TGA Submission – ACMS Meeting July 2015

Regarding the following proposal:

Codeine	To delete the Schedule 3 entry for codeine, and reschedule the current Schedule 3 codeine entry to Schedule 4 due to potential issues of morbidity, toxicity and dependence. Consideration may be given as to 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 may be given as to whether the Schedule 2 entry for codeine should also be amended.

In addition to the well-recognised harms associated with inappropriate use of over the counter codeine that result from co-ingestion of non-steroidal anti-inflammatory drugs or paracetamol (such as gastrointestinal bleeding, renal impairment and hepatic injury) over the counter codeine is the prime local candidate for induction of medication overuse headache[1].

Medication overuse headache occurs in patients with preexisting headache disorders when they consume opioids on a regular basis. The diagnostic criteria for medication overuse headache indicate codeine use on as little as 10 days per month is sufficient to exacerbate underlying headache[2], thus patients are susceptible to this debilitating condition even when using codeine as per the pack recommendations (i.e. 3 days of use at recommended dose 4 x per month). World-wide medication overuse headache is believe to affect 1-2% of the general adult population[3-5], equating to roughly 380 000 Australians.

Medication overuse headche is a notoriously difficult condition to treat with extremely high relapse rates of up to 70% at 4 years[6]. In addition, medication overuse headache impacts considerably on the quality of life of affected individuals and imposes a large economic burden upon society. As with other forms of chronic headache, medication overuse headache inflicts high intangible costs upon sufferers, resulting from disruption of family lives and other relationships, impediment of social roles and career opportunities and a reduced sense of individual well-being[7-9]. The economic burden of medication overuse headache is a cumulative consequence of the direct expenses associated with utilization of health care resources and the indirect costs resulting from increased sick leave and reduce performance in the workplace. European data from 2011[10] indicates medication overuse headache costs approximately $4800 per patient per year, equating to a total cost of medication overuse headache up to roughly $1 824 000 000 in Australia each year.

For all over the counter medications the benefits must outweigh the associated risks. There is no documented evidence of additional analgesia when low dose (<30 mg) codeine is added to paracetamol in any pain state. There is no evidence of benefit in adding low dose codeine to ibuprofen in pain states such as migraine, tension type headache, back pain, period pain, osteoarthritis. The only evidence suggesting a modest potential benefit when low dose (<30 mg) codeine is added to ibuprofen results from a single study in patients with post-operative pain, and results were barely significant[11]. Post-operative pain is by default one of the few pain conditions that does not require an over-the-counter solution to ensure access to treatment as the patient will undoubtedly have access to a doctor or dentist during the procedure. If deemed appropriate the doctor/dentist could provide a prescription for codeine.

As evidence to support the efficacy of low dose codeine is lacking, while evidence of significant and costly harm is apparent, I support the proposal to reschedule codeine-containing analgesics to schedule 4.

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Current overuse of Schedule 3 analgesics containing codeine

The text below sets out my observations and opinions obtained as part of my job as an inspector with the [redacted] I visit hundreds of pharmacies annually.

Any views expressed below are mine and do not necessarily represent those of the Authority.

Over the decades, no drug has been shifted around the scheduling regime as much as codeine. Its control, in Australia at least, has long been a problem for governments. The most recent change took effect on 1 May 2010 when all non-prescription analgesics that contained codeine were placed in Schedule 3 and maximum pack sizes were introduced. The new arrangements were well publicised in both the professional and mainstream news media. Despite all of the rescheduling and regulation, problems of excessive consumption, abuse and morbidity, especially in recent years continue.[1,2] Thus, the codeine genie was let out of the bottle before the rescheduling.

In the 1970s, the Senate produced a report entitled: *Another side to the drug debate--a medicated society?* [3] If that were true then, it is truer now, having regard to the quantity of analgesics taken, whether by self-selection, pharmacist recommendation or medically prescribed. In respect of the latter, the consumption of narcotic analgesics for non-malignant pain has reached alarming levels.[4,5,6]

It is timely to review the situation.

In the course of my numerous inspections of Victorian pharmacies, I examine quantities of selected Schedule 3 products and ask pharmacists for their views on the present scheduling and regulatory arrangements for Schedule 3 codeine medicines.

I have formed the opinion that the initiatives (re-scheduling and pack size limitations) introduced in 2010 have had little impact on the consumption of codeine-containing medicines. I am told that sales figures have climbed back to the levels that existed when some of the products were in Schedule 2. It would be useful to obtain figures from the manufacturing industry.

Of the many products captured by the schedule entry, several stand out in terms of demand. These are:

- Ibuprofen 200 mg with codeine phosphate 12.8 mg (Nurofen Plus and Panafen Plus as well as a number of lesser known brands having the same amounts of actives.) These are available in pack sizes of 12, 15, 24, 30, with 30 being the maximum S3 pack size.
- Paracetamol 450 mg, codeine phosphate and doxylamine succinate 5 mg, represented mainly by Mersyndol. The pack has long been 20 tablets but a 40 tablet is also now on the market.
- Paracetamol 500 mg with codeine phosphate 15 mg, the best known brand being Panadeine Extra. This was only available in small packs but recently a 40 tablet pack has also been marketed.

There does not appear such a strong demand for paracetamol 500 mg with lesser doses of codeine phosphate, as exemplified by [redacted] This might be explained because the ibuprofen-codeine formulation does indeed provide superior analgesia and the public are “voting with their feet”. To the extent that analgesia can be measured objectively, it is only ibuprofen (400 mg) with codeine phosphate (25.6 mg) that has been shown to be superior to ibuprofen 400 mg, alone, using a dental pain model.[7,8]

One pharmacist said that people were asking for the combination product when, in many cases, either ibuprofen or paracetamol would be expected to suffice, subject to dose and frequency of administration. In the case of the older formulations, such as [redacted], there are no conclusive data to show that the presence of codeine phosphate makes or does not make a useful contribution to the analgesic action of paracetamol.[9] The longevity of this formulation might suggest that it provides superior analgesia to paracetamol alone.

Observations

My practice is to examine and record the quantity of stocks of the above dot-pointed products and if the quantity is large, to seek an explanation of why large amounts are held, especially if they are on display to the public, albeit behind the counter. For example, one northern suburbs pharmacy had about 500 packets of [redacted] another, larger, pharmacy, in the south eastern area stocked Nurofen Plus in the maximum pack only, being 30 tablets – the ethics of which are questionable. I conclude from these stock holdings that there is an unusually high demand and there is little supervision of the supply, much less a refusal, despite the obligations imposed under the regulations and good professional practice. Simply to record the sale, even if on a voluntary basis, does not reduce the problem of excessive demand and supply.

From comments made, about 80 percent of sales for the above formulations are made at the request of the purchaser and 20 percent on the pharmacist's initiative.

A large majority of pharmacists were of the opinion that the present controls were not working adequately, partly because it was very difficult for them to tell whether a person was lying and in such cases, purchasers knew what questions would be asked and how they should respond.

One and only one pharmacist said that the ibuprofen-codeine combination should be deregistered and a number have expressed the opinion that some or all of the products in question, most notably ibuprofen-codeine, should be transferred to Schedule 4.

Most, however, saw a need for a non-prescription codeine analgesic but with extra regulatory controls. Nearly all favoured compulsory recording on the computer, as with prescribed medicines, and proof of identity. There are no such requirements in Victoria at present, although earlier regulations required that Schedule 3 codeine-containing medicines could be supplied only if the purchaser was “known to the pharmacist”.[10] While recording the supply would alert pharmacists in the one pharmacy to excessive supplies or too frequent supplies to an individual, it would be of little assistance in stopping pharmacy-shopping. Of those favouring this initiative, nearly all said that it should be combined with a variant of the successful Project STOP for pseudoephedrine.

Project Stop

There are some practical problems with Project STOP, these being a slow response time (“clunkiness”) on the computer, the lack of real-time information and a website that could be more user-friendly. The time involved to most pharmacies already pressured by heavy dispensing loads and related work would be a burden if the present demand continued and if recording and the use of a modified Project STOP were required. The second problem with using Project STOP is an ethical one. Project STOP was designed to track sales of pseudoephedrine with the aim of detecting illicit manufacturing in clandestine laboratories to produce methylamphetamine. The data so obtained can be viewed by other pharmacists and the police. With codeine, there is no current evidence of its conversion to morphine or heroin and no potential offences on the part of the purchaser. The technology could be modified so that, in the case of codeine purchasers, transfer of data to the

police would be blocked.

Geographical and other issues

I am satisfied that some pharmacists are paying minimal if any regard to their legal and professional obligations. If they were, why would they keep hundreds of packets of these drugs in stock? There is also the intractable conflict that arises between foregoing revenue and ethics. This is reminiscent of the days when the bromureides were in Schedule Three until the 1970s when they were transferred to Schedule Four.

Also noticeable is that pharmacies in lower socio-economic areas - mainly outer suburban – appear to hold excessive stocks. I mention Narre Warren, Frankston South, Melton South, Fountain Gate, Pakenham and Broadmeadows as examples. Reasons given for the large sales were attributed to superior efficacy of ibuprofen with codeine , especially in migraine headache; relief of pain due to toothache, because of many people being unable to afford a visit to the dentist. Another reason is that in these areas, there are new housing developments with tradesmen suffering from sore backs and other muscular conditions.

For [redacted], it is thought that it is used as a night-time sedative, rather than for its analgesic properties. A packet of any of the above products is cheaper than alcohol.

As well the outer suburban areas mentioned above, there is heavy demand in some country towns, Shepparton and Bairnsdale being cases in point.

The outer suburban locality of Narre Warren (east of Dandenong,Victoria) must surely have the highest incidence of migraine in the country, judging by the quantity of [redacted] stocked at a warehouse style pharmacy.

There is a strong demand in the central business district of Melbourne for ibuprofen with codeine, but less in the well-established residential suburbs.

United Kingdom and New Zealand developments

All packs of “P” medicines sold in the United Kingdom must now state on the front of the main label in large font “Codeine is addictive” and state that the product is for three days use. In New Zealand, the same words are used but are printed in small type at the end of the text on the back of the packet. It is a moot point whether such a warning would make much or any difference.

Some Australian manufacturers are now using the United Kingdom text on their printed labels and others are providing stickers stating the same information.

Options

1. Do nothing.
2. Further reduce the pack size to 16 tablets.
3. Transfer all codeine-containing analgesics to Schedule 4, without any phase-in period to avoid stockpiling. The consequential effects on general practitioners and hospitals and costs to government (through Medicare) might be excessive and many patients with legitimate short-term needs are likely to be disadvantaged.
4. Leave in S3 and impose by regulation, an obligation to demand and obtain identification and record the supply.
5. As in 4 and add a modified version of Project STOP.

6. As in 2, and add 4 or 5.
7. See below – A way ahead?

In a sense, combining codeine with ibuprofen or paracetamol is analogous to cigarette smoking in that it is codeine and nicotine that gets you dependent and the tars and ibuprofen or paracetamol that cause damage in large doses.

If a person has persistent pain, they should be consulting their medical practitioner for a thorough examination and diagnosis, as the RASML statement affirms.

A way ahead?

In 1946, a regulation was made in Victoria that enabled certain prescription-only medicines to be made available for supply at the pharmacist's discretion, provided a prescription had been written initially by a medical practitioner.[11] In other words, there were no restrictions on the number of repeats. Each time the medicine was dispensed and recorded, the prescription would be stamped and endorsed with the date of supply and the prescription returned to the patient. Such an arrangement would not help in cases of pain when the patient could not see a doctor but if the present S3 pack size were further reduced to a maximum of 18 tablets (three days supply at the usual dosing schedule) and recorded in the pharmacy computer, a reduction in the current overuse might be possible.

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Three days ago I walked into my 'favourite' pharmacy. Usually, I would ask for my standard order. I'd be given the option of "generic or original?", I would select the "original" (as always) and then get the routine response of "no more than 6 a day - take with or after food - for short term use only" (that last one always cracks me up).

There's not many pharmacies that are *this* good, but there are definitely good ones out there. I've found that the best pharmacies have a mix of extended hours (requiring several pharmacists to be on staff), a busy store (more likely to have faster processes, such as no ID required) and the most important thing - a good solid culture of "cognitive liberty".

Three days ago I walked into my 'favourite' pharmacy. Three days ago I came to terms with how much I had let down my [redacted] and three days ago, my favourite pharmacy showed me just how wrong the systems of pain management and drug regulations really are.

For the last two years I have been dodging, hiding, manipulating and simply rorting the system of pharmacist-only pain medications, specifically Codeine, in the form of [redacted].

In the beginning, it started as a way to relax. To forget the stress of having two young children, a stressful job, renovating a home and the recent death of my father. During the first 12 months I regularly stopped taking it for periods at a time and convinced myself that I could stop whenever I wanted… but I never did...

What started as a weekend de-stressing routine, gradually turned into an "every-other-day" habit. I went from a few pills here and there, to multiple packets per week. Before I knew it, I was consuming a packet a day… and then *two* packets. By the time I was two years in I had formed a *massive* addiction. I was taking *at least* two packets a day (30 packs, not 24) and then up-to, and quite regularly, 3 or 4 packets a day (90 to 120 pills).

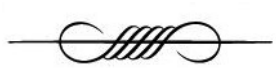
As my Codeine usage grew, so did my knowledge of how to get it. The logistics of supporting this kind of habit is almost a full-time job in itself and coupled with having quite a demanding full-time job already, I had to become quite efficient at sourcing it. Whilst I did try at some stages to use illegal methods of obtaining it, it was never my primary method. In fact, it was easier (and in most cases cheaper) to obtain it directly from a pharmacy.

I've thought long and hard about the decisions I've made over the last two years. I accept full responsibility for the position that I am in, and also the position I have placed others in, especially my family and friends.

My attitude towards both drug use and its legislation has changed a lot over the two years. I have tried to consider every argument for and against different forms of legislation and control, more so in the hope of finding a method that would have prevented, or at least stopped my addiction before it went as far as it did.

I understand that the issues are varied and the nuances of each one are not something I want to address here. What I do want to do, however, is provide at least some insight into the issues held by the existing controls.

Which gets me back to the pharmacy...



So three days ago I walked into my favourite pharmacy to start on a Methadone program. Deciding to start the program was one of the hardest decisions I have had to make, but in my mind it represents the ultimate step to curing my addiction. By choosing my 'favourite' pharmacy as for the location of the program I also felt that I was making a deliberate choice to step away from Codeine.

On my way to the pharmacy I was the most nervous I have been in a long time. I was nervous about the effects of the Methadone, I was nervous about the process of getting the Methadone and I was most nervous of how the pharmacist would react to my prescription.

Given the amount of times I have been to this pharmacy to purchase Nurofen Plus, I was pretty sure that I would be recognised. I was also sure (given the amount of Codeine I have purchased) that the pharmacist would join the dots and understand my addiction was the Codeine.

As I handed over the prescription, the look I got from the pharmacist was... well… blank. Whether I was recognised or not was hard to tell and his reaction to putting me on the program seemed mechanical. Honestly, I think I was hoping that seeing me take this step might make him think about the ease at which he hands the Codeine out. I guess I was hoping that the contradiction of requiring little or no reason for dolling pills out, then having to treat those same people with a Methadone program might spark some kind of moral obligation or emotion.

If it did or not, I couldn't initially tell, until another customer walked in. As I had finished signing the rules of the Methadone program, a middle aged man walked up to the prescription counter. The pharmacist left me to attend to the man…

"A 30 pack of [redacted] please."

"Generic or original?"

"Original please."

"Okay - No more than 6 a day - take with or after food - for short term use only..."

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May 6th 2015

The Secretary
Advisory Committee on Medicines Scheduling

To the Secretary,

I write to encourage the rescheduling of low-dose codeine to prescription-only status in Australia.

By way of introduction, I am a physician and Professor of Medicine, Pediatrics and Health Policy at the [redacted] where I am the Head of the Division of Clinical Pharmacology and Toxicology. I am a specialist in Internal Medicine, Clinical Pharmacology and Medical Toxicology, and previously worked for 5 years as a pharmacist. I maintain an active research program in drug safety, and since 2009, my colleagues and I have published more than 20 articles related to the harms caused by opioids.

The sale of codeine at any dose without a prescription is a dangerous practice. In Canada, codeine has been sold this way for decades, and I have seen the resultant harms firsthand. While I understand the importance of pain and the desire of patients for ready access to analgesics, I believe there are several reasons why this practice should be discouraged. In the interest of brevity and keeping your attention, I will focus on two.

1. To impart analgesia, codeine must be converted to morphine

Codeine itself is not an analgesic. It is a pro-drug metabolized to morphine by the liver. The extent of this conversion varies dramatically among individuals. Some subjects (about 7%) make no morphine, but most do, and some are genetically capable of making quite a lot. The key point here is that <u>when a patient consumes a known amount of codeine, what they are really taking is unknown amount of morphine</u>.

As you consider the rescheduling of codeine, I urge you to reframe the question slightly and ask whether the availability of morphine without prescription is in the public interest. With respect, if you do not frame it this way, you will not be taking the pharmacology of codeine into account.

2. Codeine is prone to misuse

Because most people do convert some codeine into morphine, the potential exists for misuse and even addiction. In this way, it is not wrong to consider codeine a "gateway" drug. Over the years I have cared for patients whose addiction began with OTC codeine, and many more with acetaminophen toxicity as a consequence of unchecked consumption of nonprescription codeine combined with paracetamol.

Many patients take codeine for a seemingly legitimate reason, but find the drug pleasurable and begin taking it in larger amounts, later "graduating" to prescription opioids. This is not a trivial consideration. In the United States, the CDC estimates that 175,000 people have died of opioid-related causes between 1999 and 2013, to make no mention of those whose lives have been harm by dependence and addiction. By definition, each of these patients had a "first exposure" to opioids. A key step in the mitigation of this epidemic is reducing first-time exposure to opioids at the population level. Maintaining the nonprescription status of codeine would have exactly the opposite effect. This point should not be lost on Australia, which is already grappling with the growing consequences of opioid overuse.

In summary, codeine is pharmacologically irrational, and should be viewed as morphine for the purposes of regulatory decisions. At low doses it is a poor analgesic, even when combined with paracetamol. Nonprescription codeine compounds lead an unknown number of patients to problematic opioid use and acetaminophen toxicity. On balance, the risks of these products outweigh their benefits, thereby violating a fundamental tenet of therapeutics. However, this point is not likely to be considered by patients who simply seek relief from pain without having to visit the doctor. In virtually every instance, however, these patients are better off without ready access to codeine.

I offer my enthusiastic support to the rescheduling of these products. Not only will Australians be better off if this transpires, but other countries such as Canada may be pressured to make a similar move.

Sincerely,

Over the counter codeine abuse

I am an Addiction Medicine Nurse with 13 years experience working as a Clinical Nurse Consultant. My role has been to provide a consultation and liaison service for patients presenting to hospital and in community health with alcohol and other drug presentations. This has included working for [redacted] and currently in rural Victoria working in a [redacted] providing alcohol and other drug support to four hospitals.

Abuse of over the counter codeine preparations continues to be a problem. In the hospitals it is mostly related to the abuse of [redacted] resulting in bleeding from perforated gastric or duodenal ulcers and hypokalaemia.

There were several cases at [redacted] diagnosed with hypokalaemia as a result of [redacted] abuse. This often meant an admission to the Intensive Care Unit (ICU) as the potassium levels took 2-3 days to stabilise. One of the recommendations made by The Addiction Medicine Unit was for these patients to be reviewed by ICU when presenting to the ED with hypokalaemia. Monitoring and care in ICU is necessary because hypokalaemia creates a risk of cardiac arrhythmia (potentially fatal irregularities of the heart rhythm) that can cause sudden death.

Many patients understate, deny or conceal their high dose misuse of Nurofen Plus when presenting to hospital. On one occasion I recognised a patient in the Emergency Department (ED) who had been previously seen by our service for [redacted] dependence. I noted this presentation was for gastric pain. I approached the Doctor looking after her and asked if he would like me to see his patient. He informed me that she was not abusing Nurofen Plus and that I probably did not need to see her. This young woman was understating her use and was actually taking up to 30 tablets of [redacted] a day. She was well presented and in full time employment. She had commenced taking these for period pain and headaches stating that she liked the way the medication made her feel and continued taking them on a regular basis.

It is probable that in hospitals we are just seeing "The tip of the iceberg." There may be many more people in the community that abuse over the counter codeine who have not presented to hospital and some who have presented to hospital whose diagnosis of [redacted] abuse is being missed because they do not offer information about their misuse of [redacted], or conceal or even deny this misuse.

Most of the patients presenting with serious side effects from [redacted] did not abuse alcohol or other drugs. These are members of the community who had found themselves taking Nurofen Plus for a medical condition and continued to take it, requiring more and more of it to obtain the desired effect. This resulted in them becoming dependent on the codeine and suffering life threatening side effects from taking large doses of ibuprofen. To maintain their increasing use of [redacted] it became necessary to visit multiple pharmacies to obtain their medications. Some people then become so sick and tired of visiting multiple pharmacies that it became a reason for them to seek help.

Since working in rural Victoria in a [redacted] there have been several cases of [redacted] abuse. These have been clients seeking support for alcohol or other drug dependence. None of the clients identified [redacted] as being a drug of dependence. The clients had been referred to our service for counselling and were seen by me for a medical review. It was during these interviews that their Mersyndol abuse was uncovered.

Case Study

- **40 year old single mother of 4 children who commenced using [redacted] 10 years ago when a friend told her they were good for headaches.**
- **Cannabis use - 1-2 grams Cannabis daily**
- **Amphetamine type substances - 1-2 times a week - Intravenous use**
- **[redacted] - takes 5-10 tablets at a time - takes these mostly at night to help her sleep and increases her use if she is "Running low on cannabis." She obtains these from a local pharmacy and as there are only 2 pharmacies where she lives, she travels to Melbourne visiting several pharmacies to maintain her supply. She states she feels ashamed and hates going to multiple pharmacies to obtain her Mersyndol.**
- **She went to Melbourne recently with 2 of her teenage children. During this visit her children would not let her stop at any pharmacies to purchase Mersyndol.**
- **She is now banned from one pharmacy where she lives. The pharmacy had requested a letter from her GP stating a medical reason for her continuing need to purchase multiple boxes of Mersyndol. She chose not to ask her GP for this.**
- **She admitted giving her 16 year old daughter [redacted] to manage her anxiety.**
- **The GP is not aware of her [redacted] abuse.**
- **She has justified the use of [redacted] as the medication is marketed for "Pain relief and its calming effect".**

Interviews with local pharmacies about misuse of over the counter codeine

Several rural pharmacies were visited. There were no more than 2 pharmacies in each area visited.

The pharmacists were initially quite guarded in their response but most stated they always recorded the customer's name and warned them of the side effects when not taken as directed. I reassured them that I was not there to accuse them of not selling this product responsibly, but to see if they encountered a problem with customers purchasing multiple boxes of [redacted] and [redacted].

The pharmacists reported continued abuse of both [redacted] and [redacted]. They encountered disgruntled customers who did not like being asked to leave their details and have information given to them about the safe use of these medications. Others reported seeing the same customers when working at other pharmacies. One pharmacist who had requested a GP letter for the continued use of one of these medications had been told by a locum GP that he would not be writing a letter as it was only an over the counter medication. Other customers

would not go to their GP but would go to another pharmacy to obtain these medications. Empty packets of [redacted] and [redacted] were also found outside one pharmacy.

In conclusion, unmonitored use of over the counter codeine can potentially have life threatening side effects, when combined with ibuprofen or paracetamol. The opioid dependence drives the need to take more and more of the medication in excessive doses to achieve the desired effect. Even with the monitoring of this medication by pharmacists, abuse of this medication continues to be a problem. Rescheduling of over the counter codeine preparations from a schedule 3 to a schedule 4 would result in these medications being prescribed by a GP for a specific medical condition in a limited quantity thus reducing the risk of codeine dependence and toxicity from excessive doses of ibuprofen and paracetamol.

[redacted]

[redacted]

12/05/2015

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14 May 2015

The Secretary,
Scheduling Secretariat
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Email: Medicines.Scheduling@tga.gov.au

Dear Sir or Madam,

Notice inviting public submission under Reg 42ZCZK of the Therapeutic Goods Regulations 1990: Schdeuling proposals to be considered at the ACMS Meeting, July 2015

Please find RB's response to the Consultation: Invitation for public comment – ACMS meeting July 2015 issued by the TGA on 2 April 2015. The TGA is seeking comments from interested parties on the following proposed amendments to the Poisons Standard referred by the Delegate for scheduling advice:

Substance: Codeine

Proposal:

To delete the Schedule 3 entry for codeine, and reschedule the current Schedule 3 codeine entry to Schedule 4 due to potential issues of morbidity, toxicity and dependence.

Consideration may be given as to whether all current Schedule 3 preparations should be rescheduled to Schedule 4, or whether any rescheduling should only apply to combination analgesics products containing codeine.

Consideration may be given as to whether the Schedule 2 entry for codeine should also be amended.

Issue: Potential abuse/misuse of codeine-ibuprofen combination products in general

Overview

RB is the manufacturer of Nurofen Plus, an ibuprofen-codeine combination. RB acknowledges that there have been case reports of adverse outcomes from misuse of OTC codeine containing analgesics with excessive consumption linked to codeine dependence. OTC misuse can be defined as the use of OTC medicines for a genuine medical reason but in an incorrect manner in terms of dosage or duration.

In this submission RB contends that, while recognising the genuine concern of some in the medical profession, and in the community over misuse and/or abuse of OTC codeine combination products, the incidences are very low. We are not aware of robust 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. The majority of case reports were published between 2010 and 2011. RB notes that OTC codeine combinations were re-scheduled to Schedule 3 in 2010. At the same time pack-sizes were limited to 5 days' supply. Again, we are not aware of an increased incidence of adverse events since this time. To RB's knowledge there is no published/validated evidence that adverse outcomes following misuse or addiction are widespread or that these events occur when people use these medicines as directed.

RB acknowledges that there is a low level of misuse and abuse of codeine combination analgesic products in the community, which is clearly unwelcome and RB acknowledges that more needs to be done to reduce any misuse or abuse that does occur. Careful consideration needs to be given to specific measures to reduce the incidence further rather than transferring the problem. Such measures could include additional warnings on pack regarding the potential for addiction. RB currently over-sticker packs to include such statements voluntary and work with the support of Pharmacists in their broader educational programs. 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.

1. OTC Codeine-containing analgesics – the current situation

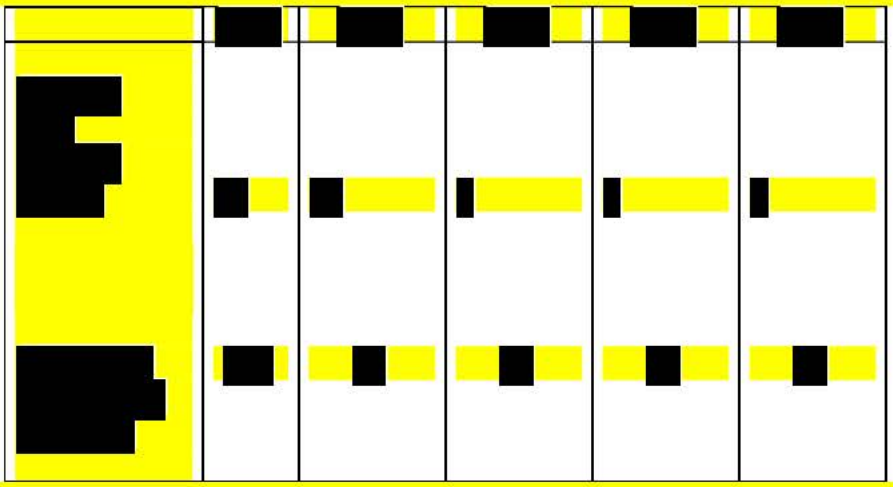
OTC codeine-analgesic combinations, including Nurofen Plus, were developed to give thousands of people world-wide significant relief from strong pain, over and above the use of a single analgesic active alone, without a visit to the doctor. It is longstanding Australian Government and medical professional policy to have a well-educated community with the knowledge to self-select for their health needs, including pain relief, without a prescription from the doctor.

Currently OTC codeine-combination analgesics are only available behind the counter in pharmacy after mandatory consultation with a pharmacist. As a Pharmacist Only (S3) medicine, pharmacists are required to determine whether it is appropriate to supply codeine containing analgesics. They are required to assist the consumer with appropriate product selection and recommend an alternative analgesic option where necessary. Pharmacists are highly trained professionals to assist consumers make the appropriate choice for medicines.

