EDITED SUBMISSIONS RECEIVED IN RESPONSE TO THE NOTICE INVITING SUBMISSIONS ON MATTERS REFERRED TO THE:

Advisory Committee on Chemicals Scheduling – 21 June 2011 (ACCS#2); and
Advisory Committee on Medicines Scheduling – 22 June 2011 (ACMS#3).

Regulation 42ZCZL, Therapeutic Goods Regulations 1990 (the Regulations)

A delegate of the Secretary of the Department of Health and Ageing publishes herein all valid public submissions made in response to the invitation contained in the notice inviting public submissions for ACCS#2 and ACMS#3 (the June 2011 meetings), with the closing date of 13 May 2011.

In accordance with the requirements of subsection 42ZCZL of the Regulations these submissions have been edited to remove information that a delegate considers to be confidential.

As advised in the notice inviting public submissions, it was up to the person making the submission to highlight any information which they wished to request be considered as confidential. Material claimed to be commercial-in-confidence has been considered against the guidelines for the use and release of confidential information set out in Chapter 6 of the Scheduling Policy Framework (SPF), issued by the National Coordinating Committee on Therapeutic Goods. The SPF is accessible at www.tga.gov.au/industry/scheduling-spf.htm.

Discrete submissions have been grouped by item. However, a number of applicants provided submissions that related to multiple items. These submissions on multiple items have been separately grouped.

LIST OF SUBMISSIONS

1. ACCS #2

Item	Number of public submissions
1.2 Saflufenacil	1
1.4 Naphthalene	1

2. ACMS #3

Item	Number of public submissions
2.1.1 Loperamide	3 (and in 1 submission under item 2.3)
2.1.2 Nicotine	2 (and in 1 submission under item 2.3)
2.1.3 Orphenadrine+paracetamol	3 (and in 1 submission under item 2.3)
2.1.4 Cough and cold preparations	9 (and in 1 submission under item 2.3)
2.2.1 Rabeprazole	2 (and in 1 submission under item 2.3)
2.3 Submissions on multiple matters	1

[redacted]

1.2 Saflufenacil - submission 1 of 1.

[redacted]

[redacted]
13 May 2011

The Secretary
Scheduling Secretariat
GPO Box 9848
Canberra ACT 2601

Email: SMP@health.gov.au

Dear Sir

Public Comment submissions to 21 June 2011 meeting of the Advisory Committee on Chemical Scheduling (ACCS)

We refer to the pre-June 2011 Advisory Committee Meeting Notice inviting public submissions with respect to certain substances, addressing a matter raised in s.52E of the Therapeutic Goods Act 1989.

[redacted] wishes to provide information for ACCS consideration for the matters/substances addressed in the attached submissions.

[redacted] is an interested party and stakeholder with regard to the substances nominated in the submissions and would appreciate being advised of the Committee's considerations, with the opportunity for further submission, if appropriate.

We look forwards to ACCS's further advice. Should the committee require any additional information from [redacted] at this stage please do not hesitate to contact me on [redacted]

Yours faithfully,

[redacted]

[redacted]

Advisory Committee on Chemical Scheduling
Meeting: 21 June 2011

Agenda Item 1.2
Saflufenacil – proposal to reschedule from Schedule 7 to Schedule 6. The delegate is also seeking advice on potential cut-offs from Scehdule 6 to Scheudle 5, including the possibility of a 70% cut-off limit to water dispersible granule formulations.

[redacted] notes the current classification of saflufenacil as a Schedule 7 substance. We are encouraged that science can prevail and that the committee is considering a more appropriate scheduling. We support the proposal to reschedule as described above.

[redacted] will supply agricultural chemical products containing saflufenacil to resellers for retail sale within Australia. This new molecule has been evaluated via a tri-country arrangement between Australian, Canadian and the USA regulatory authorities. This product has subsequently been launched successfully in USA and Canada.

[redacted] is an interested party and stakeholder with regard to the substance nominated in this submission and would appreciate being advised of the Committee's considerations, with the opportunity for further submission, if appropriate.

Public submissions that address matters mentioned in section 52E of the Therapeutic Goods Act 1989 have been invited.

S52E (1) (e) the dosage and formulation of a substance
The committee may take into account the dosage and formulation of a substance under Section 52E (1) (e). [redacted].

For clarity, since the original submission to APVMA was many years ago [redacted]

S52E (1).and may take into account the labelling, packaging and presentation of a substance

- It is suggested that this product will [redacted].
- The proposed pack size for [redacted]
- The product will be labelled in accordance with advice from [redacted] and the APVMA's most recent Ag Labelling Code.

1.4 Naphthalene 1 of [redacted]

13 May 2011

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Email: SMP@health.gov.au

Dear Sir/Madam

Public Comment Submission to the June 2011 meeting of the Advisory Committee on Chemicals Scheduling (ACCS)

We refer to the notice published on 13 April 2011 inviting public submissions, with respect to certain substances, addressing a matter raised in s.52E of the *Therapeutic Goods Act 1989.*

[redacted]

[redacted] wishes to provide information on **naphthalene** for consideration at the June 2011 meeting of the ACCS. Please see attached submission.

[redacted] is an interested party and stakeholder with regard to the nominated substance and would appreciate being advised of the Committee's considerations, with the opportunity for further submission, if appropriate.

We look forward to further advice from the ACCS. Should the Committees require any additional information from [redacted] at this stage please do not hesitate to [redacted]

Yours faithfully

[redacted]

[redacted]

National Drugs and Poisons Schedule Committee

Meeting: 21 June 2011

Agenda Item 1.4

Naphthalene

Background

[redacted] understands that this scheduling re consideration has been triggered by concerns raised by a professor of neonatal medicine with regard to products containing naphthalene and the risks they pose to new born babies with a genetic disorder glucose-6-phosphate dehydrogenase (G6PD) deficiency.

G6PD-deficiency can lead to breakdown of red blood cells (hemolysis). It is our understanding that for adults and older children, hemolytic episodes are usually brief because the body continues to produce red blood cells, and therefore relatively harmless in itself. The main concern is for infants when the blood brain barrier is not yet fully developed; breakdown product of haemoglobin from lysed red blood cells (bilirubin) may potentially enter the brain and be deposited in cell bodies which may cause irreversible damage, potentially leading to severe brain damage or even death.

We note that for GD6P-deficient individuals, haemolytic episodes can be triggered by a number of factors including severe stress, infections, certain foods such as broad beans, certain medicines such as anti-malarial drugs, aspirin and nonstreoidal anti-inflammatory drugs, and certain chemicals including naphthalene.

