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15 October 2015

The Secretary
Scheduling Secretariat
Advisory Committee on Medicines Scheduling
GPO Box 9848
Canberra ACT 2601

Email: Medicines.Scheduling@tga.gov.au

RE: Interim decision to up-schedule OTC codeine to Schedule 4

Dear Sir or Madam

I am writing to express our strong disagreement with the Federal Government Medicines Scheduling Delegate's interim decision to reschedule codeine.

[redacted] is a member of [redacted], the largest and most diversified Australasian marketer, wholesaler and distributor of healthcare, medical and pharmaceutical products.

As an organisation that provides quality healthcare products and has daily contact with a wide spectrum of people across Australia, we sincerely believe the change will cause unnecessary hardship and pain for a vast number of individuals.

Our healthcare system, including community pharmacy, is one of the best in the world. Australian pharmacists are highly-trained professionals who help people towards managing their health and leading an active, happy and balanced lifestyle.

For many Australians, community pharmacy is often their only realistic option for accessible and affordable healthcare, so the planned rescheduling will impact them significantly. In addition, it will place a completely unacceptable time and cost loading on our already stressed health system.

Indeed, much greater thought must be given to the impact of this proposed change with a full regulatory impact assessment the most sensible course.

While we acknowledge the debate being conducted around the efficacy and misuse of codeine for the small percentage of the population, the proposed rescheduling is a very blunt tool to address

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either of these concerns. Further analysis of data is required to avoid a hasty decision which could have extensive unintended repercussions.

The National Health and Medical Research Council (NHMRC) of Australia says:

> "*There is no evidence that the use of opioids for treatment of severe pain leads to opioid dependence or addiction*."

It goes on to say:

> "*Traditional methods of opioid administration include oral, intramuscular, subcutaneous, intravenous and continuous intravenous routes. These methods each have advantages and disadvantages in different groups of patients, but are more likely to be effective when the dosage regimen is tailored to the individual. The patient's need for pain relief should be seen as more important. Patient-controlled analgesia (PCA) allows patients to adjust the degree of pain relief to their own desired level of comfort and tolerance of side effects*." [1]

Every day millions of Australians responsibly access OTC products, some of which contain codeine. They use these products safely and sensibly to manage their healthcare needs. In contrast, the Delegate argues that "codeine was the opioid drug of dependence for 1,038 clients". This identified group equates to less than 0.001% of the population – less than one in 23,000! Even allowing for a higher number of non-identified individuals in this category, to increase the pain, discomfort and inconvenience of so many everyday Australians because of the issues of so few is simply not a fair or balanced response in a democratic society.

Further, there has been no evidence put forward by the Delegate that the rescheduling of codeine will significantly reduce its misuse by those with an addiction. Experience shows that many, if left without suitable support, will 'doctor shop' to maintain their access[2].

The rational action should be to help those with an addiction, not punish those who are doing the right thing.

The arguments put forward for re-scheduling also fail to give proper weight to the flow-on effects of the change. A huge number of people – migraine sufferers, for example – know, often through hard-won experience, that they require immediate treatment with codeine to relieve their pain. Therefore, they will have no choice but to go to a GP or, if there are no appointments available, flood into hospital emergency departments. Conversely, these patients could attempt to 'persevere with the pain' which could have further consequences for their wellbeing.

Moreover, patients with acute pain presenting to a GP are typically prescribed oxycodone/endone which has a higher concentration of opiates and therefore a greater risk profile to patients.[3]

By delaying access to effective relief, everyday Australians will remain in pain for an unacceptable period of time. It will significantly increase workload and waiting times at GP clinics and hospital emergency departments. It will also severely impact the nation's health expenditure and work force

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productivity, which could well compromise emergency services and GP access for others who truly need them.

Research by Macquarie University[4] found that the up-scheduling of pharmacist-only analgesics would cost $675 million a year. Almost $170 million would come from Medicare for additional doctor visits. It would cost patients some $70 million. Lost productivity and delayed treatment would cost more than $400 million.

There seems to have been no thought given to the fact that these costs – physical and financial – will be borne unduly by the older, sicker and poorer sections of our society. Similarly, people in rural and remote locations with already reduced access to GPs and hospital emergency departments will suffer disproportionate distress, inconvenience and cost.

The Delegate's suggestion that people – to avoid these painful delays, inconveniences and costs – should have a prescription on hand makes little sense. Not only would such 'just in case' prescriptions put GPs in an ethical dilemma, they would also provide an open door for codeine abusers, negating the apparent primary reason behind the drive to reschedule. In addition, it would likely increase the number of adverse events through self-medication of higher dose opioids such as endone/oxycodone.

We also strongly disagree with the unsupported claim that the new non-opioid analgesics (ibuprofen plus paracetamol) can be an automatic replacement for existing codeine medications (see **Appendix A**). It is well known that ibuprofen is not recommended for large numbers of Australians with a number of conditions[5] including:

- Hypertension (3.7 million Australian adults[6]);
- Asthma (2 million[7]);
- Stroke (440,000[8]);
- Heart attack (350,000[9]); and
- Pregnant women (300,000[10]).

Recent labelling changes to non-steroidal anti-inflammatory drugs (NSAIDs) further reinforce that these products are not a simple 'straight swap'.

In addition the NHMRC clearly states in its GP guidelines for acute pain management:

> "*The adverse effects of NSAIDs are potentially serious and it is imperative that contraindications are respected (Levels of evidence II and III).*"[11]

To add to the problem, ibuprofen and paracetamol vary widely in their interaction with a vast range of other drugs people might be taking. This could result in medications being ineffective or, potentially, harmful.

These non-opioid analgesics should be seen as an addition to our arsenal of pain medications and not a replacement for products which are safely and effectively helping people every day.

To further support our objection to the interim decision, please refer to **Appendices B and C**. These appendices provide counter argument from a scientific and evidence based point of view to the rationale of the Delegate's interim decision. This examination has been done in accordance with section 52E of the Therapeutic Goods Act (1989).

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Our other great concern is that, if this unnecessary rescheduling does go ahead, the proposed implementation date of 1 June 2016 is completely unachievable.

Such a short timeframe will inflict significant financial losses across the industry – from manufacturers to community pharmacies – and lead directly to a shortage of medications because of the time needed to source and deliver replacement products. Patient risk could be increased as a short time frame does not allow for suitable education processes around alternatives to be implemented.

Analgesics containing codeine equate to 25% of the pain medication (by volume) sold by pharmacies. These large volumes have a significant logistical implication. This has not been appropriately considered by the Delegate. Within [redacted] we typically place orders for codeine products 12-18 months in advance to meet public health needs.

If the interim decision is allowed to stand, there will need to be much greater consultation with the industry to ensure businesses, large and small, are resourced appropriately, are not unfairly financially penalised and to ensure no patient goes without necessary treatment.

In addition, if the decision is allowed to stand, consideration needs to be given to the wider healthcare sector which would require re-education, training and support to prepare for the large scale migration of patients from one healthcare sector to another and one medication to another.

It is clear that the Delegate has failed to consider all clinical evidence and clinical practice guidelines around opiate use in acute pain. Further, linking codeine-containing cold and flu products with NHMRC level IV evidence (the lowest form of evidence), is not reasonable. Failure to assess all published data, to properly balance the greater healthcare implications, and to consider the broader commercial implications calls into question the credibility of the entire interim decision.

In our view, rather than rescheduling there are a number of actions that should be first implemented, monitored, reviewed, assessed and then long term decisions can be made. These include:

- Greater support (multi-disciplinary team) for those dealing with opioid misuse
- National real-time monitoring and data collection
- Mandatory front-of-pack warning labels
- Mandatory pack size reduction for analgesics
- Multi-disciplinary team management for those living with chronic pain
- Public health education about the appropriate use of codeine and associated risks
- Increased training and tools for pharmacists to identify people at risk of addiction and hypermetabolism or hypo metabolism
- Training for pharmacists on counselling “at risk” patients
- Adding S3s to MyHR (E-health record) to allow doctors and pharmacists to monitor medication history (with patients who opt out of MyHR not being able to receive codeine-based products)

Also attached as **Appendix D** to the submission are six letters from well-credentialed, experienced and respected community pharmacists with a personal view of the impact of the interim decision on their patients and business.

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The interim decision to reschedule OTC codeine to Schedule 4 is a significant over-reaction that will have widespread, unfair and inequitable consequences and will cause considerable distress to a huge number of Australians.

Yours sincerely,

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Appendix A

A comparative analysis on the clinical safety and efficacy of substituting codeine combined analgesics (CCAs) with paracetamol and ibuprofen combinations

Neither Nuromol® (paracetamol 500mg, ibuprofen 200mg) or Maxigesic® (paracetamol 500mg, ibuprofen 150mg) should be considered therapeutic substitutes for the Schedule 3-registered paracetamol and codeine combined analgesics (CCAs). Codeine is considered a weak opioid analgesic[1] recommended in the over-the-counter setting for relief of mild-to-moderate pain. Currently available as a schedule 3 registered medicine in combination with paracetamol, it may be the treatment of choice for many patients in whom Non-Steroidal Anti-Inflammatories (NSAIDs) may be contraindicated due to intolerances, pre-existing health conditions, pending surgeries, or administration of concomitant medicines which may interact.

Differences in side-effect profile preclude treatment of some patient groups

Ibuprofen, as a non-selective Non-Steroidal Anti-inflammatory[1], is not recommended in multiple patient groups where combination codeine and paracetamol preparations may be (see **figure 1**).

Contraindication / Precaution	**Ibuprofen (at doses contained in Nuromol® and Maxigesic®)**	**Codeine (at doses contained in Panadeine®)**
Allergy to active drug or drug class[1, 2,3]	✗	✗
Airways disease (Asthma , COPD) [1,2]	✗	✓
Coagulation disorders [1]	✗	✓
History of myocardial infarction[1,3]	✗	✓
History of stroke[1,2,3]	✗	✓
Heart failure[1,2,3]	✗	✓
Hypertension[1,2]	✗	✓
Peptic ulcer disease[1,2,3]	✗	✓
Gastric bleeding [1,2,3]	✗	✓
Inflammatory bowel disease[1,2, 3]	✗	✗
Renal impairment[1,2,3]	✗	✓*
Hepatic impairment[1]	✓*	✗
Peri-operative periods[1]	✗	✓**
Elderly[1,2,3]	✗	✓

Pregnancy planning[1]	✗	✓
Pregnancy[1,2,3]	✗	✓
Breastfeeding[1,2]	✓	✗*
Electrolyte abnormalities[1]	✗	✓
Sedation[1]	✓	✗
Pheochromocytoma[1]	✗	✗
Respiratory / CNS depression[1,2,3]	✓	✗
Children <12[1,2,3]	✓	✗
Constipation / bowel obstruction[1]	✓	✗
History of substance abuse[1,2,3]	✓	✗
Biliary tract surgery[1,2,3]	✓	✗
Uncorrected adrenocortical abnormalities[2]	✓	✗
CYP2D6 ultra-rapid metabolism[1,2]	✓	✗
Diarrhoea secondary to psuedomembranous colitis[2]	✓	✗
Cardiac arrhythmias[3]	✓	✗
Urinary tract surgery or stricture[3]	✓	✗
✓= may be recommended ✗= avoid		
* = has been used with caution / monitoring ** = excluding biliary tract and urinary tract surgery		

Figure 1. Patients usually deemed suitable candidates for Ibuprofen VS Codeine containing medicines based on their medical history, intolerances and physical characteristics (Note: other patient-specific factors many need to be considered before safely recommending a product to an individual)

Differences in drug-drug interactions precluding treatment of some patient demographics

Differences in drug-drug interactions preclude treatment of some patient groups

Due to the many differences in pharmacology between ibuprofen and codeine, there is wide variation between listed drug-drug interactions[2] (see **figures 2 & 3**). As a result, the products Nuromol® and Maxigesic® may not be able to satisfy the therapeutic need of patient groups who previously used codeine-containing analgesics concomitantly with medicines which interact with ibuprofen.

Nalorphine hydrobromide	Naltrexone	Midazolam	Flunarizine
Naloxone hydrochloride	Naltrexone hydrochloride	Midazolam hydrochloride	Hydroxyzine embonate
Naloxone hydrochloride dihydrate	Nitrous oxide	Midazolam maleate	Hydroxyzine hydrochloride
Selegiline hydrochloride	Nortriptyline hydrochloride	Nitrazepam	Ketotifen
Methylphenidate hydrochloride	Pentazocine	Oxazepam	Ketotifen fumarate
Quinidine bisulfate	Pentazocine hydrochloride	Potassium clorazepate	Levocabastine hydrochloride
Quinidine sulfate	Pentazocine lactate	Ritonavir	Lignocaine
Amitriptyline hydrochloride	Pentobarbitone sodium	Temazepam	Lignocaine hydrochloride
Amoxapine	Phenobarbitone	Triazolam	Mebhydrolin napadisylate
Amylobarbitone	Phenobarbitone sodium	Eltrombopag olamine	Meclozine hydrochloride
Amylobarbitone sodium	Primidone	Pregabalin	Mepyramine maleate
Buprenorphine	Propofol	Methotrimeprazine	Methdilazine hydrochloride
Buprenorphine hydrochloride	Protriptyline	Methotrimeprazine hydrochloride	Pheniramine aminosalicylate
Butobarbitone	Rifabutin	Methotrimeprazine maleate	Pheniramine maleate
Clomipramine hydrochloride	Rifampicin	Antazoline hydrochloride	Phenyltoloxamine citrate
Desflurane	Sevoflurane	Atovaquone	Pizotifen malate
Desipramine hydrochloride	Trimipramine	Azatadine maleate	Promethazine
Diethyl ether	Alprazolam	Azelastine hydrochloride	Promethazine hydrochloride
Dothiepin hydrochloride	Bromazepam	Brompheniramine maleate	Promethazine theoclate
Doxepin hydrochloride	Chlordiazepoxide	Chlorcyclizine	Thiethylperazine malate
Enflurane	Chlordiazepoxide hydrochloride	Chlorpheniramine maleate	Thiethylperazine maleate
Ethanol	Ciprofloxacin	Clemastine	Triprolidine hydrochloride
Etomidate	Ciprofloxacin hydrochloride	Cyclizine	Apraclonidine hydrochloride
Halothane	Ciprofloxacin lactate	Cyclizine hydrochloride	Brimonidine tartrate
Imipramine hydrochloride	Clobazam	Cyclizine lactate	Chloral hydrate
Isoflurane	Clonazepam	Cyproheptadine hydrochloride	Chlormethiazole
Ketamine hydrochloride	Diazepam	Dexchlorpheniramine maleate	Clozapine
Maprotiline hydrochloride	Flunitrazepam	Dimenhydrinate	Thalidomide
Methoxyflurane	Flurazepam hydrochloride	Diphenhydramine hydrochloride	Zopiclone
Methylphenobarbitone	Lamotrigine	Diphenylpyraline hydrochloride	
Nalbuphine hydrochloride	Lorazepam	Doxylamine succinate	

Figure 2. Drugs reported to interact with codeine[3]

Lithium carbonate	Lumiracoxib	Magnesium trisilicate	Dexamethasone
Lithium chloride	Methyclothiazide	Methylprednisolone	Dexamethasone sodium phosphate
Phenindione	Metolazone	Methylprednisolone acetate	Digoxin
Warfarin sodium	Parecoxib sodium	Methylprednisolone sodium succinate	Doxazosin mesylate
Aspirin	Paroxetine hydrochloride	Nadroparin calcium	Enalapril maleate
Choline salicylate	Paroxetine mesilate	Neomycin sulfate, oral	Enoxaparin sodium
Diflunisal	Probenecid	Neomycin sulfate, parenteral	Eprosartan mesylate
Methotrexate	Quinethazone	Neomycin sulfate, topical	Ethanol
Salicylamide	Rofecoxib	Neomycin undecenoate	Fludrocortisone acetate
Salol	Sertraline	Netilmicin sulfate	Fluocortolone
Sodium salicylate	Sertraline hydrochloride	Olmesartan medoxomil	Fosinopril sodium
Tacrolimus	Valdecoxib	Paromomycin	Framycetin sulfate
Tenofovir disoproxil fumarate	Alfuzosin hydrochloride	Perindopril arginine	Gentamicin
Bendrofluazide	Amikacin sulfate	Perindopril erbumine	Gentamicin sulfate
Bumetanide	Amiloride hydrochloride	Phenoxybenzamine hydrochloride	Glibenclamide
Celecoxib	Beclometasone dipropionate	Phentolamine mesylate	Gliclazide
Chlorothiazide	Beclomethasone dipropionate	Prazosin hydrochloride	Glimepiride
Chlorthalidone	Betamethasone	Prednisolone	Glipizide
Citalopram hydrobromide	Betamethasone acetate	Prednisolone acetate	Hydrocortisone
Cyclopenthiazide	Betamethasone dipropionate	Prednisolone hexanoate	Hydrocortisone acetate
Dapoxetine hydrochloride	Betamethasone sodium phosphate	Prednisolone sodium phosphate	Hydrocortisone sodium succinate
Escitalopram	Budesonide	Prednisone	Irbesartan
Escitalopram oxalate	Candesartan cilexetil	Proscillaridin	Kanamycin
Ethacrynic acid	Captopril	Quinapril hydrochloride	Lisinopril
Etoricoxib	Chlorpropamide	Ramipril	Lisinopril dihydrate
Fluoxetine	Cholestyramine	Spironolactone	Losartan
Fluoxetine hydrochloride	Cilazapril monohydrate	Streptomycin	Losartan potassium
Fluvoxamine maleate	Colestipol hydrochloride	Tamsulosin hydrochloride	Magnesium carbonate
Frusemide	Cortisone acetate	Telmisartan	Magnesium hydroxide
Hydrochlorothiazide	Cyclosporin	Terazosin	Magnesium oxide
Indapamide hemihydrate	Dalteparin sodium	Terazosin hydrochloride	Magnesium oxide heavy
Tinzaparin sodium	Ginkgo biloba leaf extract dry conc.	Pentosan polysulfate sodium	Timolol maleate
Tobramycin	Grepafloxacin	Prasugrel	Brimonidine tartrate
Tobramycin sulfate	Levofloxacin	Reteplase	Hydralazine hydrochloride
Tolazamide	Lypressin	Rivaroxaban	Misoprostol
Tolazoline hydrochloride	Moxifloxacin hydrochloride	Sodium clodronate	Aluminium hydroxide
Tolbutamide	Nalidixic acid	Streptokinase	Aluminium hydroxide gel
Trandolapril	Norfloxacin	Tenecteplase	Aluminium hydroxide gel, dried
Triamcinolone acetonide	Ofloxacin	Ticlopidine hydrochloride	Adefovir dipivoxil
Triamterene	Ornipressin	Treprostinil sodium	Phthalylsulfathiazole
Valsartan	Pemetrexed	Urokinase	Silver sulfadiazine
Zidovudine	Pemetrexed disodium	Zoledronic acid	Sulfabenzamide
Alendronate sodium	Phenytoin	Acebutolol hydrochloride	Sulfadiazine
Baclofen	Phenytoin sodium	Alprenolol hydrochloride	Sulfadiazine sodium
Ciprofloxacin	Terlipressin	Atenolol	Sulfadoxine
Ciprofloxacin hydrochloride	Trovafloxacin	Betaxolol hydrochloride	Sulfamethizole
Ciprofloxacin lactate	Vasopressin	Bisoprolol fumarate	Sulfamethoxazole
Clopidogrel	Voriconazole	Carvedilol	Sulfathiazole
Clopidogrel besilate	Abciximab rmc	Celiprolol hydrochloride	
Clopidogrel hydrogen sulfate	Adrenal extract	Esmolol hydrochloride	
Desmopressin	Alteplase	Labetalol hydrochloride	
Desmopressin acetate	Danaparoid sodium	Levobunolol hydrochloride	
Enoxacin	Dasatinib	Metoprolol	
Eplerenone	Desvenlafaxine	Metoprolol succinate	
Felypressin	Eltrombopag olamine	Metoprolol tartrate	
Fleroxacin	Epoprostenol sodium	Nadolol	
Fluconazole	Eptifibatide	Nebivolol hydrochloride	
Fosphenytoin sodium	Heparin calcium	Oxprenolol hydrochloride	
Gatifloxacin sesquihydrate	Heparin sodium	Pindolol	
Ginkgo biloba	Heparin, porcine	Propranolol hydrochloride	
Ginkgo biloba leaf	Heparinoid	Sotalol hydrochloride	
Ginkgo biloba leaf dry	Iloprost trometamol	Timolol	

Figure 3. Drugs reported to interact with ibuprofen[3]

Differences in duration of action and dosage of paracetamol and ibuprofen

The pharmacokinetics of ibuprofen and paracetamol are not suitably well matched to be combined in a single dosage form which would force simultaneous administration times and prevent individual dosage titration of anti-inflammatories which some patients may prefer.

A dose of 400mg of ibuprofen, the recommended maximum intake at a single dose[1,3], would be required in most patients to optimise the therapeutic efficacy of taking ibuprofen. The product Maxigesic® (containing paracetamol 500mg and ibuprofen 150mg) recommends a dose of up to 2 tablets (resulting in an ibuprofen intake of only 300mg per dose) every 6 hours over 24 hours[4,7]. This may result in sub-optimal pain relief in some patients who usually achieve the most adequate pain alleviation with single doses of 400mg at a time. The product Nuromol® (paracetamol 500mg, ibuprofen 200mg) recommends lower dosages still, with only one tablet three times a day recommended for Australian patients[6]. Even if patients were dosed at the maximum of 2 tablets three times a day (as is recommended in UK Nuromol® product information), a maximum dose of only 3000mg of paracetamol daily is reached (as opposed to a maximum of 4000mg daily which can be reached using paracetamol-only products or CCAs)[8], which may not optimise the therapeutic efficacy of paracetamol in some patients.

Furthermore, paracetamol and ibuprofen have differing durations of action, which may correspond to different optimal timing of doses. In healthy subjects, paracetamol has a half-life ranging from 1.9-2.5 hours[9] but a duration of action of 4-6 hours[10,13]. Ibuprofen has a similar half-life ranging from 1.8-2 hours[11] and duration of action of 4-6 hours for 200mg dosing, but at least 6 hours duration of action for 400mg dosing[12]. Therefore, optimal therapeutic duration of action may not be achieved in patients using the combination paracetamol and ibuprofen product Nuromol® due to its inherently pre-determined dosage regimes.

Lastly, oral dosage formulations containing ibuprofen are recommended to be taken with or shortly after meals to minimise risk of gastric adverse effects[1,2]. The product Maxigesic® recommends 6 hourly dosing (4 times a day)[5,7] which may not correspond fully with the common frequency of mealtimes (3 times a day).