It is also important to note that currently pack sizes are limited to five days' supply. This means that a single pack cannot, on its own create a physiological dependency. For dependency to occur, a consumer must interact repeatedly with a pharmacist if more pain relief is needed. The pharmacist is ideally placed to advise the consumer and refer them to a GP or pain clinic for further management.

RB therefore conclude that the current scheduling of codeine analgesic combinations is appropriate. Rescheduling would not provide any tangible benefits but would result in disadvantages to consumers and increased economic burden.

[redacted]



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3. Assessing relative risks

The risks associated with abuse of codeine combination medicines need to evaluated from a risk/benefit perspective against other substances of abuse to provide a true estimate of risk to the wider community, rather than to a smaller population who already abuse other substances.

A change in scheduling of codeine combination medicines would deny access to proven community pain relievers for the vast majority to 'protect' a very small minority who, often due to their addictive personality and pattern of substance abuse, expose themselves to potential harm.

One of the impacts of rescheduling to Schedule 4 is an increase in consumers visiting Doctors. Doctors' visits, apart from being costly to the community, also usually involve time away from work and loss of productivity for the individual. If pain relief is not adequate, acute pain can have a very negative impact on the life of a consumer and their family. Those using codeine-combinations appropriately will be disadvantaged and there will be unnecessary burdens on the healthcare systems. RB are aware that ASMI have data to show the likely economic impacts and that they will be including this in their submission on this matter.

3.1 Proposed actions to reduce risks

Even though RB believes that the level of abuse/misuse of codeine-containing analgesics is currently very small, we acknowledge the genuine concern among a number of healthcare professionals and the wider community.

The PSA has recently launched new resources for pharmacists to assist them to provide counselling to consumers seeking to manage pain and addiction issues. We feel that time is needed for these initiatives to show their full benefit.

RB believes the best patient outcomes will depend on a collaborative approach rather than problem shifting. RB therefore will work closely with pharmacists, The Pharmacy Guild, the Pharmaceutical Society of Australia (PSA) and other stakeholders to put measures in place to minimise the risk of abuse/misuse. Consistent with our ethics as a responsible manufacturer our position is as follows

- Collaborative educational programs to maintain high levels of awareness amongst pharmacists and consumers about the appropriate use of codeine-combination analgesics to reduce the risk of misuse and abuse.

- RB supports a real-time monitoring system coupled with pharmacist training, guidelines and protocols, to allow pharmacists to detect consumers who may be purchasing large quantities of codeine-combination analgesics, and refer them to a GP or pain clinic for intervention.

- RB do not oppose a reduction in pack size to 3 days for OTC codeine containing analgesics, consistent analgesics, consistent with UK pack size and front of pack labeling statement which states a 3 day duration of use.

4. Conclusions and Recommendations

In the absence of compelling validated community incidence data demonstrating an increased risk from codeine analgesic combinations and with consideration of the risk/benefit profile to the Australian community, RB recommends:

- That the current scheduling for OTC ibuprofen-codeine combination products remain as S3;
- RB will work with relevant stakeholders (e.g. pharmacists, the PG, PSA) to ensure that this category of medicine can be used appropriately with the maximum benefit to the wider community in terms of short term, accessible relief for strong pain; and
- RB Support additional warnings on pack in relation to the potential for codeine addiction and we do not oppose a reduction in pack size, consistent with UK pack size and statements.

Yours sincerely,

[redacted]

[redacted]

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14 May 2015

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Dear Sir or Madam,

Notice inviting public submissions under Reg 42ZCZK of the *Therapeutic Goods Regulations* 1990 Scheduling proposals to be considered at the ACMS Meeting, July 2015

We refer to the notice inviting public comment under Regulation 42ZCZK of the *Therapeutic Goods Regulations* and would like to provide comment on some of the scheduling proposals that will be referred to the July 2015 meeting of the ACMS.

ASMI (Australian Self Medication Industry) is the peak body representing companies involved in the manufacture and distribution of consumer health care products (non-prescription medicines) in Australia. ASMI also represents related businesses providing support services to manufacturers, including advertising, public relations, legal, statistical and regulatory consultants.

ASMI appreciates the opportunity to provide public comment in relation to ACMS agenda scheduling proposals. We wish to address relevant matters under section 52E of the *Therapeutic Goods Act* 1989.

Please find enclosed, under cover of this letter, ASMI's comments in relation to the following scheduling proposal that will be considered by the ACMS at the July 2015 meeting:

Codeine

To delete the Schedule 3 entry for codeine, and reschedule the current Schedule 3 codeine entry to Schedule 4 due to potential issues of morbidity, toxicity and dependence.

Consideration may be given as to 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 may be given as to whether the Schedule 2 entry for codeine should also be amended

Comment is presented as a separate attachment.

As an industry representative, ASMI is a key stakeholder in scheduling matters and we are keen to provide further input as required. We look forward to the Delegate's interim decisions and greater detail on the final scheduling proposals.

Please contact me should you require any further clarification relating to this submission.

Yours sincerely,

[redacted]

Agenda item 1 - Codeine

Proposal to delete the Schedule 3 entry for codeine, and reschedule the current Schedule 3 codeine entry to Schedule 4 due to potential issues of morbidity, toxicity and dependence.

Consideration may be given as to 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 may be given as to whether the Schedule 2 entry for codeine should also be amended

ASMI Comment

Background

ASMI acknowledges that there have been case reports of adverse outcomes in some patients when excessive amounts of OTC codeine containing analgesics have been consumed as a result of codeine dependence. These reports have been published over the past several years, with the majority of case reports published between 2010 to 2011.

ASMI assumes that it is these issues that have prompted the above re-scheduling proposal and notes that no information has been provided to stakeholders or respondents on the nature of the evidence provided to the ACMS.

For the purposes of this submission, ASMI has assumed that the re-scheduling proposal is based on these reports of morbidity and rare cases of mortality following misuse and abuse of codeine containing analgesics.

At the outset it should be noted that the majority of people who use OTC codeine containing analgesics and cough and cold products do so responsibly and appropriately and there has been no evidence provided that adverse outcomes following misuse or addiction are widespread problems, or that these problems can occur with short term use as per the labelling instructions.

Following re-scheduling to Schedule 3 in 2010 following a decision on scheduling by the NDPSC, OTC pack sizes of OTC codeine containing analgesics have been limited to 5 days' supply. A 5 day pack size cannot on its own instigate dependence and it is excessive duration of use and dose escalation which may predispose to dependence. Repeat purchases are needed for this to occur.

ASMI acknowledges that misuse and addiction are serious problems especially for the individuals affected and the healthcare professionals treating them. These concerns warrant special attention from healthcare professionals, pharmacists and industry and a range of measures that mitigate risk should be adopted. These include labelling and tracking mechanisms, as detailed further in this submission.

ASMI notes that the proposal currently before the ACMS also includes cough and cold products for which ASMI can find no evidence of harm, misuse or abuse and for this part of the proposal there is no apparent rationale for any re-scheduling, other than the presence of codeine in the formulations.

ASMI has no understanding of the basis for proposals to re-schedule cough and cold products containing codeine and to ASMI's knowledge there have been no reports of adverse outcomes or abuse of codeine containing cough and cold products. The proposal to reschedule cough and cold products will be addressed below in a separate section.

ASMI believes that the current scheduling of codeine containing analgesics and cough and cold medicines is appropriate; that there are unintended and possibly costly consequences to re-scheduling and that there are many other measures that can be implemented to curb addiction and misuse.

1. OTC Codeine Containing Analgesics

Nature of the problem

ASMI understands that the issues which have prompted the re-scheduling proposal are the various harms associated with misuse due to dependence on codeine containing analgesics.

ASMI is aware of the publications of Australian case reports in the literature of gastrointestinal harm,[1,2,3] renal effects,[2] hypokalaemia associated with dependence or misuse of codeine containing analgesics,[2,4,5,6] noting that the majority of the cases occurred between 2005 to 2008 which is before the NDPSC recommended smaller pack sizes and re-scheduling of these products to Schedule 3, implemented in May 2010.

For the purposes of this submission ASMI does not intend to review or reiterate the adverse events and morbidity that have been reported as a result of dependence on codeine containing analgesics. We acknowledge the harm that can occur with misuse or abuse of codeine containing analgesics and this is not disputed.

In providing comments to the scheduling proposal, the following relevant questions will be addressed in this submission:

- whether re-scheduling codeine containing analgesics to Schedule 4 (S4) is the most appropriate way of minimising harm from misuse or dependence
- what activities are currently being undertaken to address concerns around misuse, abuse and dependence
- what further actions can be taken to mitigate risks towards consumers who are most at risk while allowing access for responsible users, i.e. a risk based approach

[1] Dutch M. Nurofen Plus misuse: an emerging cause of perforated gastric ulcer. MJA 2008; 188(1):56-7
[2] Frei M et al. Serious morbidity associated with misuse of over-the-counter codeine-ibuprofen analgesics: a series of 27 cases. MJA 2010; 193(5):294-6
[3] McDonogh M. Misuse of codeine-containing combination analgesics. MJA 2011; 194(9):486
[4] Ernest D, Chia M, Corallo C. Profound hypokalaemia due to Nurofen Plus and Red Bull misuse. Crit Care Resusc. 2010; 12(2):109-10
[5] Page C et al. Life threatening hypokalaemia associated with ibuprofen-induced renal tubular acidosis. MJA 2011; 194(11):614
[6] Ng J et al. Life-threatening hypokalaemia associated with ibuprofen-induced renal tubular acidosis. MJA 2011; 194(6): 313-6

- whether cough and cold products are part of any problems relating to abuse, misuse or dependence

Evidence of low prevalence of misuse, abuse, dependence

Following the June 2009 meeting of the NDPSC, OTC codeine containing analgesics were re-scheduled from Schedule 2 to Schedule 3 and changes were made to pack sizes, limiting the supply of OTC codeine containing analgesics to 5 days. At that meeting, no changes were made to the scheduling of OTC cold and flu products containing codeine, however pack sizes were limited to 6 days' supply. These changes were implemented in May 2010.

Published articles on the issue of harm resulting from OTC codeine containing analgesics consistently refer back to the case reports that were documented between 2005 – 2008 and reported by Frei (2010)[2], McAvoy et al (2011)[7], McDonough (2011)[3], Robinson et al (2010)[8], Dutch (2008)[1] and Ernest et al (2010)[4], noting that some of these reports pertain to single case reports only and some include New Zealand reports.

Most published literature from 2011 onwards relates back to the 2005 – 2008 case reports that were published in 2010 and 2011 referred to above. There appear to be fewer case reports published in the literature from 2011 onwards. ASMI is not suggesting that this indicates that there were no reports of harm and anticipates that there may be some unpublished reports. However, this information, together with sales data and the activities being undertaken by pharmacists, indicates that the number of cases in Australian and New Zealand are very small in relation to the sales of the products concerned. The regulatory actions of 2010 together with increased awareness among pharmacists as well as consumers may already be having a positive impact.

ASMI does not have access to unpublished data or hospital records on reports of harm since access to codeine containing analgesics was tightened post - 2010. The TGA Database of Adverse Event Reports (DAEN) lists 50 cases of abuse/dependence/misuse since 2010, and we believe that this figure includes the cases detailed in the literature.

Given the large number of people using these products and the volume of sales, adverse events such as dependence and misuse or abuse are low in comparison and the vast majority of people use these products appropriately. Separate submissions from ASMI members will provide detail on sales volumes and usage.

It is crucial that any decisions on scheduling that have the potential for increased costs and other unintended consequences are based on strong recent evidence rather than evidence from pre-2010.

Sales and Marketing data

An ASMI member company has provided some Australian sales data for OTC codeine containing analgesics. The detail of this data will be provided confidentially by the relevant member in their respective submission however ASMI can provide the following general information:

[7] McAvoy BR, Dobbin MDH, Tobin CL. Over-the-counter codeine - misuse and harm in Australia and New Zealand. *N Z Med J* 2011; 124: 29-33.

[8] Robinson GM, Robinson S, McCarthy P et al. Misuse of over-the-counter codeine-containing analgesics: dependence and other adverse effects. N Z Med J 2010; 123:59-64.

- There has been an overall reduction in sales of OTC ibuprofen and codeine / OTC paracetamol + codeine containing analgesics between 2009 and 2014 (based on IMS data, which monitors supply through warehouse to pharmacies)
- Sales of ibuprofen plus codeine continue to show downward trends since 2010, with sales of paracetamol plus codeine having dropped then plateaued (IMS data)
- Sales of single ingredient non-codeine containing analgesics (paracetamol or ibuprofen) have been slightly increasing during this time, suggesting substitution of non-codeine containing analgesics

This information, which will be expanded upon by the sponsor(s) concerned, indicates that the scheduling amendments implemented in 2010 have been having an impact and there have been gradual shifts in sales of analgesics since then.

Potential consequences of rescheduling OTC codeine containing analgesics to Schedule 4

It is acknowledged that pharmaceutical drug misuse in Australia is a complex and emotive issue and a number of strategies that involve all stakeholders will be needed to help address problems of abuse or misuse. Stakeholders include consumers, pharmacists, GPs as well as specialists in the field of pain management.

ASMI does not believe that rescheduling all OTC codeine containing analgesics to Schedule 4 represents a neat, simple solution to the problems described. Although it is difficult to predict the exact impact of any up-scheduling of OTC codeine containing analgesics to Schedule 4, it is likely that there will be consequences that will have significant impact on consumers as well as pharmacists and medical practitioners, mainly busy GPs.

Below are some potential consequences and concerns that may arise as a result of up-scheduling:

- A Schedule 4 entry is no guarantee against misuse or abuse. Misuse and abuse of prescription opiate and psychoactive drugs has escalated significantly over the past several years[9].
- When patients visit a doctor, there exists a risk that they may be prescribed a higher strength opiate (either single ingredient or combination) by the medical practitioner, as many patients will indicate that single ingredient painkillers are inadequate for treating their pain. Some doctors may prescribe the 30 mg codeine (Forte) combination analgesics or other stronger PBS listed medicines which are commonly prescribed for acute pain conditions, e.g. dental pain, some back pain and injuries – as both the high strength and low strength codeine combination products will be in the same schedule. Prescribing of higher strength opiates may carry even higher risks to some consumers as they have a greater potential for addiction compared to the lower dose codeine analgesics.
- Even if a GP does not prescribe a higher strength opiate, a larger quantity of the lower strength (currently OTC) codeine containing analgesic (e.g. 30 or 50 pack) will be prescribed together with repeats if the doctor judges that the user is legitimate. This may predispose to more harm than the scenario where a patient must present to the pharmacy on repeated

[9] Dobbin M. Pharmaceutical drug misuse in Australia. Australian Prescriber 2014; 37(3):79-81

occasions to buy smaller quantities, particularly if an effective real time monitoring system is introduced.

- GPs will be seeing patients who would otherwise be seeing a pharmacist. There will be an attendant increase in healthcare costs due to Medicare consultations, a budgetary area which is currently under strain and patients will also bear the cost of additional patient co-payments. Consumer behaviour research shows that consumers will go to their doctor if they cannot access their medicine from their pharmacist, with 62% indicating they would visit their GP or a medical centre, and 3% of these patients indicating that they would go to an Emergency Department[10].

- It is foreseeable that additional pressure will be placed on GPs / Medical Centres / Emergency Departments who may not have the time and resources to adequately deal with the significant increase in consultations. Some codeine containing combination analgesics are on the PBS, so it is likely that costs will shift from OTC purchase to PBS subsidised purchases, adding further to costs to the government.

- Should non-PBS OTC codeine combination analgesics be up-scheduled, patients will require a private prescription so the cost of the medicine to patients will also increase significantly.

- There are no mechanisms for prescription monitoring and doctor-shopping monitoring for patients who have addiction and misuse problems. Therefore the problems will in all likelihood continue unnoticed until harm occurs. Effective and frequent monitoring of purchases is the key to identifying excessive and inappropriate use, and the pharmacy is the most appropriate avenue for this to occur.

Undermining trust in pharmacists

As a Pharmacist Only (S3) medicine, pharmacists are required to be involved with each product request to determine whether it is appropriate to supply an OTC analgesic containing codeine. They are required to assist the consumer with appropriate product selection, counsel on appropriate use and to recommend an alternative analgesic option where it is warranted.

Pharmacists are highly trusted to appropriately advise on S3 medicines and have professional practice standards and guidelines to enable them to fulfil this role. Pharmacists are increasingly being seen as experts in medication management and are taking on extra responsibilities with medication reviews, advice on medicines and other services. They support the principles of Quality Use of Medicines (QUM) and follow competency and quality standards as part of their practice.

ASMI believes that the majority of users of codeine containing analgesics use the products responsibly. Pharmacists have recently implemented further activities in the area of risk mitigation with the use of cautionary & advisory labels as detailed in the new edition of the Australian Pharmaceutical Formulary (APF 23)[11], consumer information leaflets and updated pharmacist training. This indicates that pharmacists are aware of concerns around addiction and are updating and revising their practices in response to this.

Up-scheduling codeine containing analgesics to S4 may be seen to undermine trust in pharmacists and imply that pharmacists have not managed this category sufficiently, despite the fact that the

[10] Macquarie University Centre for the Health Economy (MUCHE). Consumer Behaviour Fact Book – Understanding consumers' use and attitudes towards OTC medicines, vitamins, minerals and supplements. March 2015

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

majority of users of these products do so appropriately and pharmacists have demonstrated commitment to education, consumer awareness and quality care frameworks over many years.

Likelihood of increased costs to patients and the health system

If OTC codeine-containing analgesics are rescheduled then legitimate users of the products will be inconvenienced and out-of-pocket as they will have to do to their doctor to obtain a prescription for the product. Both consumers and the healthcare system will be unnecessarily burdened.

ASMI approached the Macquarie University Centre for the Health Economy (MUCHE)[10] for some research into the economic value of OTC medicines, and as part of this an economic analysis of the impact of up-scheduling of S3 analgesics was conducted, with the following findings:

"Faced with the scenario of their Schedule 3 (S3) Pharmacist Only analgesics no longer being available over-the-counter at their local pharmacy, the research indicates that adult consumers would go to their doctor to continue to access their preferred medication. Only about a quarter would use an OTC alternative. If Pharmacist Only analgesics were up-scheduled to prescription only the cost to the system would be considerable. Currently, these medicines make up 22% of the volume of analgesics sold in pharmacies, so the decision to up-schedule would cost $675 million. Of this, almost $170 million is the direct cost to Medicare for additional doctors' visits, $25 million is borne by insurance companies and $70 million will be paid by individual consumers. The indirect costs of lost productivity and delayed treatment are over $400 million."

The vast majority of responsible users will be inconvenienced and there will be increased costs to the healthcare system with any rescheduling.

ASMI believes that targeted approaches and interventions to identify and assist people at risk of misusing or abusing the products are the most appropriate solution to the problems and pharmacists have a crucial role to play in this respect. Addiction is a medical problem that requires specialist care, however not all users are addicts and up-scheduling these products gives the implication that the majority of users are not using the products appropriately.

Activities currently being undertaken to address concerns of misuse, abuse and dependence

Labelling

During 2009, Medsafe made a decision requiring sponsors of OTC codeine containing products to include a statement regarding duration of use and risk of addiction on the back of pack labelling of affected products -

"*Do not use for more than 3 days. Codeine is an addictive substance."*

Many sponsors of Australian products also included this statement on their harmonised packs, even though the TGA has not made any changes to RASML requiring updated warning statements.

Some ASMI member companies have started to voluntarily apply front of pack warning statements similar to the above statement, not only as a means of raising awareness and educating consumers but also as a way of enabling pharmacists to counsel patients in a non-confrontational way.

ASMI supports the use of front-of-pack warning statements, and for these warning statements to be applied to branded as well as private label products. These warnings mirror those used in the UK where these combination products remain available without a prescription as Pharmacy Medicines.

Pharmacy Initiatives to address the problems associated with abuse, misuse and dependence

Pharmacists are required to be involved in every sale of a Schedule 3 medicine. ASMI believes that pharmacists have an important role to play in minimising inappropriate use of OTC medicines and The Pharmaceutical Society of Australia (PSA) and the Pharmacy Guild of Australia (PGA) have been undertaking educational activities and training for pharmacists not only to raise awareness but to assist them in identifying people misusing OTC codeine containing analgesics.

A PSA Guidance for provision of S3 combination analgesics containing codeine (updated 2015) has been in place, providing pharmacists with guidance in assessing patient needs including when to refer, selecting and making the appropriate recommendation, provision of counselling including written information as well as identifying conditions for which codeine containing analgesics may not be appropriate.

The latest edition of the Australian Pharmaceutical Formulary and Handbook (APF 23)[11] includes a new section on OTC codeine containing analgesics with new consumer information leaflets and a new Cautionary and Advisory label sticker for pharmacists to include on the front of pack. These initiatives have been complemented by further information and continuing professional education for pharmacists.

ASMI believes that the above initiatives of the PSA, which have been implemented relatively recently are a step in the right direction and pharmacists should be given time to fully implement these practices and assess their success before any changes to scheduling are contemplated.

ASMI Member Initiatives

The issue of misuse and addiction to OTC codeine-containing analgesics is an issue which the self care industry takes very seriously. Medicines should always be used as directed.

ASMI and its members work closely with the pharmacy profession to maintain high levels of awareness amongst pharmacists and consumers about the appropriate use of these products.

As mentioned above, some ASMI members have voluntarily introduced prominent front of pack warning statements on product labelling, modelled on the mandatory UK front of pack labelling which the MHRA introduced in 2009. The wording states “Can cause addiction. Do not use for more than 3 days”. The effectiveness of front of pack labelling will be increased if this is extended across all products including house brands and generic / private label brands.

ASMI member companies have also been active in providing educational programs for healthcare professionals, including CPD modules for pharmacists to assist with quality use of medicines in the supply of OTC codeine containing an analgesics.

<u>Further actions that can be taken to mitigate risk</u>

Any Initiatives undertaken should serve to both detect people who may be currently misusing the products as well as educate and monitor current and future users to prevent them from exceeding the recommended dose or taking the products for longer than necessary.

In addition to the mandatory introduction of front of pack warnings, further actions that should be considered include:

- A real-time monitoring system coupled with pharmacist training, guidelines and protocols, to allow pharmacists to identify consumers if they begin to purchase inappropriate quantities of codeine-combination analgesics, and refer them to a GP or

pain clinic for intervention. A modified Project STOP system currently in use for pseudoephedrine may be suitable.

- Full implementation, by the PSA and/or other pharmacy bodies, of a program to equip pharmacists with the information they need to counsel and educate consumers about the appropriate use of codeine containing analgesics as well as related topics such as management of chronic pain, identification and management of medication overuse headache, accompanying mental health concerns such as anxiety and insomnia which can also lead to problematic use.
- Improved collaboration between pharmacists, doctors and other services to assist people with these concerns.
- Improved consumer education and updating of the Product Information and Consumer Medicine Information to include information on the risk of addiction when the dose or recommended duration of use are exceeded.

As outlined previously limiting the pack size to 5 days was implemented to effectively mitigate the risk of dependence, however ASMI would consider a reduction in pack size to 3 days for OTC codeine containing analgesics.

2. Codeine containing cough, cold & flu products

Cough and cold products that contain codeine typically also contain a decongestant such as phenylephrine / pseudoephedrine in addition to a non-opiate analgesic such as paracetamol. The product indications include pain however this is always in the context of, or associated with cold and flu symptoms. These medicines should not be confused with or classed as analgesics.

The NDPSC considered the scheduling of cough and cold products that contain codeine in 2009, and a decision was made that the scheduling was appropriate and should not be changed, as there was no evidence that misuse of cough and cold medicines containing codeine was occurring. A pack size limit of 6 days' supply was implemented. The NDPSC also stated that the self-limiting nature of cold and flu, low likelihood of dose escalation and the multiple therapeutically active ingredients in these products may diminish abuse or misuse. There were no reports indicative of abuse or misuse.

Since the scheduling decision in 2009, there has been no evidence to suggest that misuse or abuse has been occurring and there has been no evidence of "morbidity, toxicity and dependence" associated with these products, as suggested in the ACMS agenda item description.

ASMI therefore assumes that the basis for the request to reschedule codeine containing cough and cold products concerns:

- The presence of codeine in the formulation per se, irrespective of the fact that there has been no demonstration of concerns with misuse or abuse
- Concern of a theoretical potential for misuse or abuse if consumers shift their purchases to cough and cold products

ASMI believes that the current scheduling of codeine containing cough and cold products is appropriate and that any decision on scheduling should be based on evidence and data concerning the products involved.

No evidence of abuse or misuse

Regarding OTC codeine containing cold and flu medicines, there has been no documented abuse or misuse in the literature in Australia and New Zealand (as per a preliminary literature search), nor have there been any reports to the TGA Database of Adverse Event Notifications (DAEN).

ASMI is of the view that there is no case for amending the scheduling of codeine containing cold and flu preparations as there is no evidence of harm from misuse, abuse or dependence.

Evidence suggests that consumers can appropriately self-treat with codeine containing cough, cold & flu products and that these products are used for symptom relief on a short term basis.

Data that will be provided (confidentially) by an ASMI member indicates that there has been no transfer of demand from OTC codeine containing analgesics to cold and flu products that contain codeine. It will be demonstrated that there has been no increase in demand for codeine containing cold and flu products.

Potential consequences of up-scheduling

As discussed above in relation to codeine containing analgesics, any change in scheduling for OTC codeine containing cough, cold and flu products will be likely to drive more people to their doctor

to obtain products they have previously used for symptomatic relief of colds and flu, which are generally self-limiting and easily recognised and treated by consumers.

As discussed above this will result in more presentations to GPs, higher costs to Medicare and co-payments, and higher costs of the medicines and this will significantly impact government costs and individual consumers' costs.

3. Scheduling Factors in summary

Section 52E(1)(a) - Risks and benefits

- Benefits:
    - OTC Codeine containing analgesics offer an option for consumers to treat short term moderate pain particularly when single ingredient analgesics do not provide adequate relief. Clinical studies have shown that OTC codeine containing combination analgesics are more efficacious than placebo and single ingredient analgesics.[12,13]
    - 5 day pack does not on its own cause dependence or abuse. When used as directed for a short duration, these products have a good safety profile.
    - Availability from pharmacists ensures advice and availability when needed, without the need for an appointment and associated Medicare costs. Pharmacists have a Protocol for supply as well as consumer educational material and front of pack labels to allow them to more easily raise the subject of inappropriate use with consumers. Pharmacists can refer when needed.
- Risks:
    - The reported risks of dependence and abuse particularly with excessive use over a prolonged period of time. Prolonged use at supra-therapeutic doses can lead to harm.
    - For some people, differences in drug metabolism mean that there can be variability in response, which alters efficacy and tolerability.

Section 52E(1)(b) – Purposes for use and extent of use

- Indicated for short term use for moderate to severe pain associated with headache, dental pain and other types of pain.
- Front of pack labelling provides instructions that the products are for three days use only and that codeine can be addictive.

Section 52E(1)(c) – Toxicity

- Toxicity typically occurs with longer term use at higher than recommended doses, following dependence or misuse.
- The type of harm seen is usually dependent on the non-opiate analgesic that forms part of the combination (ibuprofen, paracetamol)

[12] Toms L, Derry S, Moore RA, McQuay HJ. Single dose oral paracetamol (acetaminophen) with codeine for postoperative pain in adults. Cochrane Database Syst Rev 2009; (1):CD001547

[13] Derry S, Karlin SM, Moore RA. Single dose oral ibuprofen plus codeine for acute postoperative pain in adults. Cochrane Database Syst Rev 2013;(3):CD010107

Section 52E(1)(d) - Dosage, formulation, labelling, packaging and presentation

- Supply is limited to 5 days use. The products are intended for short term use.
- Labelling of many branded products will include warning statements consistent with those used in the UK, such as “Can cause addiction. Do not use for more than 3 days” following voluntary implementation by some ASMI member companies. This is already being phased in and should be extended.
- Pharmacists have updated their supply protocol, undertaken educational activities and now are required to use a Cautionary and Advisory Label following the inclusion of OTC codeine containing analgesic warning statements in the APF 23. Consumer education leaflets are also provided as part of these measures.

Section 52E(1)(e) - Potential for abuse

- A five day pack on its own is not an instigator of addiction.
- The risk of dependence and abuse increases if the products are taken for prolonged periods at higher doses than recommended.
- A real-time reporting system such as that used for pseudoephedrine is likely to be a very effective way to mitigate risk, by identifying pharmacy shoppers and targeting those who require referral for specialised care.