[redacted] is unaware of any specific regulatory consideration of naphthalene in the context of this sensitive sub-population, other than by the National Drugs and Poisons Schedule Committee (NDPSC), the predecessor to the ACCS and ACMS, at the October 2003 and February 2004 meeting. It is our understanding that the concerns recently raised over the risks posed by naphthalene on new born babies with G6PD deficiency was considered at this meeting, and current controls in SUSMP were considered appropriate. This decision was reiterated at the June 2006 meeting of the NDPSC.

As far as we are aware, all international considerations of naphthalene has focused on the ingestion hazard for young children as the main hazard of concern when considering naphthalene.

In 2008, the United States Environmental Protection Agency (US EPA) considered naphthalene as a candidate for re-registration and determined that products containing naphthalene are eligible for reregistration provided that specified label amendments were made. There were also limitations placed on the physical form of naphthalene to be supplied to discourage children eating the product. Loose forms of mothballs cannot be supplied from September 2013, unless in child-resistant packaging.

While inhalation risks were considered by the US EPA, we note that based on scientific evidence available at the time of the reregistration consideration, the US EPA concluded that inhalation does not represent a risk of concern. We understand that the carcinogenic and non-carcinogenic potential of naphthalene resulting from inhalation exposure is currently being reassessed by the USEPA Integrated Risk Information System (IRIS) program. There is also research being conducted by industry on the pharmacokinetics of naphthalene. US EPA will apparently re-visit naphthalene inhalation risk when these studies are completed.

Health Canada, when it granted re-registration of naphthalene in Canada in mid-2010, reached a similar conclusion as the US EPA and called for further mitigation through utilizing child-resistant packaging to reduce ingestion risk.

[redacted] notes that the SUSMP currently requires that naphthalene in ball, block, disc or pellet form for domestic use only be supplied in a device which prevents removal and ingestion of its contents.

Naphthalene products are not available in the EU since the mid 2009; they were withdrawn from the market due to lack of commercial interest by manufacturers during the review of biocide products.

Submission

The invitation for public comment to the June 2011 ACCS meeting has specifically sought information on the proposal to increase the current restrictions through scheduling on domestic use of naphthalene, including (but not necessarily limited to) mothballs, blocks, discs, pellets or flakes. We understand that the delegate is particularly seeking advice on:

1. Expanding the container requirements for domestic use of camphor and naphthalene under SUSMP Part 2, Labels and Containers, paragraphs 28 and 29 to apply to flake forms of naphthalene.
2. Rescheduling some, or all, forms of naphthalene for domestic use from Schedule 6 to Schedule 7 or Appendix C. This consideration may include the potential for a low concentration cut-off. Particular consideration is likely to be given to further restricting loose or flaked forms of naphthalene.
3. In addition to domestic pesticidal use (mothballs etc), information on other domestic uses is particularly being sought to help define potential regulatory impact from increasing current restrictions.

[redacted] considers that the above three options have been put forward to address three distinct issues. We believe that these points are:

- Ingestion risk,
- Risks for G6PD deficients individuals, and
- Other uses of naphthalene.

We will therefore provide information under these separate headings.

Ingestion risk

[redacted] notes that currently, the flake form of naphthalene for domestic use is the only form of naphthalene that is not required to be sold in a device which prevents removal and ingestion of its contents. While we are unsure of the reasons behind this exception, it appears that the NDPSC had considered the risks posed by different physical forms of naphthalene. The October 2003 meeting of the NDPSC consideration of naphthalene was triggered by a registration of naphthalene flakes with the APVMA.

We hypothesize that due to their convenient size, mothballs, blocks and cakes are more likely to be picked up and ingested or sucked by children. Because flakes are smaller and arguably less appealing, it may be less likely to be picked up and ingested by young children. [redacted] only supply flake form of naphthalene for household use, and they have not had any incident reports relating to their product. Unfortunately, we have no other data to support our hypothesis.

Unlike Australia, the US EPA and Health Canada consideration of the ingestion risk for naphthalene has focused on the size of naphthalene as an indicator for risk of ingestion by children. Neither countries have indicated special packaging requirement for large blocks or cakes (> 2.5 inch diameter; approximately 7cm), but have indicated special packaging requirement for loose mothballs. [redacted] has assumed that this includes flakes. These requirements come into force on 30 September 2013.

[redacted] respectfully requests that the risk management consideration of the Committee be consistently aligned with the likelihood of ingestion by children. If the Committee believes that the size of naphthalene is the key to determining the level of ingestion risk, then we believe that the scheduling consideration should be aligned with the US EPA and Health Canada. However, if the consideration of ingestion risk is based on the appeal to young children and the ease with which the naphthalene can be picked up, then we believe that the current scheduling requirements are appropriate.

If the Committee considers that the ingestion risks for young children for naphthalene flakes is equal to or greater than ingestion risk for mothballs, blocks, discs or pellets and therefore packaging changes may be required, we request that a minimum 2 years transition be considered. This would align with US EPA special packaging requirement timeline of 30 September 2013.

Risks for G6PD deficient individuals

[redacted] notes that the risks to the G6PD deficient individuals have been considered by the NDPSC in 2004 and 2006. As far as we are aware, no new information has emerged since these considerations.

While we agree that the risks posed by naphthalene to new born babies and young children with G6PD deficiency is high, we note that naphthalene is neither the cause of the G6PD deficiency, nor the only trigger for a hemolytic crisis in G6PD deficient individuals.

[redacted] also understands that there are currently products registered with the APVMA that do not display relevant warning statements required for naphthalene products, particularly statement 105, Appendix F (Do not use on the bedding or clothing of infants or in the bedrooms of children three years of age or less). We believe that these should be addressed.

It is our understanding that the APVMA has powers to request amendments to existing labels. This may be the best mechanism for ensuring that naphthalene is not used in bedding or clothing of infants and children, which should address the risks for G6PD deficient infants.

Other uses of naphthalene

Naphthalene is an impurity that exists in many hydrocarbon solvents including kerosene, diesel, mineral turpentine and light mineral oils.

Hydrocarbon solvent (HYDROCARBONS, LIQUID) parent entry is in Schedule 5. Naphthalene parent entry is in Schedule 6, with no exemptions for impurities or cut-off levels provided.

It is our understanding that the risks posed by naphthalene as an impurity in hydrocarbon solvents is not of regulatory concern. [redacted] therefore requests that the Committee consider exemption for naphthalene when present in hydrocarbon solvents as an impurity. We suggest the following wording:

Schedule 6

NAPHATHLENE except in liquid hydrocarbons as an impurity.

