTC CCA is low
- The risk of harm among all users of OTC CCA is low
- The risk of harm among abusers of OTC CCA is high.[35]

In spite of this, the Interim Decision states the following:

> *Rescheduling to Schedule 3 has not achieved the required reduction in harm to affected individuals. Since the rescheduling of codeine in 2010 there hasn't been the reduction that might have occurred.*[36]

[31] Section 52E(1e)- *Therapeutic Goods Act 1989*
[32] Cooper, R. J. (2013). Over-the-counter medicine abuse–a review of the literature. *Journal of substance use*, *18*(2), 82-107.
[33] Roxburgh, A., Hall, W. D., Burns, L., Pilgrim, J., Saar, E., Nielsen, S., & Degenhardt, L. (2015). Trends and characteristics of accidental and intentional codeine overdose deaths in Australia. *The Medical journal of Australia*, *203*(7), 299-299.
[34] Roxburgh, A et al. (2015). Trends and characteristics of accidental and intentional codeine overdose deaths in Australia.
[35] Interim decisions & reasons for decisions by delegates of the Secretary to the Department of Health – October 2015, 14

The Guild questions the evidence behind this assertion, particularly as the NDPSC did not provide definitive figures of abuse/misuse in 2009. It is also not clear what the term "required reduction" means in the context.

The Guild also notes that industry specific data indicates that in the three years immediately following the rescheduling of codeine products from Schedule 2 to Schedule 3 in 2010, there was a 12 per cent decline in OTC codeine medicines sales in terms of units sold.[37] This is in contrast to an increase in pain medications dispensed on the PBS over the same period as shown in the table below.

Substance	**Increase in volume sales (2010-2013)** [38]
Prescription codeine	3 per cent
Tramadol	3 per cent
Oxycodone	15 per cent

While the rescheduling of codeine from Schedule 2 to Schedule 3 has had an impact (demonstrating the role pharmacists play in determining the therapeutic need for Pharmacist Only products), the rapid increase in volume and misuse/abuse of prescriptions opioids such as oxycodone demonstrates scheduling alone cannot be expected to fully address misuse and abuse.

Rescheduling appears to be a blunt instrument to manage abuse/misuse. As mentioned in our pre-meeting submission, there are more effective measures where combined with the introduction of a real-time monitoring system that are likely to more effective in addressing abuse/misuse without restricting access to the majority of patients who use these products safely and effectively, these include:

- Mandatory warning labels advising consumers of the potential for dependence from prolonged use of these products (greater than 3 days);
- Ongoing education for pharmacists;
- Consumer awareness campaign (further information provided under Additional Matters that the secretary considers necessary to protect public health).

Scheduling Policy Framework

The following comments are made in the Interim Decision:

> *It should be noted that the following factors for a Schedule 3 medicine in the Scheduling Policy Framework (SPF) are not met:*
>
> - *Codeine does not meet the SPF scheduling factors for inclusion in Schedule 3. In particular, criterion 2 is not satisfied – i.e. "The use of the medicine at established therapeutic dosages is not expected to produce dependency. Where there is a risk of misuse, abuse or illicit use identified, the risk can be minimised through monitoring by a pharmacist."*

Codeine in Schedule 3 products are only indicated for the treatment of acute pain and are sold in small packs (maximum 5 days' supply). Studies show that dependence is associated with the regular/prolonged use of codeine usually related to the treatment of chronic pain conditions.[39] [40] Studies conducted in Australia indicate that patients who are susceptible to codeine dependency are more likely

[36] IBID, 15
[37] Nielsen Pharmacy Scan, Jan 2010 – May 2013
[38] PBS expenditure and prescriptions www.pbs.gov.au/info/browse/statistics#Expenditure . These figures do not account for medicines dispensed as a private script over this period.
[39] Sproule, B. A., Busto, U. E., Somer, G., Romach, M. K., & Sellers, E. M. (1999). Characteristics of dependent and nondependent regular users of codeine. *Journal of Clinical Psychopharmacology*, *19*(4), 367-372.
[40] Ford, C., & Good, B. (2007). Dependence on OTC drugs: Over the counter drugs can be highly addictive. *BMJ: British Medical Journal*, *334*(7600), 917.

to have taken well above the recommended doses of OTC codeine and have taken it for considerably longer periods of time than recommended.[41]

Cases examining morbidity associated with misuse of over-the-counter codeine-ibuprofen analgesics indicated that patients were taking mean daily doses of 435-602 mg of codeine phosphate and 6800-9400 mg ibuprofen. These amounts are greatly in excess of what a patient can obtain in a single pack of Schedule 3 codeine product and the stipulated maximum daily dose of 100mg of codeine that must be included as part of the labelling.[42]

The evidence suggests taking Schedule 3 codeine medicines, when used as directed to treat episodic pain at the maximum daily dose and maximum treatment period has little risk of producing dependency. This reflects previous statements made by the NDPSC in 2009 that stated the proportion of all users who abuse OTC CACC and the risk of harm among all users of OTC CACC is low. It is when patients exceed the recommended daily doses and/or prolong their use beyond what is recommended the risk is evident.

Therefore the Guild believes a Schedule 3 listing for CCAs is consistent with the SPF.

In order to ensure patients do not obtain codeine products in quantities that are likely to produce dependency, a real-time monitoring system needs to be implemented so that pharmacies can determine where and when patients have previously purchased Schedule 3 codeine products and therefore make a fully informed determination regarding the therapeutic need for a product.

Rescheduling these products to Schedule 4 will simply shift the problem to medical practitioners who will have the same difficulty in determining whether a patients' previous and current use is consistent with therapeutic guidelines.