Potential for drug misadventure due to the introduction of an unfamiliar combination

The introduction of a new combination analgesic into the community pharmacy environment in the setting of removing a different but pre-existing one creates potential for confusion and medicine-related mishap. Not all patients may be aware of the removal of their usual codeine-containing analgesic from Schedule 3 availability. As a result, consumers may request Nuromol® or Maxigesic® as a substitute with the understanding that they are interchangeable. This is a particular risk for the elderly patient cohort who may be visually and/or cognitively impaired but have a high requirement for over-the-counter analgesics. The confusion caused by similar-appearing products is a risk with the introduction of new combination medicines into the marketplace in replacement of medicines such as Panadiene®. The hazards of look-alike and sound-alike products (LASA) have been well documented and identified as one of the largest causes of medication selection and administration errors worldwide[14]. The name Nuromol® itself has similar

phonetic components to the product name Nurofen® which could be a source of confusion for consumers. An additional hazard is related to the fact that Nuromol® will be intended for schedule 3 registration[15] and so likely to be stocked in the same geographical location in pharmacies where CCA's were kept. The consequences of Nuromol® or Maxigesic® being mistaken for Paracetamol-only, Ibuprofen-only, or codeine-containing analgesics could range potentially from treatment failure, to overdose of one of the components, accidental co-administration of two NSAIDs, allergic reactions, medicine interactions, or severe adverse effects due to pre-disposing patient-specific risk factors.

Comments on claims and references used in the Maxigesic® and Nuromol® Advertisements

- Maxigesic®'s claims to "deliver 2.7 more times than paracetamol and 2 times more ibuprofen than Nuromol®" appears to be unreferenced, and a claim drawn upon the advertised drug content of Maxigesic®'s competitor rather than it's bioavailability which would be a true measure of drug "delivery".
- The Merry et al[16] study used to substantiate Maxigesic®'s efficacy only involved a comparison of the efficacy of combined paracetamol and ibuprofen to the efficacy of its separate components. The combination of paracetamol and codeine was not tested against Maxigesic® in this study.
- Both the Merry et al[16] study of Maxigesic® and the Daniels et al[17] study of Nuromol® tested their products only in the clinical setting of oral surgery, not in the settings of ailments the products have been advertised for (headache, migraine, backache, period pain, sore throat, arthritis, etc.)
- The Maxigesic® advertisement appears to recommend its use in "daily pain"; this simultaneously omits specifying the recommended conditions to treat while suggesting this product can be considered for ongoing "daily" use. Ongoing or "long-term" use of OTC medicines is not recommended without medical supervision.

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Appendix B

Objection to Proposed Amendments to the Poisons Standard: Proposal to reschedule codeine to Schedule 4

INTRODUCTION

In response to current proposals to up-schedule codeine-based products, [redacted] would like to express their concerns on behalf of their consumers and a healthcare system of which they have been a part of since 1845. Up-scheduling codeine-containing medicines will have serious consequences for the patient community and the healthcare industry. [redacted] requests the Delegate to consider the following actualities of codeine, as required under section 52E of the Therapeutic Goods Act 1989[16.] and in doing so reconsider a decision which may prove extremely detrimental to both our over-exerted health system and the Australian public's quality of life.

Assumptions made about the recently publicised codeine-related addiction statistics from the 2015 MJA study (Roxburgh et al, National Drug and Alcohol Research Centre) do not take into account all of the factors involved in substance abuse.

[in relevance to: 1(e), Section 52E, Therapeutic Goods Act 1989]

Chronic addiction to pharmaceuticals is a multi-faceted, psychological disorder. Development of substance abuse depends on the vulnerabilities of the individual, the perception of the drug as a rewarding stimulus, the tendency of the individual to be impulsive and form habits[1,2], and social and cultural influences. Pseudoaddiction and psychological dependence can also represent significant but often under-recognised causes of analgesic addiction[36]. The phenomenon of pseudoaddiction can be described as a syndrome of behaviour caused by inadequate pain management[34]. This behaviour is characterised by persistent demands for stronger analgesia, misinterpreted as addiction, and then mistrust between patient and clinician as the patient strives to convince their health care providers of their unrelieved pain[34,35]. This can result in patients self-medicating to the extent of causing harm or death, while never intentionally misusing the analgesic[35]. The aforementioned study (Roxburgh et al) did find an increase in codeine related deaths between 2000 and 2013, but also mentioned that almost half of the reported deaths were accidental overdoses and a third were intentional self-harm[28]. There is no comparison mentioned regarding possible increasing rates of overall OTC medicine abuse or overall OTC-medicine-facilitated deaths. It would appear that the main aspects of this study could be interpreted as more of a commentary about the incidence of poor mental health, suicidal tendencies, and low understanding and respect of medicines in the community. In addition to pre-existing mental health disorders, this study also found that a notable proportion of individuals abusing codeine suffered from chronic pain, suggesting scope for the healthcare system to improve its management of this patient cohort[28]. Overall however, there appears to be very limited evidence to conclude that the initiation of an opioid itself, such as codeine-containing analgesics (CCAs), is a causative factor in the development of opioid addiction[21]. The notion that over-the-counter availability of

CCAs is turning multitudes of unsuspecting patients into addicts is a misconception. In fact, in another study of 12,000 patients initiated on opioid medications, there were only four patients without a prior history of substance abuse who developed a dependence on that medication[21]. This appears to indicate that other dynamics such as tendencies of psychological addiction and maladaptive behaviours of the individual are more likely drivers of opioid abuse than the simple introduction of an opioid. Mental health disorders and polysubstance abuse is common to individuals addicted to over-the-counter codeine products[3]. Roxburgh et al found that most codeine-related deaths during the period of 2000-2013 (1201, 83.7%) were attributed to multiple drug toxicity[28]. In a 2011 Australian and New Zealand study, over 38% of Australian codeine-abusers were reported to be using alcohol and other drugs, and 28% were identified as having a mental health disorder[3]. As polysubstance abusers by their very nature have more than one outlet for addiction, the restriction of supply of codeine to this cohort will not necessarily result in drug abstinence. It is even possible that the removal of OTC CCAs may cause these individuals to simply rely more heavily on other, potentially more harmful substances to satisfy them. More rational approaches could include implementing social policies and support services to address the marginalisation, social exclusion, stigma, and poor insight common to drug abusers[2].

Codeine continues to meet the Poisons Standard criteria consistent with current scheduling of the relevant Schedule 2 and Schedule 3 codeine-containing products.

[in relevance to: 1(b,e), Section 52E, Therapeutic Goods Act 1989]

While the *AHMAC Scheduling Policy Framework for Medicines and Chemicals* may be open to interpretation, the scheduling factors remain in support of the continued current scheduling of over-the-counter codeine. While it has been debated, this is particularly true of Criterion 2 of Schedule 3 requirements:

> *"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."*

The distinguishably low dose and low quantity available over-the-counter is *not* expected to produce dependency. The average daily intake of codeine-containing tablets amongst Australian over-the-counter codeine-abusers is 50 tablets, and the daily quantity of codeine intake is 640mg[3]. This quantity of consumption is not achievable with the purchase of a single unit of the highest dose and highest pack-size (Panadeine Extra, Paracetamol 500mg/ Codeine Phosphate 15mg, Qty 40) of codeine-based over-the-counter products. Also, the addiction risk associated with the purchasing of all codeine products is in fact minimised already by not just the supervision, but the mandatory direct involvement of the pharmacist in the sale as per current scheduling requirements and fundamental pharmacist training.

In addition, over-the-counter codeine products *do not* specifically meet the Criteria for Schedule 4, in particular, Criterion 1;

"...diagnosis, management or monitoring of chronic pain conditions requires medical or dental intervention before use"

Or, Criterion 7;

"...its use has contributed to, or is likely to contribute to, communal harm"

While codeine, like many over-the-counter products, has been used in practice long-term in some special cases, it is not considered first-line treatment for the chronic pain referred to in Criterion 1. It is recommended for limited duration courses of short-lived, mild-to-moderate incidental pain[4,5], and this type of use is the proviso on which pharmacists approve codeine-product sales. This is not a recommendation which has been significantly revised recently, and therefore is not supporting of any need for corresponding new changes to the schedule.

Regarding Criterion 7, it is not even-handed to single out codeine as a specifically "harmful" substance, as it is likely that over the history of community pharmacy practice many over-the-counter products have contributed to, through misuse, abuse or misadventure, some type of communal harm. Abuse of over-the-counter products is not limited to codeine, but has been identified in the use of dextromethorphan, sedating antihistamines, nasal decongestants and laxatives[8]. Medicines inherently have potential for both benefit and detriment depending on the circumstances of their use; these risks are managed adequately already by the Poisons Scheduling in Australia and supervising community pharmacists.

Low dose codeine has, and can, be efficacious for short-term pain relief as it is currently recommended. It does not cause "escalation up the pain-ladder". It cannot, as has been suggested, be practically replaced by "direct administration" of opioids such as morphine.
[in relevance to: 1(a), Section 52E, Therapeutic Goods Act 1989]

It has been argued that codeine, as a "weaker" opioid[9], is a poorer choice of pain management whose use encourages poly-pharmacy and more rapid escalation of more potent analgesics. A small improvement in relief gained from using CCAs may be sufficient to meet a consumer's needs and prevent unnecessary visits to the GP for stronger analgesics. The World Health Organisation's Analgesic Ladder also recognises codeine as having a valid role in modern pain management as a Step 2 drug, and goes on to suggest that the combination of codeine and paracetamol may be in fact more effective and better tolerated in many patients than the schedule 4 item tramadol[8,9]. Furthermore, it has not yet been conclusively established in human studies that codeine can induce the "escalation up the pain-ladder" by way of the phenomenon hyperalgesia [22].

Lastly, patient convenience and tolerance of analgesics are important but occasionally forgotten factors in analgesic choice. While stronger opioids like morphine can produce more pronounced side effects in their prescription-only available forms, the side-effect profile of codeine is usually mild[9] and likely even more tolerable in the low doses currently conveniently found over-the-counter. Strong opioids, due to their toxicity and

abuse potential, are also only available on prescription and therefore not a convenient option for consumers.

Removing over-the-counter access to codeine has the potential to significantly impair the quality of life of some of our most vulnerable patient groups, including pregnant women and the elderly.
[in relevance to: 1(a,b), Section 52E, Therapeutic Goods Act 1989]

There is a high prevalence of persistent pain in elderly adults[10]. This patient group may occasionally require the intermittent use of low-dose codeine-containing analgesics to self-manage their pain and provide autonomy in their lifestyle. Physical changes in the aging adult body include decreased renal function, a condition which makes Non-Steroidal-Anti-Inflammatories (NSAIDS, which are currently available over the counter) an unsuitable choice of pain relief when codeine is unavailable. Low-doses of codeine in this setting should not be viewed as ineffective: due to the altered pharmacokinetics of this medicine in the elderly, low-dose codeine (in combination with paracetamol) may be potent enough[10] for their needs. A 2009 study (J.H Friday et al, in the setting of acute pain of extremity injuries) also demonstrated that the paracetamol-codeine combination achieved similar analgesic effectiveness to ibuprofen[30]. There is also low potential for abuse in the aged consumer demographic: 95% of Australians identified as addicted to over-the-counter codeine products were less than 45 years old[3]. As our population ages, problems relating to reduced access to analgesics will only become more apparent with time and codeine restriction. Due to the reduced mobility and social isolation seen in some elderly patients, it may not always be possible to obtain a prescription for codeine-based analgesics from a local doctor in a timely fashion.

Similar to the elderly patient cohort, pregnant women will be disadvantaged for choice for non-prescription analgesics if codeine is up-scheduled. As a result of the physical challenges of gestation, many women experience some pain during their pregnancy[6]. Codeine has a safety classification of Category A in pregnancy[6,12]. Provided it is used for short time periods at the lowest effective dose, it is considered a safe, convenient and viable option for women to manage mild, intermittent pain[5,11]. As with renally impaired older Australians, over-the-counter NSAIDs are not an appropriate substitute for codeine in pregnancy due to their Category C safety classification[5,11].

Short courses of low-dose codeine consumption in breastfeeding is not necessarily an absolute contraindication[11]. There are risks associated with ultra-rapid CYP2D6 polymorphism metabolisers and codeine consumption which can be identified and prevented.
[in relevance to: 1(a,b,c), Section 52E, Therapeutic Goods Act 1989]

There has been some debate as to the risk of codeine use during breastfeeding. Codeine has been used in combination with paracetamol to adequate effect for many women in whom other analgesics are not preferable, including as soon as directly after birth to manage post-caesarean pain[29]. Like many analgesics, codeine is excreted into breast milk[11]. The degree of excretion is related to maternal metabolism, with the resulting relative infant dose estimated at only 8.1%[11]. The consequences of codeine consumption in patients with the ultra-rapid (UM) metabolising CYP2D6 genetic polymorphism has been documented in case studies[12,23]. However, most of these studies demonstrating higher adverse effects of codeine in the UM patient cohort have been done using single doses of 30mg. This single dose is only achievable in an OTC product setting using two tablets of

the highest-strength OTC codeine product, Panadeine Extra, whose sale is restricted by pharmacist discretion. Lastly, the prevalence of the UM CYP2D6 genetic polymorphism itself has been estimated at only 1-2% of patients[12]. These statistics are arguably not significant enough to contraindicate all patients from accessing codeine for analgesia. Conversely, variants of CYP2D6 can in fact result in poor opiate metabolism[37]. Even so, genetic testing for this polymorphism is available, and could be recommended for patients specifically indicated for treatment with codeine. This may be required in the many cases where codeine is determined to be the preferred analgesic.
While alternative pain control medicines are preferred in the breastfeeding setting, codeine may still be the treatment of choice in some individuals[11] who have allergies, intolerances or contraindicating medical conditions which may preclude the use of agents including NSAIDs[27]. With limited consumption, pharmacist counselling, genetic screening where indicated, and informed patient consent, codeine-based Schedule 3 items can be used in practice to good effect where other analgesics are undesirable.

There is not yet enough evidence of "cold & flu" codeine-containing schedule 2 formulations being targeted specifically by consumers with codeine-abuse behaviours to substantiate a need to change to schedule 3. Also, suggestions that these products are therapeutically redundant in the pharmacy as treatment for cough is misguided as the only schedule 2 products recommended for dry cough in the community pharmacy setting contain dextromethophan and pholcodine.
[in relevance to: 1(b,e), Section 52E, Therapeutic Goods Act 1989]
Furthermore, the single dose quantity of 30mg of codeine is not achievable using the Schedule 2 "cold & flu" formulations, which contain 9-9.6mg of codeine phosphate per tablet at most[24,25](18-19.2mg per dose of 2 tablets) negating the need to up-schedule "cold & flu" products to schedule 3 to reduce access.

Concerns regarding codeine use in children are not in proportion to actual risk in the community pharmacy environment. There is limited (if any) evidence of widespread use of codeine in children under 12 years of age to justify restrictions affecting what is almost entirely an adult formulation commercial range.
[in relevance to: 1(a,b,c), Section 52E, Therapeutic Goods Act 1989]
While there are valid safety concerns detailed by the TGA[12], there is limited potential for harm to persons aged under 12 posed by the availability of current schedule 3 codeine-based products. The majority of these over-the-counter products in Australian pharmacies are strictly adult formulations, with accompanying adult doses of paracetamol, and therefore are not approved by pharmacists for sale to or for a child. In the case where consumers are between 12 and 18 years old and have undergone tonsillectomy or adenoidectomy for sleep apnoea, the advice of a prescriber should be sought as to safe analgesic selection[12].

Should the option of schedule 3 codeine-containing products be removed from local pharmacies, it is likely that it will encourage doctor-shopping for prescription codeine and unnecessary presentations to emergency departments.
[in relevance to: 1(b,e,f), Section 52E, Therapeutic Goods Act 1989]

Rural or otherwise geographically isolated patients may particularly be disadvantaged[16] and so may resort to this behaviour. Emergency departments are already targeted by substance abusers as a means to obtain prescriptions for opioids and other medicines[13,14]. Apart from increasing the workload of hospital ED departments[16], the new influx of codeine-prescription-seeking patients will make it more difficult for the treating medical staff to discern which presenting patients are there to facilitate their drug abuse. As emergency departments are typically staffed with rotating personnel unfamiliar to the patient and their pain-relief needs, it is possible that patients may be unnecessarily prescribed stronger analgesics than is therapeutically required[16]. By having to resort to seeing hospital doctors in place of their unavailable GPs, patients may be inadvertently introduced to more potent avenues of addiction and potential for adverse effects.

Improved labelling to include visible warnings and reductions in commercial pack size should not be considered a futile option in reducing CCA-related harm (see figure 1).

[in relevance to: 1(d), Section 52E, Therapeutic Goods Act 1989]

While codeine-addiction has proved a difficult social condition to alleviate, there are many less extreme and potentially more effective strategies that can be implemented. While some may declare labelling and pack size changes a weak option, these simple measures have been proved in other settings to reduce long term measures of harm to the population. Changing labelling to include more obvious warnings about addiction risks may allow new consumers to make informed decisions about their analgesic choices while reminding them more noticeably about addiction potential. This strategy may prevent new cases of codeine dependence. Boxed warnings have been used to good effect for many registered medicines by prompting more scrutiny in product selection[26]. A notable and very effective implementation of packaging warnings in the setting of reducing addiction is that of the tobacco industry[31]. It has been found that mandatory label warnings which are large, graphic and comprehensive are effective in communicating health risks, with pictorial warnings the most associated with an increased motivation to quit[31,32]. Harm reduction by reducing commercial pack size has also been demonstrated in a 2013 study which described the result of the UK September 1998 pack-size reductions for paracetamol products[17]. This change in regulation resulted in an estimated 43% reduction in paracetamol-related deaths over the 11.25 year study period[17].

Doctors and pharmacists need to be empowered to recognise and intervene in the activity of codeine-abusers, optimally facilitated by a real-time monitoring and recording system (see figure 1) . Patients should also be educated frankly about the risks of over-the-counter medicine misuse and abuse.

[in relevance to: 1(e), Section 52E, Therapeutic Goods Act 1989]

Weaknesses in the primary care system need to be addressed before rescheduling is considered. Prescribers and pharmacists need to be educated specifically in recognising and managing drug-seeking behaviour specific to over-the-counter medicines. Over-the-counter-product addictions can be incorrectly perceived as “unproblematic” or “different” to other drug-addictions, and so current approaches employed by health professionals may not be suitable[18]. Without the opportunity for early intervention, it is likely that despite supply restrictions, patients may continue to find ways to source codeine.

While pharmacists already question patients to ascertain Schedule 3 product appropriateness, they should be empowered to take up a more active role in preventing codeine-abuse-driven sales. It has been noted on occasions in practice that while CCA consumers are questioned regularly by pharmacists, they are seldom challenged or denied sale[18]. This is a valid area for improvement. Where pharmacists are concerned about a codeine-product sale, they may record requests of over-the-counter items through their dispensing software. While this is a useful tool in preventing codeine abuse within the pharmacy setting, this practice is neither specifically mandatory nor one which allows other pharmacies to view or benefit from the premises-specific records. Fortunately, ASMI and The Pharmacy Guild of Australia are developing a prototype real-time monitoring system similar to the pseudoephedrine sale monitoring program Project Stop. Project Stop was developed as an initiative of The Guild in an effort to reduce the number of pseudoephedrine sales to those seeking to supply illegal methamphetamine laboratories. This decision-making tool designed for pharmacists records the identity of the patient along with their product request to make it easier for pharmacists to identify repeated and potentially harmful purchasing behaviours[19]. The first trial of Project Stop in Queensland was a considerable success, implicated in the 25% decrease in the number of clandestine laboratory detections over a 12 month period[20,33]. A monitoring system such as this could have a significantly useful application in the campaign against codeine abuse and negate the need for scheduling revisions.

The issue of inappropriate OTC CCA use in chronic pain should be directly addressed and the current scheduling be maintained to preserve access to those in whom they are legitimately indicated. Pharmacists need to be encouraged to identify and refer poorly controlled chronic pain cases to prevent psuedoaddiction. Prescribers need continuing professional development on modern pain management strategies to prevent their patients from ineffective self-medicating behaviours.

[in relevance to: 1(b,e), Section 52E, Therapeutic Goods Act 1989]

Community pharmacists need to be empowered to utilise their clinical skills in recognising excessive use of OTC CCAs as possible cases of pseudoaddiction. If pharmacists intervene early, patients may be able to access more effective pain relief for their condition from their doctor and prevent the cycle of pseudoaddiction. Prescribers in turn need to be supported in access to chronic pain services to refer their patients when necessary, in addition to up-to-date evidence-based continuing education on treatment choices. Both prescribers and pharmacists should work to foster patient-clinician trust especially in cases of chronic pain. Engaging with patients about their pain management strategy and discussing options transparently may prevent chronic pain sufferers from resorting to ineffective self-selection of analgesia.

Intervention	Practical implementation
Educate pharmacists and prescribers regarding • CYP2D6 polymorphism and codeine metabolism • OTC codeine dependence as a unique addiction with a unique patient demographic • Contraindications to codeine use in children • Avoiding codeine initiation in patients with a history of alcohol and / or substance abuse • Appropriate and evidence-based therapy in chronic pain	• Continuing professional education facilitated by professional regulatory bodies • Encourage transparent, realistic, and up-to-date discussion about the available and effective chronic pain relief options between pharmacists, prescribers and their patients to prevent ineffective chronic self-medication • Taking a patient's full medical history to identify at-risk behavioral profiles, reaction after previous treatment with codeine and counsel on risks of codeine consumption
• Empower pharmacists and pharmacy staff to recognise, prevent and report suspected codeine abuse in the community pharmacy setting	• Continuing professional education facilitated by relevant regulatory bodies • Pharmacists to minimise stock facings of schedule 3 products • Pharmacists to enforce the one-pack-per-customer-only strictly • Pharmacists to enforce the referral of all patients with chronic pain self-medicating with OTC codeine-containing analgesics without medical supervision to their GP • Ensure that detecting and managing risks of OTC product abuse is a topic thoroughly addressed in tertiary education institutions offering pharmacy qualifications
• Employ real-time monitoring/recording system for OTC codeine product requests	• Implement the prototype monitoring system The Pharmacy Guild has developed and ensure its use is mandatory • Define baseline statistics and key performance indicators of the practice to evaluate its efficacy • Pending availability of this system, pharmacists to record all sales of OTC CCAs on patient profiles using their dispensing software
• Change labelling and pack-size where appropriate in a manner which reflects the restrictions of use	• Include boxed warnings on codeine-containing products to alert consumers more obviously to CYP2D6 metabolizer polymorphisms and potential for addiction. • Reduce the pack sizes of schedule 3 codeine-containing analgesics to contain at least less than the amount of codeine contained in the commercial packs of schedule 4 medicines
• Address the implicit mental health problems and drug & alcohol use of the community which are significant drivers for OTC	• Direct more resources to social welfare services and the mental healthcare system

medicine abuse	
• Ensure the public is aware of the risks of using and misusing OTC medicines	• Public education including medication safety awareness in schools • Use signage in pharmacies to remind the community of the role of the pharmacist in assisting them with analgesic selection and the need to disclose relevant medical history before requesting OTC medicines

Figure 1. Summary of strategies to implement in preference to CCA up-scheduling to address codeine dependence and misadventure in the community

CONCLUSION

With a combination of community and professional education, alterations in product packaging, and implementation of a real-time monitoring program, we are able to make a substantial impact in the epidemiology of codeine-addiction. These strategies may help us achieve this goal without infringing on the professional responsibilities of pharmacists and rights of patients to timely and preferred pain relief.