Summary

It is [redacted] view t hat while th e physical f orm of naphthalene is an important factor whe n considering the level of ingestion risk by children, it has littl e to no impact on the risks posed t o G6PD deficient individuals. When stored in an airtight cont ainer as dir ected, there would be lit tle difference in the amount of naphthalene "soaked up" by clothing or bedding stored with mothballs, flakes or bl ocks. Further, if all products have relevant directions o n packagin g including the warning statement agai nst use with children's bedding or clothing, we believe th at these risks would be a dequately addressed. It is our un derstanding that the issues with labels of old er products registered with the APVMA could b e addressed by the APVMA, by requesting t hat registrants amend the existing labels.

We also believe that th ere has bee n a differen ce in appro ach to consideration of ingestion r isk between the US EPA / Health Canada and the NDPSC. If the Commit tee believes that Australia should align with the USA and Ca nada, i.e. the view that the size det ermines the likelihood of ingestion, then relevant packaging should be recommended for small naphthalene p roducts such as flakes and mothballs, but removed from other larger forms of naphtha lene. If however the ris k consideration is based on the app eal to childr en and like lihood of be ing picked up, then we believe that the current scheduling requirements are appropriate.

If packaging changes are considered necessary, then we re quest that there be min imum 2 yea rs transition time.

[redacted] also respectfu lly recomme nds that t he Committee consider exempting naphthalene in hydrocarbon solvents as an impurity. As far as we are aware, no con cerns have been raised regarding the presence of naphthalene in these types of solvents.

[redacted]

12/05/2011 12:09 PM

To <SMP@health.gov.au>
cc
bcc
Subject Loperamide [SEC=No Protective Marking]

History: This message has been replied to.

DOCUMENT NOT YET CLASSIFIED

Dear Sirs

Re: 2.2 Loperamide - proposal to reschedule loperamide in packs of eight dosage units or less, up to a maximum of one days' supply, from Schedule 2 to unscheduled.

As a consultant gastroenterologist of some thirty years standing, I would support an application for a switch in listing for loperamide from S2 to unscheduled. A one day or maximum eight tablet supply would allow excellent symptom control for patients with acute infectious (viral or bacterial) gastroenteritis and would not be detrimental to the course of the illness or cause delay in diagnosis. Patients could be advised to see their GP if symptoms persist beyond this time or if they had more worrying features such as rectal bleeding. These caveats could be included on the packaging.

[redacted]

[redacted]

DOCUMENT NOT YET CLASSIFIED

2.1.1 Loperamide 2 of 3.

[redacted]

05/05/2011 09:37 PM

To <SMP@health.gov.au>
cc
bcc
Subject Availability of loperamide outside the pharmacy setting [SEC=No Protect

History: This message has been replied to.

DOCUMENT NOT YET CLASSIFIED

Dear Sir/Madam,
I am a gastroenterologist [redacted] and I believe loperamide should be more readily available for patient use for two reasons. Firstly, loperamide is a common medication in any traveller's medication kit and used frequently and safely in this setting in the absence of medical/pharmacist advice and there is no reason it cannot be used similarly in the community. Secondly, the fact that loperamide is already available in a general sales environment through the internet makes restricting the location of physical sales a lot less relevant.

Regards,
[redacted]

DOCUMENT NOT YET CLASSIFIED

[redacted]

13 May 2011

Comments by [redacted] to the Advisory Committee for Medicines Scheduling – Meeting of 22-23 June 2011

Proposal

2.2 Loperamide – proposal to reschedule loperamide in packs of eight dosage units or less, up to a maximum of one days' supply, from Schedule 2 to unscheduled.

Guild position

[redacted] does not support the proposal to exempt packs of 8 dosage units or less of loperamide from scheduling.

Contact person:

[redacted]

Background

Loperamide is an anti-propulsive that binds to the opioid receptor in the gut wall. Consequently, it inhibits the release of acetylcholine and prostaglandins, thereby reducing propulsive peristalsis and increasing intestinal transit time. Studies suggest that loperamide may increase the tone of the anal sphincter, reducing incontinence and urgency. It is indicated for the symptomatic treatment of acute and chronic diarrhoea. It is not a curative treatment.

Loperamide 2mg tablets and capsules in packs of 20 dosage units or less are currently listed in Schedule 2 of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP).

Quality Use of Medicines

Quality Use of Medicines (QUM) is one of the central objectives of Australia's National Medicines Policy[1]. [redacted] believes that QUM is best supported by the supply of medicines through a pharmacy with access to specialised professional support and advice from a pharmacist. As such, we have traditionally opposed exempting medicines from scheduling because we have been concerned that the proposed arrangements may facilitate use of the medicines in a manner that does not align with QUM principles. There are no controls or quality assurance processes in place for the supply of medicines through the grocery channel and grocery customers can purchase one or one hundred packs of medicines exempt from scheduling without any question asked about the condition, the patient history or the use of the medicine.

Key Points

1. Primary treatment for diarrhoea is rehydration
2. Essential to facilitate triaging for health care professional intervention as anything more than mild, short-term diarrhoea without complications warrants investigation
3. Important to protect the most vulnerable patient groups, particularly the young, elderly, debilitated and people whose first language is not English
4. The inclusion of warnings and directions on packs does not surmount the issues associated with poor consumer health literacy without the opportunity for counselling
5. The risk factors associated with loperamide use warrant management through the pharmacy sector
6. Access through the pharmacy sector is more than adequate and provides access to health professional advice to support QUM objectives

Comments

We note that this issue was considered by the National Drugs and Poisons Schedule Committee (NDPSC) in both June 2009 and June 2010 and in both instances the

[redacted]

proposal was rejected. It would be beneficial to have access to this most recent application for exemption to understand whether new evidence or reasoning is being introduced in order to specifically target our response.

Without access to the application, [redacted] has considered the proposal to exempt packs of 8 dosage units or less of loperamide 2mg from scheduling with particular reference to the following subsections of the *Therapeutic Goods Act 1989 – Section 52E (1)*:

(a) the risks and benefits of the use of a substance

- When determining whether a medicine is sufficiently risk free to allow it to be exempt from scheduling and available without the opportunity to consult a health professional, it is essential that the safety of the most vulnerable of the population are protected. Such groups would include children and the elderly, as well as those with co-morbidities or taking multiple medicines for chronic conditions.

- In an epidemiological study in Italy regarding the prevalence of diarrhoea in old age, the most common causes were infectious diseases (19%) and drug use (16%). Regardless of the cause, the treatment of elderly patients with diarrhoea must include rehydration and nutritional support.[2] For these people, where causes relate to infection or medicine side-effects, it is essential that they have access to advice from a health professional. This would not be encouraged by having packs of loperamide available through the grocery sector.