Section 52E(1)(f) - Other matters

- The newly implemented PSA initiatives will all serve to enable more effective interaction with customers, provide an avenue to educate and counsel them and thereby mitigate risks. The need to educate consumers will be the same regardless of the scheduling.
- These measures, coupled with universal adoption of label warnings and a real time reporting system will be the most effective way of targeting the individuals most at risk while not inconveniencing or increasing costs for people who use the products appropriately.

Overseas Regulatory Status

- Concerns about harms associated with dependence, abuse and misuse are not limited to Australia.
- Other comparable regulatory authorities have assessed these matters in reviews of safety and classification
- Low dose codeine containing analgesics are classified as Pharmacy Medicines in some key markets:
    - UK: Pharmacy Medicines with the mandatory labelling warning statements described above. Pack size limited to three days.
    - New Zealand
    - Canada
    - Denmark
    - France

- Ireland
- South Africa, which also has a real time monitoring system

In Australia, many sponsors have harmonised products with New Zealand that utilise the same labelling for both markets. It is very important for scheduling to be aligned across Australia and New Zealand to enable the distribution of products with the same labelling in both markets. As New Zealand in particular is a small market and supply of non-harmonised product will add to costs associated with separate packaging and labelling runs of lower order quantities. A move to Schedule 4 in Australia will have cost implications for New Zealand.

Conclusion

OTC codeine containing analgesics

ASMI believes that the current scheduling of OTC codeine containing analgesics is appropriate. The majority of consumers use the product responsibly for the short term treatment of moderate to severe pain for self-limiting conditions. In relation to the sales of the products, the number of cases of harm from addiction is low in comparison – indicating that while the harms are significant for those affected and those who treat them, the problem is not widespread so more specific and targeted interventions are needed to address those at most risk.

ASMI does not believe that a move to Schedule 4 provides a simple solution which will solve the problems that can arise as a result of misuse or addiction. ASMI takes the issue of harm very seriously and supports the new education and counselling initiatives undertaken by pharmacists, the new Cautionary & Advisory labelling of the APF 23 as well as more effective monitoring which could be achieved by a real time monitoring system such as a modified Project STOP system. This would enable better detection and referral of vulnerable people while not inconveniencing those who use the products correctly. Many ASMI members have voluntarily implemented prominent front of pack warning statements on the risk of addiction and a treatment duration of 3 days use.

As part of Schedule 3 supply requirements, pharmacists must provide consumers with counselling and advice on use of these products and ensure that supply is in accordance with the protocol for supply. Should these products be up-scheduled, then the legitimate users of these products will require a prescription – which will be costly, inconvenient and most likely result in purchase of a larger quantity on prescription (e.g. 30 or 50 tablets), and this in itself may predispose to use for longer than needed.

OTC Cough, cold & Flu products containing codeine

ASMI believes that the current scheduling of cough, cold and flu products is appropriate. These products are not labelled or marketed as analgesics. No evidence has been provided that these products are being misused and no information has been made available on the basis of the scheduling proposal.

ASMI assumes that the proposal is based on a hypothetical risk that misuse may occur by those who are misusing codeine. There is no evidence to support this position and sales data indicates that the product usage is predominantly seasonal and there has been no indication of a growth in demand since the codeine containing analgesics were rescheduled to Schedule 3 in 2010.

The Pharmacy Guild of Australia

Consumer Survey of Schedule 3 products containing codeine April 2015

Background

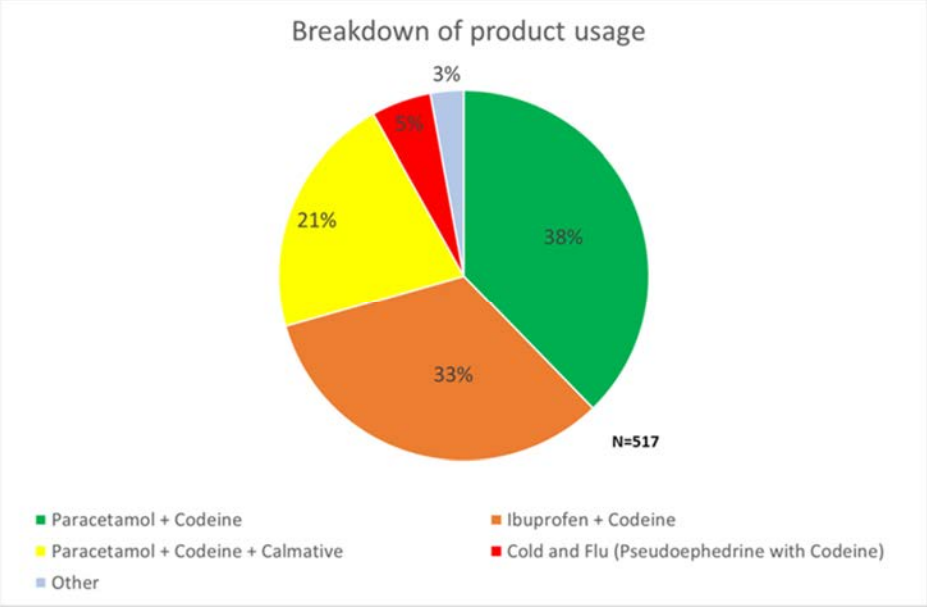
The Advisory Committee on Medicine Scheduling (ACMS) will consider at its July 2015 meeting, a proposal to delete the Schedule 3 entry for codeine, and reschedule the current Schedule 3 codeine entry to Schedule 4 due to potential issues of morbidity, toxicity and dependence.

In preparing a response to this proposal, the Guild conducted a consumer survey in April 2015 to determine usage patterns regarding these products, their views on recording of their details and the likely course of action if these products became prescription only.

The survey was distributed to the community pharmacies across the country via the Guild Branch Committees. The surveys were completed by consumers who purchased a Schedule 3 product during the period the week of 20 -27 April 2015 and a total of **517** responses were received.

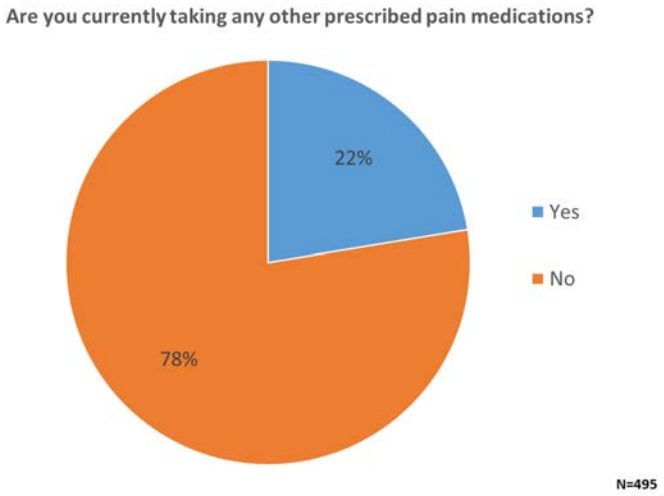
Results

Question 1 – Products purchased



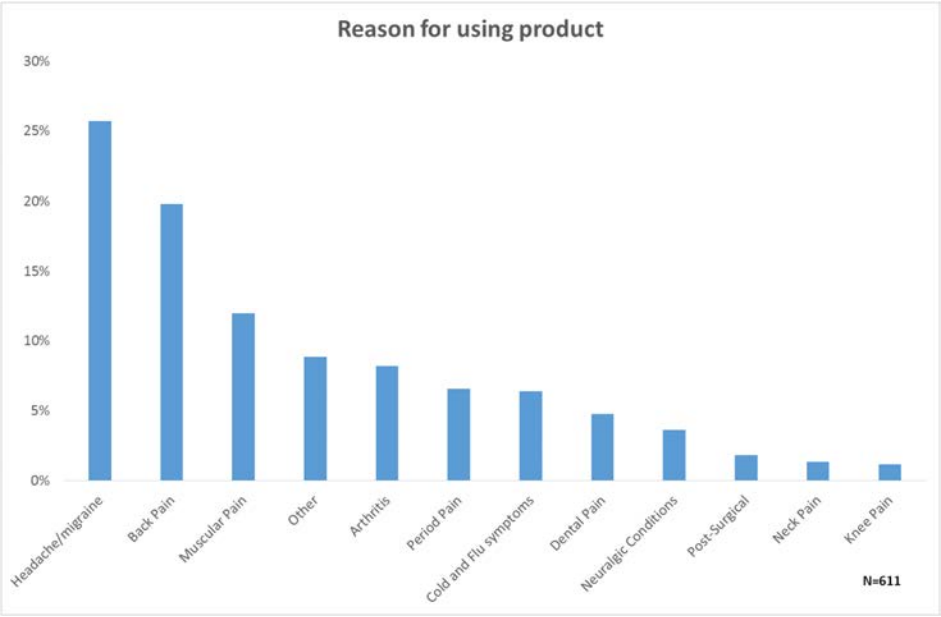
The graph above shows 39 per cent of respondents purchased a paracetamol+codeine combination product (e.g. Panadeine ®) with one-third purchasing an ibuprofen/codeine product. Approximately one in five (21 per cent) purchased a paracetamol product also containing calmative (e.g. Mersyndol ®) and 5 per cent purchased a cold and flu product containing codeine.

Question 2 – Concurrent use of prescribed pain medication with OTC codeine products



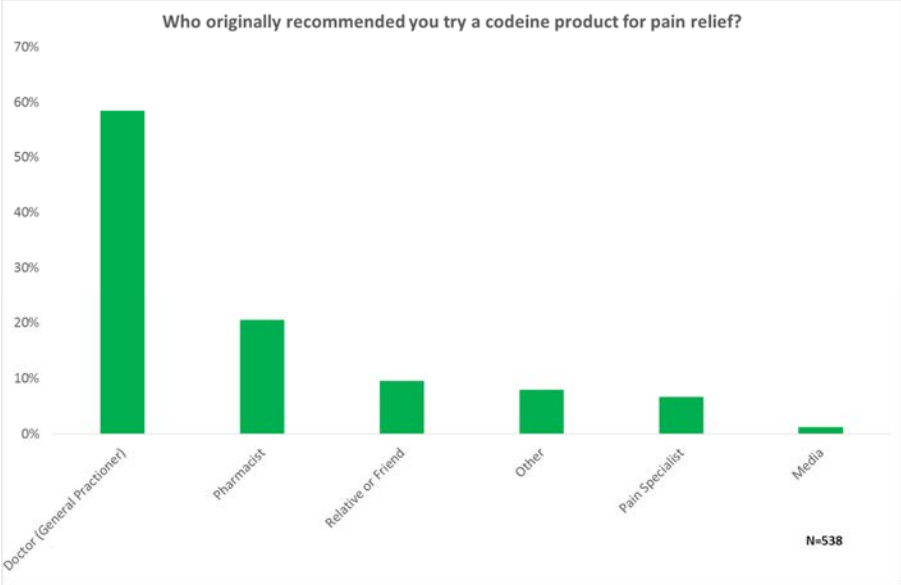
Approximately three-quarters (78 per cent) of respondents indicated they were not taking prescribed pain medications concurrently with over-the-counter products containing codeine.

Question 3 – Why are consumers using OTC codeine products?



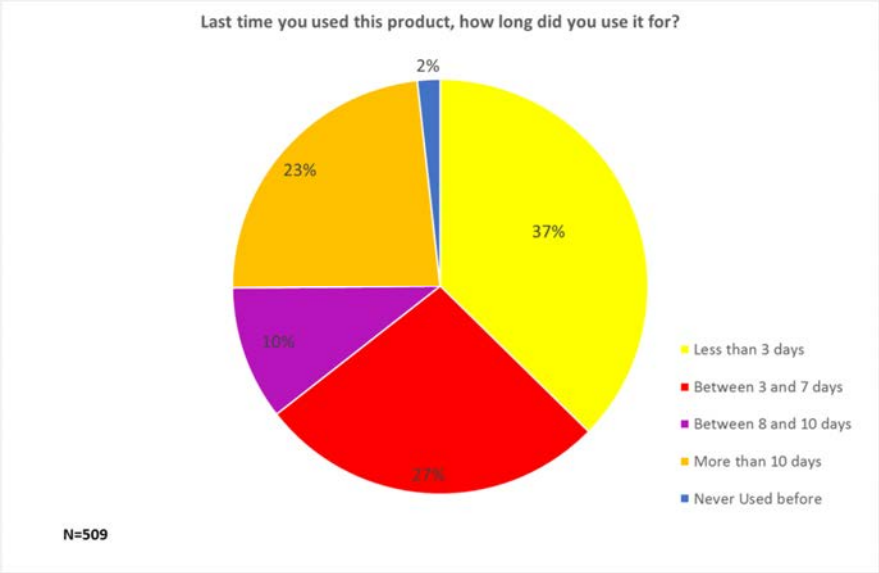
Consumers are using OTC codeine products for a variety of conditions. The most conditions nominated were headache/migraine (26 per cent), back pain (20 per cent) and muscular pain (12 per cent). The 'other' category comprised a variety of conditions including fractures, leg pain as well as hip pain. Several respondents indicated they were taking their selected product for multiple conditions.

Question 4 – Who is recommending consumers use OTC codeine products?



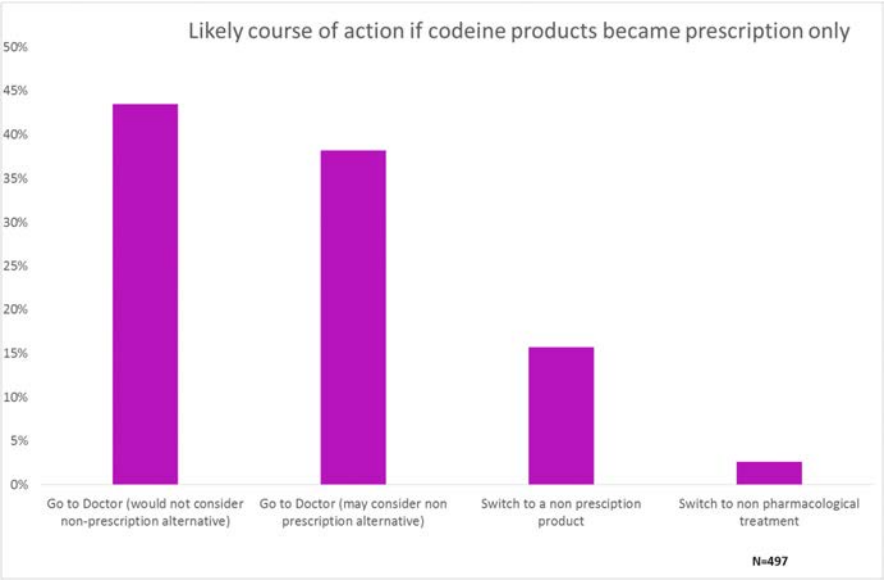
More than half (58 per cent) of respondents indicated a general practitioner had original recommended an OTC codeine product for their particular condition. Approximately one-fifth (21 per cent) had been recommended by a pharmacist and 9 per cent by a relative or friend. The 'Other' category consisted mainly of dentists recommending such products to treat dental pain.

Question 5 – How long are consumers using OTC codeine products?



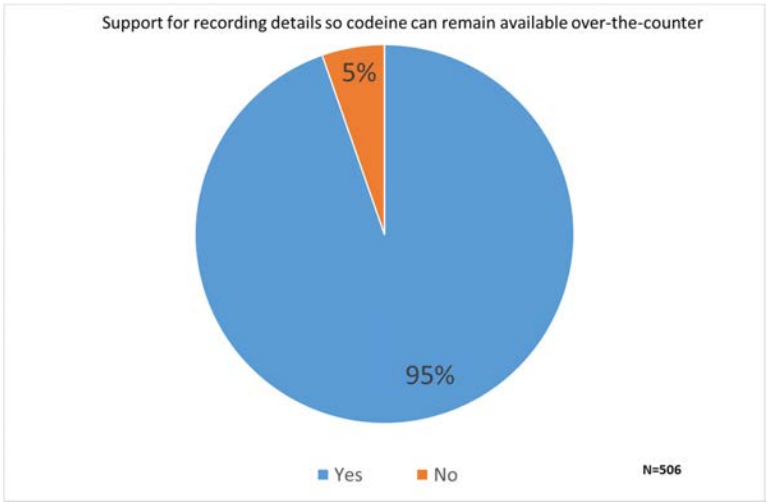
Nearly two-thirds (64 per cent) of respondents indicated the last time they used their specific product, they used it for 7 days or less. Approximately one-quarter (23 per cent) indicated they used an OTC codeine product for more than 10 days, in some cases long-term (year or more) or constant use.

Question 6 – If codeine products became prescription only, what would consumers likely do?



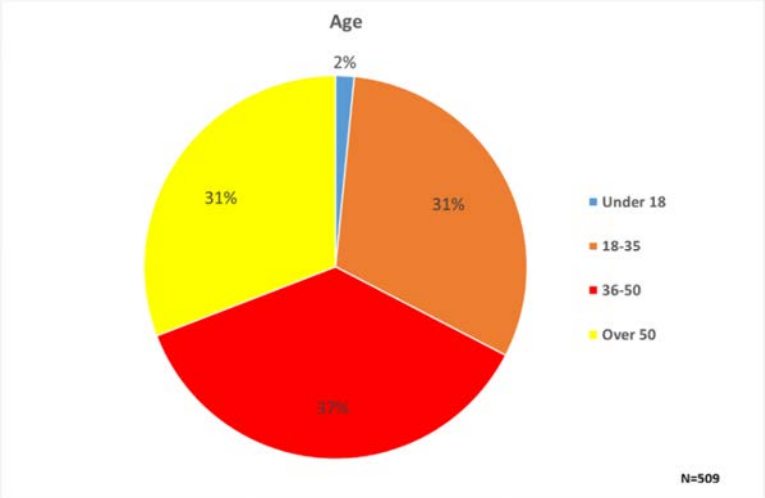
The vast majority (81 per cent) of respondents indicated they would most likely visit a doctor to obtain a prescription for the codeine product they were using. More than half indicated they would not consider an alternative medication available over-the-counter. Only 16 per cent of respondents indicated they would stop using codeine products and switch to another non-prescription product.

Question 7 – Would consumers be prepared to have their details recorded to obtain codeine products over-the-counter?



The overwhelming majority of respondents (95 per cent) indicated they were prepared to have their personal details recorded by the pharmacist when obtaining codeine products if this meant these products would remain available over-the-counter.

Question 8 – Age groups



The 36-50s age group were the most common groups of respondents (37 per cent) with approximately one third of respondents (31 per cent) aged between 18-35 and Over 50 respectively. Only 2 per cent of respondents were under 18.

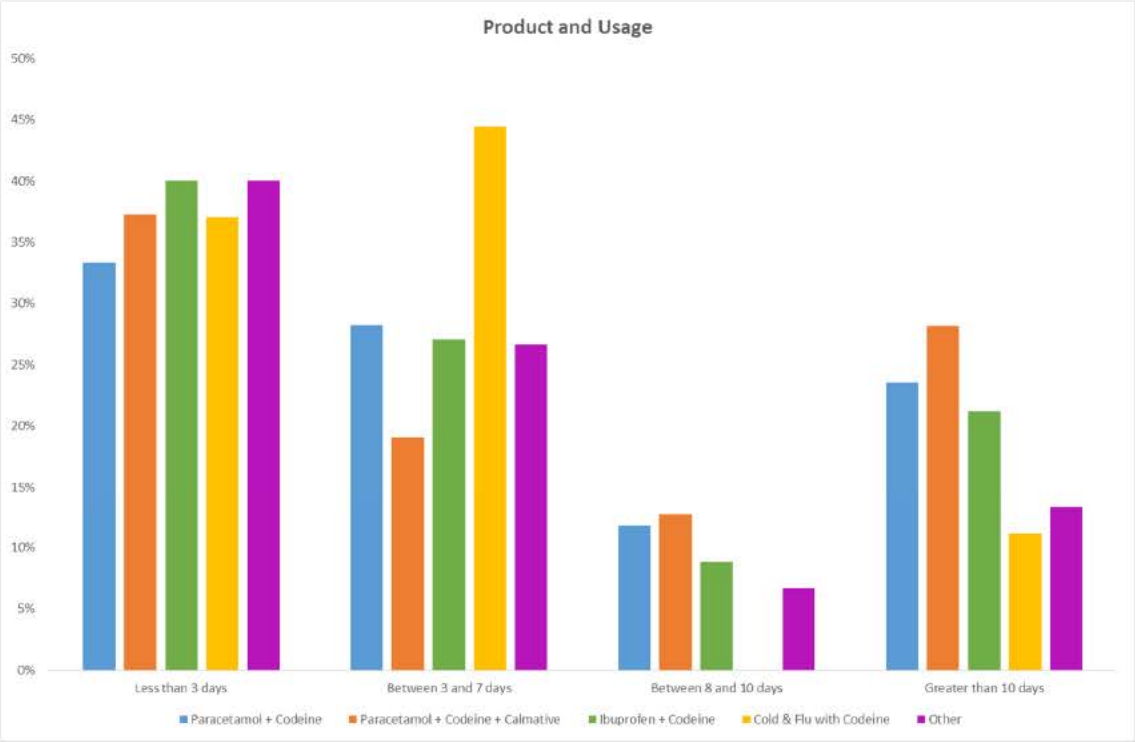
COMPARISON ANALYSIS

The comparison analysis investigates respondents' answers across two question to determine whether they are any significant correlations that indicate particular patterns across key areas such as product type demographics or health condition.

Product and usage

Product	Less than 3 days	Between 3 and 7 days	Between 8 and 10 days	More than 10 days
Paracetamol and Codeine	33%	28%	12%	24%
Paracemtamol, Calmative and Codeine	37%	19%	13%	28%
Ibuprofen and Codeine	40%	27%	9%	21%
Cold & Flu (pseudoephedrine) product with codeine	37%	44%	N/A	11%

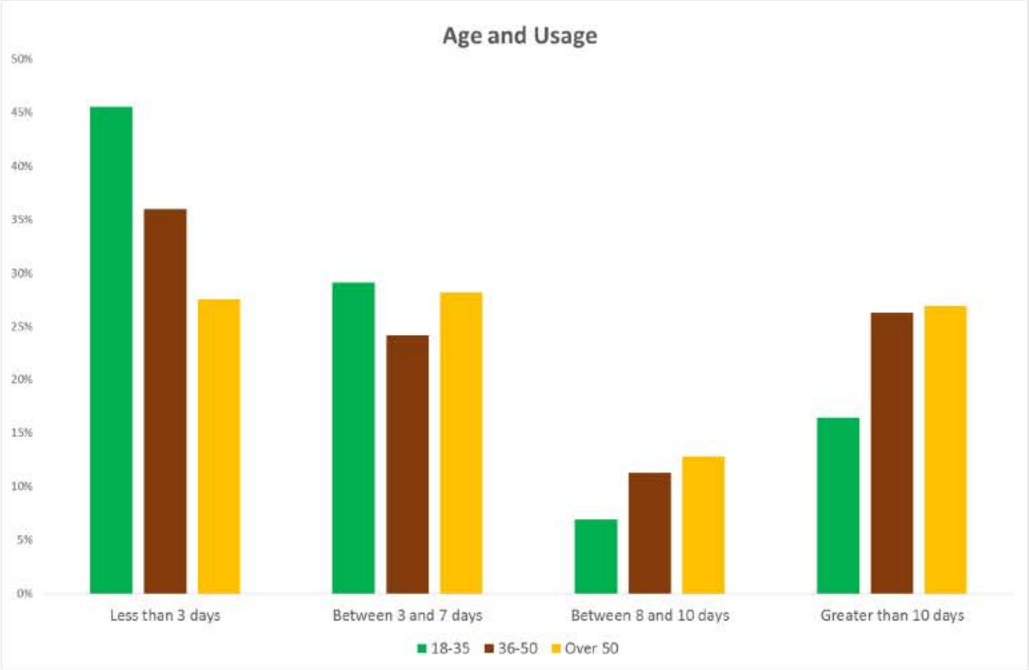
No significant difference in usage with a particular product found except for cold and flu products where the number of days usage is lower, with a greater number of respondents using these for 7 days or less.



Age Category and Usage

Product	Less than 3 days	Between 3 and 7 days	Between 8 and 10 days	More than 10 days
18-35	46%	29%	7%	16%
36-50	36%	24%	11%	26%
Over 50	28%	28%	13%	27%

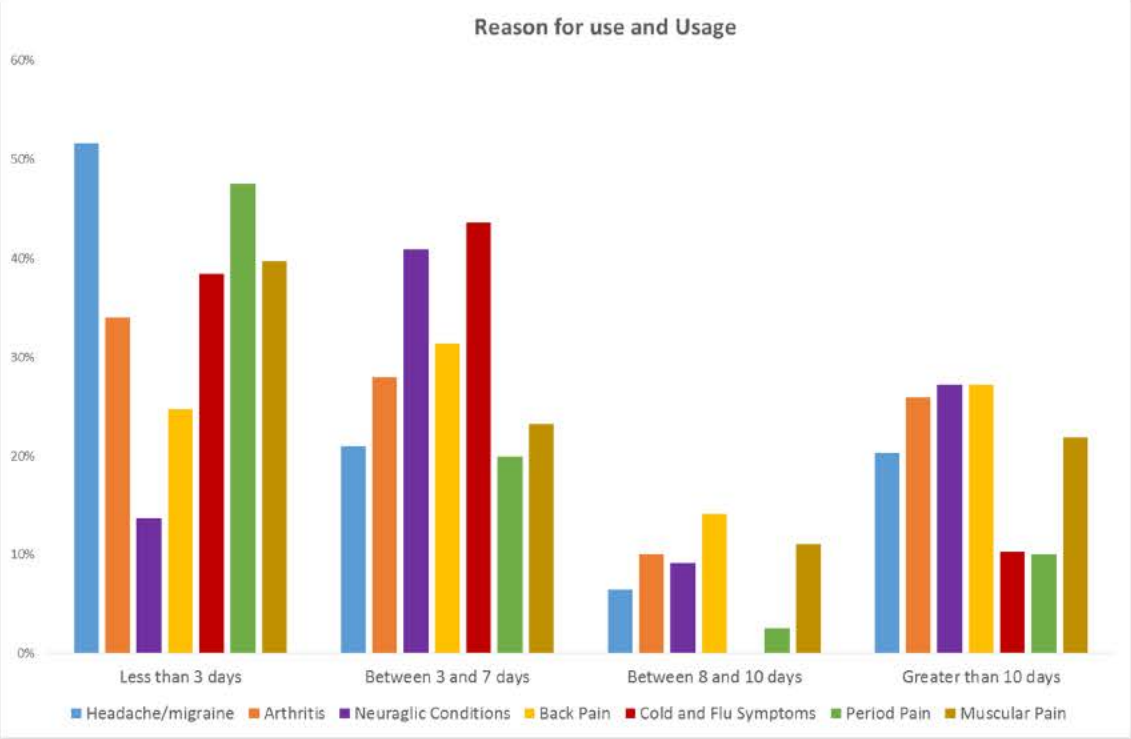
Respondents in the older age groups (36-50 and over 50) are more likely to use these products longer than 10 days compared to the respondents under 35. This may be an indication of these age groups more likely to suffer from chronic pain conditions. *NOTE (Due to the low number of respondents under the age of 18, this age group was excluded from this table).*



Reason for Use (condition) and Usage

Product	Less than 3 days	Between 3 and 7 days	Between 8 and 10 days	More than 10 days
Headache/migraine	52%	21%	6%	20%
Arthritis	34%	28%	10%	26%
Neuraglic Conditions	14%	41%	9%	27%
Back Pain	25%	31%	14%	27%
Cold and Flu Symptoms	38%	44%	0%	10%
Period Pain	48%	20%	3%	10%
Muscular Pain	40%	23%	11%	22%

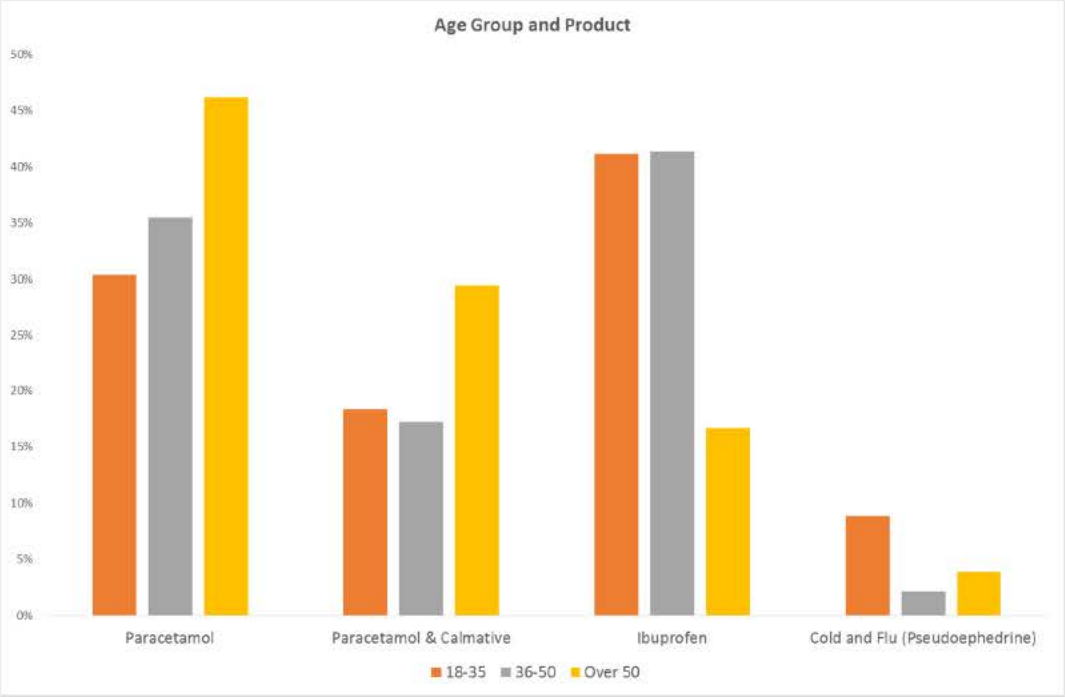
Most people with cold and flu and period pain are taking the medicines for 7 days or less. Sufferers of neuralgic conditions, headache/migraine, arthritis, back pain and muscular pain tend to use the products for more than 10 days.