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Appendix C - Claims and evidence table

Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
1	Risks of medication misadventure through polymorphic metabolism, deliberate misuse/abuse combined with the relative lack of efficacy compared to safer products.	a,e	The prevalence of the UM CYP2D6 genetic polymorphism has been estimated at only 1-2% of patients[1], arguably not significant enough to contraindicate all consumers from codeine as an analgesic	Patients to undergo genetic assessment to ascertain CYP2D6 polymorphism status prior to codeine treatment	Further education and support (such as a real-time monitoring/recording system) needs to be given to community pharmacists to empower them to recognise and address over-the-counter codeine abuse. Prescribers also require education to recognise and treat over-the-counter codeine addiction as the unique substance abuse problem that it is
2	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. Codeine demonstrates marked variability in its transformation to morphine in different individuals, with the potential for very severe toxicity in ultra-rapid metabolisers.	a	Reduced benefit VS risk in some patients does not mean the benefits of codeine are therapeutically obsolete in the community. Over-the-counter codeine-containing products which do not specifically contain an additional antitussive agent are not marketed or recommended by pharmacists for relief of cough. Pholcodine and dextromethophan preparations currently available over the counter are available for this purpose[2]	Patients to undergo genetic assessment to ascertain CYP2D6 polymorphism status prior to codeine treatment.	In Caucasian populations, 8% to 10% of people are poor metabolisers; however 3% to 5% are ultrarapid metabolisers (Stamer & Stuber, 2007; Madadi et al, 2009). Those who are ultrarapid metabolisers (carriers of the CYP2D6 gene duplication) have significantly higher levels of morphine and morphine metabolites after the same dose of codeine (Kirchheiner et al, 2007 LevelIV). There are large inter-ethnic differences in the frequencies of the variant alleles. For example, the proportion of ultrarapid metabolisers is higher (up to 29%) in Middle Eastern and Northern African populations, and lower (0.5%) in Asians (Stamer & Stuber, 2007); the proportion of poor metabolisers is lower in Asians and African Americans (Holmquist, 2009).
3	OTC intended for management of acute self-limiting pain, however, there is inappropriate use for chronic pain.	b	There is insufficient evidence to conclude widespread use of over-the-counter codeine to treat chronic pain, especially as it is not recommended for this indication in Australian Therapeutic Guidelines[3]. There is also insufficient evidence to conclude abuse by chronic pain sufferers, or the initiation of codeine as a factor in addiction development in patients without a prior history of substance abuse[5]	Further education and support (such as a real-time monitoring/recording system) needs to be given to community pharmacists to empower them to recognise and address over-the-counter codeine abuse. Prescribers also require education to recognise and treat over-the-counter codeine addiction as the unique substance abuse problem that it is	Interpatient opioid requirements vary greatly (Macintyre & Jarvis, 1996 Level IV) and opioid doses therefore need to be titrated to suit each patient. Reasons for variation include patient age and gender, genetic differences and psychological factors as well as opioid tolerance.
4	Purpose is questioned since benefit is low.	b	Benefit may be considered low in cases where analgesic needs are high or in chronic pain situations, but it does not mean that it is therapeutically obsolete. Low dose codeine can be useful in elderly patients who may not be able to tolerate NSAIDS, and pregnant women who not only are unable to take NSAIDs due to safety data[2,13], but are conscious of medication consumption during pregnancy, preferring to take the lowest effective doses possible.	Educate and empower pharmacists to recognise suspicious purchasing behaviours and treatment failure in those patients not responding to codeine.	

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Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
5	The purposes for which codeine is intended to be used are for Schedule 2 products for the "treatment of coughs and colds" and for Schedule 3 products for the "temporary relief of strong pain and discomfort associated with a number of different medical conditions."		The use of the word "coughs" as in the phrase "coughs and colds" is likely intended as a descriptive reference to the condition of the self-limiting viral upper-respiratory tract infection rather than an explicit indication for the product, as pharmacists do not recommend codeine-containing products strictly for the purposes of cough (unless the product contains a strictly antitussive agent), but for general cold & flu relief. In practice, pharmacists recommend pholcodine or dextromethophan preparations[2].	The wording in our regulations could be changed to exclude "cough" from the indication of schedule 2 codeine-containing cold & flu preparations to reflect current pharmacy practice, rather than the rescheduling of a product which otherwise complies with it's schedule 2 requirements.	Meta-analyses have shown that the risk of side effects from opioids administered by PCA is similar to the risks from traditional methods of systemic opioid administration, (Hudcova et al, 2005 Level I).
6	Codeine shares the properties of other opioid analgesics and is potentially capable of producing dependence and, in overdose, respiratory depression and reduced level of consciousness.	a	While codeine shares a similar side-effect profile to other opioid analgesics, the severity of the effects are generally considered milder and less problematic than the schedule 4 varieties of opioids. The argument that codeine is equally capable to producing the same dependence, respiratory depression, reduced consciousness and risk of overdose cannot be substantiated as it does not take into account many patient-individual characteristics such as CYP2D6 polymorphism status, opioid naivety, pharmacokinetics specific to physical distributions, or tolerance and perception of the side-effects.	Patients to undergo genetic assessment to ascertain CYP2D6 polymorphism status prior to codeine treatment. Pharmacists to also be encouraged to refer patients to doctors if they report a history of poor tolerance to or adverse events involving opioid analgesics	A number of studies investigating hypoxia in patients receiving opioids for pain relief, have found that measurement of respiratory rate as an indicator of respiratory depression may be of little value and that hypoxaemic episodes often occur in the absence of a low respiratory rate (Catley et al, 1985 Level IV; Jones et al, 1990; Wheatley et al, 1990 Level IV; Kluger et al, 1992 Level IV). As respiratory depression is almost always preceded by sedation, the best early clinical indicator is increasing sedation (Ready et al, 1988; Vila et al, 2005; Macintyre & Schug, 2007).
7	Codeine, as a prodrug, causes its direct toxicity primarily through its biotransformation into morphine. The metabolic polymorphism discussed above leads to major variability within the population in terms of the extent and rapidity of this conversion to morphine. Ultra-rapid metabolisers, who have an accelerated rate and higher extent of conversion, are exposed to morphine concentrations that are many-fold higher than those reached in poor metabolisers. This variant is found in up to 10% of Caucasians, and higher proportions of populations of North African, Oceanic and Middle Eastern origin. Very few individuals are aware of their own metaboliser status, and it would thus be very difficult to protect ultra-rapid metabolisers by way of warnings. High concentrations of morphine in the plasma can lead to serious sedation and respiratory depression, and potentially to death.	a,c	The prevalence of the UM CYP2D6 genetic polymorphism has been estimated at only 1-2% of patients[1], arguably not significant enough to contraindicate all patients from codeine as an analgesic, especially at the low doses currently available over the counter	Patients to undergo genetic assessment where possible to ascertain CYP2D6 polymorphism status prior to codeine treatment	
8	The potential for severe adverse effects at "usual" doses in ultra-rapid metabolisers is such that codeine appears to be an unsuitable candidate for OTC availability, with either S2 or S3 scheduling. This conclusion applies equally well to the products intended for treating coughs and colds, and those intended for the treatment of pain.	a,c	The term "usual doses" needs to be defined in order to substantiate this claim. While it has been noted that consumers who are ultra-rapid metabolisers of codeine are at higher risks of adverse effects from codeine-containing products, studies documenting this phenomenon appear to involve single test doses of 30mg of codeine[6]. The codeine available in combination cold and flu products (eg. Codral Cold & Flu New Formulation, Demazin PE Cold & Flu) ranges from 9-9.6mg of codeine per tablet (18-19.2mg per recommended single dose)[7,8]. Therefore the studied single dose of 30mg is not achievable using recommended dosage of the Schedule 2 “cold & flu” formulations , negating the need to upschedule these products to schedule 3 based on the UM-risk line of reasoning.	Pharmacists to deny sale of Schedule 2 & 3 codeine-containing items to patients with a suspected or known history of poor tolerance of opioids, possibly relating to UM CYP2D6 status, and patients recommended to undergo genetic assessment prior to codeine treatment wherever possible.	

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Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
9	Changing the labelling and decreasing the pack size will not adequately address the problem of misuse and dependence.	d	Changing labelling to include more obvious warning about addiction risks may allow new consumers to make informed decisions about their analgesic choices while reminding them more clearly about the potential for dependence. Boxed warnings have been used to good effect for many registered medicines by prompting more scrutiny in product selection[4]. Harm reduction by reducing commercial pack size has been demonstrated in a 2013 study which described the result of the UK September 1998 pack-size reductions for paracetamol products[9]. This change in regulation resulted in an estimated 43% reduction in paracetamol-related deaths over the 11.25 year study period[9].	Include boxed warnings in the labels and negotiate a pack-size reduction	
10	Current labelling and packaging include insufficient warnings, and that there should be clear warning labels stating the risks of addiction and dependence, the risks of harm from the paracetamol or ibuprofen, and the risk of death. Access to codeine in Australia is inconsistent, in that the total amount of codeine available in a pack of Panadeine Extra® (40 tablets containing 15mg each) is the same quantity as that available in a pack of codeine phosphate (20 tablets containing 30mg each), which is included in Schedule 8 and recognised to have potential for abuse or addiction.	d	As described above, changing labels and pack sizes of schedule 3 codeine-containing products is an achievable and potentially very effective way to maintain access to analgesia while reducing risk of misuse and addiction	As above, Include boxed warnings in the labels and negotiate a pack-size reduction with manufacturers	
11	Some sources, including the Panadeine® product information, suggest or imply that before taking codeine a person should know their CYP4502D6 status, and this in turn means that no person should be able to self-administer codeine that has been obtained OTC. It is argued that the benefit of medical supervision that would be obtained with a rescheduling to S4 includes the ability of the prescriber to discuss with the patient the risks of excessive opiate effect, and provide advice about actions to take if this occurs. This argument applies equally well to products currently available in both S2 and S3.	a,c	While it is recommended where possible that genetic testing be done before codeine treatment, patients who have had codeine previously at same or similar doses to good effect without incidence of adverse effects such as sedation should not be precluded from being able to self-administer codeine from OTC sources	Pharmacists to be empowered to deny sale of Schedule 2 & 3 codeine-containing items in situations where patients have a suspected or known history of poor tolerance of opioids, possibly relating to UM CYP2D6 status, and patients recommended to undergo genetic assessment prior to codeine treatment.	
12	Increasing amount of evidence for harm from abuse.	e	The recent highly publicised statistics from the National Drug and Alcohol Research Centre did find an increase in codeine related deaths between 2000 and 2013, but also mentioned that almost half of the reported deaths were accidental overdoses and a third were intentional self-harm[19]. There is no comparison mentioned regarding possible increasing rates of overall OTC medicine abuse or overall OTC medicine facilitated suicide attempts. It would appear this study could be interpreted as more of a commentary about the incidence of poor mental health, suicidal tendencies, and low understanding and respect of medicines in the community.	We need to improve the public's understanding and respect of medicines to help prevent not just codeine-related deaths, but all medicine-related deaths. Our national drug and mental health management strategies need to be improved as a priority over restricting codeine availability as it is clear that codeine use is only one factor in the majority of deaths described in this study, which reported a wider history of substance abuse problems, chronic pain, and injecting drug use as associated characteristics in the deaths	

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Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
13	Codeine is emerging as an increasingly commonly used drug of abuse internationally and in Australia. Data from the national opioid pharmacotherapy statistics in 2013 showed that codeine was the opioid drug of dependence for 1,038 clients receiving opioid substitution pharmacotherapy. The actual number was likely to be higher than this because of missing data. Another recently published study of 902 people who inject illicit drugs found that about one third had misused OTC codeine during the preceding six months.	e	The recent highly publicised statistics from the National Drug and Alcohol Research Centre did find an increase in codeine related deaths between 2000 and 2013, but also mentioned that almost half of the reported deaths were accidental overdoses and a third were intentional self-harm[19]. There is no comparison mentioned regarding possible increasing rates of all OTC medicine abuse or possibly medication-related suicide attempts. It would appear this study could be interpreted as more of a commentary about the incidence of poor mental health, suicidal tendencies, and low understanding and respect of medicines in the community.	We need to improve the public's understanding and respect of medicines to help prevent not just codeine-related deaths, but all medicine-related deaths. Our national drug and mental health management strategies need to be improved as a priority over restricting codeine availability as it is clear that codeine use is only one factor in the majority of deaths described in this study, which reported a wider history of substance abuse problems, chronic pain, and injecting drug use as associated characteristics in the deaths	
14	Misuse of OTC codeine products including deaths resulting from hepatic injury, gastrointestinal perforations, hypokalaemia and respiratory depression.	a,c	Risks of morbidity and mortality from these side effects have always been detailed in the product information. Risk of similarly serious adverse affects is possible with many medicines. Codeine was originally included in Schedule 2 and 3 products because this risk rightfully was perceived as low in the majority of the population so long as the product was used as per product recommendations and patient selection by a supervising pharmacist. In addition, risk of hepatic injury from paracetamol and gastric perforations from NSAIDs such as ibuprofen will not be removed by upscheduling codeine as these items will still be available to consumers in their isolated form.	Pharmacists need to improve their vigilance and exercise their role in patient selection when it comes to allowing consumers to purchase products containing paracetamol and NSAIDs by checking for risk factors and purchasing behaviours which could predispose them to serious side effects. The public needs further education on what their pre-existing health conditions mean for analgesic selection and be encouraged to disclose them to the pharmacist when making a purchase.	
15	Genetic influence on codeine's action complicates risk and benefit decisions, and leads to questions regarding the role of codeine in clinical practice.	a	The prevalence of the UM CYP2D6 genetic polymorphism has been estimated at only 1-2% of patients[1], arguably not significant enough to contraindicate all patients from codeine as an analgesic. For patients in whom other analgesics are deemed unsuitable (allergies, intolerances, elderly, pregnant women, poorly controlled asthmatics, gastrointestinal ulceration, pre-eclampsia, renal impairment), codeine may be the treatment of choice and spare the use of more potent opioids. Making codeine far from obsolete in clinical practice	Patients to undergo genetic assessment to ascertain CYP2D6 polymorphism status prior to codeine treatment wherever possible. Doctors and pharmacists to be educated to be more scrupulous about patient selection for codeine therapy and utilise 1st line analgesics where possible.	
16	An appropriately qualified practitioner needs to assess the risk before making the decision that codeine will be used.	b	It is not reasonable for patients who have had codeine before at same or similar doses to good effect without incidence of adverse effects such as sedation to be precluded from being able to self-administer codeine from OTC sources. A practitioner should assess risk in patients if using codeine for the first time and/or has a history of poor tolerance to opioid analgesics	Patients to undergo genetic assessment to ascertain CYP2D6 polymorphism status prior to codeine treatment. Doctors and pharmacists to be educated to be more scrupulous about patient selection for codeine therapy and utilise 1st line analgesics where possible.	

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Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
17	A recently released combination of two non-opioid analgesics (ibuprofen plus paracetamol) appears to be more effective than the CCAs, with a number needed to treat (NNT) of 1.5. This combination would fill any gap left by the unavailability of CCAs over the counter, giving consumers access to a more effective analgesic without requiring a prescription and without the risks of the marked variability in pharmacokinetics or abuse potential that are associated with codeine.	a	Low dose codeine preparations may be the treatment of choice in patients unable to tolerate aspirin or ibuprofen, and therefore CCAs cannot be replaced by paracetamol/ibuprofen combinations.	Maintain current schedulling	
18	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.	a	A "minor" analgesic effect needs to be specified in order to validate this statement. Also, a "minor" improvement in relief in addition to that of paracetamol or ibuprofen alone may be what is appropriate for a consumer's needs. Low dose codeine preparations may be the treatment of choice in patients unable to tolerate aspirin or ibuprofen, and therefore CCAs cannot be replaced by paracetamol/ibuprofen combinations.	Maintain current schedulling	
19	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.	c	The prevalence of the UM CYP2D6 genetic polymorphism has been estimated at only 1-2% of patients[1], arguably not significant enough to contraindicate all consumers from codeine as an analgesic	Patients to undergo genetic assessment to ascertain CYP2D6 polymorphism status prior to codeine treatment	
20	Codeine is an opioid which must be metabolised by CYP2D6 to its active metabolite, morphine, for its analgesic effect. Different genetic groups show significant variations in metabolism of codeine. Of particular concern are "ultra-rapid" metabolisers, where the accelerated metabolism of codeine to morphine results in an increased risk of morphine toxicity and adverse events.	c	The prevalence of the UM CYP2D6 genetic polymorphism has been estimated at only 1-2% of patients[1], arguably not significant enough to contraindicate all consumers from codeine as an analgesic	Patients to undergo genetic assessment to ascertain CYP2D6 polymorphism status prior to codeine treatment	
21	The function of the enzyme carrying out that transformation is genetically controlled and highly variable between individuals because of the existence of multiple forms of the relevant gene; the difference in exposure to morphine following a standard dose of codeine can be up to 45-fold higher in ultra-rapid metabolisers compared with poor metabolisers.	c	This study being referred to compared the difference in exposure to morphine of ultra-rapid metabolisers to poor metabolisers, which naturally would have produced a significant result. However, as the issue of poor metabolisers does not present a necessary harm to consumers of codeine, for this results discussion to be valid the UM results need to be compared to extensive metabolisers which represent 77-92% of patients[1].	Patients to undergo genetic assessment to ascertain CYP2D6 polymorphism status prior to codeine treatment	
22	Ultra-rapid metabolisers are therefore at risk of morphine overdose, with potentially fatal consequences, following "usual" doses of codeine.	c	"Usual" doses of codeine must be defined. Many studies claiming this have been based on single doses of 30mg, which is a dose only achievable in one of the many CCA products available under Schedule 2 and 3 registration	Patients must be encouraged to use the lowest effective doses of OTC CCAs for the shortest time period possible.	
23	Individuals rarely know their metaboliser status, and testing is not readily available.	c	Not all individuals may be aware of their metaboliser status or have ready access to testing, but they may have used codeine in the past at similar doses to good effect without incidence of adverse outcomes. These patients could reasonably be allowed low test doses of codeine if codeine was the analgesic drug of choice.	Prescribers need to be educated to know when to implement genetic testing for individuals with no prior experience with codeine where codeine is considered the drug of choice. The public needs to be educated on the variability of adverse effects that can occur depending on their metaboliser polymorphism status.	
24	All other opioids are at least Schedule 4.	f	All other opioids are at least schedule 4 as they are deemed more potent (and so have been considered to have higher potential for harm and abuse) and more likely to have higher toxicity risks than the CCAs included in Schedule 2 and 3.	Maintain current scheduling of opioids	

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Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
25	The approved indication for the S3 codeine products is for the "temporary relief of strong pain and discomfort associated with a number of different medical conditions". It is noted that there is significant use of S3 codeine products for longer term relief of chronic pain and a number of public submissions by consumers have noted that this is how they use it.	b	The term "chronic" needs to be defined in this argument as either continuous dosing or intermittent temporary dosing. Schedule 3 codeine containing analgesics may be recommended for temporary relief of headache, muscle pain, period pain, arthritis, neuralgia, migraine headache, cold & flu , tension headache, back pain, toothache, dental procedures, sore throat, and fever[12]. All these conditions may be recurring complaints, which may justly indicate recurring treatment with CCAs. It is the pharmacist's and prescriber's responsibility to recognise inappropriate frequency of use of CCA's and investigate more long-lasting treatments for conditions where appropriate.	Further education and support (such as a real-time monitoring/recording system) needs to be given to community pharmacists to empower them to recognise treatment failure through inappropriate frequency of purchase. They need to be able to refer patients to their physicians for formal assessment and management of conditions that appear truly chronic and poorly managed by OTC codeine products.	
26	The management of chronic pain would be better achieved by having medical practitioner input with appropriate advice on non-medicine treatments and appropriate medicinal treatment for the chronic pain, rather than self-treating with long term codeine containing analgesics (CCAs).	b	This is already a practice in community pharmacy, where patients are given education by the pharmacist on non-pharmacological methods of relieving chronic conditions (eg. by counselling with the aid of the Self Care cards produced by the Pharmaceutical Society of Australia). Pharmacists also refer patients suspected of treatment failure to see their GPs for assessment. Given that family physicians are not always available to be seen, there is still a need for OTC codeine analgesics to manage patient's pain pending appointments	Pharmacists to be encouraged to counsel on non-pharmacological pain relief and refer for chronic conditions as necessary	
27	The presence of codeine in OTC combination analgesics contributes to severe adverse outcomes associated with over dosage of the paracetamol or ibuprofen component, because the development of dependence on codeine leads to overuse of the combination. Anecdotally some abusers of OTC codeine products are consuming 30 to 70 tablets/capsules per day of the CCAs.	c	The combination of paracetamol or ibuprofen with codeine can effectively meet the needs of patients who comply to the recommended dosage. The side effects of the paracetamol and ibuprofen component are to be expected from abuse at that "anecdotally" reported level. However, it is at the patient's own risk if they choose to knowingly consume more than the dose clearly recommended on the product packaging. It is not even-handed to remove access to an analgesic for a responsible majority because a minority knowingly misuses the product despite packaging warnings	Further education and support (such as a real-time monitoring/recording system) needs to be given to community pharmacists to empower them to recognise and address over-the-counter codeine abuse. Pharmacists and prescribers should be encouraged to investigate over-the-counter codeine analgesic abuse as a potential causes of new cases of kidney and liver impairment or gastric ulceration.	
28	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.	f	All countries have a unique and complex healthcare system which caters in turn to a unique and complex demographic. They may differ in ease of access to general practitioners and have a different range and potency of other OTC analgesic products. It is difficult to make a comparison between Australia and other countries to justify making a decision which could be beneficial for other nations but detrimental to Australia.	Maintain current scheduling of opioids	

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Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
29	Codeine is also a Prescription Medicine in the USA, Hong Kong, Iceland, India, Japan, the Maldives, Romania, Russia, and the United Arab Emirates.	f	All countries have a unique and complex healthcare system which caters in turn to a unique and complex demographic. They may differ in ease of access to general practitioners and have a different range and potency of other OTC analgesic products. It is difficult to make a comparison between Australia and other countries to justify making a decision which could be beneficial for other nations but detrimental to Australia.	Maintain current scheduling of opioids	
30	There is no evidence that low dose codeine combination analgesics provide any additional analgesia over optimal dosing of paracetamol, aspirin or ibuprofen.	a	There is not "no evidence" that low dose codeine combination analgesics (single doses <60mg of codeine, or 2x 30mg) is more effective than paracetamol alone, there is "limited evidence"[11]. Low dose codeine preparations may be the treatment of choice in patients unable to tolerate aspirin or ibuprofen and therefore has a need as an OTC treatment	Patients should be aided in selecting the most effective and appropriate analgesic for them, which may or may not include a schedule 2 or 3 CCA, taking into account their individual tolerances and medical history	
31	In February 2009 NDPSC decided that:				
32	Based on the currently available information from Australia, the evaluator concluded that there was potential for significant harm from OTC combination analgesics containing codeine (CACC) and even death, and it was not possible to accurately estimate the associated risk, although the following were reasonably assumed:	c			
33	the proportion of all users that abuse OTC CACC is low.	b			
34	the risk of harm among all users of OTC CACC is low.	c			
35	the risk of harm among abusers of OTC CACC is high.	c,e	The risk of harm of abuse of all medicines can be considered high. An indicator of morbidity and/mortality needs to be described to validate this statement	Further education and support (such as a real-time monitoring/recording system) needs to be given to community pharmacists to empower them to recognise and address over-the-counter codeine abuse. Prescribers also require education to recognise and treat over-the-counter codeine addiction as the unique substance abuse problem that it is	
36	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.	a	If there is not yet "sufficient "information available at this time regarding the efficacy of low dose CCAs then the decision of rescheduling should at least be postponed till such data is available	Population studies into the use of low-dose codeine and it's perceived efficacy amongst patients and doctors need to be done prior to decisions about rescheduling. In the meantime, further education and support (such as a real-time monitoring/recording system) needs to be given to community pharmacists to empower them to recognise and address over-the-counter codeine abuse.	
37	The NDPSC rescheduled OTC codeine-containing combination analgesics to Schedule 3 in 2010, with the aim of increasing surveillance of codeine medication usage by pharmacists to ensure quality use of medicines, as it was recognised that there is a potential for harm if used inappropriately. The Schedule 3 entry included limits on the maximum daily dose and pack size, and restrictions on the quantities of codeine in divided (and undivided) preparations.	d	See below	See below	
38	Rescheduling to Schedule 3 has not achieved the required reduction in harm to affected individuals. Since the rescheduling of codeine from 2010 there hasn't been the reduction in risk that might have occurred.	f	It has not been stated how the "reduction in risk" has been measured to validate this comment.	A real-time monitoring/recording system such as Project Stop needs to be given to community pharmacists to empower them to recognise and address over-the-counter codeine abuse, as well as a means to record usage statistics to track perceived "reduction in harm".	