- Loperamide can cause tiredness, dizziness or drowsiness, and it is advised to use caution when driving a car or operating machinery[3]. Generally, because the body is not accustomed to these effects, they are more noticeable with acute, short-term treatments such as that proposed if loperamide were available through the grocery sector

- There is a potential interaction with tranquilisers or alcohol[4] which may also impact on a person's ability to safely drive.

- [redacted] believes the safety profile of loperamide for the treatment of diarrhoea aligns more with that for listing in Schedule 2 of the SUSMP, being the least restrictive classification for a medicine while facilitating access to health professional support and advice.

(b) the purposes for which a substance is to be used and the extent of use of a substance

- Stool is 60 to 90% water. In Western society, stool amount is 100 to 200 grams per day in healthy adults and 10 grams per kilogram in infants, depending on the amount of unabsorbable dietary material. Diarrhoea is defined as stool weight of greater than 200 grams per day. However, many people consider any increased stool fluidity to be diarrhoea.[5] This demonstrates that the symptoms of diarrhoea can be ambiguous and self diagnosis is not necessarily a simple matter. Support and advice should be available where possible, particularly for people that may

[redacted]

have underlying gastrointestinal problems or who would benefit from a referral to a doctor for further investigation.

- The primary goal of treating any form of diarrhoea, whether viral, bacterial, parasitic or non-infectious, is preventing dehydration or appropriately rehydrating persons presenting with dehydration. Anti-motility agents such as loperamide should be considered only in adult patients who are not febrile nor having bloody/mucoid diarrhoea.[6]

- Most cases of acute diarrhoea are self limiting and do not require drug treatment. Rehydration is the optimum treatment. If diarrhoea is prolonged or there is associated vomiting, blood in the stool, fever, or signs of dehydration, medical consultation is advised.

- Antidiarrhoeals should not be used for acute diarrhoea in children as they do not reduce fluid and electrolyte loss and may delay expulsion of organisms and may cause adverse effects. While a short course of antidiarrhoeals may be warranted in adults to control symptoms of acute diarrhoea, assessing and correcting dehydration and electrolyte disturbance is a priority. This is particularly important in those at greater risk of adverse outcomes from such disturbances – such as the elderly or those with diabetes, cardio vascular conditions or impaired renal function. In such cases, it is more essential that access is to appropriate advice rather than an anti-motility agent.

- People often underestimate the dehydrating effect of diarrhoea, especially if it results from an acute infection in a hot climate. Dehydration may be less noticed in the elderly who often fail to experience appropriate thirst.[7]

- Complications may result from diarrhoea of any aetiology. Fluid loss with constant dehydration, electrolyte loss and even vascular collapse sometimes occur. Collapse can develop rapidly in patients who have severe diarrhoea or are very young, very old or debilitated.[8]

- For patients that present with chronic diarrhoea, it is important to consider other causes such as coeliac disease and inflammatory bowel disease. Any alarm symptoms such as rectal bleeding or weight loss need further assessment.[9]

- A recent article[10] in the Medical Journal of Australia indicates that Australia is in the grip of a new strain of *Clostridium difficile*, the most common infectious cause of nosocomial diarrhoea for which the severity of infection can vary from mild diarrhoea to pseudomembranous colitis, toxic megacolon and death. The article advises that Australia must learn from overseas experiences and to implement necessary interventions. Community pharmacists are well placed to assess whether patients with mild diarrhoea have had any recent hospitalisation to facilitate referral for further investigation, particularly for people seeking to purchase larger quantities or who have had symptoms for greater than 24 hours. This type of support is not available from the grocery sector.

- Loperamide is commonly included as part of a traveller's first aid kit, particularly when travelling overseas. The traveller would benefit from interaction with

[redacted]

pharmacy personnel who could also assist them in checking they are prepared for other medical contingencies, including vaccination and malaria prophylaxis.

- Some people with chronic diarrhoea may require long-term treatment with anti-motility agents. This should be a specialist decision.[11] Regular non-prescription purchase of loperamide or the purchase of multiple packs can be managed within the pharmacy sector in line with QUM principles. If small packs of loperamide are exempted from scheduling, there is no quality assurance processes to restrict the number of packs purchased at any given time or how frequently a person purchases these products without access to professional intervention.

- There are significant risks attached with misdiagnosis or misuse of loperamide. While mild diarrhoea may be a nuisance, depending on its cause, it can develop into a life-threatening condition. A pharmacist has the capacity to assist people with mild diarrhoea without complications and to refer complicated cases to the doctor for further investigation. With the availability of loperamide through grocery outlets, there is no professional support and advice available and there can be significant consequences from delayed referral for complicated cases.

(c) the toxicity of a substance

- Loperamide is contraindicated in people with a hypersensitivity to loperamide and in children under 12 years of age. It should also be avoided when inhibition of peristalsis is to be avoided[12].

- Due to possible anticholinergic effects, loperamide should be used with caution in people with glaucoma, pyloric obstruction, significant gastric retention, or intestinal stasis[13].

- There is limited data on use in pregnancy or lactation, although it is known to cross the placental barrier and to be detected in milk in animals. As such it is a Category B3[14] drug with regards to pregnancy and is not recommended in either pregnancy or lactation.

- With such safety concerns, even short-term treatment of acute diarrhoea is better managed through a pharmacy where patients have access to professional advice from a pharmacist and pharmacy assistants who are trained to triage and refer to the pharmacist when appropriate.

(d) the dosage, formulation, labelling, packaging and presentation of a substance

- We note that applications for medicines to be exempted from scheduling typically assert that the key to safe and efficacious use of medicines that are exempt from scheduling is responsible labelling that addresses the known areas of potential concern. However, health literacy is a serious issue and we are concerned that not only do people not read the labels, but when they do, they often don't understand what they are reading.

[redacted]

- A survey[15] conducted by the Australian Bureau of Statistics (ABS) identified 46% of Australians aged 15 to 74 years as not having sufficient literacy skills to meet the complex demands of everyday work and life, and that on the health scale, 60% attained scores below the minimum requirement to meet everyday needs.

- The ABS survey also identified that only 36% and 38% of people whose language was not english attained scores at or above the level that demonstrated sufficient prose and document literacy respectively to meet everyday needs.

- As such, [redacted] has concerns that even small pack sizes may be inadvertently misused by people who do not understand the directions or the precautions. There would be a risk of administration to children or the elderly, or use for extended periods without consulting a health professional.

- Retaining loperamide to supply from a pharmacy may not resolve this issue in every instance, but it ameliorates it and provides consumers with the opportunity to receive informed advice and/or consultation with a health professional if required.