Any other matters that the Secretary considers necessary to protect public health[43]

Overseas classifications of codeine

The Interim Decision makes the following statements in relation to the available of codeine in other countries:

> *In Europe codeine is not an OTC medicine (i.e. is a prescription only medicine at least) in 13 countries being Austria, Belgium, Croatia, the Czech Republic, Finland, Germany, Greece, Italy, Luxembourg, Portugal, Slovakia, Spain and Sweden.*
>
> *Codeine is also a Prescription Medicine in the USA, Hong Kong, Iceland, India, Japan, the Maldives, Romania, Russia, and the United Arab Emirates.* [44]

The Guild cautions against making direct comparisons regarding the availability of codeine in other countries given the significant differences in the scheduling systems. For example, the Unites States does not have any OTC schedules meaning all non-prescription medicines can be sold in a non-pharmacy setting with no controls over supply. As a result, there are several medicines that are available OTC in Australia that require a prescription in the Unites States.

[41] Nielsen, S., J. Cameron, and N. Lee. "Characteristics of a non-treatment-seeking sample of over-the-counter codeine users: implications for intervention and prevention." *Journal of opioid management* 7.5 (2010): 363-370.
[42] Poisons Standard July 2015 – Schedule 3 listing codeine www.comlaw.gov.au/Details/F2015L00844
[43] Section 52E(1f)- *Therapeutic Goods Act 1989*
[44] Interim decisions & reasons for decisions by delegates of the Secretary to the Department of Health – October 2015, 14

There are also many other countries where low dose codeine products are available OTC and are classified as Pharmacy Medicines. These include:

- United Kingdom – All codeine products must have mandatory labelling warning of the potential for addiction. In addition, pack size is limited to three days' supply.
- New Zealand (the country whose scheduling system most closely resembles Australia)
- Canada
- Denmark
- France
- Ireland
- South Africa – have a real-time monitoring system

Consumer Awareness Campaign

There is a lack of awareness within the Australian public that *Pharmacist Only* Medicines are not available for purchase without a pharmacist's assessment for appropriateness and safety. The Guild are working with the consumer groups and other relevant stakeholders in this regard. To complement this, the Guild are supporting pharmacists with their professional obligations in managing requests and recommendations for CCAs and other *Pharmacist Only* Medicines.

Additional impacts of scheduling decision

The Guild notes the following comment made in the Interim Decision:

> *Potential unintended consequences and disadvantages of a decision to reschedule CCAs to S4 need to be considered. One would be a reduction in the availability of analgesics for moderate to severe pain, although the evidence suggests that the addition of codeine adds only a minor additional analgesic effect over and above that of the ibuprofen or paracetamol in the combination product. The recent introduction of a paracetamol/ibuprofen combination may fill this niche more effectively than the CCAs have done, without the disadvantages of codeine. A reduction in the availability of a drug known as an anti-tussive agent, despite the lack of evidence available to support this, would also occur, but significant actual disadvantages are unlikely to occur. No other potential disadvantages to the community are readily identified.*[45]

The Guild has already highlighted problems with the statements made in the Interim Decision regarding combination ibuprofen/paracetamol products are alternatives for all patients. The Guild has also noted evidence in relation to the efficacy of low-dose CCAs over single ingredient analgesics.

In addition, the Guild does not believe the full consequences and disadvantages of this scheduling decision have been properly considered. Several potential unintended consequences that must be formally considered include:

- The decision to reschedule codeine will add significant costs to the MBS and PBS as well as patient's out of pocket expense;

- For patients who do not have easy and/or affordable access to a prescriber in their local area, their pain management is likely to suffer. This is likely to be a significant factor in rural/remote areas. This in turn may result in:
    - An increase in presentations to emergency departments, which increase health costs for State/Territory Governments; and

[45] Interim decisions & reasons for decisions by delegates of the Secretary to the Department of Health – October 2015, 14

- Patients self-medicating with non-therapeutic products such as alcohol or illicit substances.

- The scheduling changes will require many sponsor companies to reformulate their products to remove the codeine if they wish to keep supplying the product as an OTC product. The process of reformulation and re-registering the product with the TGA will likely extend well beyond the current proposed implementation date of June 2016. Alternatively, some products may be discontinued meaning the products will no longer be available in any schedule. This could result in a shortage of cold and flu products for the start of the 2016 winter season. This could also lead to further demand on emergency hospital services.

Furthermore, many medical practices (particularly practices in rural/remote and lower socioeconomic areas) have limited additional capacity to see more patients, hence it will be challenging for these practices to accommodate the likely substantial increase in visitors to obtain prescriptions for codeine. This will likely result in reduced availability of medical practitioner services and an increase in waiting time for all patients. Patients who reside in regional, rural and remote areas would be most impacted, given the time and cost to visit a medical practitioner is substantially greater compared to metropolitan areas.[46]

Given the sheer magnitude and extent the proposed scheduling amendment will cause to a wide range of stakeholders, the Guild believes it is imperative that a formal regulatory impact statement (RIS) be conducted prior to any decision on rescheduling. This RIS should also examine the comparative risk/benefits of implementing a national real-time monitoring system as an alternative strategy.

Recommendation

The Guild believes that given the widespread implications and cost of the rescheduling proposal, it is imperative that a formal regulatory impact statement (RIS) be conducted prior to any decision on rescheduling. The RIS should also examine the comparative risk/benefits of implementing a national real-time monitoring system as an alternative strategy.

[46] National Health Performance Authority Media Release 01 October 2015 – People 2 to 3 times more likely to avoid seeing a GP due to cost in some areas