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Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
39	Codeine is increasingly a drug of abuse in Australia, and some individuals have developed severe adverse effects from the high doses of paracetamol and ibuprofen that accompany the use of large numbers of tablets in a codeine-dependent person. A pack of CCA available under S3 contains the same total dose of codeine as a pack of codeine available only under S8.	e	The combination of paracetamol or ibuprofen with codeine can effectively meet the needs of patients who comply to the recommended dosage. The side effects of the paracetamol and ibuprofen component are to be expected from abuse at that "anecdotally" reported level. However, it is at the patient's own risk if they choose to knowingly consume more than the dose clearly recommended on the product packaging. It is not even-handed to remove access to an analgesic for a responsible majority because a minority knowingly misuses the product. Reduction in pack sizes can be an effective way to reduce the amount of total codeine available per Schedule 3 pack and potentially reduce risk of paracetamol or ibuprofen overdose	Reduce Schedule 3 pack sizes to contain less than the amount available in schedule 4 and 8 codeine products	
40	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.	e,f	It has not been stated what the criteria or key performance indicators for adequately "addressing" OTC codeine abuse is. Also, substance addiction is a complex problem and it should not fall solely to "the industry" or "pharmacy organisations" to remedy what is one of society's significant social issues	Further education and support (such as a real-time monitoring/recording system) needs to be given to community pharmacists to empower them to recognise and address over-the-counter codeine abuse. The program will need to be trialled with clearly defined performance indicators to assess it's success at reducing codeine dependence. Prescribers also require education to recognise and treat over-the-counter codeine addiction as the unique substance abuse problem that it is. The public to be educated as the real risks of OTC product abuse.	
41	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.	a	The "very little" analgesic effect must be defined to validate this statement. Also, small increases in analgesia additional to paracetamol or ibuprofen alone may be appropriate for the consumer's pain requirements. This may avoid GP appointments where an unnecessarily more potent analgesic with a less tolerable side-effect profile may be prescribed. NSAIDs such as ibuprofen are not appropriate in many patient populations (eg. pregnant women, the elderly, renally impaired, history of GI ulceration[2], etc)	Patients should continue to be aided by a pharmacist in selecting the most effective and appropriate analgesic for them, which may or may not include a schedule 2 or 3 CCA, taking into account their individual tolerances and medical history	
42	CCAs do not meet the criteria required for Schedule 3, particularly that they are not "substantially safe in use but require professional advice or counselling by a pharmacist", and cannot be said to "not require close medical management." Rather, it would be more appropriate for CCAs to be prescribed so that consumers can be warned about the potential risks and adverse effects can be more closely monitored.	c,f	CCA's do meet the criteria for Schedule 3 and as they are considered safe to use in the majority of the population at the recommended low dosage without medical supervision as use is intended as short term. Studies including the recent 2015 MJA study[19] have shown that the incidences of harm reported have been largely from overdoses and intentional abuse. The professional advice for safe use is already available from the pharmacist in it's current scheduling. Boxed warnings specifically referring to the potential risks and adverse effects can easily be implemented to caution consumers	Include boxed warnings in the labels	

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Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
43	Concurrently the Advisory Committee on the Safety of Medicines (ACSOM) has recently considered the risks of codeine use in children, and codeine use in persons who are ultra-rapid metabolisers of codeine. Excerpts from the meeting statement from ACSOM 28 state:	c			
44	ACSOM agreed that the risks of respiratory depression and possible death in the context of ultra-rapid metabolism associated with codeine outweigh the benefits of codeine for all indications in children under the age of 12 years.	c	Regarding the concern of codeine use in children, while there are valid safety concerns detailed by the TGA[1], there is limited potential for harm to persons aged under 12 posed by the availability of current schedule 3 codeine-based products. The majority of these over-the-counter products in Australian pharmacies are strictly adult formulations, with accompanying adult doses of paracetamol, and therefore are not approved by pharmacists for sale to or for a child. In the case where consumers are between 12 and 18 years old and have undergone tonsillectomy or adenoidectomy for sleep apnoea, the advice of a prescriber can be recommended before sale to assess the risks and benefits associated with this higher risk age group.	Schedule 2 and 3 CCA's should not be used in children under 12, especially since the majority of these products are adult formulations and do not get recommended to persons under 12 in any case.	
45	As it is not possible to identify in advance the subgroup of children who are at increased risk of toxicity (e.g. through being an ultra- rapid metaboliser), the committee's advice relates to the risks for all children under the age of 12.	c	The majority of CCAs are adult formulations and therefor not recommended to children under 12 years regardless of their metaboliser status.	Schedule 2 and 3 CCA's should not be used in children under 12, especially since the majority of these products are adult formulations and do not get recommended to persons under 12 in any case.	
46	ACSOM also agreed that the risks associated with codeine outweigh the benefits of codeine for analgesia in children under the age of 18 years who have undergone tonsillectomy or adenoidectomy for sleep apnoea, for the same reasons as for children under the age of 12 years, as above. This is consistent with the United States Food and Drug Administration (US FDA) position that codeine use after adenotonsillectomy is contraindicated. The committee also noted that there have been a number of adverse event cases observed that are not clearly explained but may relate to sleep apnoea.	c	In the situation where consumers are between 12 and 18 years old and have undergone tonsillectomy or adenoidectomy for sleep apnoea, the advice of a prescriber can be recommended before sale to assess the risks and benefits associated with this higher risk age group.	In the situation where consumers are between 12 and 18 years old and have undergone tonsillectomy or adenoidectomy for sleep apnoea, the advice of a prescriber can be recommended before sale to assess the risks and benefits associated with this higher risk age group.	
47	ACSOM also agreed that the risks to breastfed infants associated with ultra-rapid metabolism of codeine by their mothers outweigh the benefits of codeine for any indication by breastfeeding mothers.	a,c	Like many analgesics, codeine is excreted into breast milk. The degree of excretion is related to maternal metabolism, with the resulting relative infant dose estimated at only 8.1%[13]. The prevalence of the UM CYP2D6 genetic polymorphism itself has been estimated at only 1-2% of patients[1]. These statistics are arguably not significant enough to contraindicate all breastfeeding women from codeine as an analgesic. Even so, genetic testing for this polymorphism is achievable, and it could be recommended that patients specifically indicated for treatment with codeine undergo genetic screening. This may be required in the many cases where codeine is the preferred analgesic. While alternative pain control medicines are preferred in the breastfeeding setting, codeine may still be the treatment of choice in some individuals[13] who have allergies, intolerances or contraindicating medical conditions which may preclude the use of agents including NSAIDs.	Consider alternatives to analgesics in the breastfeeding setting, although if codeine is the medicine of choice, use the lowest effective dose for the lowest time possible[13]. Monitor the baby for excessive drowsiness, irritability or poor feeding. Recommend genetic testing during gestation for women in whom codeine is the preferred agent so that a decision can be made as to the safety of codeine in breastfeeding	

Appendix C - Claims and evidence table

Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
48	As a mother's knowledge of her own experience with codeine (and indirectly, metaboliser status) does not predict the infant's response, breastfeeding should be a contraindication for codeine.	c	Like many analgesics, codeine is excreted into breast milk. The degree of excretion is related to maternal metabolism, with the resulting relative infant dose estimated at only 8.1%[13]. The prevalence of the UM CYP2D6 genetic polymorphism itself has been estimated at only 1-2% of patients[1]. These statistics are arguably not significant enough to contraindicate all breastfeeding women from codeine as an analgesic. Even so, genetic testing for this polymorphism is achievable, and it could be recommended that patients specifically indicated for treatment with codeine undergo genetic screening. This may be required in the many cases where codeine is the preferred analgesic. While alternative pain control medicines are preferred in the breastfeeding setting, codeine may still be the treatment of choice in some individuals[13] who have allergies, intolerances or contraindicating medical conditions which may preclude the use of agents including NSAIDs.	Consider alternatives to analgesics in the breastfeeding setting, although if codeine is the medicine of choice, use the lowest effective dose for the lowest time possible[13]. Monitor the baby for excessive drowsiness, irritability or poor feeding.	
49	ACSOM noted the following contraindications which were recommended in the TGA's safety review to be included in the codeine Product Information - use in children under the age of 12 for any reason; use in people of any age known to be ultra-rapid metabolisers; use in children younger than 18 years of age who have undergone adenotonsillectomy for obstructive sleep apnoea; and use by breastfeeding mothers.	c	In the situation where consumers are between 12 and 18 years old and have undergone tonsillectomy or adenoidectomy for sleep apnoea, the advice of a prescriber can be recommended before sale to assess the risks and benefits associated with this higher risk age group.	In the situation where consumers are between 12 and 18 years old and have undergone tonsillectomy or adenoidectomy for sleep apnoea, the advice of a prescriber can be recommended before sale to assess the risks and benefits associated with this higher risk age group.	
50	The committee noted that the OTC availability of codeine-containing medicines supported a general perception in the community that codeine is safe. Therefore, communication of the contraindications by label changes alone was not likely to achieve the desired outcome of risk reduction. Additional measures including education and the possible rescheduling of codeine-containing medicines also needed to be considered. The committee supported consistency and harmonisation in labelling across all codeine-containing medicines, especially regarding advice to breastfeeding mothers.	c,f	The community needs to be educated that the use of all medicines are never without risk. Label changes and education which includes information regarding breastfeeding safety should be considered	The community needs to be educated that the use of all medicines are never without risk. Label changes and education which includes information regarding breastfeeding safety should be considered	

Appendix C - Claims and evidence table

Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
51	Activities to reduce the use of codeine cannot occur in isolation from consideration of alternative pain management strategies. Pain management strategies that do not include codeine needed to be carefully defined and their implementation carefully considered. For example, direct administration of morphine could be considered as an alternative and the issues of analgesic polypharmacy and escalation up the 'pain ladder' also require consideration in the development of any pain management strategies that omit codeine.	f,	This is already a practice in community pharmacy, where patients are given education by the pharmacist on alternative pain strategies of relieving chronic conditions without the use of medicines (eg. by counselling with the aid of the Self Care cards produced by the Pharmaceutical Society of Australia). Pharmacists also refer patients suspected of treatment failure to see their GPs for assessment. Given that family physicians are not always available to be seen, there is still a need for OTC codeine analgesics to manage patient's pain pending appointments. "Direct administration of morphine" is however neither a practical or necessarily safer alternative to OTC codeine use. The World Health Organisation's Analgesic Ladder recommends codeine as having a valid role in modern pain management as a Step 2 drug, and goes on to suggest that the combination of codeine and paracetamol may be in fact more effective and better tolerated in many patients than the schedule 4 item tramadol[14,15]. Furthermore, it has not been conclusively established that codeine can induce the "escalation up the pain-ladder" by way of the phenomenon hyperalgesia in human studies[16]. Lastly, patient tolerance of analgesics is an important but occasionally a forgotten factor in analgesic choice. While stronger opioids	Pharmacists should be encouraged to continue to counsel on non-pharmacological strategies for pain relief. They should also be empowered to recognise treatment failure and refer to physicians to prescribe more effective therapy.	
52	It should be noted that the following factors for a Schedule 3 medicine in the Scheduling Policy Framework (SPF) are not met:	?			
53	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."	f	The distinguishably low dose and low quantity available over-the-counter is not expected to produce dependency. The average daily intake of codeine-containing tablets amongst Australian over-the-counter codeine-abusers is 50 tablets, and the daily quantity of codeine intake is 640mg[10]. This quantity of consumption is not achievable with the purchase of a single unit of the highest dose and highest pack-size (Panadeine Extra, Paracetamol 500mg/ Codeine Phosphate 15mg, Qty 40) of codeine-based over-the-counter products. Also, the addiction risk associated with the purchasing of all codeine products is in fact minimised already by not just the supervision, but the mandatory direct involvement of the pharmacist in the sale as per current scheduling requirements and basic pharmacist education.	It must be enforced in pharmacist that only one pack at a time is to be sold to consumers. In addition, further education and support (such as a real-time monitoring/recording system) needs to be given to community pharmacists to empower them to recognise and address over-the-counter codeine abuse.	
54	Codeine containing analgesics should now be included in Schedule 4 because codeine meets the factors in the Scheduling Policy Framework required for Schedule 4, and particularly the following factors:	f			

Appendix C - Claims and evidence table

Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
55	In particular, use at established therapeutic dosage levels may produce dependency (criterion 3).	e	The distinguishably low dose and low quantity available over-the-counter is not expected to produce dependency. The average daily intake of codeine-containing tablets amongst Australian over-the-counter codeine-abusers is 50 tablets, and the daily quantity of codeine intake is 640mg[10]. This quantity of consumption is not achievable with the purchase of a single unit of the highest dose and highest pack-size (Panadeine Extra, Paracetamol 500mg/ Codeine Phosphate 15mg, Qty 40) of codeine-based over-the-counter products. Also, the addiction risk associated with the purchasing of all codeine products is in fact minimised already by not just the supervision, but the mandatory direct involvement of the pharmacist in the sale as per current scheduling requirements and basic pharmacist education.	It must be enforced in pharmacist that only one pack at a time is to be sold to consumers. In addition, further education and support (such as a real-time monitoring/recording system) needs to be given to community pharmacists to empower them to recognise and address over-the-counter codeine abuse.	
56	Codeine also meets SPF Schedule 4 criterion 1 (diagnosis, management or monitoring of chronic pain conditions requires medical or dental intervention before use and, although OTC codeine products are intended for short-term use, many consumers use them for chronic pain without medical intervention) and criterion 7 (its use has contributed to, or is likely to contribute to, communal harm).	b	While codeine has been used in practice long-term in some special cases, it is not considered first-line treatment for the chronic pain referenced in Criterion 1. It is recommended for limited duration courses of short-lived, mild-to-moderate incidental pain[3,17] and this type of use is the proviso on which pharmacists approve codeine-product sales. This is not a recommendation which has been significantly revised recently, and therefore is not supporting of any need for corresponding changes to the schedule. Regarding criterion 7, it is not even-handed to single out codeine as a specifically "harmful" substance, as it is likely that over the history of community pharmacy practice many over-the-counter products have contributed to, through misuse, abuse or misadventure, some type of communal harm. Abuse of over-the-counter products is not limited to codeine, but has been reported to also include dextromethorphan, sedating antihistamines, nasal decongestants and laxatives[18].	Maintain current scheduling of opioids. Pharmacists to refer patients with chronic pain managed unsupervised with CCAs to their GP	
57	Other issues:				
58	Codeine alone is ineffective as an analgesic in doses <60mg (number needed to treat (NNT) to achieve one patient obtaining a 50% pain relief response is 12).	a	The low efficacy results in the study do not mean that low-dose codeine is an obsolete therapy in all patients, as metabolism and efficacy across the population is varied and could provide certain patients with effective pain relief depending on their metaboliser polymorphism and side-effect tolerability. Low-dose codeine may still meet the analgesic requirements of some patients while avoiding GP appointments where an unnecessarily more potent analgesic with a less tolerable side-effect profile may be prescribed.	Patients should continue to be aided by a pharmacist in selecting the most effective and appropriate analgesic for them, which may or may not include a low-dose codeine-containing analgesic, taking into account their individual tolerances and medical history	

Appendix C - Claims and evidence table

Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
59	Compound analgesics containing codeine plus paracetamol or codeine plus ibuprofen, show minimal analgesic benefit compared to the simple analgesics (paracetamol or ibuprofen) alone.	a	The "minimal analgesic benefit" needs to be defined in order to validate this statement. Furthermore, "minimal analgesic benefit" does not mean "no analgesic benefit", and therefore does not mean that low-dose codeine is an obsolete therapy in all patients. Metabolism and efficacy across the population is varied[1] and could provide certain patients with effective pain relief depending on their metaboliser polymorphism and side-effect tolerability. Low-dose codeine may still meet the analgesic requirements of some patients while avoiding GP appointments where an unnecessarily more potent analgesic with a less tolerable side-effect profile may be prescribed.	Patients should continue to be aided by a pharmacist in selecting the most effective and appropriate analgesic for them, which may or may not include a low-dose codeine-containing analgesic, taking into account their individual tolerances and medical history	
60	In up to 10% of the population (poor metabolisers), it is ineffective but can still cause harmful effects.	c	In this patient population, other analgesics should be recommended following treatment failure. Lack of efficacy in this minority should not justify the removal of low-dose CCAs from the effective use of the majority.	Patients should continue to be aided by a pharmacist in selecting the most effective and appropriate analgesic for them, which may or may not include a low-dose codeine-containing analgesic, taking into account their individual tolerances and medical history. Genetic assessment as to metaboliser polymorphism status should be undertaken in circumstances where	
61	In up to 4-10% of the population (ultra-rapid metabolisers), it can cause life threatening toxicity.	c	In this patient population, other analgesics should be recommended following treatment failure. Lack of efficacy in this minority should not justify the removal of low-dose CCAs from the effective use of the majority.	Patients should continue to be aided by a pharmacist in selecting the most effective and appropriate analgesic for them, which may or may not include a low-dose codeine-containing analgesic, taking into account their individual tolerances and medical history. Genetic assessment as to metaboliser polymorphism status should be undertaken in circumstances wherever possible when codeine is the analgesic of choice	
62	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.	c	The prevalence of the UM CYP2D6 genetic polymorphism itself has been estimated at only 1-2% of patients[1]. These statistics are arguably not significant enough to contraindicate all consumers from codeine as an analgesic. Even so, genetic testing for this polymorphism is achievable, and it could be recommended that patients specifically indicated for treatment with codeine undergo genetic screening. This may be required in the many cases where codeine is the preferred analgesic. While alternative pain control medicines are preferred in the breastfeeding setting, codeine may still be the treatment of choice in some individuals[13] who have allergies, intolerances or contraindicating medical conditions which may preclude the use of agents including NSAIDs. If the patient has used codeine previously in the same or similar doses to good effect without experiencing side effects it is not unreasonable for that patient to continue to use codeine containing analgesics without prior genetic testing	Patients should be aided in selecting the most effective and appropriate analgesic for them by their pharmacist, which may or may not include a schedule 2 or 3 CCA, taking into account their individual tolerances and medical history. Genetic screening should be recommended prior to using CCAs for the first time wherever possible	