  In the interest of public safety, it is essential that support is aimed at the lowest common denominator. For people with limited health literacy such as those from culturally and linguistically diverse (CALD) or lower socio-economic backgrounds or who are poorly educated, relying solely on having information on a medicine pack is not appropriate if there is any risk of misuse.

(e) the potential for abuse of a substance

- Although it has the lowest addiction potential of all opioids, loperamide may cause sedation, nausea and cramps[16].

- [redacted] believes there is more a risk of inappropriate use than abuse associated with unrestricted access to loperamide.

(f) other matters in public health interest

- One of the most common arguments for proposing medicines to be exempt from scheduling is that availability through the grocery channel provides greater after-hours access. With the wide distribution of pharmacies and the ever increasing number that operate 7 days a week with extended trading hours, this argument now lacks base. In fact, in country areas, pharmacists provide after-hours patient access for urgent cases and in some jurisdictions, regulations for store trading hours mean that after-hours pharmacy access is as good as or better than that through the grocery sector.

  As an example, a recent analysis of access in metropolitan areas showed:

  - In Western Australia, pharmacy has no restricted trading hours as it is a 'specialty retail store'. There is a majority of pharmacies operating 7 days a week and 2 pharmacies open for 24 hours a day. In contrast,

[redacted]

supermarkets have restricted trading hours and can open until 9pm Monday to Friday, until 6pm on Saturday, and cannot trade on Sunday.

- In Brisbane, there are no pharmacies or supermarkets that open for 24 hours a day. There are 3 pharmacies that open until 11pm and the majority operate 7 days a week. There are restrictions on trading hours for supermarkets which can open on weekdays until 9pm and till 6pm on weekends.

- In Adelaide, there are no 24 hour pharmacies, however there are 2 pharmacies that open to midnight each day. Because of trade restrictions in South Australia, supermarkets can only open until 9pm on weekdays, and till 5pm on weekends. They also cannot open on public holidays.

- In Melbourne, there are 2 pharmacies that are open for 24 hours a day and the majority operate 7 days a week. By comparison, there is only 4 Coles and no Woolworths supermarkets that are open for 24 hours a day

- It is also common for pharmacies in both rural and metropolitan areas to offer delivery services for customers in their local area, where even patients without internet access can discuss the condition over the phone with a pharmacist for delivery at a convenient time.
- Under the Fair Work Act 2009 which came into effect from 1 July 2009, pharmacists are allowed to issue certificates as proof of legitimate absence from work. [redacted] has developed a reference guide[17] with input from key clinical stakeholders with recommendations for the issue of a 24 hour certificate for patients with diarrhoea and when to refer the patient to a doctor. Maintaining access to anti-diarrhoeal medicines through community pharmacy facilitates health professional intervention as well as access to sick certificates as part of the referral process.
- Exempting small packs of medicines from scheduling for access through the grocery sector does not meet QUM principles if there is no quality assurance processes to restrict the number of packs that can be purchased at a single time or to manage chronic users who do not have health care professional support. With access through the grocery sector, multiple packs can be bought in a single transaction without question. Within the pharmacy sector, pharmacy assistants are trained to ask clinically relevant questions and facilitate consultation with a pharmacist if appropriate. They are also trained to note 'red flags' for referral to the pharmacist, such as requests for multiple packs or repeat purchases, pregnancy, breast-feeding or people taking other medicines or presenting with other symptoms such as vomiting or fever.

Conclusion

The use of anti-motility agents can assist the symptomatic relief of diarrhoea in adults with no other complications, however their use is second line to other treatment such as rehydration. The proposal to allow loperamide to be exempt from scheduling in pack sizes of 8 or less is not supported by [redacted] as it is critical that those most at risk of adverse outcomes, such as children, the elderly, or those with chronic health conditions, are encouraged to access advice and consultation with a health professional if needed.

[redacted]

Pharmacy continues to provide more than adequate access to these medicines along with professional advice and support in line with QUM principles.

Reference Sources:

[1] http://www.health.gov.au/internet/main/publishing.nsf/Content/National+Medicines+Policy-1
[2] F Baldi, MA Bianco, G Nardone et al; Focus on acute diarrhoeal disease
[3] Imodium® Product Information: eMIMS
[4] Ibid
[5] Merck Manuals Online Medical Library; http://www.merckmanuals.com/professional/sec02/ch008/ch008c.html#sec02-ch008-ch008b-165
[6] Guidelines for the management of acute diarrhoea; Department of Health and Human Services; USA http://www.docstoc.com/docs/40638820/Guidelines-for-the-Management-of-Acute-Diarrhea
[7] Thompson WG; Managing Diarrhea; International Foundation for Functional Gastrointestinal Disorders; 2009
[8] Op cit Merck
[9] Op cit eTG
[10] Stuart RL and Marshall C; Clostridium difficile infection: a new threat on our doorstep; MJA Vol 194 No.7; 4 April 2011
[11] Australian Medicines Handbook - loperamide
[12] Op cit eMIMS
[13] Op cit eMIMS
[14] Category B3: evidence of foetal harm in animals, significance of which is uncertain in humans.
[15] ABS 4228.0 – Adult Literacy and life Skills Survey, Summary Results, Australia, 2006 (Reissue); www.abs.org.au
[16] Op cit: Thompson WG
[17] www.guild.org.au under Issues and Resources

[redacted]

[redacted]

[redacted]

12 May 2011

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Email: SMP@health.gov.au

Invitation for public comment – ACMS meeting 22 June 2011

2.3 Nicotine – proposal to amend the Schedule 4 entry to exempt from scheduling when used for human therapeutic use as an aid in withdrawal from tobacco smoking:

- **nicotine oromucosal film; and**
- **nicotine inhalation cartridges for oromucosal use.**

These proposed exemptions are similar to the exemptions for nicotine in chewing gums, lozenges, and preparations for sublingual, transdermal or oromucosal spray use when used as an aid in withdrawal from tobacco smoking.

[redacted] advice is also sought on potentially expanding the nicotine exemption to include all oromucosal uses.

The current Schedule 4 (S4) entry reads:

NICOTINE in preparations for human therapeutic use except:

(a) when included in Schedule 2; or

(b) for use as an aid in withdrawal from tobacco smoking in chewing gum, lozenges, or preparations for sublingual, transdermal or oromucosal spray use.

The current Schedule 2 (S2) entry reads:

NICOTINE for use as an aid in withdrawal from tobacco smoking in preparations for inhalation.

[redacted] appreciates the opportunity to provide comment to this proposal. We wish to express our support of the proposal to expand the exemption from scheduling to include all oromucosal uses.