Age and Product

Age	Paracetamol and Codeine	Paracetamol, Calmative and Codeine	Ibuprofen and Codeine	Cold & Flu (pseudoephedrine) product with codeine
18-35	30%	18%	41%	9%
36-50	35%	17%	41%	2%
Over 50	46%	29%	17%	4%

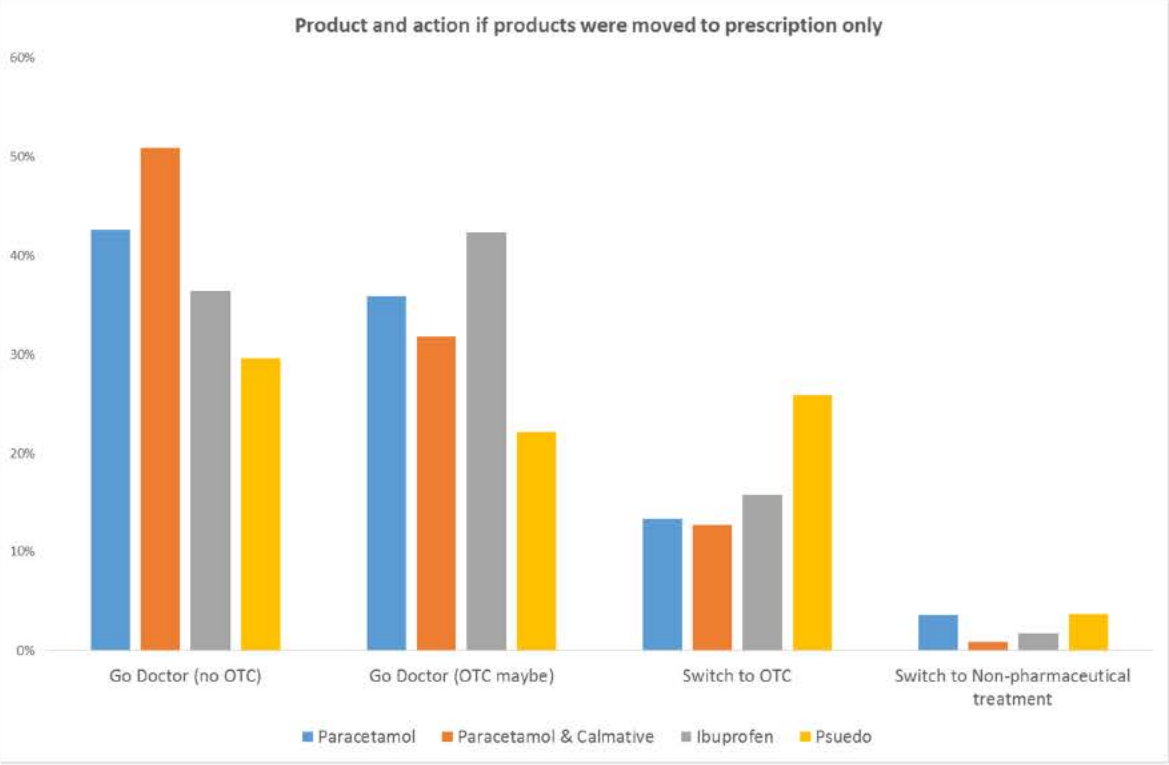
Respondents who are over 50 seem to be using more of paracetamol combination products whereas people in the age group of 18-50 use ibuprofen combination product more. *NOTE (Due to the low number of respondents under the age of 18, this age group was excluded from this table).*



Product and action if products were moved to prescription only

Product	Go to Doctor (not consider OTC alternative)	Go to Doctor (may consider OTC alternative)	Switch to OTC alternative	Switch to non-pharmaceutical alternative
Paracetamol and Codeine	43%	36%	13%	3%
Paracetamol, Calmative and Codeine	51%	32%	13%	1%
Ibuprofen and Codeine	36%	42%	16%	2%
Cold & Flu (pseudoephedrine) product with codeine	30%	22%	26%	4%

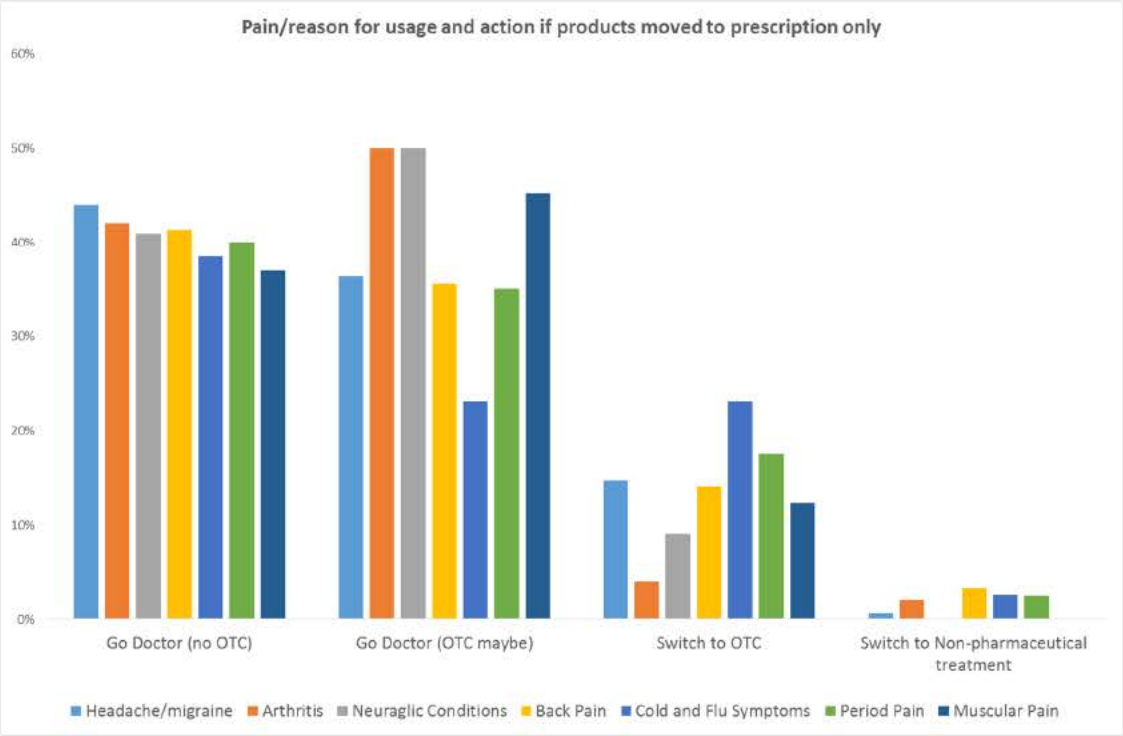
People using pseudoephedrine combination products are most likely to switch to an alternative product available over-the-counter, whereas people using paracetamol combination products are more likely to visit a doctor to obtain a prescription for a same/ similar product.



Pain/reason for use and action if products move to prescription only

Reason for use	Go to Doctor (not consider OTC alternative)	Go to Doctor (may consider OTC alternative)	Switch to OTC alternative	Switch to non-pharmaceutical alternative
Headache/migraine	44%	36%	15%	1%
Arthritis	42%	50%	4%	2%
Neuralgic Conditions	41%	50%	9%	N/A
Back Pain	41%	36%	14%	3%
Cold and Flu Symptoms	38%	23%	23%	3%
Period Pain	40%	35%	18%	N/A
Muscular Pain	37%	45%	12%	N/A

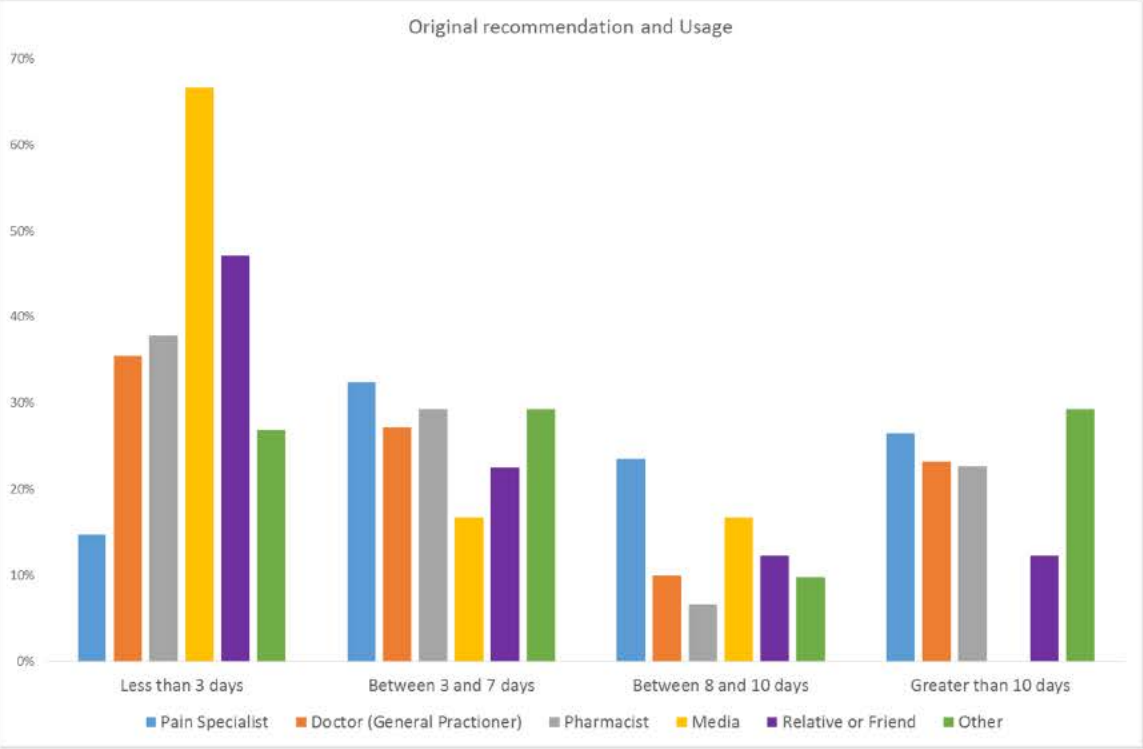
People suffering from arthritis and neuralgic conditions are the least likely to switch to another over-the-counter medication in the event codeine combination products move to prescription only (preferring to go to the doctor to obtain a prescription for these products. People experiencing cold and flu symptoms and period pain are the most likely to switch to another non-prescription product.



Product Recommendation and Usage

Recommended by	Less than 3 days	Between 3 and 7 days	Between 8 and 10 days	Greater than 10 days
Pain Specialist	15%	32%	24%	26%
Doctor	35%	27%	10%	23%
Pharmacist	38%	29%	7%	23%
Media	67%	17%	17%	0%
Relative or Friend	47%	22%	12%	12%

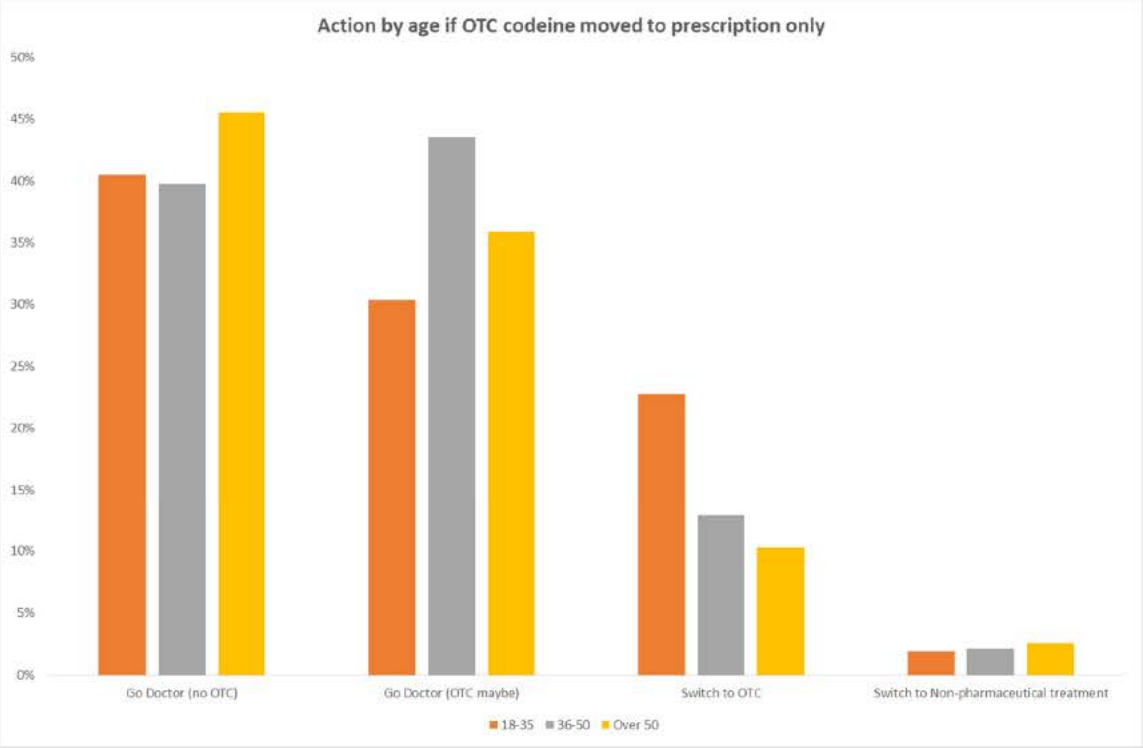
It appears that people are using the product for a longer period if it was originally recommended by a health professional (doctor, pharmacist, pain specialist).



Age and Choice of Alternative Product

Age	Go to Doctor (not consider OTC alternative)	Go to Doctor (may consider OTC alternative)	Switch to OTC alternative	Switch to non-pharmaceutical alternative
18-35	41%	30%	23%	2%
36-50	40%	44%	13%	2%
Over 50	46%	36%	10%	3%

Respondents in the 18-35 age group were more likely to switch to an alternative product available over-the-counter in the event combination analgesics containing codeine became prescription only. Only 10 per cent of respondents aged over 50 would switch to alternative OTC medicine. *NOTE (Due to the low number of respondents under the age of 18, this age group was excluded from this table).*



APPENDIX 1 – Consumer Survey

The Pharmacy Guild of Australia

ANALGESIC SURVEY

Dear Customer

We are asking you to take part in a short survey about pain relieving medications (analgesics). Certain pain relief products are currently being reviewed and the Pharmacy Guild is seeking information regarding use of these products to support the quality use of medicines.

All data will be confidential and non-identifiable. When you have completed this survey, please return the survey to the pharmacist.

1. Which particular product did you purchase today?

- ☐ Paracetamol + Codeine product (e.g. Panadeine ®, Codapane®)
- ☐ Ibuprofen + Codeine product (e.g. Nurofen Plus ®)
- ☐ Paracetamol + Codeine + Calmative (e.g. Mersyndol ®, Dolased ®)
- ☐ Cold & Flu with Codeine (e.g. Codral ® Cold & Flu)
- ☐ Other (Specify) _____

2. Are you currently taking any other prescribed pain medications?

- ☐ Yes
- ☐ No

3. What was the main reason for purchasing this product today?

- ☐ Headache/ migraine
- ☐ Arthritis
- ☐ Neuralgic Conditions
- ☐ Back Pain
- ☐ Cold and Flu symptoms
- ☐ Period Pain
- ☐ Muscular Pain
- ☐ Other (Specify) _____

4. Who originally recommended you try a product containing codeine for pain relief?

- ☐ Pain Specialist
- ☐ Media (e.g. Internet, TV, magazine)
- ☐ Doctor (General Practitioner)
- ☐ Relative or Friend
- ☐ Pharmacist
- ☐ Other (Specify) _____

5. The last time you used this product, approximately how long did you use it for?

- ☐ Less than 3 days
- ☐ Between 8 and 10 days
- ☐ Between 3 and 7 days
- ☐ More than 10 days (Specify) _____
- ☐ N/A never used product before

6. If regulatory changes meant in the future all codeine products required a prescription in order to be obtained, please indicate your most likely course of action?

- ☐ I would go to the doctor to obtain a prescription and I would **not** consider any other non-prescription products
- ☐ I would stop using codeine products and use another product that was available without a prescription
- ☐ Most likely I would go to the doctor to obtain a prescription but I may consider other analgesic products available without a prescription
- ☐ I would stop using medicines all together and try a non-medication therapy (e.g. physiotherapy)

7. Rather than being required to obtain a prescription would you instead be prepared to have your details recorded by a pharmacist when purchasing a codeine product so it could remain a non-prescription medicine?

- ☐ Yes
- ☐ No

8. Please indicate your age

- ☐ Under 18
- ☐ 18-35
- ☐ 36-50
- ☐ Over 50

Thank you for your participation

The Pharmacy Guild of Australia

Advisory Committee for Medicines Scheduling

July 2015 Meeting

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

- **Codeine**

May 2015

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Contents

Proposal 1.1 – Codeine – Amendments to Schedule 2 and 3 entries

ACMS Proposal: (To delete the Schedule 3 entry for codeine, and reschedule the current Schedule 3 codeine entry to Schedule 4 due to potential issues of morbidity, toxicity and dependence. Consideration may be given as to 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 may be given as to whether the Schedule 2 entry for codeine should also be amended.)

Overview

The Pharmacy Guild of Australia recognises concerns relating to patient safety due to misuse of combination analgesics containing codeine (CACC) and agrees some action needs to be taken.

However, the Guild is opposed to the proposed scheduling changes that would make over-the-counter (OTC) codeine products Schedule 4 medicines as we do not agree that the proposed scheduling changes will address the potential issues of morbidity, toxicity and dependence.

The Guild contends adverse events arising from OTC CACC since it was rescheduled to Schedule 3 in 2010 are small relative to the large number of users, and as such the risk of harm from OTC CACC among all users of these drugs is likely to be low. The Guild considers the proposed scheduling changes are a blunt instrument to address misuse and abuse of these medicines. The Guild believes that the proposal would not only be ineffective at addressing concerns of abuse, but also could also have unintended consequences such as increased use of higher strength CACC in larger packs or more potent opioids.

Implementation of a mandatory real-time monitoring system in community pharmacy would be more effective and economical to assist in identifying at-risk consumers, facilitate access to education materials and support appropriate referral when required. Project STOP, currently used to monitor pseudoephedrine sales in real time, could be modified for monitoring the supply of CACC. This system could be implemented quickly without restricting availability for the majority of consumers who use OTC CACC safely and effectively.

The Guild supports the continued availability of currently available CACC in Schedule 3. It is a matter of public health that these products remain available to treat mild to moderate pain when it occurs. Existing scheduling of these products allows timely access to important analgesic medicines in an environment where an appropriate level of pharmaceutical supervision exists.

The Guild highlights the duty of care community pharmacists have to the Australian community with the health and wellbeing of the consumer as their primary concern. As such the Guild is supportive of the measures that will contribute to the quality use of medicines and help achieve the best health outcomes. We believe that education initiatives are key to improving consumer awareness regarding the risks associated with taking OTC CACC for longer than recommended periods, particularly with products containing ibuprofen. Such education campaigns contribute to the quality use of medicines and decrease the likelihood of the product being used inappropriately.

In preparing a response to this proposal, the Guild conducted a consumer survey in April 2015 to determine usage patterns regarding these products, their views on recording of their details and the likely course of action if these products became Schedule 4.[1] There was a total of 517 respondents across all States and Territories.

Based on the results of the survey and other evidence cited in this submission, the Guild has put forward a number of recommendations and measures that can be implemented such as:

- real-time monitoring system;
- changes to the packaging and labelling;
- education for health professionals; and
- consumer awareness campaign including pain management support tools such as migraine/headache treatment diary/plan to achieve better health outcomes.

Guild Recommendations

1. Cold and flu preparations containing codeine (Schedule 2 phenylephrine products and Schedule 3 pseudoephedrine products):

The Guild is not aware of any evidence of misuse for these products. The Guild recommends the ACMS excludes these preparations from any rescheduling considerations.

2. Combination analgesic products containing codeine:

2.1 The current scheduling of these products as Schedule 3 remains appropriate.

2.2 In order to address the issue of abuse and dependence in a small proportion of consumers, a national real-time monitoring system should be developed and implemented as a matter of priority.

2.3 Warning labels advising consumers of the potential for dependence from prolonged use of these products should be mandatory.

2.4 The Guild is also committed to ongoing and improved education material for pharmacists (including pain management and migraine management support tools) and active participation in the development of a consumer awareness campaign in partnership with other stakeholders.

2.5 There is no compelling evidence that OTC paracetamol or aspirin products in combination with codeine are subject to widespread abuse/misuse. However, in relation to ibuprofen, the TGA's Database of Adverse Event Notifications (DAEN) indicates an over-representation of adverse events for this combination for dependency and abuse. Therefore, the specific combination of ibuprofen/codeine could be considered separately to reduce the maximum days' pack size for these from 5 days to 3 days in Schedule 3.

[1] Attachment 1 - Pharmacy Guild consumer survey report, April 2014

The risks and benefits of the use of a substance[2]

ACMS proposal: Consideration may be given as to whether the Schedule 2 entry for codeine should also be amended.

The Guild believes the current Schedule 2 classification for codeine is appropriate. The current classification stipulates that codeine is only available as a Schedule 2 medicine in preparations for the treatment of cough and colds and must be compounded with phenylephrine and no more than one analgesic substance.[3]

Data cited by the Guild indicates that usage of these products is relatively small compared to the use of combination analgesic products containing codeine (CACC) indicated specially for pain relief. Furthermore, there was no increase in the usage of these codeine/phenylephrine products in the four years following the rescheduling of CACC products from Schedule 2 to Schedule 3 in 2010.[4] This suggests that combination phenylephrine/codeine products are not targeted by consumers who may be codeine dependent. The Guild therefore believes there is no evidence from a risk perspective to suggest moving codeine/phenylephrine products into Schedule 3 is warranted.

Availability of phenylephrine/codeine products in Schedule 2 facilitates timely access for consumers who require cold and flu treatments containing analgesics ingredients such as paracetamol and codeine. It also reduces the need for consumers to take separate analgesic products to treat associated pain synonymous with cold and flu such as headaches, muscle aches and sinus pain.

Recommendation

The Guild believes the current Scheduled 2 classification for codeine remain appropriate. There is no evidence Schedule 2 codeine products are misused/abused by consumers with a codeine dependency. The likelihood of consumers becoming inadvertently addicted to codeine via these products is very low.

[2] Section 52E(1a)- *Therapeutic Goods Act 1989*
[3] Poisons Standard 2014 http://www.comlaw.gov.au/Details/F2015L00128
[4] See Johnson & Johnson submission to ACMS July meeting

The purposes for which a substance is to be used and the extent of use of a substance[5]

The consumer survey conducted by the Guild (n=611[6]) indicates these products are being used for a variety of indications and the majority of consumers report appropriate use for a genuine therapeutic need. The graph below describes the range of conditions consumers reported treating with OTC CACC products. The most common conditions reported include headache/migraine, back pain and muscular pain.

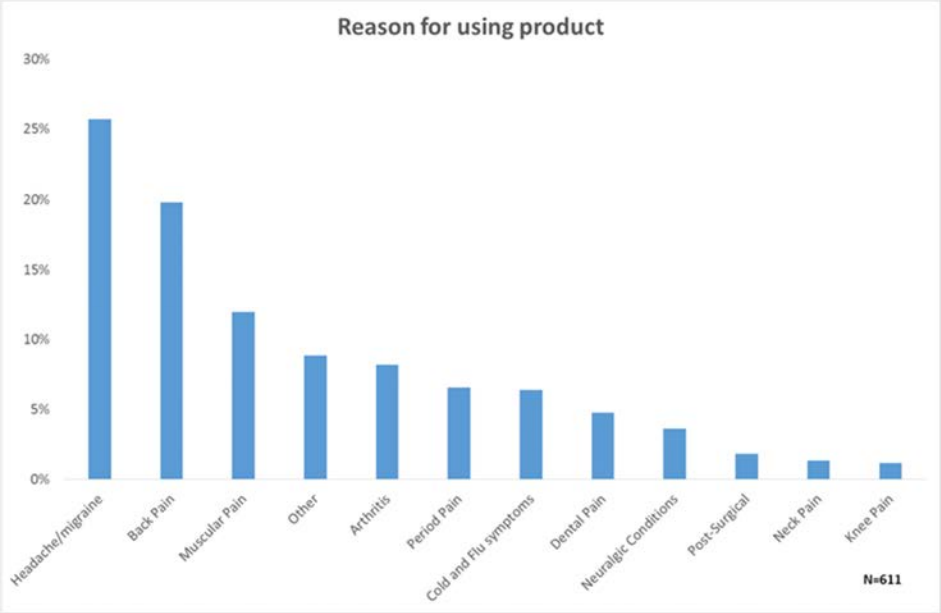

Figure 1 – Guild consumer survey of Schedule 3 products containing codeine, April 2015- Reason for use

ACMS proposal: Deleting the Schedule 3 entry for pseudoephedrine/codeine combination products

The Guild does not support rescheduling combination pseudoephedrine/codeine products into Schedule 4. The Guild believes the current scheduling remains appropriate. There is no evidence to suggest that pseudoephedrine/codeine products are subject to misuse/abuse and usage of these products is considerably lower than CACC. The likelihood of a consumer inadvertently becoming addicted to codeine via these products is low, given colds and flu are temporary conditions with symptoms generally dissipating within a few days.

Survey data indicates 81 per cent of consumers used cold and flu products containing codeine for 7 days or less.[7] The TGA's Database of Adverse Event Notifications (DAEN) records that there have only been five adverse events recorded for these products over the past 5 years with no events recorded related to abuse or dependency.[8]

[5] Section 52E(1b)- *Therapeutic Goods Act 1989*
[6] Some of the 517 respondents indicated there were using the product for multiple pain conditions
[7] Attachment 1 - Pharmacy Guild consumer survey report, April 2014
[8] Attachment 2 - Database of Adverse Event Notifications – Pseudoephedrine products containing codeine

In addition, as the supply of pseudoephedrine-based products are monitored by Project STOP (an online real-time monitoring system), any inappropriate or excessive use of these products would likely be brought to the attention of the pharmacist for intervention.

Recommendation

The Guild believes the current scheduling for pseudoephedrine /codeine products remains appropriate.

There is no evidence to suggest these particular products are a target for consumers who may be codeine dependent and sales of these products are already tracked in real time via Project STOP. Moving these products to Schedule 4 would simply to increase costs to consumers and the health system.

The dosage, formulation, labelling, packaging and presentation of a substance[9]

Reducing the pack size for Schedule 3 combination ibuprofen/codeine products

The current Schedule 3 entry for OTC CACC permits pack sizes of up to 5 days' supply. Given the number of adverse events for ibuprofen/codeine products relative to other products, [10, 11] it may be beneficial to reduce this limit for these types of CACC to 3 days' supply. Reducing the maximum pack size would require consumers who are using ibuprofen/codeine products regularly to have more frequent interaction with the health system in order to obtain these products. This increases the likelihood that inappropriate use will be detected, more pharmacist intervention and advice provided and greater referrals made to doctors and pain specialists for pain management reviews.