Appendix C - Claims and evidence table

Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
63	It was suggested that there were options to try and minimise the abuse related to CCAs by either expanding Project Stop or real-time monitoring of CCA use.	e,f	A real-time monitoring/recording system similar to Project Stop is currently under development by the Pharmacy Guild of Australia. It allows pharmacists to recognise and address over-the-counter codeine abuse. It also provides data for the purchasing trends of CCAs that can be analysed to measure the effectiveness of the program as an intervention	The prototype monitoring/recording system should be implemented as soon as possible, and the data collected from it's use should be analysed to measure the effectiveness of the program as an intervention	
64	Project Stop relates to the monitoring of sales of pseudoephedrine and is a police related activity to prevent diversion of pseudoephedrine as a precursor for illegal methamphetamine manufacture.	e,f	Project Stop also empowered pharmacists to be able to recognise patterns of abuse, document sales and alert other pharmacies of their suspicions by recording rejected product requests. It was not just a police-related activity but a tool which guided pharmacist professional discretion	The prototype monitoring/recording system should be implemented as soon as possible, and the data collected from it's use should be analysed to measure the effectiveness of the program as an intervention	
65	The Project Stop website states its role as:	e,f			
66	Project STOP is an initiative of the Pharmacy Guild of Australia to address the problem of precursor diversion through Australian Community Pharmacies. The most common precursor sourced through the community pharmacy channel is Pseudoephedrine which can be used in the illegal manufacture of methamphetamines.	e,f	As discussed above	As discussed above	
67	Project STOP is an online tool which provides decision support to pharmacists who need to establish whether requests for products containing Pseudoephedrine are legitimate. It also assists pharmacists in meeting their state regulatory recording requirements where they exist.	e,f	As discussed above	As discussed above	
68	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.	e,f	CCA's are able to be recorded in the Project Stop program, however the function has not been formally recommended for that use. A prototype program has been developed as an initiative by the Pharmacy Guild of Australia.	The prototype monitoring/recording system should be implemented as soon as possible, and the data collected from it's use should be analysed to measure the effectiveness of the program as an intervention	
69	Real-time monitoring of medicines is not currently in place in any jurisdiction other than Tasmania where it is restricted to S8 medicines. There is no formal implementation of real-time monitoring across Australia and whether its implementation would it is unsure whether it would ever come down to S3 medicines.	e,f	Real-time monitoring is currently being utilised through Project Stop for S3 medications, although it is not considered mandatory procedure in all pharmacies	Real-time monitoring of CCA's should be made mandatory Australia-wide	
70	In both Project Stop and real-time monitoring the onus on prevention of supplying CCAs would fall on pharmacists when dealing directly with consumers.	e,f	The onus for preventing supply where appropriate for ALL scheduled medications falls on the pharmacist. This is an existing arrangement for which the pharmacy profession is responsible specifically for. Real-time monitoring systems do not alter this arrangement, but rather facilitates more informed decisions for pharmacists as to whether they should allow sale	The prototype monitoring/recording system should be implemented as soon as possible, and the data collected from it's use should be analysed to measure the effectiveness of the program as an intervention	
71	Another option considered was decreasing the pack size of CCAs from the current limit of five days with a recommended daily dose not exceeding 100 mg of codeine to a pack size limit of three days' supply as has occurred in the United Kingdom. However decreasing the available pack sizes of OTC codeine products might help reduce the incidence of new users becoming dependent on codeine, but is unlikely to be effective for those who are already dependent.	d	Reducing pack size could be a viable option to reduce the number of new users while reducing the progression of addiction in existing users. Harm reduction by reducing commercial pack size has been demonstrated in a 2013 study which described the result of the UK September 1998 pack-size reductions for paracetamol products[9]. This change in regulation resulted in an estimated 43% reduction in paracetamol-related deaths over the 11.25 year study period[9].	Reduce Schedule 3 pack sizes to contain less than the amount available in schedule 4 and 8 codeine products	

Appendix C - Claims and evidence table

Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
72	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, 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.	f	The main alternative to codeine products are NSAIDs, which are not suitable for use in many patient populations (eg. renally impaired, pregnancy)[3]. Some physicians are reluctant to supply prescriptions for "just in case" purposes as it discourages patients from seeking help. Also, prescriptions for schedule 4 medicines have a 12 month expiry date while schedule 8 medicines have a 6 month expiry date. Prescribers may also prescribe items more potent than the needs of the patient. At the time of prescribing, the severity of the patient's pain in an anticipated future episode which may or may not occur is impossible to predict. Lastly, this practice encourages the hoarding of analgesic prescriptions, which increases the presence of analgesic prescriptions in the community. This then may make it more difficult for the dispensing pharmacist to determine if a prescription has been diverted for illegal use	Maintain current scheduling of opioids	
73	To be consistent with the interim decision to remove the S3 entry for codeine and for the issues around codeine in the 12 and under population as recommended by ACSOM the S2 entry should also be deleted.	f	In a 2011 study on Australian CCA abusers, the average strength of the formulation of choice for abuse based on daily intake was around 12mg[10]. This indicated that the preferred formulations sought for abuse purposes are of the higher strengths available over the counter. The codeine available in combination cold and flu products (eg. Codral Cold & Flu New Formulation, Demazin PE Cold & Flu) ranges from 9-9.6mg of codeine per tablet (18-19.2mg per recommended single dose). Furthermore, most observational studies in OTC codeine abuse appear to involve combinations with paracetamol or ibuprofen rather than Cold & Flu formulations. Therefore, there is not enough supporting evidence to justify the upscheduling of schedule 2 CCAs to schedule 3 simply based on a need to be "consistent".	Maintain current scheduling of opioids	
74	There are alternative OTC analgesic products for short-term pain relief.	f	Other alternative analgesic products available include:	Patients should be aided in selecting the most effective and appropriate analgesic for them by their pharmacist, which may or may not include a schedule 2 or 3 CCA, taking into account their individual tolerances and medical history. Genetic screening should be recommended prior to using CCAs for the first time wherever possible	
			oral NSAIDS (not suitable for patients with renal impairment, pregnancy, allergy, gastric ulceration, heart failure, unmanaged hypertensive conditions, poorly controlled asthma)		

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Argument number	Delegates interim decision arguments	Section 52E matter category	[redacted] response	[redacted] recommendation	
			paracetamol as a single agent (not always potent enough to meet the analgesic needs of the patient		
			Topical products such as NSAID gels (not appropriate for application on broken or sensitive skin, penetration not sufficient for pain relief of all conditions, only suitable for musculoskeletal complaints, some (low) risk of adverse effects from systemic absorption)		
References	1."Codeine use in children and ultra-rapid metabolisers – Pharmacovigilance and Special Access Branch Safety Review"; The Therapeutic Goods Administration; 2015.				
	2. "Dextromethophan", "Pholcodine", "Ibuprofen"; AMH Online; Australian Medicines Handbook; 2015.				
	3. "Codeine"; eTG Complete; Melbourne: Therapeutic Guidelines Limited; 2015 March				
	4. O'Connor, N R; "FDA Boxed Warnings: How to prescribe drugs safely"; Am Fam Physician; 2010; 81(3):298-303; (http://www.aafp.org/afp/2010/0201/p298.html)				
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	6. Kircheiner, J et al; "Pharmacokinetics of codeine and it's metabolite morphine in ultra-rapid metabolisers due to CYP2D6 duplication"; Pharmacogenomics J; 2007; 7(4):257-65;				
	7. Codral Cold & Flu; Codral, Johnson & Johnson Pacific Pty Limited; March 2015; (http://www.codral.com.au/cold-and-flu-products/tablets/codral-cold-flu)				
	8. Demazin PE Cold & Flu Relief Tablets; Demazin, Bayer; 2015; (http://www.demazin.com.au/en/product-detail/demazin-pe-cold-flu-relief-tablets/				
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	10. McAvoy, B et al; "Over-the-counter codeine analgesic misuse and harm: characteristics of cases in Australia and New Zealand"; *New Zealand Medical Journal* ; 2011, 124:29-33.				
	11. Murnion, B; "Combination analgesics in adults"; *Aust Prescr* , 2010(33):113-5; (http://www.australianprescriber.com/magazine/33/4/113/5)				
	12. "Panadeine"; Consumer Medicines Information; GlaxoSmithKline; (http://www.medicines.org.au/files/gwcpanad.pdf)				
	13. "Ibuprofen"; "Codeine"; *Pregnancy and Breastfeeding Medicines Guide* ; The Royal Women's Hospital; 2014.				
	14. Iedema, Joel; "Cautions with codeine"; Australian Prescriber; 2011; (http://www.australianprescriber.com/magazine/34/5/133/5)				
	15. World Health Organisation; "WHO Analgesic Ladder: which weak opioid to use at step 2?"; Best Practice Journal; 2008; 18:20-23; (http://www.bpac.org.nz/BPJ/2008/December/docs/bpj18_who_ladder_pages_20-23.pdf)				
	16. Johnson, J et al; "Codeine-induced hyperalgesia and allodynia: investigating the role of glian activation"; Transyl Psychiatry; 2014; 4(11)e482 (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4259992/)				
	17. Spooner, C et al; "Social determinants of drug use"; National Drug and Alcohol Research Centre, University of New South Wales; 2004; (http://www.racgp.org.au/your-practice/guidelines/silverbook/common-clinical-conditions/pain-management/				
	18. Cooper, R J; "Over-the-counter medicine abuse – a review of the literature"; J Subst Use; 2013; 18(2):82-107; (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3603170/				
	19. Roxburgh, A et al; "Trends and characteristics of accidental and intentional codeine overdose deaths in Australia"; Med J Aust; 2015; 203(7):299; (https://www.mja.com.au/journal/2015/203/7/trends-and-characteristics-accidental-and-intentional-codeine-overdose-deaths)				

Appendix D

[redacted]

To Whom It May Concern:

I am a community pharmacist that is deeply concerned about the interim decision to re-schedule codeine-containing analgesics to S4 (Prescription Only Medicine).

This decision will mean that my customers who use these products safely and effectively will find pain relief medications more expensive and more difficult to obtain.

For example we have many migraine sufferers who walk in to the pharmacy requesting codeine-based products to relieve an acute attack. We determine a therapeutic need and give appropriate counseling via a pharmacist. Under proposed changes these customers whilst experiencing a migraine would have to find a doctor at short notice to obtain a prescription. Not only would this cause stress and delay for the patient, it would also place further stress on our health system.

Our number one priority is the health and well being of our customers. Maintaining the Schedule 3 classification with implementation of real time monitoring service that is a clinical decision support tool will help address codeine misuse issues, whilst not penalising those using the products responsibly and who urgently need medication to manage their pain.

My customers want medications to be affordable and they want to be able to get them when they need them to manage their own lives.

Yours Sincerely,

[redacted]

[redacted]

TO WHOM IT MAY CONCERN

I am a community pharmacy owner, with partnership in three stores on the [redacted] The store I practice most in is in a semi-rural town on the outskirts of [redacted]. We trade extended hours, 7 days a week, 364 days a year. We are quite busy after hours and on the weekend due a lack of available GPs in our area. I have been asked by Symbion to make comment in support of reconsidering the schedule change of OTC codeine containing products from S3 to S4.

I take pride in my work as a pharmacist, and I can honestly say through thorough history taking techniques and substantial clinical knowledge, make accurate judgement when products containing codeine are appropriate, and when they are not. If these products are moved to S4 this will deprive the majority of patients requiring combination codeine products, who use the product appropriately, from a safe, and effective medication when they need it most.

At night, and on the weekends and public holidays, I see many patients with illness that simply can't get in to a GP, and that require treatment that can be adequately treated with these products. If the pharmacist can not supply a treatment that can treat these acute pains, such as tooth ache, injury, and back pain, then the patient has no option but to present to a hospital emergency department. This added cost to the healthcare system would be massive.

If I did not feel completely confident and comfortable in being able to supply these products I would not write this letter. I can honestly say that the pharmacist is the best trained and most readily accessible health care team member to supply and counsel these products.

Surely there are other measures that can be adopted first, such as reduced pack size, and expanded warnings and patient education? I would be strongly in favour of this before any change to scheduling, and further risk analysis could occur for a more informed and appropriate recommendation.

I'd like to also point out these changes will affect some Cold and Flu preparations that have a very small dose of codeine for suppression of cough. This will lead to another range of effective products for minor aliments being unavailable for patient when they need them in the acute setting.

It is my understanding the Pharmacy Guild of Australia currently has under development a nationwide real time monitoring system that will even solve the problem for that small minority that do misuse and occasionally successfully obtain codeine untruthfully from the pharmacist.

I urge to please reconsider this decision.

[redacted]

To whom it may concern

I write to express my concern regarding the recent TGA decision to up-schedule to S4 medications containing codeine.

My experience in my community pharmacy in [redacted] Western Australia is that many customers rely on these products to manage various pain situations, dry cough and the symptoms of influenza and the common cold.

I understand the concerns that some in the community misuse codeine and that this issue must be addressed. However, the decision to restrict codeine to S4 will restrict access for consumers who have a genuine need and safely manage the medications and get relief from symptoms. With symptom relief they are able to continue their daily lives without debilitating pain, cough or cold symptoms. To deny these consumers the access to these medications because of the misuse of a small section of the community is contrary to their right to look after their health.

I am aware of the health issues of misuse particularly in products combined with paracetamol and ibuprofen, and the associated health costs. I am also aware that many of this group have addictive personalities and will misuse even if these products are re-scheduled to prescription only.

At [redacted] we follow the the protocols of the PSA and QCCP to make decisions on the appropriateness of a customers request for a codeine based product. As our workflow includes a pharmacist in the front of store we engage the customer in a conversation around their request. However a real time data base of purchase history that was available to us to check for pharmacy shopping would support our decisions, and highlight consumers who are abusing the medications.

This scheduling change would increase dramatically the cost to the consumer of access to these products they genuinely need and are experienced in self medicating to relieve appropriate symptoms. The purchase price as a prescription would be higher, in addition to the cost of the GP visit. As well the difficulty in getting an appointment to a GP is something we hear regularly.

The need to have an appointment with a GP will put further pressure on the health budget which we a often reminded is already exceeding the governments ability to fund.

From a health perspective I can see a movement for pain sufferers to increase the use of over the counter NSAIDS to manage minor pain. This could lead to other health issues in the community.

It is imperative that we implement a data base monitoring of purchase habits to restrict abusers accessing excessive quantities of these codeine contain medications.

Finally, we should enable the majority of the population to continue looking after there own health and wellbeing.

Yours sincerely

[redacted]

[redacted]

9th October 2015

To whom it may concern,

My name is [redacted] and I am the Proprietor of [redacted] I have worked in pharmacies on the border of New South Wales and Victoria for more than [redacted] years. I would like to discuss the interim decision to reschedule codeine products to prescription only. I am very aware of the benefits to my patients that codeine provides both in the access through me and the relief from pain. I am a professional pharmacist and take the time with all my patients to discuss the use of codeine for their pain, utilising non-analgesic methods to complement their treatment. I feel this interim decision suggests I do not do my job properly, I also feel it take the individuals rights away to manage their own medications. In rural and remote regions it will also impact patients who have difficulty accessing doctors and put further pressure on hospitals when patients are unable to relieve their pain.

I ask that this decision be delayed to allow time to create a real time monitoring system to cover the few transient patients that who aren't cared for by the same pharmacy.

Yours Sincerely

[redacted]

[redacted]

12th October 2015

TO WHOM IT MAY CONCERN

I am writing in response to moving OTC codeine medicines to prescription only.

As a community pharmacist, dealing with and screening many day to day problems, I believe moving codeine containing medicines to Prescription only is unlikely to address the issues of dependency and abuse.

My belief is it would result in an added unnecessary burden on our local Doctors, who are already work over loaded, and add significant extra costs to both consumers and the health systems.

Our Pharmacy prides itself in having well educated staff to screen patients, counsel and provide excellent information on the use and side effects of codeine based products. We are all trained from reputable educators including PSA (Pharmaceutical Society of Australia) and the Pharmacy Guild, as well as online & in store training.

In our local community there is a good network between GPs, Pharmacists and other health professionals which has been successful in combating any unnecessary use or abuse of codeine based products.

Yours Sincerely

[redacted]

[redacted]

[redacted]

Friday 9th October 2015

To Whom it may concern

We are the owners of a local community pharmacy in [redacted] NSW.
The reason for this letter is to express our dismay in the interim decision to upschedule low dose combination Codeine medication.

We strongly feel that relegating all Codeine products to schedule 4 is destined to disadvantage the vast majority of patients who are effectively and safely managing their pain.

In our pharmacy, we see pain cases (both acute and chronic) on several occasions daily, which we manage with Codeine based products as the available alternatives in some cases simply aren't adequate. These are situations, where intervention from a GP is not necessary and adequate pain relief is sustained by way of low dose Codeine analgesia. Our patients trust us to recommend a medication that will alleviate the pain that they are suffering and as health professionals, we have been trained to choose what would be appropriate.

Removing Codeine from Schedule 3 and from our minor ailment arsenal will make our customers lives more difficult, as well as ours. We are likely to see patients take medication that is not appropriate as it is too hard to get in and see a Dr or inconvenient. We are also concerned that rates of inappropriate use (overdose) of other pain relieving products will increase as patients increase their dose of lower strength alternatives in order to achieve the same level of pain they have previously experienced with products now beyond their reach. Additionally, there are numerous patients for whom OTC anti inflammatories are contraindicated. With the upscheduling of Codeine products, the only analgesic a pharmacist could recommend is Paracetamol which for a vast majority of pain types, simply isn't sufficient.

We think it is also worthwhile noting that in our daily practice, we see patients struggling with addiction to prescription opiates such as Oxycodone. These patients have these issues despite Oxycodone being a schedule 8 medicine and having the highest level of restrictions placed upon it's prescribing. Prescribers are faced with the same issues that Pharmacists are - a lack of adequate tools to assess whether a patient is genuine or doctor shopping.

We are Pharmacists who are highly trained and capable of assessing suitability of low dose Codeine, this is not under question. Why then in this era of technology, are we not exploring a real time monitoring program to highlight Codeine product misuse rather than upscheduling which will only shift the problem to General Practitioners? GP's will be faced with the same issues that happen in pharmacy as we don't have a system in place to indicate addiction and overuse.

[redacted]

All that will be achieved is a lack of access of a vital medication to the vast majority of patients who are legitimate users.

We strongly urge you to reconsider this decision and to look for a solution that will successfully reduce abuse and misadventure. Upscheduling is not the answer.

Kind Regards,

Consumers
Health Forum
of Australia

Submission in response to Interim Decision on Proposed Amendments to the Poisons Standard (Medicines)

October 2015

Introduction

The Consumers Health Forum of Australia (CHF) is the national peak body representing the interests of Australian healthcare consumers. CHF works to achieve safe, quality, timely healthcare for all Australians, supported by accessible health information and systems.

At its meeting in August 2015 the Advisory Committee on Medicines Scheduling (ACMS) considered the proposal to reschedule codeine products that currently are on Schedules 2(S2) and 3(S3). CHF put in a submission opposing the proposed rescheduling.

The ACMS recommended the deletion of the current Schedule 2 and 3 entries for codeine and the amendment of the current Schedules 4 and 8 entries to reflect this change. The delegate's interim decision accepts the recommendation from the ACMS. The proposed implementation date is 1 June 2016.

Since the interim decision became public CHF has been contacted by a large number of consumers raising their concerns about reduced access to codeine based products to manage their conditions. Their concerns included the increased costs of getting a S4 product; difficulty in accessing, particularly out of hours and where there are waiting times to see a GP; and resentment at being labelled substance misusers when they believe that they are responsible users with a track record of successfully self- managing their pain.

We welcome the opportunity to provide comments on the interim decision as we want to ensure that Australian health consumers have access to affordable and appropriate medicines to ensure we have the best health outcomes as well as the best use of health care resources.

Issues

It is important to distinguish between the Schedule 2 codeine products which are used in preparations for coughs and colds and those on Schedule 3.

Schedule 2 Products for coughs and colds

In our initial submission we did not address the proposal to move S 2 products of coughs and colds up to S4 in detail although we did oppose the proposal. We still oppose that move.

We are suggesting consideration be given to move these products from S2 to S3.

These products have low dosages of codeine and the potential for them to do harm is less than with the S3 analgesics but there is still some risk and we think consumers need a higher level of protection. We do not think that any products containing codeine should be freely available for consumers to just pick up off the shelf for the same reasons outlined in the decision relating to the 'up-scheduling of S3 codeine products and because consumers need to be better informed of harms and alternatives.

We support the addition of warning labels on front of pack for such products but believe that is not sufficient information for consumers. By moving these products to S3 we ensure that the consumers need for and suitability for such a product is assessed by a pharmacist. This would give the

pharmacist the opportunity to explain that there are other non-codeine products that are available and also go over the potential problems with using a codeine product.

The use of such products would then be captured in the proposed real time recording system for S3 products being developed by the Pharmacy Guild. This would then provide useful data on people's use of these products which may or may not point to the need for further action in the future.

This change would ensure consumers are making a more informed decision about the products they are using whilst continuing to give them access without the need to go to a GP with all the associated cost of such a visit. We are concerned that consumers and the system would incur significant additional costs if people had to go to a GP and get a script but it is difficult to quantify exactly what those costs would be as we do not know how many would decide not to pursue this choice if it means incurring the time and trouble to go to a GP. For those that decide not to pursue a script due to cost barriers, there are then other potential costs such as increased absenteeism and lost productivity.

Schedule 3 Analgesics containing codeine

CHF acknowledges that there is a significant body of evidence that shows the problems that can arise from the use of OTC codeine analgesics. There is also evidence that the number of people overusing codeine and the numbers presenting with symptoms of toxicity and dependence is growing. We share the Faculty of Pain Medicine's and other clinicians concerns about this growing problem. However we believe they still only account for a minority of people who use codeine.

However this misuse is not restricted to over the counter purchases as we know we that people can and do misuse prescription products. Rescheduling will not address the issue of codeine misuse.

We believe the majority of users, particularly those using it for ongoing or chronic pain, are using responsibly and many would be doing so as part of a pain management plan that they have developed with their doctor.

The decision to move to S4 would have significant cost implications for the consumer, through out of pocket expenses, and the government through additional MBS rebates. That funding could be redirected to the three measures we outline below which we believe would be effective in reducing misuse of codeine.

We are recommending three measures that should be implemented before the final decision is taken on rescheduling to S4.

These are:

- Introduction of pharmacy level real time recording to capture time/date and reason for purchase as it happens.

  This gives pharmacists the opportunity, once they have assessed that codeine based products may be suitable for a consumer, to see what other codeine products have been bought and when to inform their decision on selling the product to the consumer.

  In its advice to the delegate the ACMS cites the fact that OTC sales data is incomplete. The implementation of a national system of real time recording would address that issue and the development of such a system is well advanced.

- Improved pain management resources and a public awareness campaign on the quality use of pain medicines.

  In its advice the ACMS questioned the therapeutic benefits of codeine for pain management and claimed it's the benefits of its use were low. Given that it if often prescribed and/or recommended as an OTC product by health professionals there is clearly a need for better education on both its benefits and risks to clinicians and consumers.

  There is a lack of good, community-based pain management programs to help people living with unrelieved pain and to get consumers to move away from codeine they need to be offered an alternative that works for them.

  The delegate reinforces the view that codeine analgesics are for "temporary relief of strong pain and discomfort" and this needs to be highlighted to both health professionals and consumers when discussing pain relief and pain management, particularly for people with chronic pain.

  There need to be a broad community awareness campaign, probably run by NPS Medicinewise to educate consumers about the potential health issues related to the use of certain OTC medications and what alternatives may be available to them.

- Introduction of mandatory front of pack warnings about codeine's potential for addiction and to ensure pharmacists warn people of this when dispensing codeine products.

Conclusion

CHF does not support the proposed rescheduling of all codeine to Schedule 4 at this point in time. We do not think the delegate has given enough consideration to the significant system wide costs of the rescheduling or the loss of access to a range of medications that do have some benefits to consumers.