Nicotine Replacement Therapy (NRT) has been proven to be an effective preventive health medicine for use as an aid in withdrawal from tobacco smoking. It was first switched in 1988 (chewing gum) and since then a number of different dosage forms have become available. As each new dose form is evaluated, confidence is generated that the various routes of administration of this active have similar profiles in relation to Risks and benefits, Purpose, Toxicity, and Potential for abuse. The TGA's *Australian Regulatory Guidelines for OTC Medicines* requires clinical studies to support the introduction of new dosage formats to demonstrate equivalence of efficacy and safety. [redacted] believe there is now sufficient evidence to support exempting <u>all</u> oromucosal use from the Schedule 4 entry.

[redacted] notes that the term 'Oromucosal' is not defined in the *SUSMP* or in the *TGA Approved Terminology for Medicines*. It is defined in the monograph for Oromucosal Preparations (1807) of the British and the European Pharmacopoeias 2011 (see excerpt below). This definition covers the existing and proposed dose

[redacted]

forms to be considered in this proposal with the exception of medicated chewing gum. The monograph technically excludes medicated chewing gum and chewable tablets, having their own monographs.

The term Buccal is defined in the *TGA Approved Terminology for Medicines* as “pertaining to the cheek cavity”. This definition is not as broad as oromucosal and does not cover the sublingual route of administration.

Taking the definitions into account and to avoid the potential of unintentional removal of a dose form from the exemption, [redacted] suggest that either:
1. The TGA establish a definition for ‘oromucosal’ route of administration that is inclusive of all dose forms absorbed locally in the mouth (including chewing gum) and for S4 entry be amended to read:

NICOTINE in preparations for human therapeutic use except:

(a) when included in Schedule 2; or

(b) for use as an aid in withdrawal from tobacco smoking in preparations for transdermal or oromucosal use.

OR

2. The S4 entry be amended to read:

NICOTINE in preparations for human therapeutic use except:

(a) when included in Schedule 2; or

(b) for use as an aid in withdrawal from tobacco smoking in chewing gum or preparations for transdermal or oromucosal use.

[redacted] support this proposal and believe it is supportive of the principle of minimum effective regulation. We hope these comments are helpful to the committee’s deliberations and look forward to the Delegate’s decisions.

Yours faithfully

[redacted]

Excerpt from the European Pharmacopoeia

OROMUCOSAL PREPARATIONS

(Ph Eur monograph 1807)

Oromucosal Preparations comply with the requirements of the European Pharmacopoeia. These requirements are reproduced below.

This monograph does not apply to dental preparations or to preparations such as chewable tablets (0478), medicated chewing gums (1239), oral lyophilisates and other solid or semi-solid preparations that are intended to be chewed or dispersed in the saliva before being swallowed.

Definition

Oromucosal preparations are solid, semi-solid or liquid preparations, containing one or more active substances intended for administration to the oral cavity and/or the throat to obtain a local or systemic effect. Preparations intended for a local effect may be designed for application to a specific site within the oral cavity such as the gums (gingival preparations) or the throat (oropharyngeal preparations). Preparations intended for a systemic effect are designed to be absorbed primarily at one or more sites on the oral mucosa (e.g. sublingual preparations). Mucoadhesive preparations are intended to be retained in the oral cavity by adhesion to the mucosal epithelium and may modify systemic drug absorption at the site of application. For many oromucosal preparations, it is likely that some proportion of the active substance(s) will be swallowed and may be absorbed via the gastrointestinal tract....

...Several categories of preparations for oromucosal use may be distinguished:

gargles,
mouthwashes,
gingival solutions,
oromucosal solutions and oromucosal suspensions,
semi-solid oromucosal preparations (including for example gingival gel, gingival paste, oromucosal gel, oromucosal paste),
oromucosal drops, oromucosal sprays and sublingual sprays (including oropharyngeal sprays),
lozenges and pastilles,
compressed lozenges,
sublingual tablets and buccal tablets,
oromucosal capsules,
mucoadhesive preparations.

[redacted]

Friday, 13 May 2011

The Secretary
Scheduling Secretariat
GPO Box 9848
Canberra ACT 2601

[redacted]

Dear Scheduling Secretariat

Re Advisory Committee of Medicines Scheduling- June 2011 meeting
Item 2.3 Nicotine

[redacted] supports the proposal to amendment the Schedule 4 entry for nicotine to exempt from scheduling oral mucosal films when used for human therapeutic use, as an aid in withdrawal from tobacco smoking.

Background

Cigarette smoking remains the single most common cause of premature death from cancer, cardiovascular disease, lung disease and other illnesses. The Tobacco Working Group of the Preventative Health Taskforce believes that if prevalence of daily smoking were to reduce to 9% or less by 2020, smoking would continue to decline until rates were so low that it would no longer be one of our most important health problems. Despite much success, ongoing efforts to reduce smoking prevalence are needed if these goals are to be reached.

Current nicotine replacement therapy (NRT) products have been available on the market for over two decades initially as prescription medicines and subsequently over-the-counter (OTC). These products have enabled close to 6 million smokers to quit successfully. The success of NRT products in helping people quit successfully has significantly complemented public health tobacco control initiatives. These initiatives have been further enhanced by broadening the accessibility and the indications for use of NRT products.

Oral nicotine formulations are the most popular form of NRT used by smokers wishing to quit. The appeal is likely to be due to familiarity and the ability to provide some oral gratification. Smokers often seek convenient and discreet forms of NRT to assist with quitting. Consequently, industry has invested in developing new oral dose formats to meet the varying needs of current and futures smokers who are wanting to quit. Nicotine containing oral mucosal films offer a new, fast dissolving, discreet option for smokers who wish to quit.

Please find following details supporting the exemption from scheduling of nicotine containing oral mucosal strips.

Safety of nicotine containing oral mucosal strips

The safety of NRT has been well established. It has a wide safety margin and the extensive experience with NRT (over 20 years of use) has demonstrated that it has a favourable safety profile with few significant untoward effects, even in those with cardiovascular disease or who use NRT and smoke.

[redacted]

Nicotine Lozenge and Gum, are extremely well-tolerated. The exposure to nicotine with 'other oral mucosal forms' of nicotine are likely to be the same as those associated with the lozenge and/ or gum.

Oral mucosal strips containing [redacted] of nicotine are bioequivalent to [redacted] and as such oral mucosal strips are as safe and effective as the [redacted] Lozenge. Consequently, broadening the current exemption from scheduling for nicotine to include oral mucosal films posses no risk to public health and safety.