Mandatory addiction warning labels

The Guild notes that in 2009 the UK Medicines and Healthcare products regulatory agency introduced a requirement where CACC are required to carry a prominent warning label advising consumers of the risk of addiction. The package of measures included changes to indications, labels and leaflets, pack size, and advertising.[12]. Some product sponsors in Australia, such as Reckitt Benckiser, voluntarily apply such labels to their CACC products. Other companies have been encouraged by the Australian Self Medication Industry adopt this approach.[13]

[9] Section 52E(1d)- *Therapeutic Goods Act 1989*

[10] Attachment 3 - Database of Adverse Event Notifications – Ibuprofen containing codeine products

[11] Attachment 4 - Database of Adverse Event Notifications – Paracetamol containing codeine products

[12] Drug Safety Update: Over-the-counter painkillers containing codeine or dihydrocodeine, 2009, Medicines and Healthcare Products Regulatory Agency, London, https://www.gov.uk/drug-safety-update/over-the-counter-painkillers-containing-codeine-or-dihydrocodeine

[13] Dow A, Nurofen to label packets with addition warning The Age Online, Melbourne, 09/12/2013 http://www.theage.com.au/national/nurofen-to-label-packets-with-addiction-warning-20131208-2yzep.html

The main advantage of this approach is that it would reduce the risk of people becoming addicted to codeine while allowing easy access for consumers who use the products appropriately. Such warning labels would complement and reinforce the instructions provided by the pharmacist at the point of sale.

Recommendation

The Guild recommends mandatory warning labels to highlight risk of misuse and dependency. The warning label should be of appropriate size and caution against inappropriate regular use of these products for migraine and headache.

The Guild believes supports reduction of pack size for OTC codeine products to a maximum of 3 days' supply for ibuprofen/codeine combination products. However, the Guild contents reduced pack size in Schedule 3 alone (i.e. without a monitoring system), will not address misuse and dependence.

The potential for abuse of a substance[14]

The Guild recognises some consumers misuse and abuse OTC CACC products. However, overall prevalence of misuse appears to be extremely low in comparison to total use.

An analysis of the TGA's Database of Adverse Event Notifications (DAEN) indicates that since combination analgesics containing codeine were moved from Schedule 2 to Schedule 3 (May 2010 – January 2015), there have been a total of 101 adverse events reported for all CACC over this time. Relative to the number of packs sold over the same period (based on annual sales of 16 million[15]) and the number of people using the product (6 million Australians aged 14 years and over report using OTC codeine analgesics)[16], the adverse events rate is very small.

Nonetheless, the Guild notes that an analysis of the adverse events **by analgesic type** indicates combination ibuprofen/codeine products are responsible for over half the number of adverse events reported. Specifically for adverse events related to dependency and abuse, this is mostly attributable to ibuprofen/codeine products. There were no adverse events related to dependency or abuse attributable to pseudoephedrine[17] or aspirin[18] in combination with codeine.

Evidence suggests the prevalence of dependency and abuse varies significantly depending on which analgesic is combined with codeine, indicating different safety profiles and therefore the entire class of CACC medicines should not be considered for rescheduling.

Therefore, the potential dependency and abuse of ibuprofen products should be handled separately by further reducing minimum pack size, mandatory warning labels and real time recording and monitoring.

[14] Section 52E(1e)- *Therapeutic Goods Act 1989*
[15] The National Pharmacy Scan, Nielsen (Jan 2012-Dec 2013)
[16] Australian Institute of Health and Welfare 2014. National Drug Strategy Household Survey detailed report 2013.Drug statistics series no. 28. Cat. no. PHE 183. Canberra: AIHW.
[17] Attachment 2 - Database of Adverse Event Notifications – Pseudoephedrine products containing codeine
[18] Attachment 5- Database of Adverse Event Notifications- Aspirin/codeine combination products

Schedule 2 codeine products

The TGA's Database of Adverse Event Notifications (DAEN) indicates there have been just three adverse events related to Schedule 2 products containing codeine (cough and cold products containing phenylephrine) over the last 5 years with none of these events related to dependency or abuse.[19] Therefore, these preparations should be excluded from consideration for rescheduling.

Recommendation

The available evidence suggests that the rate of adverse events is low compared to the use of the products.

There is no justification for re-scheduling of other combination analgesics (paracetamol, pseudoephedrine, aspirin and phenylephrine).

However, in relation to ibuprofen, the TGA's Database of Adverse Event Notifications (DAEN) indicates an over-representation of adverse events for this combination particularly for dependency and abuse. Therefore, the specific combination of ibuprofen/codeine could be considered separately to reduce the maximum days' supply available for these products at the Schedule 3 classification from 5 days to 3 days.

Any other matters that the Secretary considers necessary to protect public health[20]

Other matter 1: Costs associated with up-scheduling

Cost to Medical Benefit Schedule (MBS)

Rescheduling OTC CACC products to Schedule 4 will result in substantial costs to Medicare through an increase in doctors' visits, and will place additional workload on already overburdened GPs.[21]

As shown in the Figure 2 below, the majority (81 per cent) of respondents indicated they would most likely visit a doctor to obtain a prescription for the codeine product they were using. More than half of this group indicated they would not consider an alternative medication available over-the-counter. Only 16 per cent of respondents indicated they would stop using codeine products and switch to another non-prescription product.

[19] Attachment 6 - Database of Adverse Event Notifications – phenylephrine containing codeine
[20] Section 52E(1f)- *Therapeutic Goods Act 1989*
[21] Creswell, A. Weary trooper on the front lines of an overburdened system, 15/10/2011 http://www.theaustralian.com.au/archive/national-affairs/weary-troopers-on-the-front-lines-of-an/story-fn9iqmqf-1226167069588 (accessed 05/05/2015)

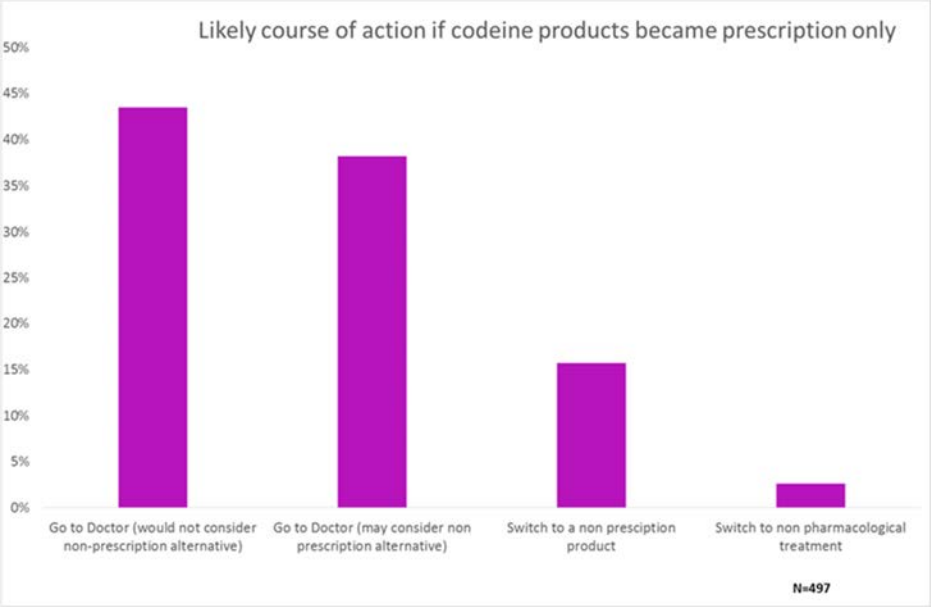

Figure 2 – Guild consumer survey of Schedule 3 products containing codeine, April 2015

When examined across age (See Figure 3), in every age category the majority of respondents indicated they would most likely visit a doctor to obtain a prescription for the codeine product they were using. These findings suggest an increase in doctor visits will not be isolated to older consumers who may already be regularly visiting a doctor, but demand will also increase among younger age groups, who may visit a doctor purely to obtain a prescription for CACC.

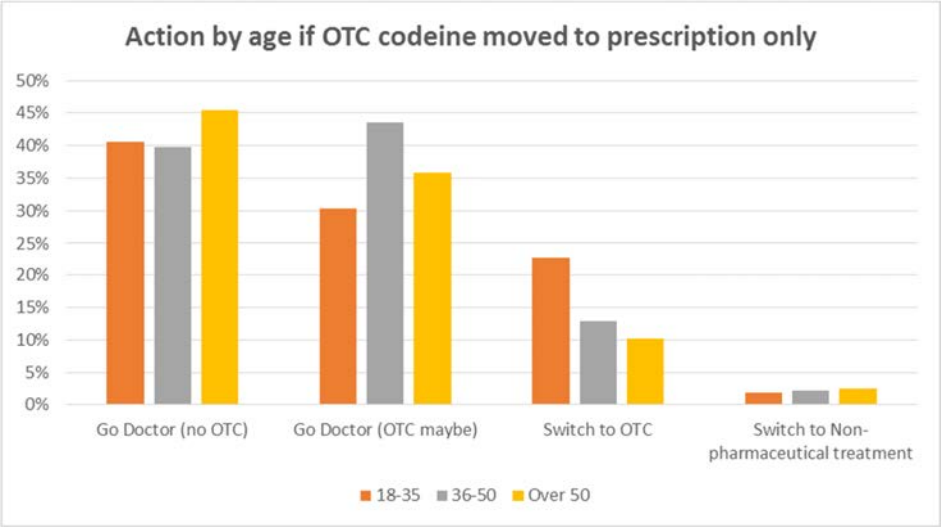

Figure 3 – Guild consumer survey of Schedule 3 products containing codeine - Action by age April 2015

These findings are broadly consistent with a consumer survey conducted by Macquarie University which found that 63 per cent of respondents would visit a doctor to obtain an analgesic/pain relief medication if it became unavailable over the counter.[22]

[22] The Value of OTC medicines in Australia – March 2014, The Macquarie Centre for the Health Economy

The Macquarie University report also found if current Schedule 3 analgesics were up-scheduled to Schedule 4, the costs to Medicare alone in additional doctor's visits would equate to approximately $170 million a year. If Schedule 3 cold and flu products were also up-scheduled this would add another $115 million in Medicare costs.[23]

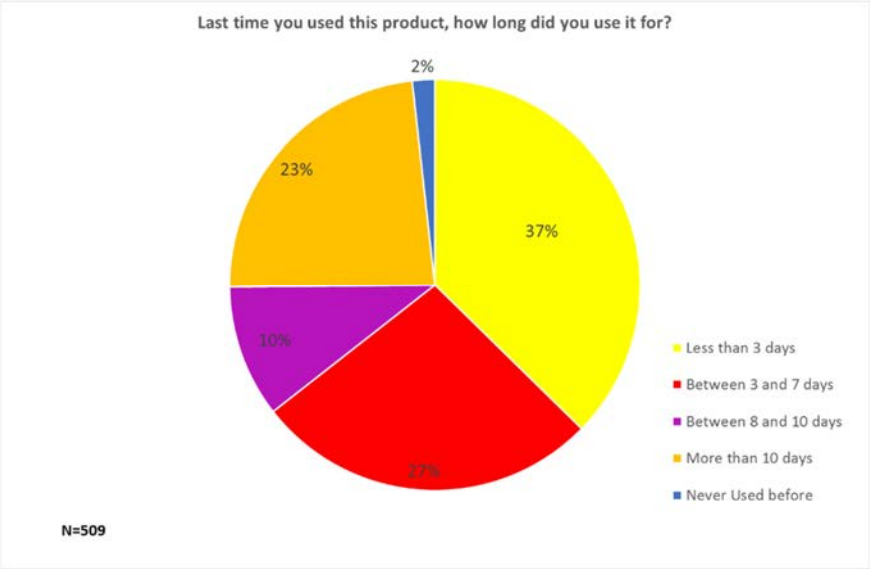

Figure 4– Guild consumer survey of Schedule 3 products containing codeine, April 2015- Age groups

Cost to Pharmaceutical Benefits Scheme (PBS)

Up-scheduling OTC codeine products to Schedule 4 is also likely to have cost implications for the Pharmaceutical Benefits Scheme (PBS), particularly if doctors elect to prescribe consumers higher strength codeine products or other opioids listed on the PBS.

As an example, doctors may choose to prescribe a combination analgesic containing a higher dose of codeine (30mg) (OTC CACC can only contain a maximum of 12mg). In addition, such products are available for consumers under the PBS which may make it a more affordable option over the course of the year due to the PBS Safety Net scheme. The total PBS cost of supplying the paracetamol/codeine products (such as Panadeine Forte ®) in the last financial year was approximately $12 million.[24] This is likely to increase if all CACC products were moved to Schedule 4.

[23] Ibid

[24] http://medicarestatistics.humanservices.gov.au/statistics/do.jsp?_PROGRAM=%2Fstatistics%2Fpbs_item_standard_report&itemlst=%2701215Y%27&ITEMCNT=1&LIST=1215Y&VAR=BENEFIT&RPT_FMT=5&start_dt=201307&end_dt=201406

Cost to Consumers

In addition to the additional costs borne by the government, through increased MBS and PBS expenditure as mentioned above, there will also be additional costs to consumers through out-of-pocket expenses.

The aforementioned Macquarie University report estimated the cost to individual consumers from up-scheduling would be $70 million a year.[25] The additional costs of visiting a doctor to obtain a prescription could be prohibitive for many consumers, leading to poor health outcomes and potentially lead to self-medicating with non-therapeutic products such as alcohol. Studies conducted in the USA indicate that up to 25 per cent of people experiencing pain self-medicate with alcohol.[26] This can lead to variety of other health issues and in some cases increase sensitivity to pain, thus compounding their existing pain problem(s).

Other matter 2: Effective of up-scheduling and potential unintended consequences

The Guild's consumer survey reveals more than half of respondents indicated a General Practitioner had originally recommended they use a product containing codeine for pain relief as shown below.

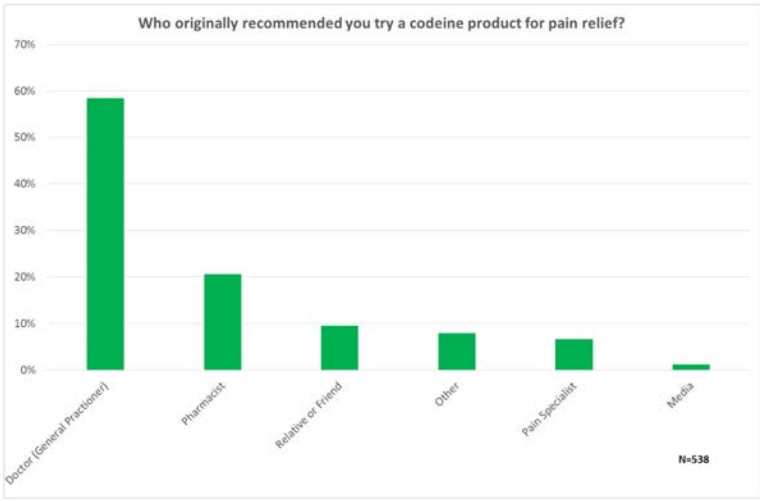

Figure 5 – Guild consumer survey of Schedule 3 products containing codeine, April 2015- Product Recommendation

There is little evidence that indicates up-scheduling products to Schedule 4 as a stand-alone measure reduces the rate of misuse and abuse of medicines, given the medicines that are classified as Schedule 4 and Schedule 8 can also be subject to misuse and abuse.[27]

[25] The Value of OTC medicines in Australia – March 2014, 8

[26] Egli, M., Koob, G. F., & Edwards, S. (2012). Alcohol dependence as a chronic pain disorder. *Neuroscience & Biobehavioral Reviews*, *36*(10), 2179-2192.

[27] National Drugs Strategy 2012-15, Pharmaceutical Drug Misuse in Australia: Complex Problems, Balanced Responses. NCETA 2011

There is also potential for consumers to be unnecessarily prescribed more potent pain relieving opioid medicines which could compound dependence and overdose issues. The National Drug and Alcohol Research Centre reported that oxycodone prescriptions increased in Australia by more than 150 per cent in just 5 years. Another study put this figure at 180 per cent.[28] This has caused concern among experts that these medicines are being overprescribed, which is leading to increased prevalence of dependence and diversion.[29] This suggests rescheduling medicines, in isolation of other measures, does little to reduce rates of misuse and abuse and only serves to increase costs to consumers and the health system.

As mentioned, re-scheduling all current OTC CACC products to Schedule 4 will likely lead to a large increase in the number of people visiting GPs to obtain analgesic medicines. Combined with the separate government budget proposal to remove certain paracetamol products from the PBS, it is likely there will be an additional large cohort of patients who will be seeking other PBS listed analgesics, which might lead to an increase in prescriptions for higher dose CACC or stronger pain medicines.

Other matter 3: Pharmacy Education and Consumer Awareness Campaign

The Pharmacy Guild of Australia online pharmacist training on Schedule 3 analgesic medicines

The Guild has developed an online training course designed to increase a pharmacist's knowledge of common Schedule 3 pain medicines to improve health outcomes for their patients. This course assists pharmacists to provide the best advice to patients requesting S3 pain medicines with the following learning topics.

- the epidemiology and societal impact of pain in Australia
- the physical and emotional influences on how we manage pain and how we experience sensations of pain
- how a health care practitioner's perceptions of a patient's pain condition can influence the management of their pain
- various classifications of pain
- the appropriate indications and counselling points for Pharmacist Only analgesics
- the advantages and disadvantages of combination analgesic Pharmacist Only Medicines

The Pharmacy Guild of Australia supporting Pain Management Network – consumer campaign

The Guild partnered with the NSW Ministry of Health and the Agency for Clinical Innovation (ACI) in July 2014 to raise awareness of a new online resource to assist people living with chronic pain. The *Pain Management Network* offers practical tools, resources and information to manage chronic pain, drawing upon the latest scientific evidence.[30]

[28] www.abc.net.au/news/2014-04-07/oxycodone-use-on-the-rise-in-australia/5372146 (Accessed 1/05/2015)
[29] IBID
[30] www.aci.health.nsw.gov.au/chronic-pain

This also included development of pharmacist continuing professional development about pain management so as to support consumers. In addition, this training should also support up-skilling pharmacists to better identify inappropriate use of over-the-counter analgesics, especially CACC.

Pharmacy online education on prescription opioid – managing misuse and dependence

The Guild has also worked with Indivior and Prime education on "*Prescription Opioid in Primary care - assessing risk and managing misuse and dependence*" online education which is CPD accredited. The course is the same as the GP course with an additional pharmacy module and is nationally available.

Pharmaceutical Society of Australia's consumer information on safe use of non-prescription codeine

The PSA has recently produced a resource developed in response to increasing reports about the damaging effects of overuse of readily available pain relievers containing codeine. [31] The resource is a useful tool to assist pharmacists to discuss appropriate pain management solutions with consumers. These codeine leaflets and inPHARMation publication which includes training modules for pharmacists and pharmacy assistants were distributed to SelfCare subscribers and pharmacy owner members of PSA in March 2015.

NPS MedicinesWise education program for GP and other health professionals

The Guild understands that the NPS MedicinesWise is planning a GP education program on chronic pain management which will also be available for pharmacists and other health professionals.

National Pharmaceutical Drug Misuse Framework for Action (2012-15)

This framework is investigating action areas relating to supporting pharmacists and other health professionals, regulation and monitoring, structural factors as well as treatment and harm reduction.[32] Effective strategies to address issues of abuse/misuse could be addressed through this framework.

Recommendation

The Guild highlights the measures currently underway to address issues of abuse and misuse of medicines and that time is needed for these initiatives to have their effect.

[31] http://www.psa.org.au/news/psa-provides-pharmacies-with-consumer-information-on-safe-use-of-non-prescription-codeine

[32] http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/Publishing.nsf/content/9C52D7D6E2C14A72CA257C3F001F009D/$File/National%20PDM%20Framework.pdf

Other matter 4: Pharmacy Assessments under the Quality Care Pharmacy Program

The Quality Care Pharmacy Program (QCPP) of the Pharmacy Guild of Australia accredits pharmacies against the Australian standard (AS85000:2011). For the last 11 years, pharmacies have been regularly assessed for compliance related to Quality Use for Medicines via a Standard Maintenance Assessment where 'mystery shoppers' pose as customers seeking non-prescription medicines in various scenarios. Cases have been scored on factors which support medicine QUM and pharmacy staff adherence to industry practice standards.

In the past, this involved pharmacies being regularly assessed for compliance related to Quality Use for Medicines via a Standard Maintenance Assessment where 'mystery shoppers' pose as customers with various scenarios regarding medicine usage and determines pharmacy staff adherence to best practice guidelines.

Analyses of the Guild's Mystery Shopper Program data have shown that pharmacies provide a higher level of intervention (regardless of medicines schedule) when they are aware that there is a potential risk to a particular consumer of the use of a particular medicine. Analyses have shown that the mean scores for the risk scenarios are higher than the 5 year mean for scenarios without risk scores across all states.

Experience with the mystery shopper program has shown that when presented with a request for a scheduled medicine by name, pharmacy staff might consider that:

- the patient has used the product before and is familiar with its use
- the product has been recommended by a another health professional
- a consumer's right to choose.

Branded advertising and consumer expectation (to be supplied a product that they ask for/self-select) appears to influence pharmacy staff behaviour, however when the staff are aware that for certain patients there is a risk associated with the products use, there is a higher level of intervention.

Symptom-based-request scenarios demonstrate there is very high compliance with profession protocols in the supply of Schedule 2 and Schedule 3 analgesic when the consumer:

- asks for assistance;
- describes their symptoms;
- does not ask for the product by brand name.

However, it appears that awareness of the risks associated with codeine-combination analgesics is not as high. This has led to profession wide approach to the supply of non-prescription codeine containing analgesics, as outlined in section 'Other matter 4'.

The mystery shopper data supports the concept, raised in the Report of the National Competition Policy *Review of Drugs, Poisons and Controlled Substances Legislation* (the Galbally Review) that the most important factor to consider in using all OTC products is the interaction between the consumer and the product being used. Therefore, scheduling appears to be a blunt instrument to regulate the supply of medicines unless other measures are in place such as medicine labelling, advertising, and pharmacy staff education regarding risk to (particular) individuals, or in this case, a real-time monitoring system.

The impact of rescheduling of over the counter codeine combination products in May 2010 has led to an improvement in scores across of all domains assessed during the time series analyses. This indicates that pharmacy staff are more vigilant about patient assessment and advice provision subsequent to the schedule change.

For example, since OTC paracetamol/codeine products were rescheduled from Schedule 2 to Schedule 3 in May 2010, the average scores pharmacies obtained in the Standard Maintenance Assessment showed a significant improvement in assessment scores as shown below.

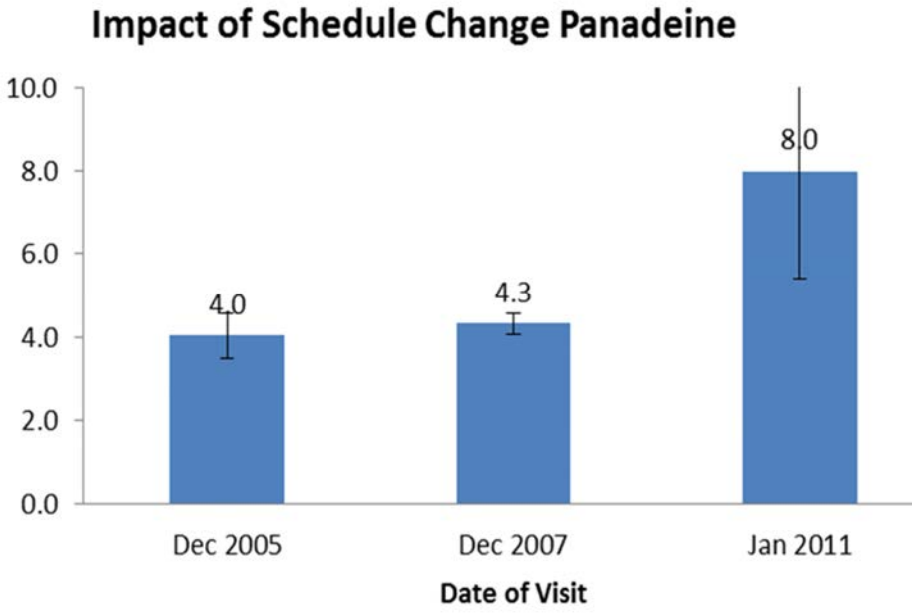

Figure 6 – Standard Maintenance Assessment Scores for Panadeine – pre and post scheduling

Other matter 5: Proposed options

Real-time monitoring

Despite the number of professional guidelines and regulations governing the sale and supply of these medicines, it is often difficult for a pharmacist to determine whether a patient may have a codeine addiction, particularly if they are visiting a number of different pharmacies to avoid detection. This is similar to 'doctor shopping' where patients visit multiple doctors to support dependency on a particular prescription medicine.

The Guild supports pharmacists routinely advising patients regarding appropriate use of Schedule 3 CACC, particularly cautioning consumer to limit use to the short term. The Guild believes a mandatory monitoring system would greatly assist the pharmacist in meeting their professional responsibility by providing an effective tool to support provision, referral and/or refusal of supply to consumers identified as misusing or abusing CACC.

The Guild considers real-time monitoring to be fundamental in ensuring Quality Use of Medicines principles are upheld in the prescribing and supply of these medicines and would address the issue of section 52E (b) "*the purposes for which as substance is to be used and the extent of use of a substance*."

The benefits of implementation of real-time monitoring systems for CACC include:

- *Targeted Regulation* – Real-time monitoring can be used to maintain appropriate and necessary access to medicines for the Australian community, whilst restricting inappropriate use.

- *Professional Decision Support* – Real-time monitoring provides powerful and pertinent data to pharmacists at the point of supply, thereby helping pharmacists determine if the supply of a medicine is appropriate. At the same time as the supply/ non-supply decision is explained to the patient, relevant clinical information can be provided, and electronic record maintained to show that this has been done.

Examples of real-time monitoring systems include:

- Project STOP, real-time recording and monitoring system for the sales of pseudoephedrine-based products. It aims to minimise diversion of pseudoephedrine into illicit manufacture of methamphetamine. Approximately 80% of pharmacies nationally are using Project STOP. In 2014:
  - a total of 2,232,281 supply requests were recorded nationally;
  - 17,997 requests were denied; and
  - 23,024 requests were recorded as safety sales.

- Electronic Recording and Reporting of Controlled Drugs (ERRCD) currently being rolled out in states and territories.

Legal Framework – Currently, recording and reporting requirements for Schedule 3 medicines vary between state/territory jurisdictions. In order to promote national consistency, an amendment should be made to the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP). This change would involve creating a new section, such as an Appendix that would list 'Pharmacist Only Medicines' that are required to be recorded in a real-time monitoring system by the pharmacy prior to being sold.

Support from consumers – In the consumer survey conducted by the Guild, the majority of respondents (95 per cent) indicated they were prepared to have their details recorded when purchasing codeine combination products if this meant these products would remain available over-the-counter. See graph below and Attachment 1 for further information.

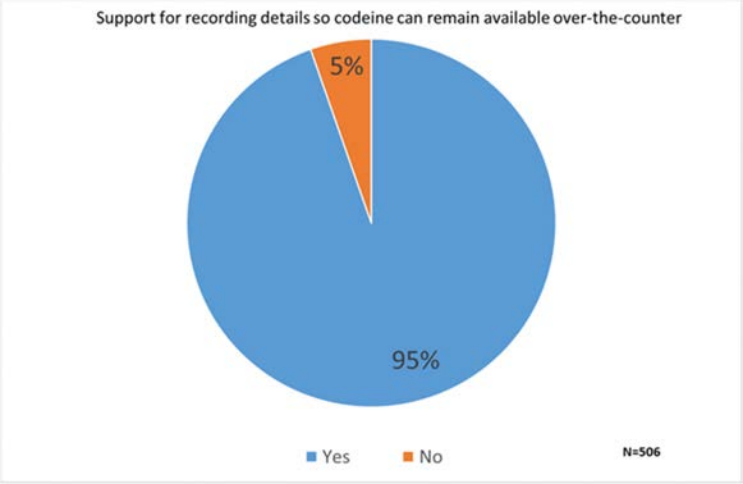

Figure 7 – Guild consumer survey of Schedule 3 products containing codeine, April 2015- consumer support for real-time monitoring

Recommendation

Regardless of the extent of codeine abuse/misuse (which the Guild contends is small relative to overall usage) the most cost effective and efficient method to address the issue of misuse/abuse is to implement a national real-time monitoring system supported by legislation that mandates the recording of CACC.