We recommend delaying the final decision for another 12 months to allow the implementation of the three measures we have detailed above to be put into place. The real time recording process would allow collection of robust data about the purchasing profile of all OTC codeine products which could help inform the final decision.

Given the costs involved for industry, which are inevitably passed onto consumers, of changing the scheduling it is important that the right decision so there will not be another change in the near future. Both consumers and industry need some certainty and adequate time to respond to changes.

Consumers Health Forum of Australia

The Consumers Health Forum of Australia (CHF) is the national peak body representing the interests of Australian healthcare consumers. CHF works to achieve safe, quality, timely healthcare for all Australians, supported by accessible health information and systems.

CHF does this by:

1. advocating for appropriate and equitable healthcare
2. undertaking consumer-based research and developing a strong consumer knowledge base
3. identifying key issues in safety and quality of health services for consumers
4. raising the health literacy of consumers, health professionals and stakeholders
5. providing a strong national voice for health consumers and supporting consumer participation in health policy and program decision making

CHF values:

- our members' knowledge, experience and involvement
- development of an integrated healthcare system that values the consumer experience
- prevention and early intervention
- collaborative integrated healthcare
- working in partnership

CHF member organisations reach Australian health consumers across a wide range of health interests and health system experiences. CHF policy is developed through consultation with members, ensuring that CHF maintains a broad, representative, health consumer perspective.

CHF is committed to being an active advocate in the ongoing development of Australian health policy and practice.

[redacted]

15 October 2015

The Secretary
Scheduling Secretariat
GPO Box 9848
Canberra ACT 2601
Email: Medicines.Scheduling@tga.gov.au

Cc: Department of Health

Dear Sir/Madam,

Notice inviting public submissions under Reg 42ZCZP of the Therapeutic Goods Regulations 1990 Scheduling proposals in relation to the interim decisions for Codeine rescheduling, October 2015

Codeine

[redacted] recognises the safety concerns relating to the misuse and overuse of Combination Analgesics Containing Codeine (CACC) and the reasons supporting the interim decision to reschedule all current Schedule 3 codeine to Schedule 4.

[redacted] also acknowledges the contrasting positions taken by a number of key stakeholders, including Pharmacy Guild of Australia, Pharmaceutical Society of Australia, Australian Medical Association, Australian Self Medication Industry, Consumer Health Forum, Australian Pain Management Association and Pain Australia.

A shared recommendation amongst these stakeholders is for the implementation of a nationwide **real-time recording and reporting system.** The system would enable pharmacists and prescribers to easily identify patients who are taking excessive quantities of CACCs, and make informed clinical decisions for the appropriate management of these patients.

Recommendation

We would like to propose [redacted] as a potential solution for real-time recording and reporting of CACC.

What is [redacted]

[redacted] was launched in Australia in late 2013 as a revolutionary Medication Management Platform designed to help patients take their medications safely, effectively and on time. [redacted] is available as an App or can be accessed online through a web browser.

[redacted] is currently available in over 1300 pharmacies across Australia and is fully integrated with all dispense systems via the GuildCare platform. This connectivity enables [redacted] to capture real time dispense information.

With almost 100,000 registered patients, [redacted] is the number one Medication App in Australia.

[redacted]r as a real time recording and reporting system

[redacted] is able to capture real time dispense data for individual patients at [redacted] enabled pharmacies, and provide visibility of this information to all other [redacted] enabled pharmacies.

Over the next 6 months, [redacted] will integrate with prescribing software, thereby closing the loop between prescribers and pharmacists. This will enable prescribers to view real time dispense information, which will facilitate continuity of care and improved patient health outcomes.

Process for recording and reporting of CACC using [redacted]

Patient requests for CACC at the pharmacy

1) Pharmacist must register patient to [redacted] (if not already registered).
2) Pharmacist must review patient history in [redacted]r to determine whether supply is appropriate. [redacted] could flag patients who have been dispensed a CACC within a certain timeframe
3) If supply is appropriate, pharmacist must dispense CACC using dispense software. Information is automatically captured in [redacted].
4) If supply is not appropriate, pharmacist must indicate in [redacted] that supply was refused. Pharmacist can provide comments regarding interaction.

Important considerations

In order for [redacted] to fulfil the requirements of a sustainable real-time recording and reporting system,

- All pharmacies and prescribers must be connected with [redacted]
- All patients supplied with CACC must be registered with [redacted]
- All CACC supplied to patients must be dispensed

[redacted] acknowledges this will require changes to the current legislative framework on a state and federal level.

Other opportunities

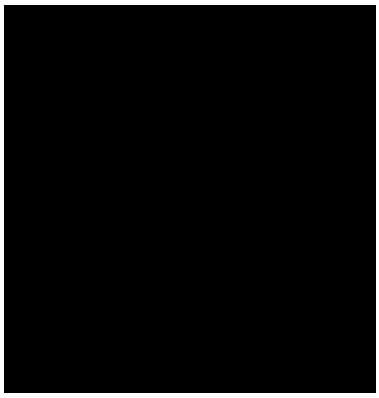
[redacted] can also be used as a real time recording and reporting system for codeine containing cold and flu preparations, pseudoephedrine, benzodiazepines and S8 medication.

[redacted] is a powerful medication management tool for patients. In addition, important safety information and warnings can be sent to target patient groups. For example, codeine addiction warning messages can be sent to patients who have been supplied CACCs.

[redacted] supports the implementation of a real time recording and reporting system for CACC to enable controlled access to these medications by patients from pharmacies.

Yours Sincerely,

[redacted]
[redacted]



15 October 2015

The Secretary
Advisory Committee on Medicines Scheduling
GPO Box 9848
Canberra ACT 2601
Email: Medicines.Scheduling@tga.gov.au

Dear Sir/Madam,

As the Executive Director of one of Australia's leading community pharmacy brands, representing the owners and pharmacists of 300 stores across the country, I am writing to express my concerns regarding the interim decision by the Federal Government Scheduling Delegate to up-schedule codeine.

It is critical to note that codeine is more than just a stand-alone pain relief product. It is also a key ingredient in a wide range of headache, flu and cold relief products.

It is our opinion that this decision, if formalised, will have several unintended consequences in terms of health outcomes for Australians and economic impacts.

The first is that there will be significant cost implications for patients, who will be left paying high fees for non-bulk billed doctor visits and then, on top of that, paying dispensing fees in the pharmacy. There will be no Federal Government subsidy and the price will be below private health insurance thresholds. The treatment of cold and flu symptoms and management of acute pain will be less accessible to a large part of society because the costs will become prohibitive.

Taxpayers in general will also be hit. There will be huge MBS cost increases at a time when the Government is attempting to rein in Medicare costs. Our research suggests that these costs could be as much as $170 million per annum[1].

From a General Practitioner (GP) perspective, there are also significant issues. The small number of people identified in the interim decision documentation who misuse these products are likely to keep going to different doctors and will ask for multiple codeine packs per script under the guise of convenience/not having to return regularly to the doctor. That system offers no monitoring of 'doctor shopping' and, because it is private and outside the PBS, this misuse will not be recorded on the MyHR electronic heath record. In addition, this will likely lengthen waiting times and block access for other in-need patients.

Furthermore, increased costs could cause genuine patients to demand stronger prescription-only medicines than are necessary, compromising the principles of the Quality Use of Medicines program. There are millions of patients who need access to codeine because they are unable to take other forms of pain relief. For example, ibuprofen is not recommended for people suffering from hypertension or asthma – conditions which impact millions of Australians.

Critically, I believe this interim decision threatens the strong nexus of trust that exists between pharmacists and their community. Our pharmacists carry out an essential frontline role in healthcare, providing outstanding professional advice and products to their community. It goes without saying that if pharmacists will no longer be able to deliver effective and affordable headache, flu and cold relief, this trusted relationship will be undermined, along with the ability to help direct people to better health choices.

There are alternative ways of solving the issues being discussed with regard to codeine.

- **Mandate the recording of codeine in the pharmacy dispense system**. This will give a full audit trail to monitor pharmacists and pharmacies and would capture any ill practice. To take this further, pharmacists could be required to submit codeine-based dispense data on a 'batch' basis at the end of each month to monitor misuse.
- **Add S3s to MyHR for better monitoring**. This would enable doctors and pharmacists to monitor medication history. If a patient wanted to opt out of MyHR, they would be unable to receive codeine-based products as S3s.
- **Adopt a 'Project Stop' system** (as per NotifyRx as in 2009). Project Stop has worked effectively in stopping the flow of product from pharmacy, and pharmacists have proven their ability to manage supply and consumption through this process.

I am fully in support of finding a solution to misuse of codeine-based products and I believe practical solutions exist. The interim decision will have severe negative impacts on our patients, on our community pharmacists and on the tax payer.

I would ask you to urgently reconsider this decision.

Yours sincerely,

1. Macquarie University. The value of OTC medicines in Australia. March 2014.

[redacted]
October 15 2015

Re: TGA Interim Decision to make codeine-based products available by prescription only from July 1 next year.

I am writing in respect to your interim decision to make codeine-based products available only by prescription from July 1 next year.

I am neither a pharmacist nor a doctor but I was for [redacted] years a Member of the NSW Legislative Assembly and I can tell you many of my former constituents strongly disagree with your interim decision.

As many pharmacists have observed, changing codeine based drugs from S3 to S4 will make little difference to the rate of over-usage of codeine-based pharmaceuticals. Doctor shopping will take the place of 'pharmacy crawling', to coin a phrase.

What is needed is compulsory real-time web-based recording of all codeine sales, so a consumer's drug purchasing habits can be monitored and, if necessary, curtailed.

Presentation of a Medicare card plus a photographic ID card in the pharmacy would be all that would be required to record the purchase. If all pharmacies were linked by internet – entirely possible in the 21st Century – it would be simple for the pharmacist to determine the amount of codeine-based drugs that had previously been dispensed, and to refuse to sell an additional packet of such drugs to an individual in accordance with Government regulations. This way, the chemist need not fear being abused because he or she refuses to supply a particular item.

This would be a vastly superior method of reducing the consumption of codeine products by the few who abuse them than the patient having to visit a doctor to obtain a prescription.

Ten years ago the pharmacy industry itself set up a system – called Project STOP – that uses a protected database to prevent the use of pseudoephedrine based products to manufacture methamphetamine. I understand that 80 per cent of pharmacies across Australia now participate in the program. If codeine is an even bigger threat to society than methamphetamine – which, frankly, I doubt – the model is certainly there for you to follow in monitoring and regulating its usage.

Country areas will be particularly disadvantaged by the TGA's proposal. Recently my [redacted] took [redacted] for a week to [redacted] in the NSW [redacted]. We arrived on a Sunday and [redacted] developed an atrocious head cold the following day. My cold arrived on the Tuesday.

There were a few Sudafed tablets in a drawer in our house but no cough mixture and the Sudafed proved useless against one of the worst colds either of us had ever experienced. So we visited the local chemist (the only one in the town, I might add) and bought some Codral which at least allowed us some measure of relief, including at night.

The next weekend was the Labour Day long weekend and both the doctor's surgery and the pharmacy were closed from lunchtime Saturday until the following Tuesday. Had your new rules been in place and the cold manifested itself on the Saturday afternoon we should have been unable to obtain any relief for our symptoms for at least three days, unless we visited [redacted], 65km distant.

So your proposed new regulation would greatly discriminate against people living in rural and regional parts of Australia. But even city dwellers would be adversely affected, as you would force them to visit a doctor virtually every time they developed a cold. My GP charges $27 over and above the bulk billing fee, or double the cost of a packet of Codral, and there is no guarantee I would be able to get in to see him at short notice..

An article in the *Sydney Morning Herald* dated October 2 2015 quotes Australian Self Medication Industry chief executive Dean Schoombie as estimating the cost to Medicare of this change at $170 million. This doesn't include the increased number of visits to hospital emergency departments, which will cost the States tens of millions of dollars – all at a time when Government budgets are stretched to breaking point.

I haven't mentioned Panadeine and Nurofen Plus in this submission, but exactly the same case could be made for them as for Codral. Requiring pharmacists to record purchases of all codeine-containing drugs on a centralised database would be by far the fairest and most cost-effective means of dealing with a problem that affects only a fraction of a percentage of the users of these products.

[redacted]

As members of the NSW Poisons Advisory Committee we would like to make some arguments against the interim decision to up-schedule codeine combination products.

As a group, we believe that patient safety is paramount and we acknowledge that codeine is misused by some members of the community, although the extent of this abuse lacks quantification.

We believe the vast majority of consumers who take OTC codeine containing analgesics take these products for the treatment of acute pain, use them for short term use, and are at no risk of becoming dependent on codeine. Hence, we believe any decision to make the current OTC codeine containing analgesics only available on prescription will significantly disadvantage the vast majority of consumers who use these products appropriately and legitimately.

If the Committee believes that there is a problem with a small number of consumers misusing OTC codeine containing analgesics, we do not see that the up-scheduling of these products is the solution to any misuse. In fact, we believe it could compound the problem, and potentially create new problems. Our arguments outlining our concerns are listed below.

1. Codeine combination products are used by the vast majority of consumers legitimately for the treatment of acute pain. By up-scheduling such products consumers, if they wish to use these products, will be forced to visit general practitioners to obtain a prescription. This will add a cost burden to Medicare, and if the GP does not bulk bill significant out of pocket costs to consumers. Furthermore, it is unlikely that most consumers will be able to obtain a timely appointment with the GP to obtain access to such products, forcing them to endure unnecessary acute pain. Alternately, these patients may present at public hospitals for treatment, increasing the burden and cost to the public health system.

2. In the delegates' interim decision it is stated that a recently released combination of two non-opioid analgesics (ibuprofen plus paracetamol) would fill any gap left by the unavailability of codeine containing analgesics over the counter. We believe this statement to be inappropriate, incorrect and ill-considered.

   There are many consumers who should not take NSAIDS such as ibuprofen. These include patients with high blood pressure, heart failure and renal impairment. In addition, patients taking anticoagulants, for example those with atrial fibrillation, and those taking low dose aspirin for cardiovascular protection should not take ibuprofen. NSAIDS such as ibuprofen can also

precipitate asthmatic symptoms and acute asthmatic attacks in around 5-10% of patients with asthma.

Ibuprofen can also have significant drug interactions. Examples include angiotensin converting enzyme inhibitors, angiotensin 2 receptor blocking agents and diuretics. These medications are used by many patients and to suggest that these patients can use ibuprofen instead of codeine is not just incorrect, it could lead to serious misadventure.

3. A further concern is that when consumers find out that they can no longer get codeine containing products OTC, they will turn to other OTC analgesics rather than go to the GP. This could lead to the inappropriate use of NSAIDS as described above, and the use of higher doses of single ingredient preparations of paracetamol and NSAIDS such as ibuprofen. As these single agents can be purchased in supermarkets and other non-pharmacy outlets without any professional advice, it seems that the potential for inappropriate use, use of doses above the recommended maximum, adverse drug reactions and drug interactions could be greatly increased.

4. We also believe that if a consumer has to go to the GP to obtain a codeine containing product, the consumer will most likely be given a prescription for a product with higher codeine content than the current OTC products, and the prescription will be for a greater number of tablets.

   We say this because data from Medicare Services Paid[1] for the period July 2014 to June 2015 indicates that when prescribing analgesics for DVA patients and given a choice of prescribing products containing either 8mg, 15mg or 30mg, 92.3% of prescriptions were for a product containing 30mg. In addition, of the prescriptions written for the 30mg product, 64% of these were dispensed on authority, meaning the consumer received multiple packs.

   In addition, currently the costs of higher codeine strengths are less expensive as they are subsidised on the PBS for the consumer. We believe that this will also encourage prescribing of higher doses.

   We thus believe that the evidence indicates that if a consumer is forced to go to the GP to obtain a codeine containing product that was previously available OTC, they will be given a higher strength product in greater volume.

5. Oxycodone is only available on prescription and its use has increased dramatically over recent years. Even with its schedule 8 listing, the misuse and harm associated with this agent is significant. In the past decade oxycodone prescribing has increased 4 fold and 800 Australian deaths were related to its use. [2,3] We believe the possibility exists that some consumers

who visit the GP for low dose codeine products may in fact be switched to oxycodone.

6. In the delegates' interim decision it was stated that "different genetic groups show significant variations in metabolism of codeine. Of particular concern are "ultra-rapid" metabolisers, where the accelerated metabolism of codeine to morphine results in an increased risk of morphine toxicity and adverse events". The interim decision goes on to say that "in up to 4-10% of the population (ultra-rapid metabolisers), it can cause life threatening toxicity".

   For those consumers who have metabolism issues regarding codeine conversion to the active metabolite (morphine), we fail to understand how the up-scheduling of these products will improve any safety concerns. Just like the pharmacist, the GP will not be able to determine the metabolic status of these patients without genetic testing, which is clearly impractical, as stated in the interim decision.

7. Although we do not have the exact numbers, it seems reasonable to conclude that codeine containing products are used by many hundreds of thousands, if not millions of Australians, every year.

   As reported in the Medical Journal of Australia[4], over the period between 2000 and 2013 there were 1444 codeine related deaths in Australia, with most of these being due to intentional or accidental overdose.

   It thus seems that the interim decision claim that in up to 4-10% of the population (ultra-rapid metabolisers), codeine can cause life threatening toxicity is not supported by the literature and would seem to be a gross over exaggeration.

8. Further, in this recent Medical Journal of Australia article[4] the authors reported that of the 1444 codeine related deaths in Australia, 48.8% were due to accidental overdose and 34.7% were due to intentional self-harm. The authors also reported that in 59.9% of cases it could not be determined whether the person obtained the codeine on prescription or obtained it OTC. However, where details were available as to the source of the codeine, in 59.9% of cases the codeine was obtained by prescription.

   It can thus seem reasonable to conclude that the majority of the codeine products involved in fatalities in Australia are prescribed, and not obtained OTC.

9. We believe that the current schedule 3 OTC Codeine supply does indeed meet the Scheduling Policy Framework for a schedule 3 medicine as there is very little risk of dependency when used appropriately for the treatment of acute pain as it is, by the large majority of patients. Pharmacists are able to reduce risk through monitoring for misuse and abuse. We would encourage the implementation of tools to assist all practitioners with their decision making around the supply of codeine. Evidence needs to be established to support arguments that suggest that the majority of OTC supply is to inappropriately treat chronic conditions.

In conclusion, we see that there is no evidence that OTC codeine is the actual problem. We do not believe that up-scheduling will solve any of the current issues that may be associated with the small minority of consumers that abuse this medicine. We see that this up-scheduling may indeed make the abuse issue worse, and force those with legitimate acute pain to suffer unduly.

Yours Sincerely

[redacted] Member of the NSW Poison's Advisory Committee

[redacted] Member of the NSW Poison's Advisory Committee

[redacted] Member of the NSW Poison's Advisory Committee

[redacted] Member of the NSW Poison's Advisory Committee

[redacted] Member of the NSW Poison's Advisory Committee

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[redacted]

[redacted]

15 October, 2015

The Secretary,
Scheduling Secretariat
GPO Box 9848
Canberra ACT 2601,

Email: Medicines.Scheduling@tga.gov.au

Dear Sir or Madam,

Notice of delegate's interim decisions under subsection 42ZCZP the Therapeutic Goods Regulations 1990 and invitation for further submissions, in relation to the ACMS Meeting of July 2015

We refer to the notice inviting further submissions and would like to provide comment in relation to the interim decision regarding codeine scheduling from the July 2015 meeting of the ACMS.

[redacted] is the manufacturer of [redacted] an ibuprofen-codeine combination analgesic.

[redacted]s position is consistent with the arguments put forward in our submission of 14 May 2015. Additional comments in relation to the interim decision are provided below.

[redacted] do not support the interim decision and our reasons are summarized as follows:

[redacted] believes that there has been a lack of transparency in the decision making. The interim decision appears to have been made in the absence of evidence to demonstrate that the incidence of misuse of codeine combinations has increased. No evidence is provided to demonstrate that the risks have become greater since these medicines were rescheduled in 2010 from S2 to S3. In the interim decision, there does not appear to have been consideration of the financial burden or impact on accessibility for consumers.

[redacted] recommends that the final decision is deferred until:

- An extensive evaluation of the financial and socio-economic implications of the interim decision has been conducted;

- Implementation of a real-time monitoring system to collect data so that an informed decision can be made after an acceptable period of time.

OVERVIEW

Evidence to Support the rescheduling to S4

- No tangible evidence is provided to support the interim-decision for re-sceduling. There is no discussion or evidence to show that "S3 has not achieved the required reduction in mis-use or harm". [redacted] are not aware of any tangible evidence that enables this level of abuse neither to be quantified nor to show it is increasing. There is no evidence of an escalating risk to public health.
- [redacted] question the interim decision in the absence of evidence to suggest that the public risk from mis-use of codeine combination products has increased post the reschedule from S2 to S3 in 2010.

Restriction of codeine to prescription only will not mitigate the risk of misuse or abuse

- There is no evidence to show that making all codeine combination products prescription only will address the concerns of misuse and abuse. All this does is increase the burden on the already overstretched healthcare system
- Evidence suggests that there are more people misusing prescription strength codeine containing analgesics than non-prescription codeine containing analgesics
- Prescription only scheduling is no guarantee against misuse or abuse and there are no mechanisms in place for prescription monitoring.
- Reviews in other jurisdictions including the UK and New Zealand, with an equivalent medicines classification system and standard of healthcare to Australia, have maintained codeine containing product availability from pharmacies without evidence of an increased risk to public health.

The proposed implementation date of 1 June 2016 is unrealistic

- The proposed implementation date of 1 June 2016 does not take into account the impact of the significant changes that would be required throughout the supply chain.
- As a global company [redacted] would need a minimum of 2 years to implement a change of this magnitude post the final determination.
- The unrealistic timeframe is compounded by the absence of consideration of expedited regulatory pathways to facilitate the approval of alternative formulations presentations, or appropriate scheduling that will be required to maintain appropriate supply and ensure a viable medicines industry in Australia.

Monitoring Programs should be introduced to understand the actual risk and provide insight in effective risk mitigation programs.