Nature of ailments or symptoms to be treated

[redacted] The indications for use will be the same as those already approved for other dose formats which are currently exempt from scheduling, that is;

- Relief of nicotine withdrawal symptoms including cravings associated with smoking cessation.
- Use as part of a smoking reduction strategy by smokers who are unable or not ready to stop smoking abruptly as a step towards stopping smoking.
- Combination therapy-use with nicotine containing transdermal patch

Self diagnosis and need for professional counselling before use

Smokers can easily identify nicotine (tobacco) withdrawal symptoms and cravings. In addition, current forms of NRT which are exempt from scheduling do not require any professional counselling before use. As oral mucosal strips will be used in much the same way as other oral dose formats which are currently exempt from scheduling, there will be no need for professional counselling before use. In addition, the packaging for nicotine containing oral mucosal strips will contain a detailed consumer medicines information leaflet which clearly specifies how to use the product.

Potential for abuse of the product

There is currently little potential for abuse of NRT products. It is expected that the potential for abuse for oral mucosal strips would be similar to that of currently marketed oral dose formats which is negligible.

The incidence of adverse effects and contraindications

The incidence of adverse effects and contraindications for NRT are well established. As oral mucosal strips are bioequivalent to the [redacted] lozenge the same adverse events and contraindications apply.

The risk of masking serious conditions

There is only a low risk of NRT masking a serious disease or compromising medical management of a disease. These have been assessed previously for other unscheduled oral dose NRT products and considered negligible. The risk of masking serious conditions when using nicotine containing oral mucosal strips can be expected to be the same as that for currently exempt oral dose NRT products.

The risk benefit profile of the product

The public health benefit profile of NRT has been well established. From an overall public health perspective, using NRT to assist quitting is always safer than continuing to smoke. Indeed, the impetus behind approving the use of such products for the OTC and then general sale environment was to improve consumer access and enhance the overall potential public health benefit.

As indicated previously, current NRT products have been available on the Australian market for over two decades initially as prescription medicines, subsequently over-the-counter (OTC) and more recently general sales. Nicotine containing oral mucosal strips are bioequivalent to [redacted] and as such the same risk benefit profile exists for this product as it does for [redacted] lozenge.

Conclusion

Broadening the exemption from scheduling for nicotine to include oral mucosal films when used for human therapeutic use, as an aid in withdrawal from tobacco smoking will facilitate greater access to safe and effective innovative NRT formats with the ultimate goal of encouraging more smokers to quit smoking. The importance of finding innovative ways of assisting smokers to quit is evidenced by the global regulatory approval of combination therapy, reduce to quit and pre cessation use of NRT.

In addition, in [redacted] view, oral mucosal films meet all the requirements for unscheduled medicine and as such an exemption from scheduling is warranted.

Kind regards

[redacted]

[redacted]

2.1.3 Orphenadrin+paracetamol - submission 1 of 3.

13 May 2011

Comments by [redacted] to the Advisory Committee for Medicines Scheduling – Meeting of 22-23 June 2011

Proposal

2.4 Orphenadrine – proposal to reschedule orphenadrine from Schedule 4 to Schedule 3 when combined with paracetamol with the following conditions:

- limited orphenadrine content per dosage unit, such as 35 mg or less;
- a limited pack size, such as 24 dosage units or less; and/or
- a restricted indication, such as when used for the relief of pain associated with skeletal muscle spasm in adults and children over 12 years of age.

[redacted] position

[redacted] supports the proposal to the Schedule 3 listing of combination products containing paracetamol and up to 35 mg of orphenadrine in pack sizes of up to 24 units.

Contact person:

[redacted]

[redacted]

Background

Orphenadrine is used as a skeletal muscle relaxant and is listed in Schedule 4 of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP). Combination products of orphenadrine and paracetamol are registered[1] in Australia for the treatment of:

- tension headaches
- occipital headaches associated with spasm of skeletal muscles in the region of the head and neck
- acute and traumatic conditions of the limbs and trunk
- sprains, strains, whiplash injuries, acute torticollis and prolapsed intervertebral disc.

Acute pain is defined as 'pain of recent onset and probable limited duration. It usually has an identifiable temporal and causal relationship to injury or disease'. Chronic pain 'commonly persists beyond the time of healing of an injury and frequently there may not be any clearly identifiable cause' (Ready & Edwards, 1992). It is increasingly recognised that acute and chronic pain may represent a continuum rather than distinct entities. [2]

Chronic pain is a common condition in Australia, estimated in 2007 to affect around 3.2 million Australians. The prevalence of chronic pain is projected to increase as Australia's population ages to approximately 5 million by 2050.[3]

Quality Use of Medicines

Quality Use of Medicines (QUM) is one of the central objectives of Australia's National Medicines Policy[4]. [redacted] believes that QUM is best supported by the supply of medicines through a pharmacy with access to specialised professional support and advice from a pharmacist. Schedule 4 medicines require supply from a prescription written by an authorised prescriber, with counselling available from a pharmacist at the time of dispensing. Schedule 3 medicines are available without prescription at the pharmacist's professional discretion. The pharmacist assesses the need and provides the necessary counselling for safe and appropriate use.

Key Points

1. The availability of an additional non-prescription analgesic product facilitates pharmacist intervention to enquire about pain control and product use for patients who regularly purchase other Schedule 3 analgesics.
2. A Schedule 3 listing provides an opportunity for pharmacists to manage safety concerns and facilitate QUM.
3. Community pharmacy is well set up and supported by professional quality assurance standards to facilitate QUM for these medicines and to manage abuse risks.

Comments

[redacted] has considered the proposal for packs of 24 dosage units or less of orphenadrine to be listed in Schedule 3 of the SUSMP when combined with paracetamol, with particular reference to the following subsections of the *Therapeutic Goods Act 1989 – Section 52E (1)*:

(a) the risks and benefits of the use of a substance

- The availability of a Schedule 3 analgesic with muscle relaxant actions increases the scope of conditions with which a pharmacist can assist patients. In addition to topical analgesic and heat therapies, the following are the most common non-prescription analgesics recommended by pharmacists:
    - aspirin with or without codeine
    - ibuprofen with or without codeine
    - paracetamol with or without codeine
    - paracetamol + codeine + doxylamine

- Many consumers who take non-prescription analgesics self treat because they do not know of alternative options. Many also believe they have a right of access to Schedule 3 products because a prescription is not needed. The availability of an additional non-prescription analgesic with muscle relaxant properties facilitates pharmacist intervention to enquire about the patient's pain control with an opportunity to review analgesic use and assess whether the patient is taking the most appropriate therapy.