Moving these products to Schedule 4 independent of other measures is unlikely to address issues of dependence but will lead to substantial increased costs to consumers and the health system in the form of additional doctor visits and PBS costs. There is also the risk that consumers previously on OTC CACC could be moved to higher strength CACC or other more potent prescription medicines.

Submission on Proposed Amendments to the Poison's Standard (Medicines)

I wish to express my opposition regarding the proposition of putting low dose (8mg) Codeine combinations on to a medical prescription only supply basis.

Several million Australians suffer from chronic pain such as migraines, period pain, chronic back pain to name a few. A substantial portion of these would obtain remarkable relief from the use of low dose Codeine/Paracetamol combinations.

On many occasions these combination medications are the only type which relieves their symptoms.

Removing the accessibility of low dose Codeine/Paracetamol combinations directly from pharmacies may result in these people using higher doses of Paracetamol and non-steroidal anti-inflammatories (NSAID) both groups having potential serious side effects.

High doses of Aspirin and other non-steroidal anti-inflammatories such as Ibuprofen, Diclofenac etc increase the risk of gastrointestinal bleeding as well as cerebrovascular bleeding.

Increased doses of Paracetamol are particularly dangerous. Even normal dosaging of Paracetamol has resulted in hepatic necrosis and death in individuals.

There has been a worldwide trend in recent years to reduce the recommended doses of Paracetamol due to concerns regarding liver toxicity and subsequent liver failure and possible death.(they may need a liver transplant)

There is only a slim margin of safety with the current recommended dosaging of Paracetamol.

To upgrade low dose Codeine/paracetamol combinations to prescription only will increase the price of these from perhaps $8.00 for 20 tablets to most likely $30.00 to $40.00 per packet once the medical consultation and pharmacy dispensing fees are taken into account.

If low dose Codeine/Paracetamol combination becomes a medically prescribed item only, it may well become a marketable commodity similar to other medically prescribed opiate analgesics.Patients may ask for stronger opiates to break in half or quarters to save money e.g panadeine forte (codeine 30mg versus 8mg).

In the United States up to two thirds of opiate overdoses are caused from high strength opiate analgesics obtained on medical prescription. Most likely the same situation will occur in Australia.

There will always be a very small percentage of people who will use any agent which gives them a "slight high". If it is not Codeine it most likely would be alcohol, aerosol propellants, glue, petrol etc.

There are also those people who suffer from **acute pain** such as severe sporting injuries with fractures,haematomas etc or those who have any form of surgery including excision of skin cancers, removal of wisdom teeth who may require something stronger than Paracetamol. In this group anti-inflammatories are often best avoided for the first 2 days as they increase the risk of bleeding from the injury or surgical site.

Paracetamol in high doses may be used unless a opiate analgesic is medically prescribed.

In summary I feel the status quo should remain with low dose Codeine/Paracetamol combinations being monitored by pharmacists.

Yours sinc

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CODEINE RESCHEDULING PROPOSAL

SUBMISSION FOR JULY 2015 ACMS MEETING

Date: April 2015 Total number of pages: 5

1 INTRODUCTION

Sanofi welcomes the opportunity to comment on the Scheduling Proposals to be considered at the forthcoming ACMS Meeting to be held in July 2015, as outlined in the Notice inviting public submissions under Reg 42ZCZK of the Therapeutic Goods Regulations 1990. This document provides the Company response to the following scheduling proposal relating to codeine:

> **Codeine**
> *To delete the Schedule 3 entry for codeine, and reschedule the current Schedule 3 codeine entry to Schedule 4 due to potential issues of morbidity, toxicity and dependence.*
>
> *Consideration may be given as to 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 may be given as to whether the Schedule 2 entry for codeine should also be amended*

As a diversified healthcare company Sanofi supplies a broad range of medicines and devices in Australia across the spectrum of prescription and non-prescription medicines. Sanofi has a large manufacturing facility in Brisbane supporting its complementary medicines portfolio and is the Sponsor for several OTC analgesic products containing a combination of paracetamol and codeine.

Sanofi is a member of ASMI (Australian Self Medication Industry), the peak body representing companies involved in the manufacture and distribution of consumer healthcare products (non-prescription medicines) in Australia. Sanofi strongly supports Quality Use of Medicines and a regulatory framework that ensures appropriate regulation commensurate with the potential risks to public health and safety. This is critical to ensure a viable medicines industry in line with the National Medicines Policy, to support continuing investment and innovation in Australia.

In responding to the above scheduling proposal for codeine, Sanofi agrees with the comments made by ASMI that the lack of specific information on the scientific and medical concerns raised limits the ability to respond appropriately. It is therefore assumed that the proposal has arisen due to concerns arising on misuse and potential dependence, however there has been no evidence presented that indicates widespread problem of misuse or addiction when these products are used appropriately and according to directions.

As this proposal has the potential to significantly impact both the industry and consumers who use analgesics products responsibly, it is disappointing that a more transparent process has not been considered warranted. Sanofi strongly endorses the views expressed by ASMI, the Australian Medical Association and the Pharmacy Guild that re-scheduling codeine containing analgesics to Schedule 4 (S4) is not the most appropriate way of minimising harm from misuse or dependence on codeine containing analgesics.

2 RESPONSE TO RESCHEDULING PROPOSAL FOR CODEINE

An outlined in the ASMI submission, after re-scheduling to Schedule 3 in 2010, OTC pack sizes of codeine containing analgesics have been limited to 5 days' supply. Given the large number of people using these products and the volume of sales, adverse events such as dependence and misuse or abuse are low in comparison, indicating that the vast majority of people use these products appropriately. Moreover, a 5 day pack size cannot on its own instigate dependence and it is excessive duration of use and dose escalation which may predispose to dependence. Repeat purchases are needed for this to occur.

Importantly, the Australian sales data for OTC codeine containing analgesics does not indicate increasing sales (a factor which may be an indication of increasing risk of misuse):

- There has been an overall reduction in sales of OTC ibuprofen and codeine / OTC paracetamol + codeine containing analgesics between 2009 and 2014 (based on IMS data, which monitors supply through warehouse to pharmacies)
- Sales of paracetamol plus codeine having dropped then plateaued since 2010 (IMS data)

Sanofi endorses the ASMI submission which details the considerations of unintended consequences of making codeine containing analgesics S4. These include the risk of consumers receiving higher strength codeine containing prescription medicines or larger pack sizes than available from a pharmacy, as well as the significant burden on the healthcare system and potential for increased costs. In the absence of prescription monitoring and the potential for doctor-shopping, patients who have addiction and misuse problems are more likely to continue unnoticed until serious harm occurs.

Sanofi fully endorses Quality Use of Medicines and considers appropriate use of OTC codeine-containing analgesics is critical to ensure mitigation of the risk of potential misuse that may lead to addiction. Sanofi supported the voluntary introduction of the prominent front of pack warning statements, modelled on the mandatory front of pack labelling introduced in the UK in 2009, that specify "Can cause addiction. Do not use for more than 3 days". As a Pharmacist Only (S3) medicine, pharmacists are required to assist the consumer with appropriate product selection, counsel on appropriate use and to recommend an alternative analgesic option where it is warranted.

Sanofi strongly believes that the front of pack statements should be made mandatory for all S3 codeine containing analgesic products. This will ensure all consumers receive packs that incorporate the appropriate warnings and thus optimize the effectiveness of the communication of potential risks. Sanofi also supports implementation of the following additional measures to detect people who may be currently misusing the products and tol educate and monitor current and future users to prevent them from exceeding the recommended dose or taking products for longer than necessary:

- As proposed by The Pharmacy Guild, a real-time monitoring system, coupled with pharmacist training, guidelines and protocols, to allow pharmacists to identify consumers if they begin to purchase inappropriate quantities of codeine-combination analgesics, and refer them to a GP or pain clinic for intervention.

  - Project STOP, currently used to monitor pseudoephedrine sales in real time, has been successful in addressing diversion and misuse and a similar approach could be implemented for codeine.

- Full implementation, by the PSA and/or other pharmacy bodies, of a program based on the PSA *'Guidance for provision of S3 combination analgesics containing codeine'* to equip pharmacists with the information they need to:
  - counsel and educate consumers about the appropriate use of codeine containing analgesics, including identification and management of medication overuse headache
  - educate and increase awareness of the management of chronic pain and accompanying mental health concerns such as anxiety and insomnia, which can also lead to problematic use.
- Improved collaboration between pharmacists, doctors and other services to assist people with these concerns, together with improved education for healthcare professionals and consumers
  - updating of the Product Information and Consumer Medicine Information to include information on the risk of addiction when the dose or recommended duration of use are exceeded to further mitigate risks of misuse.

3 RECOMMENDATION

- Sanofi does not support the proposal to reschedule codeine containing analgesics from S3 to S4 on the grounds this is not the most appropriate means of strengthening existing risk mitigation activities to minimise possible misuse.
  - The existing arrangements have not resulted in an increased trend in sales or adverse reports linked to misuse or abuse.
  - A Schedule 4 entry is no guarantee against misuse or abuse.
  - Misuse and abuse of prescription opiate and psychoactive drugs has escalated significantly over the past several years.
  - Unintended consequences of a change in scheduling may result in consumers receiving higher strengths and longer treatment durations than for products available over the counter.
- Sanofi strongly supports the introduction of additional risk mitigation measures that will further support Quality Use of Medicines by ensuring appropriate and responsible use of OTC products for short term, acute pain management including:
  - mandatory front of pack warnings *'Can cause addiction. Do not use for more than 3 days'*.
  - a national real-time monitoring system for OTC codeine containing analgesics to help manage the risk of potential misuse. This will allow pharmacists to identify consumers who may be at risk and offer early referral to a GP or pain clinic for specialist intervention.
  - comprehensive educational and support activities for both healthcare professionals and consumers.

From: katie wright [mailto:katie_wright_@hotmail.com]
Sent: Tuesday, 28 April 2015 9:47 PM
To: Medicines Scheduling
Subject: Proposed Amendments to the Poisons Standard (Medicines)

To whom it may concern,

Please see below my response to proposed amendments to the poisons standard (medicines).

1. codeine - SUPPORT
As current studies suggest that the dose of codeine in OTC products does not provide any additional therapeutic benefit but can contribute the adverse reaction burden I would support the proposal to reschedule ALL codeine containing preparations to S4. Further to my support is the knowledge that codeine containing preparations are subject to abuse, and the combination analgesic (eg paracetamol & ibuprofen), which while safe when used in dosages not exceeding the recommended maximums, contribute to significant hepatic and renal toxicity, respectively. I feel that if only S3 formulations are subject to rescheduling, persons with a codeine dependency may be forced to abuse other formulations containing codeine (eg. S2), which since these contain additions combination ingredients (eg. phenylepherine in cold and flu products), may contribute to further significant toxicity, and increase hospital admissions, increasing the cost to the government.

2. esoemprazole - DO NOT SUPPORT
- with the growing number of pharmacies, making any PPIs S2, would mean consumers have no monitoring to ongoing and/or long term use of PPIs. This may lead to an increase in adverse reactions, especially those linked to long term use eg. increased risk of pneumonia and osteoporosis.
- I believe it is outside the scope of practise for a pharmacy assistant to both diagnose GORD and suggest treatment for same. especially since the symptoms of GORD are similar to those of heart attack and any misinterpretation of these may lead to poor outcomes for consumers including death.

3. hydrocortisone plus antifungal - SUPPORT

4. naloxone - SUPPORT

5. orlistat - DO NOT SUPPORT
With the growing number of people with anorexia and bulimia the risk of abuse with this product is VERY high.

Thank you for you time in considering the above.

regards,

Katie Wright

promoting excellence in medicines management

ABN 54 004 553 806

6 May 2015

Medicines.Scheduling@tga.gov.au

Re: Consultation: Invitation for public comment – 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 proposed changes are presented below.

Codeine

In principle, because of the well documented risks associated with the appropriate and inappropriate use of codeine, SHPA would support a decision that would restrict access to all products that contain codeine (alone or in combination).

However, we note 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.

SHPA believes that changes could be made to reduce the harm associated with the use of codeine whilst maintaining reasonable access at a reasonable cost. This could be achieved through scheduling all products containing codeine (alone or in combination) to either Schedule 3 or Schedule 4.

SHPA believes a re-evaluation of products containing codeine because of changes to scheduling would lead to a decrease in the number of products:

- with a sub-therapeutic dose of codeine that are no more effective than simple analgesia[1] and
- containing codeine altogether.

The total amount of codeine available in the whole pack could be used to define if the product is scheduled in Schedule 3 or 4.

As Schedule 3 medicines are pharmacist only medicines, and in essence a pharmacist's prescription, SHPA believes that all supplies of these products should be dispensed, individually labelled and recorded by the pharmacist, to appropriately monitor and manage patient usage of codeine, as well as in the context of their other medicines.

SHPA believes that a national real-time recording and reporting system would mitigate many of the risks of the inappropriate use and diversion of codeine.

Naloxone

SHPA supports the amendment to include single use prefilled syringes for injection containing 400 micrograms/mL of naloxone or less in Schedule 3.

Esomeprazole

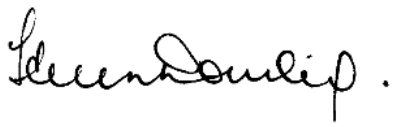
In principle SHPA does not support any amendments to create Schedule 2 entries for proton pump inhibitors (PPI). We believe that these medicines should be Schedule 3 medicines to ensure appropriate consultation and review by a pharmacist.

Allowing consumers access to this class of medicines without professional review has led to unintended consequences. A recent study published in the Canadian Medical Association Journal on the use of PPIs in older patients concluded that older adults who started PPI therapy had an increased risk of acute kidney injury and acute interstitial nephritis[2], and recommended that clinicians understand the risks of PPI therapy, monitor patients appropriately and discourage the indiscriminate use of PPIs. Another recent study in the JAMA Internal Medicine Journal concluded that recurrent PPI use is associated with elevated risk of *Clostridium difficile* infections[3] and encouraged the cessation of inappropriate PPI use.

In addition, as part of the Choosing Wisely Australia campaign, the Royal Australian College of General Practitioners (RACGP) have flagged the long term use of PPIs as one of the top five tests, treatments or procedures which should be questioned by GPs and their patients.[4]

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

Yours sincerely



Helen Dowling
Chief Executive Officer
(BPharm,DipHospPharmAdmin,GDipQIHCare,FSHP,AICD)

References

1. Analgesic Expert Group. Therapeutic Guidelines: Analgesic. Version 6. Melbourne: Therapeutic Guidelines Limited; 2012.
2. Antoniou T, Macdonald E, Hollands S, Gomes T, Mamdani M, Garg A et al. Proton pump inhibitors and the risk of acute kidney injury in older patients: a population-based cohort study. CMAJ Open. 2015;3(2):E166-E171.
3. McDonald E, Milligan J, Frenette C, Lee T. Continuous Proton Pump Inhibitor Therapy and the Associated Risk of Recurrent Clostridium difficile Infection. JAMA Internal Medicine. 2015;175(5):784.
4. Royal Australian College of General Practitioners (RACGP). East Melbourne. Australia. Available from <http://www.racgp.org.au/yourracgp/news/media-releases/choosing-wisely/>.

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6 May 2015

The Secretary
TGA Advisory Committee of Medicines Scheduling
Therapeutic Goods Administration

Dear Sir/Madam

RE: Proposed amendments to the Poisons Standard (Medicines)

Thank you for the opportunity to provide feedback on the proposed amendments to the Poisons Standard for Codeine, Esomeprazole, Hydrocortisone and hydrocortisone acetate (excluding other salts and derivatives), Naloxone and Orlistat.

Endeavour Consumer Health is the Consumer Products division of EBOS Group Ltd. We are the sponsor and supplier of hundreds of OTC products to Australian Pharmacies under the brands of Chemmart® and Pharmacy Choice®.

Codeine

It is our opinion that that the current scheduling of codeine is both entirely appropriate and responsible.

Listing codeine products as Schedule 3 (S3) pharmacist-only medicines enables patients to access pain relief quickly and effectively while receiving professional advice and health care from their pharmacist. Pharmacists are trained in medication management for good reason – their involvement mitigates the associated risks.

In contrast, rescheduling codeine products as Schedule 4 (S4) medicines would, in our opinion, create a number of problems including (but not limited to):

- Requiring patients to visit a General Practitioner (GP) in order to access codeine products means increased pressure on the GP health segment and higher costs for taxpayers;
- GP visits come at a cost and accessibility is often limited. Therefore, it's an impractical option for patients who need urgent relief;
- It may prevent people in pain getting the medicine they need due to the associated cost and time restraints; and
- It may encourage "doctor shopping".

It is our opinion that alternative control methods for substance abuse, such as Project STOP currently in place for pseudoephedrine-based products, should be considered before resorting to rescheduling.

Therefore, we are writing to reaffirm our support for the S3 scheduling of codeine and, for the reasons outlined above, our opposition to the proposed rescheduling to S4.

With regard to the other proposed amendments to the Poisons Standard:

Esomeprazole

- We support the proposal to amend the scheduling to include oral preparations containing 20mg or less of esomeprazole per dosage unit for the relief of heartburn.

Hydrocortisone and hydrocortisone acetate (excluding other salts and derivatives)

- We support the proposal to amend the scheduling of hydrocortisone and hydrocortisone acetate to include preparations for dermal human therapeutic use containing 1% or less of hydrocortisone when combined with an anti-fungal substance.

Naloxone

- We support the proposal to amend the scheduling of naloxone to include single use prefilled syringe preparations for injections containing 400mg/ml or less in S3.

Orlistat

- We support the proposal to amend the scheduling of orlistat from S3 to S2.

Once again, thank you for the opportunity to provide this feedback.

Yours sincerely,

Jennifer Luke
Executive Director
Endeavour Consumer Health

Pharmaceutical Society of Australia

Submission to the July 2015 meeting of the Advisory Committee on Medicines Scheduling

MAY
2015

Purpose

The Pharmaceutical Society of Australia (PSA) makes this submission in relation to proposed amendments to the *Poisons standard* referred by the delegate for scheduling advice for consideration by the Advisory Committee on Medicines Scheduling (ACMS) at the July 2015 meeting.

PSA's comments relate to the proposed amendments to: codeine; esomeprazole; hydrocortisone and hydrocortisone acetate; naloxone; and orlistat.

About PSA

PSA is the peak national professional pharmacy organisation representing Australia's approximately 28,000 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.

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[1] Pharmacy Board of Australia. Pharmacy registrant data: December 2014. PBA: 2015; Mar. At: **www.pharmacyboard.gov.au/documents/default.aspx?record=WD15%2f16240&dbid=AP&chksum=GlzFM3NCWODifvb2zYBDTA%3d%3d**

Recommendations

Codeine

PSA believes that Schedule 3 remains appropriate for codeine-containing analgesics to support consumer access with pharmacist oversight and tailored advice.

PSA does not support rescheduling these products to Schedule 4. A more restrictive schedule in this instance will not fundamentally address the issues of misuse and further, does not provide a holistic consumer-focussed solution.

PSA believes it is appropriate to consider amending the maximum pack size for Schedule 3 codeine given our current advice is that codeine-containing analgesics are intended for short term use, not exceeding three days.

PSA strongly urges for the implementation of a national real-time recording and reporting system to be given the highest priority and seeks the support of the ACMS in this regard.

PSA advocates for a partnership approach between consumers, health professionals, governments and industry to informing consumers about OTC medicines and promoting the quality use of medicines.

PSA suggests that the Schedule 2 entry of codeine be considered in the context of issues including: the evidence-base around the effectiveness of these medicines; the availability of other options for the management of coughs and colds; impact on community pharmacies and industry; any data on the use of these medicines and any associated trends in adverse reactions; and overseas trends and activities.

PSA strongly suggests that adequate time is required for pharmacist support tools recently launched by PSA (relating to codeine-containing OTC analgesics) to be implemented appropriately.

PSA believes consideration is warranted of innovative and collaborative research projects and Australian studies currently under way which may help inform future directions.

Esomeprazole

PSA supports the proposed inclusion of esomeprazole in Schedule 2 for oral preparations containing 20 mg or less per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease (GORD), in packs containing not more than 7 days' supply. PSA recommends the inclusion of appropriate warning statements and reference to the need to seek medical advice for certain symptoms or situations.

Hydrocortisone and hydrocortisone acetate

PSA believes 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 (with the conditions listed) in Schedule 2.

Naloxone

PSA supports the proposal to include single use prefilled syringe preparations for injection containing 400 micrograms/ml of naloxone or less in Schedule 3.

PSA suggests development of a practice support package for pharmacists would be an essential component to support this rescheduling.

Orlistat

PSA believes the involvement of pharmacists in supporting consumers through an holistic approach to weight management is important and therefore the current Schedule 3 entry for orlistat remains appropriate. PSA is firmly opposed to the proposed amendment for inclusion of orlistat in Schedule 2.

Comments on proposed amendments

Codeine

Proposal to delete the Schedule 3 entry for codeine, and reschedule the current Schedule 3 codeine entry to Schedule 4 due to potential issues of morbidity, toxicity and dependence.

Consideration may be given as to 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 may be given as to whether the Schedule 2 entry for codeine should also be amended.

Background

PSA recognises the growing use of over-the-counter (OTC) analgesics containing codeine in the community, and is concerned with the rising levels of harm associated with their inappropriate use. PSA has recently issued a position statement on *Minimising harm from the inappropriate use of over the counter analgesics*.[2]

PSA recognises that the increasing incidence of acute and chronic pain conditions and the range of pain management options available to consumers can present challenges for successful treatment. PSA re-iterates that pharmacists have a critical role in advising and supporting consumers, carers and other health professionals on appropriate pain management options.

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[2] 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**

Key issues

Key issues identified in PSA's position statement include the following.

Availability and access

PSA supports consumers continuing to have reasonable access to all codeine-containing OTC products with the advice of a pharmacist.

Pharmacists have medicines and medication management expertise and can make an assessment of the safety profile of all OTC analgesics while considering any reported trends in inappropriate use and adverse health outcomes. The suitability of codeine-containing analgesics may need to be reviewed particularly in the context of a person's metabolic profile which may result in an increased risk of toxicity for some, while others may derive minimal or no analgesic benefit. Pharmacists also have regard for the therapeutic efficacy of these products (given the information that sub-therapeutic doses of codeine are contained in these OTC preparations) in providing the best advice tailored for the consumer.

Where pharmacists have concerns about a consumer's use of OTC analgesics containing codeine, the need for a referral for medical advice would be discussed, and initiated as appropriate.

Given the appropriateness of pharmacist oversight and intervention, PSA does not support the rescheduling of codeine-containing OTC (Schedule 3) analgesics to Schedule 4 (Prescription Only Medicine). Such a move does not provide a holistic consumer-focussed solution, nor does it serve the best interest of the consumer. It is likely that the medical profession would be burdened with the need for a prescription and a majority of consumers disadvantaged with additional costs and possibly delayed treatment in having to secure a medical appointment.

Further, PSA is aware that prescription-only opioid analgesics are also associated with inappropriate use, and strongly believe that the rescheduling of products will not fundamentally address the issues of misuse.

PSA notes that packs in excess of five day's supply of codeine-containing analgesics are currently included in Schedule 4 thereby providing people who have a genuine need for chronic use to benefit from regular medical oversight.

The current professional advice provided for codeine-containing OTC analgesics includes a warning statement that they are intended for short term (three days) use only and they "can cause addiction". PSA has developed a new Cautionary Advisory Label (CAL) — see below under *Support for pharmacists*. This initiative is also largely supported by industry. Thus, PSA would suggest that it may be appropriate for the ACMS to consider an amendment to the current maximum pack size of Schedule 3 codeine.

Real-time recording and reporting

For many years PSA has expressed 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.

This is not the same as Project Stop which is being used nationally to monitor the supply of pseudoephedrine-containing medicines to prevent their diversion into the production of methamphetamine. Project Stop is regarded primarily as a law enforcement tool although its use by pharmacists is not mandatory in all jurisdictions. Pharmacists use it as a tool to identify persons who may be obtaining pseudoephedrine-containing medicines, usually from many different pharmacies, in quantities in excess of accepted therapeutic use and therefore, with a high likelihood of involvement in illicit activities.

The current Fifth Community Pharmacy Agreement (5CPA) has funds allocated for the Electronic Recording and Reporting of Controlled Drugs (ERRCD) initiative.[3] A system which integrates with both prescribing and dispensing software has the ability to provide relevant data access to prescribers and pharmacists to help inform their clinical decision-making on the use of Controlled Drugs. However, PSA believes there are synergistic opportunities and we have called for the system to be expanded to include all drugs of dependence, including OTC analgesics.

Unfortunately, the expiry of 5CPA is imminent and PSA is not informed regarding the status of implementation of the ERRCD initiative as they are being progressed separately in each state and territory. PSA is aware that real-time monitoring systems for prescribers and pharmacists were reportedly implemented in British Columbia and Canada, and noted to be an effective strategy to detect and prevent pharmaceutical misuse.[4]

PSA is aware that coronial reports in several jurisdictions have also advocated for the implementation of a system to monitor the prescribing and dispensing of drugs of dependence in real-time. A system to help minimise and prevent the misuse of codeine-containing OTC analgesics and other drugs of dependence will have a direct impact on improving the safety of consumers and carers, facilitating timely referrals when considered necessary to appropriate health professionals, and reducing unnecessary hospital admissions and mortality.

Thus, despite these potential benefits, currently the opportunity for pharmacists to be able to record and report on the dispensing and supply of particular substances and medicines including OTC analgesics containing codeine in accordance with relevant state and territory legislation is not being realised.

Partnership approach

PSA continues to advocate strongly for a partnership approach to promote the quality use of medicines by consumers, health professionals, governments and industry. This is necessary to ensure consistent messages are used and understood. It would also create synergies and efficiencies in the implementation of initiatives.

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[3] Australian Government Department of Health and Ageing, and The Pharmacy Guild of Australia. Electronic recording and reporting of controlled drugs [fact sheet]. At: **http://5cpa.com.au/files/fact-sheet-electronic-recording-and-reporting-of-controlled-drugs/**

[4] In: Australian Drug Foundation. Prevention Research Quarterly: current evidence evaluated — Pharmaceuticals. West Melbourne: ADF; 2008.

Cough and cold preparations

PSA is also aware that codeine is contained in many cough and cold preparations in Schedule 2.

Reports[5] on the effectiveness of OTC preparations for cough have indicated that codeine appeared no more effective than placebo in reducing cough symptoms.[6,7] Further, while recommendations are given that there is some supporting evidence for the use of codeine for short-term symptomatic relief of coughing associated with chronic bronchitis, its use is not recommended for cough due to upper respiratory infections due to limited efficacy for symptomatic relief.[8]

With regards to codeine's analgesic effect, PSA has previously noted the concerns raised that most OTC preparations are believed to contain sub-therapeutic doses of codeine. Whilst the lowest effective dose of codeine has not been established, there is no conclusive evidence to show that analgesics containing 8–15 mg of codeine per tablet (in combination with paracetamol, aspirin or ibuprofen) have any benefits over non-opioids alone.[9,10]

Given most coughs and colds are self-limiting, pharmacists are able to consider alternatives including non-pharmacological management.[11] PSA also recognises that, as part of their professional practice, pharmacists will consider consumer beliefs and expectations when assisting consumers to make safe and responsible self-medication choices.

Regarding consideration by the ACMS on whether the Schedule 2 entry for codeine should also be amended, PSA's response is that having all codeine-containing OTC preparations in Schedule 3 would provide consistency in consumer expectations of pharmacist intervention and provide optimal use of these products.

However, PSA regards that the following issues (and possibly others) would need to be balanced in considering a final decision.

- A substantial number of codeine-containing cough and cold products would be captured and, by adding to the current Schedule 3 codeine entry, would result in resource and workload implications for community pharmacists.

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5 Smith SM, Schroeder K, Fahey T. Over-the-counter (OTC) medications for acute cough in children and adults in community settings (Cochrane Review). 2014. At: **http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001831.pub5/pdf**

6 Eccles R, Morris S, Jawad M. Lack of effect of codeine in the treatment of cough associated with acute upper respiratory tract infection. J Clin Pharm Therap 1992;17(3):175–80.

7 Freestone C, Eccles R. Assessment of the antitussive efficacy of codeine in cough associated with common cold. *J Pharm Pharmacol* 1997;49:1045–9.