- [redacted] believes that a real-time-monitoring system should be put in place nationally as part of a package of measures including mandatory front-of-pack warnings and information resources for pharmacists and consumers.
- [redacted] has been working with ASMI and other key stake-holders pharmacy organisations to develop a prototype monitoring system using experience gained from Project STOP.
- There are no comparable mechanisms in place for prescription monitoring that provide the same level of risk oversight to mitigate potential risks

Limiting Access To Medicines increases the financial burden and disadvantages the public

- [redacted] acknowledges that there is a low level of misuse and abuse of codeine combination analgesic products in the community, which is clearly unwelcome. However, the great majority of consumers use codeine containing analgesics appropriately.
- Careful consideration needs to be given to specific measures to reduce the incidence further rather than simply transferring the problem without the knowledge that it will make a difference, reduce risk, or without consideration to the financial impact or reduced accessibility.
- Rescheduling to S4 would potentially lead to a reduction in accessibility by consumers to these medicines and increase GP visits impacting the healthcare system. The current scheduling of codeine-containing analgesics remains appropriate and should not be changed without greater analysis to demonstrate the desired outcome.
- The decision to up-schedule codeine containing analgesics will make short term self-management of acute pain more difficult and create a significant additional burden on the healthcare system and already overstretched GP resources.
- The availability of a range of pain management options that are readily accessible without the need for a prescription addresses an important medical need
- For this great majority, the decision will make these products more expensive and more difficult to obtain.

Alternative medicines for treatment of moderate to strong pain

- The interim decision relies heavily on the role of the ibuprofen plus paracetamol combination in satisfying consumer's OTC pain needs. This combination has been on the Australian market since March 2014 and there has still been a demand for S3 codeine containing analgesics. The assumption that the ibuprofen plus paracetamol combination would address the all of the unmet medical need resulting from a narrowing of the choice of available medication does not present the total picture.
- We note that this combination has only been on the market a short time and is currently scheduled as S3. The ibuprofen paracetamol combination cannot be advertised to consumers. Consumers are unaware of this product as an alternative for moderate to strong pain relief. Pharmacists and consumers are very familiar with codeine combinations, they have been on the market for many years. However with the current scheduling and limited awareness of the ibuprofen plus paracetamol combination in pharmacy, they are not the immediate option that the paper suggests. [redacted]

It is in consumer's best interest to have a range of effective OTC medicines available to them so that they have timely access to pain relief that suits their needs.

CONCLUSIONS

[redacted] believes that there has been a lack of transparency in the decision making. The interim decision appears to have been made in the absence of evidence to demonstrate that the incidence of misuse of codeine combinations has increased and risk to the public become greater since these medicines were rescheduled in 2010 from S2 to S3. There does not appear to have been consideration of the financial burden or impact on accessibility for consumers.

[redacted] recommends that the final decision is deferred until:

- An extensive evaluation of the financial and socio-economic implications of the interim decision has been conducted.

- Implementation of a real-time monitoring system to collect data so that an informed decision can be made.

Yours sincerely

[redacted]

Delegate to the secretary,

Therapeutic Goods Administration,

Department of Health.

Dear Sir/Madam,

RE: Consideration of rescheduling of OTC (over the counter) codeine containing products

Please consider the following when making your final decision on the way patients will be treated with medicines containing codeine.

My background. I am a pharmacist [redacted] I have been prescribing OTC codeine products and dispensing codeine products on prescription.

Parties with an interest in this decision:

(i) Pharmacists. Proprietor pharmacists: Pharmacists that own pharmacies are obviously going to favour making no changes. I am not going to deny we do make money selling these products. Practicing pharmacists: OTC codeine is a useful medicine to have at our disposal. There will always be info to suggest is does or doesn't work that people on both sides of the debate will refer to but many times I have used it successfully at 7pm on a Sunday night when the Dr and dentist are not available for toothache to get someone through the night. (I won't fill the page up with more examples). The use of the medicine must be left up to the prescriber (pharmacist or doctor) to decide on the needs of the patient in the particular situation they are in.

(ii) Doctors. Doctors are going to favour changing these products to only being available on prescription. They can't deny they make money when they see patients and such a change would increase their patient numbers. Doctors may point out that they see patients that have previously seen a pharmacist and had no success dealing with these products. Conversely, I see patients in my HMR and hospital roles that the doctor needs some help with. We are a healthcare team and the best results are obtained by working together. Patients that doctor shop will obtain codeine products the same way they visit multiple pharmacies now to obtain them.

(iii) Patients. The most important group of all. I can think of 3 types of patients that use codeine products:

a. Patients with a legitimate use. (Mainly period pain, dental pain, broken bones, moderate to severe type headaches).
b. Patients that are addicted to codeine. These patients visit multiple pharmacies and purchase many packs of OTC codeine. They also frequently visit many doctors and obtain codeine products through this channel too. There is currently no way to monitor or help them. A pharmacist friend of mine that locums at a few different pharmacies recently told me she has seen the same patient buying OTC codeine products in 3 stores from [redacted] (Once again I will stop at one example). I have known patients to shop around and take around 12 to 20 tablets daily to feed an addiction they know little about. At least when they come in I can have a word to them and offer them help if they ever want it. Forcing them to obtain products on the black market is moving them further away from the health system where they don't have the opportunity to ask questions or get offered help.
c. Patients that are addicted to other drugs that use codeine to alleviate their withdrawal symptoms. Heroin users are known to purchase a packet of ibuprofen/codeine and take between 12 and 20 tablets at once to treat their withdrawal symptoms. This is real. Denying them the product will not fix their problem. They are not going to look for treatment – they are going to commit crimes to get money for more heroin. Visiting a Dr instead of a pharmacist is not going to alter the problem. The Dr will make the same decision as the pharmacist. Many of these patients see doctors and pharmacists to obtain these medicines already. Some months ago I had a GP tell me they had just witnessed a patient leave the pharmacy next door and do this – the whole packet swallowed, two or three at a time as a single dose. (Again, only one example given to save time).

The solution.

After much experience, thought and discussion with many pharmacists and doctors I suggest the following measures. I will keep it short. This is a largely unseen yet very harmful problem. <u>To manage it, healthcare workers need help from the regulators (you guys) to make regulatory changes.</u> We only need a couple of things:

(i) Reduction in pack sizes. Ibuprofen/codeine products are currently available in packets of up to 30 tablets. This is the targeted combination as the patients know this medicine is safer to take in very high doses whereas the paracetamol/codeine combinations will kill you if you overdose – I am not joking – the patients know this. These pack sizes should be legally limited to 20 or 24 tabs per pack with only one packet per supply. This is enough to treat monthly period pain for a few days or to get that toothache through the long weekend etc…

(ii) Mandatory monitoring and recording of all codeine sales (whether OTC or on prescription) on a live, online database. We have experience with such a system currently used for pseudoephedrine sales. We can use this experience to set up a similar thing for codeine. This was very successful in reducing illegitimate pseudoephedrine sales whilst still allowing access for patients to be treated over the counter. Accessing a patients info should be done using the patients name and date of birth which must be proven using government issued ID (drivers licence, passport, 18+ card etc…). The use of

licence numbers etc… has had some limitations with the pseudoephedrine monitoring system we already have. I believe name and date of birth will work better. This works well to ID patients in hospital situations etc… Even if the products do change to prescription only, we will still require such a monitoring tool. Perhaps this tool could be used to monitor all opioids?

(iii) There must be a legally binding limit set for OTC purchases. For example: max of 15 packets per patient per year. Beyond this it should be illegal for the pharmacist to supply more OTC. This will take the pressure off the pharmacist when the patients are arguing for more. If a patient needs more than this they should be required to have a pain management plan written by a doctor. This written pain management plan should be required to be presented to the pharmacist with the script for any more opioid supplies to be obtained.

(iv) Training. Doctors and pharmacists will require training around any new legislation. Once we are all working together I am confident outcomes will improve. The requirements should be available for pharmacists and doctors to read in simple point form on the monitoring/recording website. Doctors should have access to this too in order to view patient purchase history when making prescribing decisions.

With such regulatory changes in place:

Codeine products that are currently OTC should not be made prescription only (although pack sizes should change).

Pharmacy sales will fall considerably.

Pharmacists will still be able to use this useful medicine to treat their patients.

Doctors will get more patients from pharmacist referrals.

Patients will get better care.

If such a system that I have recommended goes ahead I believe that only then will we see the full extent of the codeine problem, as most of these patients currently “fly under the radar” and their overuse of these products is currently unknown.

If I can be of any more help please email me back or phone me on [redacted]

I understand this letter may be available to the public. In this case I request my name, address, email address and phone number be kept confidential.

Yours sincerely,

[redacted]

15.10.2015.

Pharmaceutical Society of Australia

Submission to the October 2015 interim decisions and reasons for decisions by delegates of the Secretary to the Department of Health

OCT
2015

Purpose

The Pharmaceutical Society of Australia (PSA) makes this submission in response to the interim decisions and reasons for decisions by delegates of the Secretary to the Department of Health published on 1 October 2015.

PSA's comments relate to the proposed amendments to codeine.

About PSA

PSA is the peak national professional pharmacy organisation representing Australia's 29,000 pharmacists[1] working in all sectors and locations.

PSA's core functions relevant to pharmacists include:

- providing high quality continuing professional development, education and practice support to pharmacists;
- developing and advocating standards and guidelines to inform and enhance pharmacists' practice; and
- representing pharmacists' role as frontline health professionals.

PSA is also a registered training organisation and offers qualifications including certificate and diploma-level courses tailored for pharmacists, pharmacy assistants and interns.

[1] Pharmacy Board of Australia. Pharmacy registrant data: June 2015. PBA: 2015; Aug. At: **http://www.pharmacyboard.gov.au/documents/default.aspx?record=WD15%2f17608&dbid=AP&chksum=dYPo%2bvia3clPsjfHGE0Fag%3d%3d**

Summary

Codeine

PSA does not support the interim decision to delete the current Schedule 2 and 3 entries for codeine. Our view is that the proposal to apply a significantly more restrictive schedule to all codeine products currently in the two non-prescription schedules is not a balanced decision and does not represent a consumer-focused solution. We suggest that a coordinated multi-stakeholder, multi-faceted approach is required in order to assist those individuals susceptible to, or experiencing, harm.

PSA suggests that the type of amendment proposed by the interim decision requires the Office of Best Practice Regulation to assess whether a Regulatory Impact Statement is needed.

PSA believes the amendments proposed through the interim decision are likely to have a significant negative impact overall on pharmacists, prescribers, consumers, industry and regulators. This includes significant cost implications for all stakeholders including government.

We suggest that the potential benefits that may result (e.g. harm minimised by requiring individuals using codeine-containing analgesics inappropriately to obtain a prescription) are unlikely to offset the substantial negative impacts for consumers seeking to access codeine-containing products for appropriate use. Furthermore, the anticipated benefits of rescheduling may not be realised given the evidence of harm from the use of prescription medicines containing codeine.

Given the recent publication of outcomes from a safety review on codeine use in children and ultra-rapid metabolisers, PSA suggests those recommendations should be considered in the context of the current scheduling proposal. This would need to cover, not only the safety aspects but also the issue of lack of efficacy of codeine medicines in particular cohorts of consumers.

PSA re-iterates its call for the urgent implementation of a national system of real time recording and reporting of the prescribing and dispensing of particular medicines. PSA's view is that such a system should capture all drugs of dependence including over-the-counter codeine-containing analgesics.

PSA supports the consideration of data and outcomes of Australian research on pharmaceutical opioid analgesic dependence and treatment to help inform scheduling decisions.

PSA strongly suggests that the proposed rescheduling of codeine-containing cough and cold preparations is not warranted as there is no evidence to show a shift in demand since the rescheduling of codeine-containing analgesics to Schedule 3.

PSA highlights, once again, our considerable efforts in the implementation of professional resources to support the quality use of codeine-containing medicines. Adequate time is required for implementation of these resources to take effect and to complement related initiatives being delivered by other stakeholders.

Hydrocortisone and hydrocortisone acetate

PSA re-iterates its firm view that the current Schedule 3 entry for hydrocortisone dermal preparations (up to 1% combined with an antifungal substance) remains appropriate and ensures the quality use of these medicines. PSA does not support the proposed amendments to include hydrocortisone in Schedule 2. No new information is provided in this submission.

Comments on the interim decision on codeine

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. The proposed implementation date is 1 June 2016.

PSA takes this opportunity to submit further comments in response to the delegate's interim decisions which were published on 1 October 2015.

The significant breadth of the scheduling proposal for codeine, coupled with the complexity of issues associated with codeine and its use, has made it one of the most challenging considerations for all stakeholders.

PSA does not support the interim decision for codeine. In our view, the removal of codeine from the two OTC schedules which would result in all of these existing products moving to a category requiring a prescription, is not a balanced decision. It is not a consumer-focused solution to the harm that some individuals and the community are experiencing. We suggest changes need to be made in other ways, not by using a more restrictive schedule as a sole instrument.

PSA provides comments below on the published reasons for the decision.

Potential magnitude of impact of the interim decision

The proposal considered by the Advisory Committee on Medicines Scheduling (ACMS) consisted of three aspects:

- Proposal to delete the Schedule 3 entry for codeine, and reschedule all current Schedule 3 codeine to Schedule 4 due to issues including morbidity, toxicity and dependence.
- Consideration could include whether all current Schedule 3 preparations should be rescheduled to Schedule 4, or whether any rescheduling to Schedule 4 should only apply to combination analgesic products containing codeine.
- Consideration could include whether the Schedule 2 entry for codeine should also be amended.

PSA believes this is one of the most wide-ranging proposals involving a single substance considered by the ACMS in terms of the number of schedules covered, the number and range of products potentially impacted, relevance to the health and welfare of consumers, professional practice and workload considerations for health professionals, and consequential impact on industry and regulators.

Following ACMS consideration, the delegate's interim decision is to delete the current Schedule 2 and 3 entries for codeine. PSA believes the proposed deletion of entries across two non-prescription schedules is unprecedented, particularly for a substance which is used widely and has been for many decades in Australia. A very high proportion of people will be affected as analgesics, and cough and cold products are the two highest OTC categories used/taken by consumers. In a recent study,[2] only 4.5% and 6.9% of survey respondents, respectively, had never taken these medicines.

PSA has stated previously that the potential impact of scheduling proposals, for example, on pharmacy practice, cost to industry and regulators, and costs and benefits to consumers, must be key considerations in the scheduling decision-making process. PSA appreciates that the ACMS is generally well equipped to consider these factors. However, given the significance of the proposed amendment we believe a more formal assessment of the potential impact is required.

PSA notes the Scheduling Review Panel report[3] stated that the Office of Best Practice Regulation (OBPR) considers an assessment of regulatory impact is not required where amendments to the Poisons Standard are considered to be minor or machinery in nature. Thus the need for a Regulation Impact Statement (RIS) is not assessed for the following amendments:

- adding new substances to the Poisons Standard
- down-scheduling of substances
- correction of minor errors or inadvertent scheduling errors
- urgent scheduling when it relates to new substances or derivatives of existing Schedule 9 substances. This does not cover instances where urgent scheduling relates to up-scheduling of existing substances
- annual consolidation of the Poisons Standard.

The report further states:

> *It follows that any other type of amendments to the Poisons Standard would require the OBPR to assess whether a proposal triggers a RIS.*

PSA suggests therefore that the interim decision on the codeine scheduling proposal requires the OBPR assessment process to take effect.

Proposed implementation date

The interim decision proposes an implementation date of 1 June 2016. PSA notes this is a slightly extended timeframe (compared to the usual implementation timeframes) and is based on the

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[2] Koslow S. Consumer behaviour fact book. 2015; Mar. At: **http://www.wsmi.org/wp-content/uploads/2015/06/CONSUMER-BEHAVIOUR-FACT-BOOK_MARCH-2015.pdf**

[3] Review of arrangements for scheduling substances under part 6-3 of the Therapeutic Goods Act 1989. Report by the Scheduling Review Panel. 2013; Sep.

need to “allow time for education of consumers, pharmacists and medical practitioners regarding pain management and alternative analgesia available”.

Given the significance and magnitude of amendments which are likely to result if the proposed interim decision was confirmed, PSA strongly believes the implementation timeframe is inadequate. While industry would be in a better position to comment, PSA understands that packaging and labelling changes alone would require a substantially longer lead-in time or transition period. This is one example of the types of issues that must be canvassed and formally assessed, and in our view should trigger a RIS.

Scheduling history

As outlined in the published record of reasons, there has been considerable recent history of assessment by the ACMS (or the then, National Drugs and Poisons Schedule Committee) of appropriate scheduling of all over-the-counter (OTC) codeine-containing products.

- In 2009, it was agreed that the Schedule 2 classification of OTC codeine combinations for coughs and colds remained appropriate with an amended pack size limit. A further consideration in 2011, in the context of the review of the use of cough and cold preparations in children, resulted in a decision that there should be no change to the scheduling of codeine in cough and cold preparations.

- With respect to OTC combination analgesics containing codeine, it was confirmed in 2009 that Schedule 3 was a more appropriate classification.

These recent decisions were a result of extensive consultation and considered expert advice. They should be taken into account in the context of the current proposal.

Metabolism of codeine

The ACMS consideration and delegate’s interim decision have highlighted the impact of genetic polymorphism of cytochrome P-450 enzyme 2D6 (CYP2D6) on the metabolism of codeine and the consequential impact on efficacy for individuals. This can result in the potential for different therapeutic responses ranging from a higher risk of toxicity for an ultra-rapid metaboliser, through to lack of efficacy for a poor metaboliser.

A recent safety review report[4] notes that, currently in Australia, there are inconsistencies in the way risks associated with ultra-rapid metabolism of codeine are addressed across OTC and Schedule 4 codeine products. This review focused on codeine use in children and ultra-rapid metabolisers and therefore the resulting recommendations relate mainly to safety aspects and warnings around potential risks. Nevertheless, PSA would contend that inconsistencies in advice would apply equally to the potential for lack of efficacy which is relevant to poor metabolisers.

PSA suggests the recommendations arising from this safety review are pertinent to the current scheduling proposal. It recognises that warnings need to be standardised across all codeine-containing products. We would add that the regulator’s advice needs to be extended to include

[4] Therapeutic Goods Administration. Codeine use in children and ultra-rapid metabolisers. Canberra: TGA; 2015. At: **https://www.tga.gov.au/sites/default/files/codeine-use-children-and-ultra-rapid-metabolisers.pdf**

warnings around potential for lack of efficacy in a particular group of individuals since this can impact on safety through possible overuse. The report also recommends the provision of education to health professionals and consumers regarding the variability of codeine efficacy.

This new report clearly identifies additional measures that should be implemented in relation to all codeine products. Although the ACMS has taken into account the discussions and outcomes of the Advisory Committee on the Safety of Medicines, the information and recommendations from the safety review were not widely available during the last public consultation period and therefore were not considered by PSA. We strongly suggest the recommendations and their possible implementation warrant due consideration by the ACMS before a scheduling change decision for codeine is made.

Availability and access

As stated previously, PSA supports consumers continuing to have reasonable access to all codeine-containing OTC products with the advice of a pharmacist.[5] Pain management is a complex and subjective matter and pharmacists have a critical role in advising and supporting consumers, carers and working with other health professionals. Pain management options need to be canvassed and tailored for individual consumers, responses and outcomes monitored, and plans adjusted where necessary.

The proposed rescheduling of all codeine products to prescription only status does not serve the best interest of the consumer. The interim decision is strongly opposed by consumer organisations such as the Consumers Health Forum of Australia and the Australian Pain Management Association.

Greater restriction in access may be regarded as of benefit to some individuals experiencing harmful outcomes, however it may not necessarily equate to acceptable pain relief or better health outcomes. In addition, prescription-only opioid analgesics are also associated with inappropriate use[6] and therefore rescheduling a substance to a more restrictive category will not fundamentally address the issues of misuse.

There is also suggestion that rescheduling to Schedule 4 will provide people with the opportunity to access other treatment options in consultation with the doctor. PSA re-iterates that packs in excess of five day's supply of codeine-containing analgesics are currently already in Schedule 4 thereby providing people who have a genuine need for chronic use to benefit from regular medical oversight and the opportunity to determine if specialised treatment is necessary.

PSA believes if the interim decision was to be implemented it will have several impacts, including the following:

- It is clear that the burden on general practitioners will rise if a prescription is needed for a codeine-containing medicine (analgesic or cough and cold product). Of concern, however,

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[5] Pharmaceutical Society of Australia. Minimising harm from the inappropriate use of over the counter analgesics [position statement]. Canberra: PSA; 2015. At: **www.psa.org.au/download/policies/codeine-position-statement.pdf**

[6] Roxburgh A, Hall WD, Burns L, Pilgrim J, Saar E, Nielsen S, Degenhardt L. Trends and characteristics of accidental and intentional codeine overdose deaths in Australia. Med J Aust 2015;203(7):299.e1–7.

is that a proportion of people suggest they would go to an emergency department instead. Some people indicated they would not do anything (would "tough it out").[7]

- The flow on consequences include time off work (decreased productivity) due to the need to see a doctor or because treatment is not initiated.[8] Clearly health care expenditure would increase from increased doctor visits and additional emergency department visits.

- The Australian Self Medication Industry has stated[9] that rescheduling codeine-containing cold/flu medicines to Schedule 4 would cost the Australian economy $257 million annually. This includes costs to government of $53 million each year due to increased doctor visits, Medicare and dispensing costs, $174 million due to productivity losses caused by restricted access, and the balance of costs borne by consumers.

Monitoring consumer access

PSA restates once again its strong support for the urgent implementation of a national real-time recording and reporting system to allow for real-time monitoring of prescribing and dispensing of specific medicines.

A letter co-signed by PSA, the Pharmacy Guild of Australia, Society of Hospital Pharmacists of Australia, Australian Medical Association, Royal Australian College of General Practitioners, Royal Australasian College of Physicians, Consumers Health Forum of Australia and the Medical Software Industry Association of Australia, was recently sent to Federal, State and Territory Health Ministers calling for the urgent implementation of a national system for the Electronic Recording and Reporting of Controlled Drugs (ERRCD).

While the ERRCD is intended to capture Schedule 8 medicines, PSA's strong view is that the system should be expanded to include all drugs of dependence, including OTC codeine-containing analgesics, as appropriate and in accordance with relevant State and Territory legislation. This would provide more holistic and comprehensive information to assist prescribers and pharmacists in their informed clinical decision-making for the benefit of the consumer.

PSA understands some progress on the possible implementation of the ERRCD has already been made. We believe this is an urgent priority issue that requires collaboration and coordination across all jurisdictions. We suggest there is a clear obligation on regulators to move forward on this initiative given positive outcomes have been reported in Tasmania and overseas. Health professionals, consumers and industry are united in calling for immediate implementation of a national system for the ERRCD.

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7 Koslow S, op. cit. p. 14–5.

8 Koslow S, op. cit. p. 16.

9 Australian Self Medication Industry. New figures reveal significant costs of up-scheduling codeine containing cold/flu products [media statement]. 2015; Oct 15.