8 Bolser DC. Cough suppressant and pharmacologic protussive therapy: ACCP evidence-based clinical practice guidelines. Chest 2006;129:238S–249S.

9 Australian Medicines Handbook, 2015. p. 50, 51.

10 Derry S, Karlin S, Moore R. Single dose oral ibuprofen plus codeine for acute postoperative pain in adults (Cochrane Review). 2015. At: **http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010107.pub3/pdf**

11 Sansom LN, ed. Australian pharmaceutical formulary and handbook. 23rd edn. Canberra: Pharmaceutical Society of Australia; 2015. pp. 524–7.

- Follow-up of overseas data and reports of relevant medicines is warranted. For example, following a recent review, the European Medicines Agency has announced that the use of codeine for cough and cold is[12,13]:
    - now contraindicated in children below 12 years; and
    - not recommended in children and adolescents between 12 and 18 years who have breathing problems.
- Industry data (not available to PSA) reportedly shows no association between the fall in supply of codeine-containing analgesics (since their rescheduling to Schedule 3 in 2010) with any unexpected increase in demand for codeine-containing cough and cold products. An increase in single ingredient analgesics has apparently been observed.
- Although data is not available to PSA, industry has suggested that feedback from the community pharmacy sector and adverse drug reaction reporting figures do not raise any concerns with cough and cold products containing codeine.
- Many other options for cough and cold treatment (not containing codeine) would remain available in Schedule 2.

Support for pharmacists

PSA is committed to supporting pharmacists to provide solutions to consumers seeking to manage pain and addiction issues.

PSA provides continuing professional development and practice support resources to inform pharmacists' skills in pain management and addiction care. Topics such as options for pain relief and management, efficacy and adverse effects of OTC single ingredient and combination analgesics, codeine dependence, harm from the misuse of codeine-containing combination analgesics, consumers' perspective on pain management options and pharmacist advice and intervention, are regularly covered for pharmacist and pharmacy staff education.

Recently PSA has developed additional resources which are now being implemented:

- guidance document[14] for pharmacists to support the provision of Schedule 3 combination analgesics containing codeine;

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12 European Medicines Agency. Codeine not to be used in children below 12 years for cough and cold. 24 Apr 2015. At: **www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Codeine_cough_or_cold_in_children/Position_provided_by_CMDh/WC500186159.pdf**

13 European Medicines Agency. Codeine-containing medicinal products for the treatment of cough or cold in paediatric patients. At: **www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Codeine_containing_medicinal_products_for_the_treatment_of_cough_and_cold_in_paediatric_patients/human_referral_prac_000039.jsp&mid=WC0b01ac05805c516f**

14 Sansom LN, ed. op. cit. pp. 577–580.

- new CAL[15] 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*;

- 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 initiatives require adequate time for implementation to take effect.

Research

The misuse of codeine-containing analgesics is a concern in many countries and PSA is interested in collaborative initiatives and innovative solutions.

PSA is aware of the CODEMISUSED project[16] involving researchers, consumers, multidisciplinary health professionals and treatment providers in Ireland, United Kingdom and South Africa. A strong partnership approach is evident in this project which aims to create a model including monitoring systems, web- and pharmacy-based interventions, and educational materials for health professionals and treatment providers.

PSA also understands that several Australian studies funded through the National Health and Medical Research Council are under way to investigate pharmaceutical opioid analgesic dependence and treatment. We believe data and outcomes of such studies (yet to be published) need to be given due consideration.

Summary

PSA believes that, on balance, Schedule 3 remains appropriate for codeine-containing analgesics to support consumer access with pharmacist oversight and tailored advice. However, PSA issues a strong call for the implementation of a national real-time recording and reporting system to be given the highest priority and seeks support of the ACMS in this regard. PSA also re-iterates its advocacy for a partnership approach to informing consumers about OTC medicines and promoting the quality use of medicines.

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15 Sansom LN, ed. op. cit. p. 12.

16 Further information available at: **http://codemisused.org**

Esomeprazole

Proposal to amend the scheduling of esomeprazole to include oral preparations containing 20 mg or less of esomeprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 7 days' supply in Schedule 2.

Proton pump inhibitors (PPIs) are widely available as OTC medicines and well established for use in the relief of heartburn and other symptoms of gastro-oesophageal reflux disease (GORD).

PSA understands the current Schedule 3 entry for esomeprazole permits up to 14 days' supply of 20 mg (or less) per dosage unit.

PSA notes that from 1 June 2015, pantoprazole (20 mg or less per dosage unit) up to 7-days' supply will be included in Schedule 2. Given the comparable safety profiles generally of all PPIs and to support consistency and choice for consumer access, PSA supports the proposed amendment to include esomeprazole up to seven day's supply in Schedule 2.

However, we provide the following comments for consideration by the ACMS.

- A recommendation to seek medical advice should be included on the packaging, for example, for[17,18]:
    - atypical (e.g. cardiac-type chest pain) or alarm (e.g. painful or difficulty in swallowing) symptoms are present;
    - symptoms occur daily;
    - age less than 18 years, or over 55 years with recent onset symptoms;
    - two weeks of continuous PPI therapy has not resulted in adequate control of symptoms.

- Inclusion of a warning statement would be warranted regarding, for example:
    - increased risk of adverse effects in older people;
    - potential for significant drug interactions, including some that may require dose adjustment (e.g. citalopram, escitalopram, clomipramine).

In summary, PSA supports the amendment to the scheduling of esomeprazole as proposed.

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[17] Antoniou T, Macdonald EM, Hollands S, Gomes T, Mamdani MM, Garg AX, Paterson JM, Juurlink DN. Proton pump inhibitors and the risk of acute kidney injury in older patients: a population-based cohort study. CMAJ Open 2015;3(2):E166–71.

[18] Sansom LN, ed. op. cit. pp. 597–600.

Hydrocortisone and hydrocortisone acetate (excluding other salts and derivatives)

Proposal to amend the scheduling of hydrocortisone and hydrocortisone acetate to include preparations for dermal human therapeutic use containing 1% or less of hydrocortisone when combined with an antifungal substance (and no other therapeutically active substance) in Schedule 2 under the following conditions:

- ***in packs containing 15 g or less; and***
- ***for the treatment of tinea and other fungal skin infections; and***
- ***not labelled for the treatment of children under 12 years.***

PSA understands that dermal preparations of hydrocostisone (up to 1%) combined with an antifungal substance is currently included in Schedule 3 with an upper limit on pack size of 30 g.

PSA commented in 2013 on a proposal similar to the current one although we do not believe a smaller pack size option was given at the time. PSA did not support that proposal primarily due to concerns around the potential for greater use of fixed combination therapies which are not regarded as appropriate first-line therapy for tinea and other fungal infections.

Tinea, a relatively common skin infection, and other minor fungal skin infections are suitable for management and treatment with OTC medicines. However, there are many factors which need to be considered in order to select the best available treatment for the patient.

Examples of pharmacists' considerations include the following[19]:

- patient factors:
    - symptoms (e.g. area of body affected, type of infection);
    - age;
    - use and response to prior treatment;
    - medical history (e.g. hyperhidrosis, diabetes, HIV infection and other conditions affecting the immune system, on medication affecting the immune system);
    - lifestyle history (e.g. occupation, sports, gardening);
- medical advice may be warranted, for example:
    - signs of extensive / severe or bacterial infection are evident;
    - recurrent infection or no response to topical therapy;
    - patient has diabetes;
- recommendation of treatment:
    - selection of product with a dosage form which is appropriate to the area of infection (e.g. paint or lacquer for nail infections);
    - relevant precautions (e.g. age, pregnancy status);

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19 ibid,. pp. 564–7.

- advice on use of the medicine (e.g. dose, duration of treatment, expected outcome of treatment, possible adverse effects, supportive self-care measures);
- prevention of infections in future.

Combination corticosteroid-antifungal therapy can generally be used for severely inflamed infections with duration of treatment tailored for the condition. Patients may not appreciate that extended use of these products is not recommended. Careful monitoring of symptoms is required as it is usual to continue treatment with an antifungal only for best outcomes. Overuse of corticosteroids on their own can also exacerbate fungal infections or mask symptoms so pharmacist advice is warranted.

Thus, PSA strongly believes that the current schedule (S3) remains appropriate as it promotes appropriate use of these medicines through pharmacist intervention and oversight and minimises confusion or inappropriate use which may arise through consumer self-selection.

In summary, PSA does not support the proposal to include hydrocortisone dermal preparations (with the listed conditions) in Schedule 2.

Naloxone

Proposal to amend the scheduling of naloxone to include single use prefilled syringe preparations for injection containing 400 micrograms/ml of naloxone or less in Schedule 3.

PSA understands this product (*Naloxone minijet*) is currently included in Schedule 4 and is indicated for the complete or partial reversal of narcotic depression, including respiratory depression, induced by natural and synthetic opioids such as codeine, diamorphine, methadone, morphine and propoxyphene. It is also indicated for the diagnosis of suspected acute opioid overdosage.

The reason for the proposed amendment has not been made public and therefore it is likely to be difficult for most people to ascertain the exact rationale or evidence base for this proposal.

PSA is familiar with the collaborative work undertaken in Victoria by our state branch staff and officials with the Penington Institute in conjunction with a wide multidisciplinary stakeholder group. From this group, PSA understands that less restrictive availability of naloxone is likely to improve the lives of opioid users, their carers and friends, and the wider community and reduce the number of fatal opioid overdoses in Australia without impacting negatively on patient safety.

Naloxone is a competitive antagonist at opioid receptors. It does not possess any agonistic activity. It has not been shown to produce tolerance or cause physical or psychological dependence. It does not exhibit pharmacological activity in the absence of opioid effects.

PSA notes that naloxone is currently listed on the Pharmaceutical Benefits Scheme (PBS) as:

- a general benefit (item number 2192J for medical and nurse practitioners and 2196N for dentists); and

- an emergency drug supply item (2200T for medical and nurse practitioners).

Perusal of PBS statistics indicates that most of the use is through emergency drug supplies with 7,690 items processed nationally from July 2013 to June 2014. On the other hand, the total

number of general benefit prescriptions for individuals in the same 12-month period is reported to be only 231 with an overwhelming majority (182) prescribed in Victoria.

It is reported[20] that 687 accidental overdose deaths in 2010 were attributed to opioids. This was an increase from 2009 at 645 deaths. These deaths should be preventable. PSA believes that in the interests of good public health and given the low rate of PBS prescribing, consideration of other ways to improve access of naloxone to opioid users is warranted.

Based on the inherent safety profile of naloxone and its specific indications, PSA believes Schedule 3 access should be considered. We believe pharmacists have a role in facilitating access of this medicine to opioid users and potential overdose witnesses. However, we believe it is essential that a comprehensive training package be developed to support pharmacists in this transition and change.

We understand there are successful initiatives in many countries overseas which demonstrate that naloxone provision to potential witnesses of overdose benefits users and the community. In Australia, PSA is aware that some programs have been trialled to enhance the uptake of take-home naloxone by opioid users with positive evaluations including reports of successful overdose reversals in the community setting.

In summary, PSA supports the proposal to amend the scheduling of naloxone to include single use prefilled syringe preparations for injection containing 400 micrograms/ml of naloxone or less in Schedule 3. We suggest that the development by PSA of a practice support package for pharmacists would be an essential component to support this rescheduling and would seek the contribution of expertise and assistance through a multidisciplinary group.

Orlistat

Proposal to amend the scheduling of orlistat from Schedule 3 to Schedule 2 for oral preparations for weight-control purposes containing 120 mg or less of orlistat per dosage unit.

PSA believes the current Schedule 3 entry of orlistat (as listed above) remains appropriate, primarily from a quality use of medicines perspective. This position has been supported by PSA since 2002.

PSA strongly advocates for pharmacist involvement in an holistic approach to weight management. If orlistat is considered to be appropriate for an individual, the pharmacist will provide information and support for other associated activities to help maximise the treatment outcomes.[21] Lifestyle changes such as dietary adjustments and regular physical activity are important in helping achieve weight loss through orlistat treatment and to maintain this outcome. Overall health of the person is likely to improve and the incidence of, or likelihood to develop, weight-related comorbidities (e.g. type 2 diabetes, cardiovascular disease) is reduced.

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[20] Roxburgh A, Burns L. Accidental drug-induced deaths due to opioids in Australia, 2010. Sydney: National Drug and Alcohol Research Centre; 2014. At: **https://ndarc.med.unsw.edu.au/sites/default/files/ndarc/resources/NIDIP%20Bulletin%20-%20Accidental%20opioid-induced%20deaths%20in%20Australia%202010.pdf**

[21] Sansom LN, ed. op. cit. pp. 591–3.

Pharmacists can also support the consumer in setting realistic treatment goals and monitoring outcomes. Referral to a medical practitioner regarding assessment and treatment of any comorbid conditions is also important.

In summary, PSA supports retention of the current Schedule 3 entry for orlistat and therefore is firmly opposed to the proposed amendment for inclusion in Schedule 2.

Submitted by:

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7 May 2015

Proposed amendments referred by the delegate for scheduling advice for consideration by the Advisory Committee on Medicines Scheduling (ACMS).

Codeine

I write as a private citizen to express my dismay at the proposal to reschedule codeine as a Schedule 4 entry. Please give consideration to the many people like my family who have an inherited paracetamol tolerance. Unfortunately paracetamol has no effect at all on acute pain for myself, my mother, my grandfather and their family, and so painkillers with a low, mild dose of codeine are the only effective options available over the counter for the relief of headache and muscle and joint pain. For my family, paracetamol is less effective for pain relief than a placebo, and given its toxicity, is generally avoided. Unfortunately, as reported in the media, the ANZCA FPM submission ignores the issue of acute pain relief, where low-dose codeine is most useful, and only looks at chronic pain, where it is less so.

Thankfully Nurofen Plus and similar generics remain available, upon production of name, address, and drivers' license at a pharmacy, but without those options we would each have to visit a GP every month to get a new refill, as it would be difficult to find a doctor to prescribe, say, 3 packets – a six month supply). This would also be a needless complication when, say, getting a headache in the evening, and instead of just going to the pharmacy for more, I would need to travel much further and wait in an after-hours bulk-billed clinic, to be poked, prodded, and interviewed – by the time I got to the pharmacy after 3-4 hours of suffering, the headache would probably have resolved itself.

It should be noted that with the monitoring systems recently put in place, including chemists recording drivers' license numbers, there should be much less concern regarding pill diversion going forward. The inclusion of the toxic ingredients paracetamol and ibuprofen already prevent most misuse.

Please do not go forward with this proposal to ban the only cheap and effective over the counter temporary pain reliever available to my family.

Other proposals

The other proposals listed are all sensible changes to ease supply restrictions on safe treatments that should be available over the counter, and I support them all. For example, Esomeprazole 20MG (Nexium) has been safely available over the counter for years overseas – in the U.S., the market price at Walmart is half again cheaper than the TGA subsidised price in Australia (roughly $16 vs $30 for one months' supply).

The cheap availability of safe, long-lasting, single-dose relief for indigestion and reflux would be of substantial benefit to the Australian population.

Johnson & Johnson Pacific

Thursday, 7th May 2015

Medicines Scheduling Secretariat
Therapeutic Goods Administration
136 Narrabundah Lane
Symonston ACT 2606
Australia

Dear Sir/Madam,

Re: Public Submission – under Reg. 42ZCZK of the Therapeutic Goods Regulations 1990. ACMS meeting, July 2015

Proposal: To amend the scheduling of esomeprazole to include oral preparations containing 20 mg or less of esomeprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 7 days' supply in Schedule 2.

Johnson & Johnson Pacific (JJP) refers to the pre-July 2015 Scheduling meeting notice. JJP would like comment on the proposed amendment to the scheduling of esomeprazole.

As the panel would be well aware, all PPIs have a similar mode of action, are well tolerated with similar safety and efficacy profile with rabeprazole being slightly differentiated as it has fewer known drug interactions when compared with the other PPIs.

If the proposal to down schedule esomeprazole is deemed to be in the best interest of public health, and given the similar safety and efficacy profiles for PPIs, it would be appropriate for the panel to consider recommending that all PPIs (omeprazole, esomeprazole, rabeprazole, lansoprazole and pantoprazole) have a new entry under schedule 2 created in line with the proposed for esomeprazole and the recently approved entry under schedule 2 for pantoprazole.

Yours faithfully,

Andrew Harris, B.Sc(Hons) Ph.D
Director, Regulatory Affairs
Johnson and Johnson Pacific

The Pharmacy Guild of Australia

Advisory Committee for Medicines Scheduling

Meeting July 2015

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

- **Esomeprazole - New Schedule 2 listing**
- **Hydrocortisone – New Schedule 2 listing**
- **Naloxone – New Schedule 3 entry**
- **Orlistat – New Schedule 2 entry.**

May 12 2015

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Introduction

The Pharmacy Guild of Australia (the Guild) welcomes the opportunity to comment on proposed amendments to the Standard for the Uniform Scheduling of Medicines and poisons (SUSMP) being considered by the Advisory Committee on Medicines Scheduling (ACMS) at its meeting of July 2015.

The Guild is the national peak organisation representing community pharmacy. It supports community pharmacy in its role delivering quality health outcomes for all Australians. It strives to promote, maintain and support community pharmacies as the most appropriate primary providers of health care to the community through optimum therapeutic use of medicines, medicines management and related services.

Community Pharmacists provide professional advice about the safe use of medicines for optimal effect and are supported by a team of pharmacy assistants that are trained to communicate with the consumer to identify potential issues for referral to the pharmacist for professional intervention.

Comments on Proposed Amendments

The Guild has considered the proposed amendments to the SUSMP of relevance to community pharmacy, with particular reference where applicable to Section 52E(1) of the *Therapeutic Goods Act 1989*. We provide comments for the following proposed amendments in line with the rationale for our position provided below:

1.2- Esomeprazole - New Schedule 2 listing
1.3- Hydrocortisone and hydrocortisone acetate - Schedule 3 to Schedule 2
1.4- Naloxone – New Schedule 3 listing
1.5- Orlistat- New Schedule 2 listing

Proposal 1.2 Esomeprazole- new Schedule 2 listing

(To amend the scheduling of esomeprazole to include oral preparations containing 20 mg or less of esomeprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 7 days' supply in Schedule 2)

Overview

The Guild notes that at its November 2014, the ACMS recommended the creation of a new Schedule 2 entry for pantoprazole under the same conditions (20mg, not more than 7 days' supply) as is being proposed for esomeprazole.

Nevertheless, the Guild's position remains that Proton Pump Inhibitors (PPIs) should remain a Schedule 3 medicine to ensure safe and appropriate use and therefore does not support this proposal. As indicated in our submission to the March 2015 ACMS meeting, we support the listing of esomeprazole on Appendix H while retaining it in Schedule 3.

Risks and benefits of the use of a substance[1]

As we have stated previously, the Guild believes there are some public risks which warrants pantoprazole and other PPIs to remain a Schedule 3 medicines.

The Guild notes that NPS MedicineWise is examining the use of PPIs and believes up to 30 per cent of the 1.6 million consumers taking heartburn and reflux medicine daily could stop taking them after the course of four to eight weeks.[2]

Some reports have linked PPI use to increased risk of fractures, pneumonia, enteric infections, vitamin and mineral deficiencies, and acute interstitial nephritis.[3][4] Although the absolute risk is very low, many of the consumers in these reports were older people – a group that makes up the largest proportion of PPI users and who are at increased risk of medicine-related problems.[5]

A key point raised in the NPS report is consumers who are taking a PPI long term should have their medication treatment reviewed if symptoms persist daily as long-term use of PPIs are only recommended in selected groups. Maintaining PPIs as Schedule 3 medicines increases the likelihood that excessive or inappropriate use (particularly over the long term) can be identified by a pharmacist who can refer to a doctor if required.

The purposes for which a substance is to be used[6]

The Guild also has concerns that increased access to PPIs could result in consumers using them to treat adverse effects caused by other medicines (such as gastric problems associated with non-steroidal anti-inflammatories) and/or masking more serious health conditions e.g. gastric cancer, without health professional oversight.

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[1] Section 52E(1A)- *Therapeutic Goods Act 1989*

[2] NPS Medicinewise – *Proton pump inhibitors- too much of a good thing?* (published 16/03/2015, accessed 22/04/2015) http://www.nps.org.au/publications/health-professional/medicinewise-news/2015/proton-pump-inhibitors

[3] Madanick RD. Proton pump inhibitor side effects and drug interactions: Much ado about nothing? Cleve Clin J Med 2011;78:39–49 (Sourced from NPS MedicineWise)

[4] McCarthy DM. Adverse effects of proton pump inhibitor drugs: clues and conclusions. Curr Opin Gastroenterol 2010;26:624–31 (Sourced from NPS MedicineWise)

[5] McLean AJ, Le Couteur DG. Aging biology and geriatric clinical pharmacology. Pharmacol Rev 2004;56:163–84 (Sourced from NPS MedicineWise)

[6] Section 52E(1B)- *Therapeutic Goods Act 1989*

Any other matters that the Secretary considers necessary to protect public health[7]

The Guild is also concerned with the potential availability of pantoprazole as a Schedule 2 product through licensed non-pharmacy retail outlets in rural/remote areas. Jurisdictions license non-pharmacy outlets to supply Schedule 2 medicines in locations in which there is no pharmacy within a specified distance (from 10km in Tasmania[8] to 25km in the Northern Territory[9]). In such circumstances, there is no training for any of the retail staff and there is no access to health professional advice. Given that consumers living in rural and remote areas have generally older populations, higher levels of health risk and higher rates of chronic disease,[10,11] the risks described above may be increased. Even though the population may be small, the safety of consumers in these locations still remains an important priority.

Recommendation

The Guild recommends that esomeprazole should remain a Schedule 3 medicine with an Appendix H listing. The risk associated with prolonged use combined with the increased likelihood of a pharmacist detecting unresolved GORD symptoms when PPIs are Schedule 3 medicines warrant the current scheduling to be retained.

Proposal 1.3 Hydrocortisone and hydrocortisone acetate- Schedule 3 to Schedule 2

(To amend the scheduling of hydrocortisone and hydrocortisone acetate to include preparations for dermal human therapeutic use containing 1% or less of hydrocortisone when combined with an antifungal substance (and no other therapeutically active substance) in Schedule 2 under the following conditions: In packs containing 15 g or less, for the treatment of tinea and other fungal skin infections; and not labelled for the treatment of children under 12 years.)

Overview

The Guild does not support this proposal as it believes if a consumer requires a combination medicine for a dermal condition, their condition is at a level of severity that is not met by either product alone and requires pharmacist oversight.

The purposes for which a substance is to be used and the extent of use of a substance[12]

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[7] Section 52E(1F)- *Therapeutic Goods Act 1989*
[8] Tasmanian Poisons Act 1971 (s.27)
[9] Medicines, Poisons and Therapeutic Goods Act (3,2,s.123)
[10] National Rural Health Alliance; Fact Sheet 2 – The way forward for rural health; May 2011; www.ruralhealth.org.au
[11] AIHW – Rural Health; http://www.aihw.gov.au/rural-health/
[12] Section 52E(1B)- *Therapeutic Goods Act 1989*

It should also be noted that products which contain an antifungal as the single active ingredient are available as a Schedule 2 medicine. If both single and combination antifungal products are available in the same Schedule 2, there is a strong likelihood consumers will use a combination product as a first line treatment under the belief that such products are more effective.

The Guild is particularly concerned about risks of misuse or adverse effects of combination hydrocortisone/antifungal products in more vulnerable patient groups such as the elderly and infants. The most frequent adverse effects include dermatitis; rash; urticaria; burning; pain; atrophy; skin cracking, thinning, tightening; activation of latent and intercurrent infection.[13] There is also a risk that people may inadvertently use a combination antifungal product with other cortisone products, increasing the risk of systemic absorption and adverse effects.

The Guild also has concerns that consumers may attempt to treat skin conditions which are symptomatic of a serious underlying condition such as shingles. Hydrocortisone anti-fungal products are contraindicated for conditions such as viral skin infection (such as acute herpes simplex vaccinia, varicella rosacea; acne vulgaris; pruritus without inflammation as well as primary and secondary infections due to bacteria.[14] The risk of inappropriate self-medicating warrants the oversight of a pharmacist to determine the suitability of the product request and referral to another a medical professional if required.

Recommendation

The Guild does not support the proposal to re-schedule preparations containing 1 per cent or less hydrocortisone and hydrocortisone acetate when combined with antifungal substances for dermal use from S3 to S2. The Guild believes the severity of the condition the medicine is intended to treat with the potential adverse effects of this medicine, and the potential for inappropriate consumer self-treatment of skin conditions caused by an underlying contraindicated condition, warrants the continuation of mandatory pharmacist oversight.

[13] MIMS Online- Hydrozole Cream
[14] IBID

Proposal 1.4 - Naloxone-New Schedule 3 listing

(To amend the scheduling of naloxone to include single use prefilled syringe preparations for injection containing 400 micrograms/mL of naloxone or less in Schedule 3)

Overview

The Guild's supports a modified proposal to require naloxone as a Schedule 3 medicine to be accompanied with information that outlines key steps for consumers to take in the event of an opioid overdose either on the product label or as a pack insert. These inserts would complement the professional advice given by the pharmacist at the point of sale.

The Guild is concerned that without such information, consumers will access these products without having a sound understanding regarding the limitations of naloxone as well as how and when to administer it, particularly in an emergency situation when the product will be used.

The Guild notes in Canada[15], naloxone is sold in kits that not only contain the actual product, but also directions for recognising and responding to an opioid overdose. The Australian based Penington Institute as part of its Community Overdose Prevention and Education initiative has produced a factsheet that provides a clear and simple set of instructions on how to (and how not to) respond to an opioid overdose.[16] The Guild believes this is a good template that could be used as a pack insert.

The dosage formulation, labelling and presentation of the substance[17]

The risk profile of naloxone is consistent with a Schedule 3 classification. There is little risk of abuse, does not produce tolerance or physical or psychological dependence and even extremely high doses produce insignificant analgesia only and no respiratory depression, psychotomimetic effects, circulatory changes or miosis.[18]

Creating a new Schedule 3 entry will remove barriers to access and ameliorate legal issues regarding supplying a Schedule 4 medicine to another person, which is prohibited in certain jurisdictions.

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[15] http://www.washington.edu/news/2012/12/31/study-shows-naloxone-kits-cost-effective-in-preventing-overdose-deaths/

[16] http://www.copeaustralia.com.au/overdose/responding-to-overdose/

[17] Section 52E(1D)- *Therapeutic Goods Act 1989*

[18] Product Information- DBL™ NALOXONE HYDROCHLORIDE INJECTION https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2009-PI-00410-3&d=20150423161146224 12

Recommendation

The Guild supports a new Schedule 3 entry for naxolone with an amendment as outlined in bold "*Single use prefilled syringe preparations for injection containing 400 micrograms/mL of naloxone or less* ***when accompanied with a "responding to opioid overdose" factsheet"***

The inclusion of such a response guide will complement the professional advice given by a pharmacist and increase the likelihood that correct procedures will be followed in the event of an opioid overdose to maximise the chances of survival.

1.5 - Orlistat – new Schedule 2 listing

(To amend the scheduling of orlistat from Schedule 3 to Schedule 2 for oral preparations for weight-control purposes containing 120mg or less or orlistat per dosage unit)

Overview

The Guild does not support this proposal and believes the current scheduling is appropriate.

Risks and benefits of the use of a substance[19]

Product information for orlistat stipulates that a consumer's saturated fat intake should be monitored and there are precautions for consumers suffering a range of conditions such as peptic ulcer; cardiac, renal, hepatic, GI, endocrine, chronic psychiatric or neurological disorders, gallstones, renal stones as well as adhesion and fat soluble vitamin deficiency.[20] The large range of conditions (that are often linked to obesity) where caution is advised warrants a Schedule 3 classification to ensure mandatory oversight by a pharmacist.

The purposes for which a substance is to be used and the extent of use of a substance[21]

The Guild notes that orlistat in 120mg dose is indicated for the treatment of obese consumers with a body mass index (BMI) greater or all equal to 30 and overweight consumers with a BMI greater than or equal to 27 in the presence of other risk factors.[22]

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[19] Section 52E(1A)- *Therapeutic Goods Act 1989*
[20] MIMS online- Xenical
[21] Section 52E(1B)- *Therapeutic Goods Act 1989*
[22] Xenical® Australian Register of Therapeutic Goods - Public Summary

The Guild believes there is a fundamental need for a weight assessment and a general management plan (including lifestyle modification) to accompany treatment with orlistat and as such this warrants mandatory oversight by a healthcare professional. There may also be a need to refer consumers to a doctor for diagnosis of conditions associated with obesity such as Type 2 diabetes.

The potential for abuse of a substance[23]

The Guild believes creating a Schedule 2 entry for orlistat will increase the risk that the therapeutic indications (BMI levels) will be not be adhered to and increases the potential for misuse and abuse, particularly for consumers suffering from eating disorders such as anorexia. Having orlisat stored behind the counter and available only through interaction with a pharmacist reduces the risk orlistat will be obtained for inappropriate weight loss.

Recommendation

The Guild does not support this proposal and believes the current scheduling for orlistat remains appropriate. The need to determine consumer suitability for orlistat, in addition to the need for an accompanying management plan as well as minimising the potential for abuse warrants orlistat remaining a Schedule 3 medicine.

[23] Section 52E(1E)- *Therapeutic Goods Act 1989*

The Pharmacy Guild of Australia

Advisory Committee for Medicines Scheduling

Meeting July 2015

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

- Levocetirizine – New Schedule Listing
- Proton Pump Inhibitor – Listing on Appendix H

July 9 2015

Introduction

The Pharmacy Guild of Australia (the Guild) welcomes the opportunity to comment on proposed amendments to the Standard for the Uniform Scheduling of Medicines and poisons (SUSMP) being considered by the Advisory Committee on Medicines Scheduling (ACMS) at its meeting of July 2015.

The Guild is the national peak organisation representing community pharmacy. It supports community pharmacy in its role delivering quality health outcomes for all Australians. It strives to promote, maintain and support community pharmacies as the most appropriate primary providers of health care to the community through optimum therapeutic use of medicines, medicines management and related services.

Community Pharmacists provide professional advice about the safe use of medicines for optimal effect and are supported by a team of pharmacy assistants that are trained to communicate with the consumer to identify potential issues for referral to the pharmacist for professional intervention.

Comments on Proposed Amendments

The Guild has considered the proposed amendments to the SUSMP of relevance to community pharmacy, with particular reference where applicable to Section 52E(1) of the *Therapeutic Goods Act 1989*. We provide comments for the following proposed amendments in line with the rationale for our position provided below:

1.1- Levocetirizine – New Schedule 2 listing
1.2- Proton Pump Inhibitors – Listing on Appendix H

Proposal 1.1 Levocetirizine – New Schedule 2 listing

(Proposal to include specific entries for levocetirizine in Schedule 2, Schedule 4 and Appendix K in the Poisons Standard.

Consideration should include:

- *whether all levocetirizine preparations for oral use should be in Schedule 2; or*
- *whether levocetirizine should be exempt from scheduling in divided preparations for oral use for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:*
  (a) in a primary pack containing not more than 5 days' supply; and
  (b) labelled with a recommended daily dose not exceeding 5 mg of levocetirizine (i.e. consistent with the scheduling exemption for cetirizine.)

Overview

The Guild notes that proposal is designed to reflect the current scheduling classification (and Appendix K listing) for cetirizine. While in the main we have no objections to this proposal, we do not support the scheduling exemption for levocetirizine (up to 5 days' supply).

Risks and benefits of the use of a substance[1]

There is no public need for an exemption and we believe the risk of sedation and its potential impact on driving capacity is too great to warrant supply without facilitating access to advice from a pharmacist.

Although the second generation antihistamines are known to have similar efficacy, there is a significant difference in the extent of their sedative effects, with levocetirizine being six times more likely to result in sedation than other non-sedating antihistamines.[2] Levocetirizine is a medicine that can affect psychomotor and cognitive functions, potentially having an adverse influence on the ability to drive. Psychomotor skills include reaction times and hand-eye coordination while the ability to make appropriate decisions relates to cognitive skills. Combination with other impairing drugs, including alcohol, is noted as increasing the opportunity for impairment and the risk of serious road accidents.

Tolerance to the sedative effects of second-generation antihistamines is reported to develop after 4-5 days. However, the proposed scheduling exemption for levocetirizine is for small packs for short-term, acute treatment. If used as recommended, it is unlikely that the consumer will develop tolerance and will run the risk of sedation each time the medicine is used.

Dosage, formulation, labelling, packaging and presentation of a substance[3]

The Guild argues simply including warnings on the medicine packs is insufficient. A survey of 2500 Australians showed that 21% have driven after taking prescription or OTC medicines, despite pack warning labels, with the biggest offenders (27%) aged over 55 years of age, and the next group (25%) being drivers aged 18 to 34 years.[4] Consequently, ey experts in an Australian study on drugs and driving suggest warning labels should be supported by verbal information from doctors and pharmacists.[5]

Any other matters that the Secretary considers necessary to protect public health[6]

While maintaining levocetirizine in Schedule 2 does not mean that all consumers will interact with the pharmacist, pharmacy assistants are trained to triage and ask relevant questions to elicit which people should be seen by a pharmacist. As such, it would be expected that people taking other medicines, people for whom other

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[1] Section 52E(1A)- *Therapeutic Goods Act 1989*

[2] Layton, D., Wilton, L., Boshier, A., Cornelius, V., Harris, S., & Shakir, S. A. (2006). Comparison of the Risk of Drowsiness and Sedation between Levocetirizine and Desloratadine. *Drug safety*, *29*(10), 897-909.

[3] Section 52E(1D)- *Therapeutic Goods Act 1989*

[4] Quoted in presentation; Dr Jenny Gowan, Northern & North East valley Divisions of general Practice April 2010; http://www.druginfo.adf.org.au/attachments/064_JennyGowan_DrugsDrivingSeminar_14Apr10.pdf

[5] J Mallick, J Johnston, N Goren et al; Drugs and driving in Australia: A survey of community attitudes, experience and understanding; Australian Drug Foundation; http://www.druginfo.adf.org.au/attachments/400_Drugs_and_Driving_in_Australia_fullreport.pdf

[6] Section 52E(1F)- *Therapeutic Goods Act 1989*

treatments have not been effective, or those who are specifically concerned about the impact of sedation or other adverse effects will be referred to a pharmacist.

Recommendation

Based on the risk of sedation, particularly with short-term use, and the potential impact on driving due to impaired psychomotor and cognitive function, the Guild believes levocetirizine should remain exclusively as a scheduled medicine to facilitate access to a pharmacist for advice.

Proposal 1.2 Proton Pump Inhibitors – Appendix H Listing

(To create new Appendix H entries for the following Schedule 3 proton pump inhibitors:

- *lansoprazole;*
- *omeprazole*
- *pantoprazole; and*
- *rabeprazole)*

Overview

The Guild supports this proposal as it did with the previous proposal for esomeprazole in the past as all PPI's broadly have the same risk profile. Guild support is on the condition that all advertisements for these products highlight the mandatory role of the pharmacist in determining the suitability of the product for consumers. The Guild believes it would be of benefit to consumers to be made aware of products that can treat frequent heartburn or GORD, subject to consultation with a pharmacist.

Increase consumer awareness

Increased awareness of alternate treatments for heartburn and reflux may prompt consumers who regularly purchase antacids or ranitidine from supermarkets, where there is no potential for health advice or review, to consult their pharmacist for more information. This would provide a pharmacist with the opportunity to assess and provide other therapeutic options and/or lifestyle support as required, or to refer them to a doctor if required.

Safety Issues

There is no significant abuse potential to justify restricting direct to consumer advertising of Schedule 3 PPIs. The potential for overuse is limited by the fact PPIs are only available as OTC medicines in pack sizes of up to 14 days' supply.

The Guild believes that there is no more concern with the advertising of Schedule 3 PPIs than there is with antacids and H_2-receptor antagonists. Considering the interaction profile of antacids, and the fact that H_2-receptor antagonists are usually only indicated for the short-term management of reflux symptoms without medical advice, the advertising of Schedule 3 PPIs could actually be in the public interest as it would raise awareness of other therapies and prompt consultation with a health professional.

The Guild does not believe there is any significant concern that allowing advertising of PPIs would be detrimental to public safety.

Recommendation

The Guild has no objection to this proposal, provided all advertisements for these products highlight the mandatory role of the pharmacist in determining the suitability of the product for consumers. The listing of PPI's on Appendix H will increase awareness of effective treatments for heartburn and reflux which may in turn prompt consumers to consult a pharmacist for more information.

Pharmaceutical Society of Australia

Submission to the July 2015 meeting of the Advisory Committee on Medicines Scheduling – Proposed amendments referred by the delegate

JUL
2015

Purpose

The Pharmaceutical Society of Australia (PSA) makes this submission in relation to proposed amendments referred by the delegate for scheduling advice for consideration by the Advisory Committee on Medicines Scheduling (ACMS).

PSA's comments relate to the proposed amendments to levocetirizine and proton pump inhibitors (PPIs).

About PSA

PSA is the peak national professional pharmacy organisation representing Australia's approximately 28,000 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.

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[1] Pharmacy Board of Australia. Pharmacy registrant data: March 2015. PBA: 2015; May. At: www.pharmacyboard.gov.au/documents/default.aspx?record=WD15%2f16935&dbid=AP&chksum=bLY0lK9odtaeMo6vdAHZ9g%3d%3d

Recommendations

Levocetirizine

PSA does not object to the inclusion of specific entries for levocetirizine in Schedule 2, Schedule 4 and Appendix K of the Poisons Standard. We suggest the current scheduling exemption for cetirizine should also apply to levocetirizine.

Proton pump inhibitors

PSA supports the proposal to create new Appendix H entries for lansoprazole, omeprazole and rabeprazole. PSA notes this is consistent with the recent interim decision of the delegate to create a new Appendix H entry for esomeprazole.

Comments on proposed amendments

Levocetirizine

Proposal to include specific entries for levocetirizine in Schedule 2, Schedule 4 and Appendix K in the Poisons Standard. Consideration should include:

- ***whether all levocetirizine preparations for oral use should be in Schedule 2; or***
- ***whether levocetirizine should be exempt from scheduling in divided preparations for oral use for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when: (a) in a primary pack containing not more than 5 days' supply; and (b) labelled with a recommended daily dose not exceeding 5 mg of levocetirizine (i.e. consistent with the scheduling exemption for cetirizine).***

PSA understands that levocetirizine products registered in Australia are available as 5 mg tablets and 5 mg/ml oral drops.

Based on current available evidence, PSA believes levocetirizine has been appropriately regulated by being captured under cetirizine in the Poisons Standard. While we do not have any objections to the creation of specific entries for levocetirizine, PSA would support consistency with the current scheduling of cetirizine at least initially as we do not believe an amendment to the scheduling of levocetirizine is warranted at present.

Summary: PSA supports the inclusion of specific entries for levocetirizine in Schedule 2, Schedule 4 and Appendix K of the Poisons Standard with the same scheduling exemption as for cetirizine.

Proton pump inhibitors

Proposal to create new Appendix H entries for Schedule 3 proton pump inhibitors (PPIs) lansoprazole, omeprazole and rabeprazole.

PSA notes that in June 2015 the delegate issued an interim decision to create a new entry in Appendix H for another PPI, esomeprazole, with a proposed implementation date of 1 October 2015.

During the public consultation on esomeprazole, PSA provided a submission in support of that proposal. Our comments on esomeprazole included the following.

- PPIs, including esomeprazole, are widely available and well established as over-the-counter (OTC) medicines for use in the relief of heartburn and other symptoms of gastro-oesophageal reflux disease (GORD).

- A range of PPIs with similar safety profiles have been available as Pharmacist Only Medicines for many years with data supporting efficacy and no reports of significant new safety concerns since being included in Schedule 3 of the Poisons Standard.

- The ongoing Schedule 3 entry will best support those consumers who are most likely to benefit from esomeprazole. Pharmacists will give consideration to and support the consumer around general dose recommendations for optimal therapy, the need to assess the consumer's response to treatment, and provide appropriate and timely referral if further investigation is required.

In relation to the delegate's interim decision on esomeprazole, PSA notes several pertinent reasons cited for the Appendix H recommendation. For example, given GORD is a common presentation in pharmacy, PSA concurs that increasing public awareness of the availability of a Schedule 3 PPI in pharmacy may have public health benefits. Further, as PSA has stated in previous submissions, other less effective treatments for GORD symptoms have been advertised to consumers for many years. Therefore it is sensible to be able to make consumers aware that PPIs are safe and effective first line treatments and available with pharmacist advice.

As referred above, PSA considers the range of available PPIs to possess similar safety and efficacy profiles. Therefore the same rationale and recommendation regarding Appendix H listing should apply to lansoprazole, omeprazole and rabeprazole.

Summary: PSA supports the proposal to create new Appendix H entries for Schedule 3 PPIs, lansoprazole, omeprazole and rabeprazole.

Submitted by:

Pharmaceutical Society of Australia
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Contacts:

Dr Lance Emerson, Chief Executive Officer

Dr Kay Sorimachi, Director Policy and Regulatory Affairs
kay.sorimachi@psa.org.au

9 July 2015

9th July 2015

Medicines Scheduling Secretariat Team
Therapeutic Goods Administration
PO Box 100 (MDPI22)
WODEN ACT 2606
AUSTRALIA

Dear Sir/Madam,

RE: PUBLIC COMMENT ON THE PROPOSED INCLUSION OF PROTON PUMP INHIBITORS (PPI) INTO APPENDIX H OF THE SUSMP - PANTOPRAZOLE

Takeda Pharmaceuticals Australia Pty Ltd strongly supports the proposed inclusion of pantoprazole into Appendix H of the SUSMP, which was referred by the delegate for scheduling advice for consideration by the August 2015 Advisory Committee on Medicines Scheduling (ACMS) Meeting. As the innovator of pantoprazole in Australia, Takeda provide the following information which in accordance with Section 52E of the Therapeutic Goods Act 1989.

Potential Public Health Benefits

- The primary purpose of direct-to-consumer advertising of Schedule 3 medicines, as articulated in the TGA report which guided the NCCTG's 1997 decision to allow such advertising, is the protection of public health and improvement in health outcomes.
- Brand specific advertising disseminates information and increases consumer awareness of new medicines. Inclusion in Appendix H can therefore directly address any consumer misconception that heartburn does not need medical intervention. The ability to advertise to consumers provides a means through which it will be possible to raise awareness of the fact that the Pharmacist is able to provide advice about heartburn management and a more effective treatment option (compared to other currently available products).
- Encouraging more heartburn sufferers to seek assistance from their Pharmacists will positively impact public health by promoting a better use of professional expertise and a more timely medical consultation with resultant improvement in health outcomes.
- Without direct to consumer advertising, many consumers with frequent heartburn may continue to be unaware of the availability of a Pharmacist Only products and the potential value of discussing their condition with their Pharmacist. Pharmacist consultation can ensure they are referred appropriately.
- The March 2015 interim recommendation to include another PPI, esomeprazole, in Appendix H of the SUSMP, which will therefore permit brand-specific advertising of a PPI, now means that other PPI's such as pantoprazole which are at least as safe and efficacious should also be permitted to be included in Appendix H, due to equity of access.
- Pantoprazole has a very low potential for misuse or abuse. In addition, due to the nature of this product and respective limitations on use (small pack size available as a Schedule 2), short-term use only as Schedule 3 with pack size limitation, the likelihood of advertising of the substance leading to inappropriate patterns of medication use is considered low.

Implications to the wider Regulatory System

The proposed addition of pantoprazole to Appendix H is not expected to have an adverse

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impact on the wider regulatory system, be it through the Therapeutic Goods Advertising regulations or the Therapeutic Goods registration processes.

The provisions of the TGAC
The proposed inclusion of pantoprazole into Appendix H is not expected to have an adverse impact on any of the provisions of the TGAC nor any impact on the restricted representations currently listed in part 2 of Appendix 6 of the TGAC.

Impact of Advertising on intended use
The addition of pantoprazole into Appendix H will not result in the advertising of goods for an indication other than those included in the Australian Register of Therapeutic Goods. Pharmacist intervention is required to assess customer suitability prior to the supply of pantoprazole in accordance with the Schedule 3 pack size and indications. Given this, Takeda maintain that a change in advertising status will not result in a change of the purpose for which the product is to be used.

The responsibility of Pharmacists
Pantoprazole has been available in Australia as a Schedule 3 medicine for several years accordingly Pharmacists are well equipped to ensure that pantoprazole is only recommended to those patients for whom it is a suitable treatment option. Inclusion of pantoprazole in Appendix H will enable targeted, brand-specific advertising of the Schedule 3 presentation with the intention of helping patients access appropriate assessment and counseling from their Pharmacist.

Availability of CMI
The CMI for innovator pantoprazole (Somac Heartburn Relief) has been approved by the TGA and will be included in each presentation as a package insert. It provides clear instructions on the use of pantoprazole 20 mg as a Schedule 3 medicine, including what the product is used for, how long it should be used and what to do if sufficient symptom relief is not achieved.

Patient Education
- An Appendix H listing for pantoprazole would enable more specific communications to consumers, for existing patients this could simply be alerting them to the fact that there is a different presentation of pantoprazole available from their Pharmacist. Alternatively, for new patients, the availability of pantoprazole from their Pharmacist as a Schedule 3 presentation will be able to be clearly communicated.
- By consulting their Pharmacist, consumers would be provided with timely counseling on the range of medications available to treat their condition. This will result in more appropriate medication choice, facilitated by Pharmacist recommendation, and ensure that frequent heartburn sufferers are given access to the most appropriate treatment and or redirection to their GP.

The desire of consumers to manage their own condition
- Numerous products are currently available in Australia in the OTC category to treat GORD supporting the fact that consumers are willing to self-medicate heartburn using OTC products when required.
- Whilst the recent inclusion of pantoprazole into Schedule 2 will potentially increase consumer awareness of such products, through self-selection. It is also important to be able to advertise the Schedule 3 presentation of pantoprazole which is only available under the direction of a Pharmacist, and may be more cost-effective (due to pack size) for consumers to self-manage their condition under the appropriate supervision of their healthcare provider.

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- It is noted that there is additional requirements for the Schedule 3 presentations for pantoprazole to be appropriately labelled in accordance with the Required Advisory Statements for Medicine Labels (RASML) warning statements which will help to ensure appropriate use.

Requirements under clause 6.2(E) OF THE TGAC
Takeda Australia grant an assurance that should a new entry for pantoprazole be included in Appendix H, the requirement under Clause 6.2(e) of the TGAC to include words to the effect of "Your pharmacist's advice is required" in all advertisements for therapeutic goods containing Schedule 3 substances that are listed in Appendix H of the SUSMP will be met.

In summary, pantoprazole is a safe and effective first line treatment for consumers with frequent symptoms of gastro-oesophageal reflux disease (GORD). GORD is a common condition. Increasing public awareness of the availability of a Schedule 3 pantoprazole in Pharmacy may have public health benefits through making consumers aware of more effective treatment options. Consumers may be more likely to seek advice from a pharmacist about the most appropriate treatment option. The Schedule 3 pack size, 14 days' supply, minimises the risk of inappropriate use. The mandatory RASML warning statements will help ensure appropriate use of the product. Currently other less effective treatments for the symptoms of GORD are advertised to consumers and moving forward on the basis of the March 2015 positive consideration of esomprazole's inclusion into Appendix H, equally efficacious treatments will be permitted to undertake branded advertising.

Please be advised that independent of this proposal Takeda have submitted an application for inclusion of pantoprazole into Appendix H, as discussed with the secretariat on 8th July 2015, should the current proposal be positive, Takeda would have no issue with the withdrawal of this application.

Thank you for the opportunity to comment. Should you require any further information, please contact me on (02) 9859 6932, by facsimile (02) 9889 1264 or email reena.patel@takeda.com.

Yours sincerely,

REENA PATEL

Regulatory Affairs Director

Takeda Pharmaceuticals Australia Pty Ltd

NSW GOVERNMENT Health
Sydney
Local Health District

[redacted]
Drug Health Service
SLHD

24 April 2015

To whom it may concern Re: Support for rescheduling of naloxone from S4 to S3

The current situation in Australia regarding opioid overdoses is that approximately 1 death per day is caused by opioid overdoses. There is no national data available on non-fatal overdoses, however it has been established that non fatal overdoses have the potential to cause significant brain injuries. Overdoses are common in people who use drugs and many have witnessed peers overdosing. Most overdose deaths are preventable: Evidence would suggest that approximately 85% of overdose deaths occur in the presence of other people, Spoorer 2003.

Naloxone has been used internationally for many years with nil reports of adverse events. Naloxone has been used in countries such as Italy as an over the counter medication for many years with no reported problems.

The availability of Naloxone to be included in overdose prevention training programs would greatly assist in prevention of fatal and non fatal overdoses.

In an attempt to reduce mortality from opioid overdose, many Drug Health Services/Harm Reduction Services have been developing interventions to reduce overdose incidence and mortality. One approach being adopted both nationally and internationally is to train those at risk and/or third parties in overdose prevention and management with naloxone.

The rescheduling of naloxone to a schedule 3 would ensure wider distribution to those at risk of overdose and that includes third parties.

Kind regards
Yours sincerely

[redacted]

NSW GOVERNMENT Health
Sydney
Local Health District

[redacted]

20th April, 2015

Medicines Scheduling Secretariat
Medicines Authorisation Branch (MDP 122)
PO Box 100
Woden ACT 2606
Email: medicines.scheduling@tga.gov.au

Medicine Scheduling Secretariat,

Re: Support for rescheduling of naloxone form S4 to S3

The current situation in Australia regarding opioid overdoses is that approximately 1 death per day is caused by opioid overdoses. There are no national data available on non-fatal overdoses, however it has been established that non fatal overdoses have the potential to cause significant brain injuries. Overdoses are common in people who use drugs and many have witnessed peers overdosing. Most overdose deaths are preventable: Evidence would suggest that approximately 85% of overdose deaths occur in the presence of other people (Spoorer 2003).

The availability of Naloxone to be included in overdose prevention training programs would greatly assist in prevention of fatal and non fatal opioid overdoses.
In an attempt to reduce mortality from opioid overdose, many Drug Health Services/Harm Reduction Services have been developing interventions to reduce overdose incidence and mortality. One approach being adopted both nationally and internationally is to train those at risk of overdose in the prevention and response to overdose with naloxone. Green et al, 2008 conducted a study that evaluated drug users trained in such programs in six US cities and found that they could identify overdose symptoms and recognize when to intervene with naloxone as well as healthcare professionals. Overdose management programs with naloxone have been operating worldwide for many years have been associated with reductions in opioid overdose mortalities - to date there have been no adverse outcomes associated with these programs.

However the wider distribution of naloxone to third parties (family and friends of a person at risk of opioid overdose) is hindered due to the fact that naloxone is a schedule 4 medication and legally cannot be administered to a person without a specific prescription. The rescheduling of Naloxone to S3 would enable wider distribution and availability to high risk groups such as recently released prisoners, patients receiving opioid medication for chronic pain, patients prescribed methadone at risk of relapse and people who continue to use opioids illicitly.

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The risks of such a move must be few as adverse effects of naloxone are very rare. Probably the only significant issue is precipitation of opioid withdrawal and even if this occurred , given the short half-life of naloxone, this can be expected to last no more than 10-20 minutes.

As the clinical director of a metropolitan drug treatment service for over 15 years, I strongly support the proposal to "down schedule" naloxone and look forward to the more widespread availability of this life-saving drug,

Kind regards

TGA Consultation submission ACMS Meeting July 2015

Public consultation on the proposed amendments to the Poisons Standard (Medicines)

My name is: [redacted]

I would like to submit the following in relation to the proposed amendment for the scheduling of naloxone to include single use prefilled syringe preparations for injection containing 400 micrograms/mL of naloxone or less in Schedule 3

Suggested improvements
I support the proposed amendment for the scheduling of naloxone as stated & without improvements.
Whether or not you support the amendment/s. If you do not support the amendment/s, you may make suggestions for an alternative acceptable to you.
I support the amendment for the scheduling of naloxone.
An assessment of how the proposed change will impact on you. That is, what do you see as the likely benefits or costs to you (these may be financial or non-financial). If possible, please attempt to quantify these costs and benefits.
Having attended many client overdoses for resuscitation involving naloxone, I have no doubts that wider availability of this medication in the general community would be nothing but positive in effect. Naloxone is currently available to our clients through a prescription and after training in its use. The logistics of getting clients to wait until a doctor can prescribe them naloxone can mean that 1) doctors are diverted from the healthcare needs of other clients and 2) clients (who often lead chaotic and marginalised lifestyles due to their drug use) are sometimes reluctant or unable to wait for a doctor to become available meaning they miss out on taking naloxone with them. Availability of naloxone over the counter, and therefore at the convenience of those with most to benefit from having naloxone available such as people who inject drugs and their families and friends, would definitely increase its availability where it is most effective. This way drug users and those closest to them would be able to keep naloxone at hand 'just in case' they or someone they knew had an overdose. Over the years working with people who inject drugs in Sydney I have heard of many overdoses where the fear of police involvement from calling an ambulance has lead to an otherwise avoidable fatality. Wider availability of naloxone would certainly improve outcomes in similar situations. The length of time between reporting an overdose and waiting for an ambulance with naloxone to arrive increases the risk of fatality or brain damage. Prompt use of naloxone is critical and wider availability would mean that response times could be shortened and many more lives would be saved.

There is often someone else present during a drug overdose – wider availability of naloxone would enable these users to act promptly if an overdose occurs.

Having to access naloxone from a doctor is another barrier to uptake as people who inject drugs would have to disclose their drug use under the fear of both discrimination and possibly other legal consequences. Our clients who inject drugs often lead chaotic lives due to their using so often it can be hard for them to organise and attend doctor's appointments. By being able to get naloxone over the counter at a chemist, it means they would be much more likely to obtain both initial doses and subsequent refills.

Naloxone is a safe drug and has no effect on anyone without opioids in their system. You can't abuse it, it has no resale value, it is inexpensive to provide, fast acting and a reliable antidote for opioid overdoses.

Naloxone is simple to administer by witnesses of an overdose, with limited instruction therefore all persons should be able to administer it with simple instruction from a pharmacist along with the reminder of written directions provided with packs of naloxone .

AUSTRALIAN MEDICAL ASSOCIATION
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7 May 2015

Advisory Committee on Medicines Scheduling
Therapeutic Goods Administration

medicines.scheduling@tga.gov.au

Dear Committee

Re: Application to reschedule naloxone

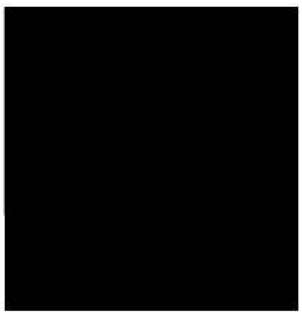
AMA Victoria supports the application to amend the scheduling of naloxone to include single use pre-filled syringe preparations for injection containing 400 micrograms/mL of naloxone or less in Schedule 3.

AMA Victoria would, however, like to note that the provision of naloxone as an over-the-counter produce at pharmacies is not a cure for dealing with drug addicted patients. The rescheduling of this substance does not replace the need for better education and support for general practitioners and addiction medicine specialists. Support must be provided to improve opportunities for doctors to provide intervention services and those services must be available to patients seeking to utilise them.

Availability and use of such products should always be considered within the context of available evidence. AMA Victoria would encourage the TGA to consider options for the monitoring and evaluation of dispensing and outcome data if this product if rescheduled.

AMA Victoria supports the rescheduling of naloxone in this manner as part of a comprehensive approach to improving intervention, treatment and support services for users of illicit drugs.

Yours sincerely



TGA Consultation submission ACMS Meeting July 2015

Public consultation on the proposed amendments to the Poisons Standard (Medicines)

My name is: [redacted]

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Whether or not you support the amendment/s. If you do not support the amendment/s, you may make suggestions for an alternative acceptable to you.
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An assessment of how the proposed change will impact on you. That is, what do you see as the likely benefits or costs to you (these may be financial or non-financial). If possible, please attempt to quantify these costs and benefits.
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There is often someone else present during a drug overdose – wider availability of naloxone would enable these users to act promptly if an overdose occurs.

Having to access naloxone from a doctor is another barrier to uptake as people who inject drugs would have to disclose their drug use under the fear of both discrimination and possibly other legal consequences. Our clients who inject drugs often lead chaotic lives due to their using so often it can be hard for them to organise and attend doctor's appointments. By being able to get naloxone over the counter at a chemist, it means they would be much more likely to obtain both initial doses and subsequent refills.

Naloxone is a safe drug and has no effect on anyone without opioids in their system. You can't abuse it, it has no resale value, it is inexpensive to provide, fast acting and a reliable antidote for opioid overdoses.

Naloxone is simple to administer by witnesses of an overdose, with limited instruction therefore all persons should be able to administer it with simple instruction from a pharmacist along with the reminder of written directions provided with packs of naloxone .