Partnership approach

PSA re-iterates the need for a strong collaborative and multi-faceted approach to assist all consumers with the quality use of codeine-containing medicines with a particular focus on those individuals who may be 'trapped' (intentionally or otherwise) in a cycle of misuse. All individuals, stakeholder groups and organisations have a role in the QUM space and innovative solutions and coordinated initiatives are urgently needed.

To this end, PSA is disappointed that there was no mention of Australian and international research in the interim decision statement. PSA re-iterates the importance and value in considering work such as:

- the CODEMISUSED project,[10] a multi-stakeholder research initiative spanning three countries, Ireland, United Kingdom and South Africa, which aims to create a model including monitoring systems, web- and pharmacy-based interventions, and educational materials for health professionals and treatment providers

- a number of National Health and Medical Research Council funded studies investigating pharmaceutical opioid analgesic dependence and treatment. It would be essential to give consideration to data and outcomes arising from such studies particularly in the Australian context.

Cough and cold preparations

PSA is surprised that the interim decision included the proposal to reschedule all codeine-containing cough and cold preparations currently in Schedule 2. PSA is not aware of any evidence which indicates these medicines are the subject of misuse seen in the codeine-containing analgesic category.

At the time when codeine-containing combination analgesics were rescheduled (to Schedule 3), PSA did have some initial concerns that codeine misuse trends may be altered, with potentially some transfer in demand to cough and cold products. However, although we do not have firsthand data, based on industry reports, PSA is informed that there has been no such outcome. We are advised that the usage patterns of cough and cold products remain as before where seasonal increase in demand is observed but no other increase in demand has been recorded.

PSA therefore strongly suggests the proposed rescheduling of codeine in Schedule 2 to prescription only status is not warranted.

Quality use of medicines initiatives

The interim decision statement refers that "industry and pharmacy organisations have not been able to fully address concerns regarding codeine dependence". PSA is disappointed that our efforts in supporting pharmacists through the provision of practice support tools do not appear to have been considered positively. These are comprehensive tools designed to support pharmacists in providing solutions to consumers who are seeking to manage pain and addiction

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[10] Further information available at: **http://codemisused.org**

issues. Other stakeholders have expressed support for these initiatives and have recognised that, with their recent introduction, more time is needed to consolidate their effect. Further consumer education campaigns are likely to be required.

The resources developed by PSA which are now being implemented include:

- guidance document[11] for pharmacists to support the provision of Schedule 3 combination analgesics containing codeine. This is a professional decision-making resource for pharmacists.

- new CAL[12] recommended for use to advise consumers of the potential for addiction with continuous use of combination analgesics containing codeine – Label 24: *FOR 3 DAYS USE ONLY, can cause addiction*.

  This resource was created by PSA because there has not been any mandatory introduction of a warning statement to the product packaging (regarding possible addiction).

  The label is also designed to highlight the need to be vigilant about short term use. Again, there has not been any regulatory decision to reduce the pack size of codeine-containing analgesics.

  It is not clear how an assessment was made by the ACMS/delegate that "changing the labelling and decreasing the pack size will not adequately address the problem of misuse and dependence" or that decreasing pack size might help reduce the incidence of new users becoming dependent "but is unlikely to be effective for those who are already dependent". The interim decision report acknowledges that "activities to reduce the use of codeine cannot occur in isolation from consideration of alternative pain management strategies".

- new consumer information leaflet, *Using codeine pain relievers safely*, which explains the possible adverse effects of inappropriate use of combination analgesics containing codeine and provides consumers a checklist of signs of codeine dependence. This tool is designed to assist pharmacists to discuss appropriate pain management solutions with consumers.

These resources are supported by PSA education and practice support modules available to pharmacists addressing issues such as pain management, difficult conversations in the pharmacy, and addiction care.

These initiatives require adequate time for implementation to take effect.

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[11] Sansom LN, ed. Australian pharmaceutical formulary and handbook. 23rd edn. Canberra: Pharmaceutical Society of Australia; 2015. pp. 577–80.

[12] Sansom LN, ed. op. cit. p. 12.

Submitted by:

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15 October 2015

promoting excellence in medicines management

ABN 54 004 553 806

15 October 2015

Medicines.Scheduling@tga.gov.au

Re: Consultation: Delegate's interim decisions – ACMS meeting, July 2015

The Society of Hospital Pharmacists of Australia (SHPA) is the national professional organisation for over 3,000 pharmacists, pharmacists in training, pharmacy technicians and associates working across Australia's health system. SHPA is the only professional pharmacy organisation with a strong base of members practising in public and private hospitals and other health service facilities.

SHPA is committed to facilitating the safe and effective use of medicines, which is the core business of pharmacists, especially in hospitals. SHPA supports pharmacists to meet medication and related service needs, so that both optimal health outcomes and economic objectives are achieved for Australians, as individuals, for the community as a whole and for healthcare facilities within our systems of healthcare.

SHPA believes that any changes to the scheduling of medicines should be driven and underpinned by the principles of patient safety. Our thoughts on three of the delegates' interim decisions are presented below.

Codeine

Given the evidence considered by the delegates, SHPA concurs that there are aspects related to codeine that do not meet the Scheduling Policy Framework (SPF) factors for inclusion in Schedule 3. In relation to this, it is criterion 2 which is critical and not satisfied: "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."

The risks can be minimised through monitoring by a pharmacist, however this requires the implementation of a national Electronic Recording and Reporting of Controlled Drugs (ERRCD) system that includes codeine, irrespective of the schedule.

For this reason, SHPA concurs that the only option available within the current interpretation of the SPF, and the lack of agreed implementation of a national Electronic Recording and Reporting of Controlled Drugs (ERRCD) system, is to reschedule codeine as detailed in the interim decision.

However, we reiterate, that this decision would introduce considerable challenges and additional financial burden to both patients (as increased out-of-pocket costs) and the healthcare system as a whole, in particular Medicare payments, including:

- requiring multiple additional attendances to doctors for prescriptions with the associated increase in claims through Medicare
- potentially more prescriptions through the Pharmaceutical Benefits Scheme (PBS); this will be dependent upon separate decisions about whether these medicines remain on the PBS
- Preventing nurses from initiating analgesic treatment in emergency departments and during hospital admissions, particularly in hospitals without full time medical staff.

The Society of Hospital Pharmacists of Australia
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SHPA believes that the option of continuing codeine as a Schedule 3 medicine should be considered with the following requirements:

1. these products are supplied as pharmacist only medicines and that all supplies of these products are dispensed, individually labelled and recorded by the pharmacist; and
2. are included in a national ERRCD system.

Irrespective of the scheduling of codeine, SHPA believes that a ERRCD system would mitigate many of the risks of the inappropriate use and diversion of products containing codeine. SHPA is a cosignatory to a letter sent to all health ministers highlighting the need for a national ERRCD. The letter notes that an ERRCD is a crucial clinical support and intervention tool to help practitioners manage the prescribing, supply and management of drugs of addiction, and to prevent harm from inappropriate use of prescription medicines. (http://www.shpa.org.au/lib/pdf/whatsnew/20150909-Joint-letter-to-Health-Ministers-re-ERRCD.pdf)

It is possible that in response to the interim decision, manufacturers may re-evaluate products containing codeine, which may lead to a decrease in the number of products. SHPA believes that manufacturers should communicate as early as possible if any product will be discontinued. Timely information will be crucial to educating consumers about their future treatment options and promoting non-pharmacological interventions in treatment plans.

Naloxone

SHPA supports the creation of a Schedule 3 entry for single use prefilled syringes for injection containing 400 micrograms/mL or less of naloxone.

Esomeprazole

As part of Choosing Wisely Australia the Royal Australian College of General Practitioners (RACGP) have flagged the long term use of proton pump inhibitors (PPIs) as one of the top five tests, treatments or procedures which should be questioned by GPs and their patients. That statement is based on the evidence that a high proportion of patients are kept on maximal doses long term when this should not be the case. (http://www.choosingwisely.org.au/recommendations/racgp)

In principle, SHPA does not support any Schedule 2 entries for PPI. Although the change would only apply to packs containing no more than 7 days' supply of the medicine, we believe that these medicines should be Schedule 3 to ensure appropriate consultation and review by a pharmacist to minimise the number of people who move to long term use of these medicines.

If you would like to discuss the issues raised in this submission or require further information, please contact us (shpa@shpa.org.au or 03 9486 0177)

Yours sincerely

[redacted]

[redacted]

15 October 2015

Generic and Biosimilar Medicines Association

Unit 4, 20 Napier Close
Deakin ACT 2600

PO Box 87
Deakin West ACT 2600

gbma.com.au

Advisory Committee on Medicines Scheduling
Therapeutic Goods Administration
Canberra

By email: Medicines.Scheduling@tga.gov.au

Re: Scheduling delegate's proposal on codeine

Members of the Generic and Biosimilar Medicines Association (GBMA) oppose the medicines scheduling delegate's proposal regarding codeine as made to the Advisory Committee on Medicines Scheduling (ACMS) in October 2015.

GBMA does not support rescheduling all current Schedule 3 codeine preparations to Schedule 4. Doing so will have a significant impact on suppliers and consequences for patient access to medicines containing codeine. GBMA notes that a number of points are made in the interim decision that relate to codeine preparations used for analgesia only. GBMA believes there is no justification for the rescheduling of cough and cold medicines containing codeine.

GBMA supports the points raised in the public submissions prior to the August 2015 ACMS meeting opposing the rescheduling of codeine, specifically the increased administrative burden and health costs associated with patients having to access a doctor in order to obtain a prescription for codeine. Additionally, GBMA would support an education campaign for patients and a national, real-time monitoring system similar to the highly successful *Project Stop* for pseudoephedrine.

GBMA strongly opposes the proposed implementation date of 1 June 2016 as this is not an achievable timeframe for such as significant change. It does not take into consideration factors such as:

- The significant volume of stock currently carried by suppliers;
- Purchase orders already in place with manufacturers;
- The time and cost associated with regulatory compliance; and
- Lead time for new orders.

GBMA suggests that any implementation date should allow suppliers sufficient time to make required changes without realising commercial losses. Therefore a more appropriate implementation date would be 1 January 2017 at the earliest.

Yours sincerely,

[redacted]

From: [redacted]
To: Medicines Scheduling
Subject: No prescription for codeine products
Date: [redacted]

To whom it may concern- by changing law to requiring a prescription in our region would add great cost - we have to see a doctor when a script is needed. A visit to doctor is $73.15! Not to mention the inconvenience of trying to get an appointment when needed.

Yours

[redacted]

[redacted]

From: [redacted]
To: Medicines Scheduling
Subject: Rescheduling Of Codeine
Date: [redacted]

[redacted]

To whom it may concern

Rescheduling codeine will be a costly, pointless exercise.

The ACMS has recommended codeine be moved to schedule 4 and made available only on prescription. The argument that codeine is dangerous to a subset of (liver enzyme) super metabolisers is insubstantial. The fact that codeine is of low therapeutic value necessarily implies the substance is of minimal toxicity. Codeine is fundamental to the useful role played by Australias approximately 6000 pharmacies in managing pain within the community without causing burden to the medicare system. If there is any substance that requires rescheduling it is alcohol and not codeine.

The following is my submission to the TGA which refutes the ACMS's reasons for change plus some additional reasons for supporting the maintenance of codeine within Schedule 3 (Pharmacist Only). Please consider the points I raise here – and take action to have this decision overturned.

Codeine is used in tablets for the relief of mild to moderate pain, often with a non-opioid analgesic such as aspirin, ibuprofen, or paracetamol. It is also used to stop coughing and to treat diahhroea.

The reasons for the recommendations of the ACMS are given here followed by the reasons I believe these points are invalid.

- Risks of medication misadventure through polymorphic metabolism, deliberate misuse/abuse combined with the relative lack of efficacy compared to safer products.

  The idea that codeine is dangerous to super metabolizers is an unnecessary overreaction. This subset of CYP450 metabolizers represent a very small percentage of the population 1-2%- and the assertion that high doses of codeine in this subset can cause severe reactions and even death – while true - is unnecessary sensationalism aimed at gaining an emotionally negative reaction.

- OTC intended for management of acute self-limiting pain, however, there is inappropriate use for chronic pain.

  How can the ACMS know what is and what isn't appropriate use for chronic pain?

- Purpose is questioned since benefit is low.

  This could also be interpreted as a reason to not upschedule codeine. If the benefit is low is it really necessary to make the substance more difficult to obtain? If codeine doesn't work as a painkiller where is the perceived danger?

- OTC sales data are incomplete.

  Will sales data be more complete when codeine is available on prescription only?

- Codeine shares the properties of other opioid analgesics and is potentially capable of producing dependence and, in overdose, respiratory depression and reduced level of consciousness.

  This is true of ALL opioids – not just codeine. Pholcodine and dihydrocodeine – useful for the treatment of dry cough as well as loperamide – useful in the treatment of diarrhoea - are capable – in large doses - of producing respiratory depression and reduced levels of consciousness. Codeine is a

mild analgesic and not the dangerous drug the ACMS makes it out to be.

- Changing the labelling and decreasing the pack size will not adequately address the problem of misuse and dependence.

  In the event codeine does become schedule 4 patients will seek out larger and larger pack sizes and quantities – given the rigmarole required to obtain a prescription. This then opens the way for unprecedented cases of misuse and severe dependence.

- Increasing amount of evidence for harm from abuse

  Without a clinical reference it is difficult to accept this point.

- Misuse of OTC codeine products including deaths resulting from hepatic injury, gastrointestinal perforations, hypokalaemia and respiratory depression.

  All substances within the poisons schedule are capable of producing death. Paracetamol is well known for the morbidity it causes – and yet it is available through supermarkets.

- Genetic influence on codeine's action complicates risk and benefit decisions, and leads to questions regarding the role of codeine in clinical practice.

  Genetic influence complicates risk and benefit decisions for all medicines and not just codeine.

- To adequately determine the clinical needs an appropriately qualified practitioner to assess risk.

  Is the ACMS suggesting every patient have their liver function tested in the event they have minor pain, like a headache? This is both onerous and impractical. Do doctors have the time - or the need - to assess every patients liver function?

A relevant point about metabolism. Phenylketonurics are at risk of severe reaction and even death from an overdose of Diet Coke and yet this product remains readily available in supermarkets.The can merely features a warning that the product contains phenylanaine (poisonous to sufferers of PKU) in super small script hidden on the side of the can alongside the ingredient and manufacturers details. Concerns about metabolism mean Diet Coke should be on script?

Codeine is a marginal pain killer, not particularly efficacious. If the molecule is put on prescription the choice to prescribe the molecule will be given to doctors. The medical profession relies on the AMH and MIMs for quick and readily digested information on the suitability of medicines - in this case in the suitability of a painkiller. Given the lack of effectiveness of codeine doctors will understandably choose more effective painkillers - stronger opiates such as oxycodone would become an increasingly popular choice - as has been the case in the UNITED STATES. Increased prescribing of oxycodone will lead to unforeseen bad results – including deaths - effects not predicted by the sudden change of re-scheduling codeine.
Monitoring the sale of codeine based products is akin to trying to "herd cats." It is pointless and impossible.

Changing codeine to schedule 4 makes it difficult to obtain for patients with minor ailments – especially given that repeat prescriptions for opioids are increasingly difficult to obtain. This will be a particular problem in rural areas.

Finally I note a perceived double standard with supermarkets Woolworths and Coles promoting the sale and use of alcohol “cheaper by the half dozen” This is inappropriate behaviour given alcohol is

a poison far more dangerous than codeine. How is the sale of alcohol allowed to continue unabated when it is responsible for far more deaths from misuse in a given population http://www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm than those attributed to the comparatively safe codeine? (impossible to quantify as codeine is metabolised to morphine in the body and detected as such in the blood of the decedent.)

Codeine is not as dangerous as the ACMS's recommendation implies – and the sudden need to change the molecule to prescription only is merely overreaction. A simple campaign run by pharmacists to stamp out potential abuse is all that's needed to ensure the continued safe and timely supply of this medicine.

Please consider my petition.

Regards

From: [redacted]
To: Medicines Scheduling
Subject: Submission on OTC supply of Codeine products
Date: [redacted]

Dear TGA

[redacted] are so relieved that the TGA is recommending that OTC codeine products are re-scheduled so that a doctor's prescription is required.

[redacted]

[redacted] has been admitted to hospital twice in the last 12 months for an emergency antidote to accidental paracetamol overdose. As you know, paracetamol overdose destroys the liver and causes deaths in young people unable to obtain a liver transplant. [redacted] Sadly, we have learnt a lot about drug addiction over the last [redacted] years. It is shocking to us that these preparations are freely available over the counter to teenagers and their later adult selves once thoroughly addicted to the codeine.

Please count us as a family devastated by the over-the-counter supply of codeine products to teenagers. Last year, we wrote to all 400 pharmacies in the [redacted] metropolitan area imploring them not to serve [redacted] codeine products. We also visit and talk to the pharmacies within a 20km radius of home most accessible by public transport.

Yours faithfully

[redacted]

[redacted]

Dear Sir/Madam

Re: Interim decisions on matters referred to an expert advisory committee (1.1)

1. Scheduling proposals referred to the August 2015 meeting of the Advisory Committee on Medicines Scheduling (ACMS #15)

1.1 Codeine

I would like to make a submission regarding the proposal to reschedule codeine containing analgesics to Schedule 4. I trust my points below address section 52E of the *Therapeutic Goods Act 1989* with respect to the benefits of the use of a substance and the purposes for which a substance is to be used.

I strongly oppose the interim decision which I understand would reschedule codeine containing over-the-counter analgesics to prescription only medication.

I suffer from migraine headaches. The symptoms can be debilitating and typically last for 24 hours After trying many different treatment approaches, I have found that I can self-manage my condition effectively and affordably using over-the-counter generic analgesic tablets containing 500mg paracetamol and 10mg codeine. I take [redacted] and experience no addiction/withdrawal complications afterwards. I cannot take NSAIDs due to allergy and paracetamol tablets alone do not help.

Importantly, I need to take the tablets within an hour or so of the onset of symptoms for maximum efficacy. This will be impossible if I need to book an appointment with a GP each time. Even if I could do so, it would become a prohibitively expensive exercise.

Thus, I submit that the rescheduling proposal would prevent me from self-managing my condition effectively and affordably.

I appreciate that there are concerns about misuse of codeine, but similar concerns over pseudoephedrine are being managed through a pharmacy based monitoring approach. If action is needed on codeine based analgesics, I would strongly advocate a similar approach so that people who use these drugs as intended are not seriously disadvantaged.

Yours sincerely,

[redacted]

From: [redacted]
To: Medicines Scheduling
Subject: No Subject
Date: [redacted]

I use codeine combination products periodicaly for [redacted] pain associated with injury - I find them very effective and I appreciate having access to them when I need them.

I am not in support on the proposal to transition OTC codeine combination analgesics to prescription only for a number of reasons:

- The proposal seems largely based on assumed risk to the population based on the theory or potential for a harmful reaction to the drug and reports of harm to very small number of people (I have been prescibed panadeine forte and other stronger medication post operatively and have never been tested for how I might metabolise these drugs).

- the summary information says the 2010 change to availability was not effective but the evidence for this is not presented.

- a 10 day consultation period for a change which will affect a large number of people does not seem appropriate at all

- The move will cause considerable inconvenience a large number of people for the sake of a few who may have issues with the medication (and who may then have issues with some other drug if codeine products are restricted). This is a real problem from my perspective. Having to see a doctor for a prescription for a product which is effective and has been available over the counter for many years is ridiculous. A half hour $10 excercise will now become potentially a half day away from work etc and a $70 cost. Further if a doctor is unavailable this may roll over into days and lead to unneccesary time away from work.

- Finally doctors have varying attitudes to prescribing pain relief - I have had experiences ranging from being told to go and lie down in a dark room (and ride out the pain) to being prescribed morphine type medications.

Regards [redacted]

[redacted]

15 October 2015

[redacted]

To Whom it may Concern
Submission to TGA

I wish to submit my views regarding the proposal to move codeine based pain relief products from over the counter to script only. I tend to feel completely powerless and insignificant in such debates but would nevertheless like to contribute.

Like the vast majority of people I am not one who consumes large quantities of pain killers in the act of joy. My pain, caused mainly by [redacted] damage due to [redacted] injury in [redacted], from years of [redacted] through my profession, is something that I have to live with and manage.

I don't have time to write much here and have been trying to get this in on time but pressures of family and work have made it difficult so I will be brief. The difficulty with having acute pain is that in the world we live in there is limited time available and so we can't just go to bed or put our feet up, or for that matter visit the doctor, every time we have aches and pains. Most of us have such fast consumer driven lives where there is limited sympathy for pain and suffering (we are all expected to 'suck it up') to some degree and get on with things. There is no slowing down due to pain.

I feel dismayed when I hear the recent discussions about too many tests that doctors are ordering for afflictions that end up being some form of arthritis or another unavoidable bodily decline and that it's costing the health system billions of dollars. The discussion was focused on the idea that people manage their own pain for simple things such as osteoarthritis rather than go down the path of endless testing to come out with the same result, that is, that the pain is still there and there is no definitive result except to confirm what the patient already suspected.

I have had many tests myself in the past and have gone around in circles and as the debate points out it took me years to realise that I simply just have to manage the pain in the best way that I can and as safely as possible. This does not mean I am taking painkillers every day but there are times when I must and this occasionally includes a stronger painkiller which contains codeine.

If this proposal is adopted it will effectively take away many people's ability to control their own pain; it will completely blow out the Medicare budget for doctors visits and it will have the opposite effect on the debate to halt unnecessary testing by in fact increasing it.

Please don't take away a simple freedom because of a handful of miscreants. Find another way such as a registration system through pharmacies so that a person's identity can, if necessary, be traced. Such a measure would surely be best for those of us who are not deviants, which would have to be a percentage in the high 90s.

If you go ahead with this 'nanny state' decision this is how I see a typical scenario playing out at the doctors:

Me: Hello Doctor, I'd like a script please for the pain in my foot and hip.
Doctor: Right okay, how long have you had this pain….
So from here I have to go over my whole life's situation, finally bringing me to the point of the pain of [redacted]
Dr: Have you thought about orthotics?
Me: you mean the $600 pair I'm wearing now, even though my podiatrist indicated that my feet are beyond orthotics.
Dr: Okay, I'm not sure you should be taking ibuprofen/codeine until we know what exactly the problem is. Let's book you in for a CT Scan.

So I convince her or him that I don't need any tests because I've had them all before and finally I walk out of there with my script, feeling as guilty as hell that I might be considered a potential addict and the whole thing has cost me a double appt because I had to talk my way through it. I go and have a cup of coffee and try not to think about the next appt in some months time where I have to explain it all again, adding to my pain.

Please consider this decision with real people in mind. Thank you for the opportunity to put my point of view.

Kind regards,
[redacted]