- Because orphenadrine shows some anticholinergic activity, it is contraindicated in patients with glaucoma, prostatic hypertrophy, obstruction at the bladder neck or myasthenia gravis. It may impair a person's ability to drive or operate machinery and should be used in caution in patients with tachycardia, cardiac decompensation, coronary insufficiency and cardiac arrhythmias.[5]

  The contraindications and precautions are very similar to a number of antihistamines with anticholinergic activity that are listed in Schedule 3 of the SUSMP. Pharmacists are well placed to make the necessary enquiries to assess whether these antihistamines are safe to use and [redacted] believes that they should not experience any additional difficulty in assessing the situation for orphenadrine products.

(b) the purposes for which a substance is to be used and the extent of use of a substance

- Back pain, back problems and disc disorders are very common in Australia, affecting around 2.8 million people (14% of the population). These problems are most prevalent among those aged 55-64 years, and are more commonly reported by males.[6]

- Of the reasons reported for seeing general practitioners, 2% are for back complaints and 1% are for headaches[7].

- The prevalence of pain increases with advancing age and pain is often undiagnosed or under-treated in older patients. Pharmacological approaches form the mainstay of therapy, alone or in combination with physical and psychological therapies.[8]

- Matching a medicine to its indication is vitally important in achieving reasonable pain control. Orphenadrine is used preferentially for muscle spasm pain.[9]

- Norgesic has been available in Australia for over 30 years and is used for conditions where pain is associated with muscle spasm. Orphenadrine is effective compared to placebo in patients with musculoskeletal conditions (primarily acute back or neck pain)[10] and a review in 1991 demonstrated superior efficacy from a combination of orphenadrine and paracetamol than with paracetamol alone or placebo.[11]

- The availability of a Schedule 3 combination product containing orphenadrine and paracetamol enhances the capacity of community pharmacists to support patients who may present with lower back pain, tension headache and other acute and traumatic painful musculoskeletal conditions.

(c) the toxicity of a substance

- Side effects are mostly associated with the anticholinergic effects and are rare at the recommended dose, consisting primarily of nausea, dry mouth or blurring of vision. Rash or drowsiness may rarely occur and symptoms disappear with dose reduction or cessation of treatment. No toxic effects have been reported.[12]

- [redacted] believes the greatest risk with inappropriate use of combination products containing paracetamol is paracetamol toxicity. This risk is enhanced by the unrestricted availability of paracetamol through the grocery sector where small packs of paracetamol tablets or capsules as well as some cold tablets are exempt from scheduling and can be purchased without any professional intervention. Patients must rely on identifying the active ingredients of all the medicines they take.

  For the proposed orphenadrine/paracetamol analgesic, this risk is somewhat mitigated if this product is Schedule 3 as pharmacists are familiar with the risk and experienced in counselling patients appropriately.

- Orphenadrine is listed as category B2 with regards to safety in pregnancy, meaning there is only limited information available but studies to date do not indicate any harm. As there are no data available regarding excretion into breast milk, it is recommended not to be used when breast-feeding.[13]

  Again, these risks are mitigated if the product is Schedule 3 as pharmacists can advise pregnant or breast-feeding women appropriately.

(d) the dosage, formulation, labelling, packaging and presentation of a substance

- [redacted] agrees that if a combination product containing paracetamol and orphenadrine is made available without prescription, Schedule 3 is the most appropriate category. This ensures that the product is packaged and labelled to facilitate patient understanding of product use and safety considerations, which is reinforced by pharmacist counselling.

- Available for over 30 years as a prescription medicine, Norgesic contains 450mg of paracetamol and 35 mg of orphenadrine and has a recommended dose of 2 tablets three times a day. With this in mind, [redacted] considers it reasonable that packs of up to 24 dosage units would meet the requirements for Schedule 3 listing as this would provide up to 4 days supply. Resupply will require pharmacist assessment with an opportunity for referral if appropriate.

  [redacted] also draws attention to guidelines[14] published by the Pharmacy Board of Australia which advise that unless there are exceptional circumstances, only one package of Schedule 2 or Schedule 3 products should be supplied at any one time. As such, it is reasonable to expect pharmacists to be professionally responsible in supplying Schedule 3 medicines as failure to comply with the Board guidelines may be considered as unprofessional conduct and subject to reprisals.

- As orphenadrine may affect a person's ability to drive or operate machinery and this risk is greatest for people who take the medicine on demand rather than regularly, [redacted] would like to see appropriate warnings included on the product label. This will provide effective backup to counselling provided by a pharmacist at the time of supply.

(e) the potential for abuse of a substance

- There is a potential for anticholinergic medicines to be misused. Information about recreational effects has been documented[15], and is similar to the risk associated with other non-prescription medicines with anticholinergic properties, including diphenhydramine, dicylomine, pheniramine and scopolamine.

  [redacted] is concerned with the potential abuse of all of these medicines, but believes this can be risk managed. For pharmacies that are accredited under the Quality Care Pharmacy Program (QCPP), pharmacists are recommended to maintain a list of non-prescription medicines that may be subject to inappropriate use in order to better monitor and manage their supply.[16]

  Schedule 3 medicines must also be stored such as to prevent public access, and to be supplied when the pharmacist has assessed appropriate and safe use. While not fool-proof, this goes a considerable way in managing the abuse potential. With medicines that are particularly problematic, such as pseudoephedrine, [redacted] with respective government agencies at federal and state levels to implement processes such as Project STOP[17].

(f) other matters in public health interest

- While there are concerns with consumer health-literacy for all medicines, access to Schedule 3 medicines facilitates counselling by a pharmacist which augments written cautions and instructions included on a product's label.

- Generally, [redacted] does not support restricted indications as part of the scheduling process as this complicates SUSMP listings. We believe restricted indications should be managed as part of the registration process for a product so that the product can be labelled with appropriate instructions and marketed accordingly.

- Should the proposed schedule change be implemented, [redacted] would be pleased to work with the sponsor and other professional organisations as required to assist with developing and/or distributing resources for pharmacists that ensures the non-prescription availability of medicines is professionally managed in line with QUM principles.

Conclusion

[redacted] supports the proposal for listing packs of up to 24 units of orphenadrine in Schedule 3 of the SUSMP when combined with paracetamol.

Reference Sources:

[1] ARTG 34044; Norgesic
[2] Acute Pain Management: Scientific Evidence; 3rd Edition 2010l; Australian and New Zealand College of Anaesthetics and Faculty of Pain medicine
[3] The high price of pain: the economic impact of persistant pain in Australia; MBF Foundation; Nov 2007; http://www.mbf.com.au/MBF/About%20MBF/Forms/MBF_Foundation_the_price_of_pain.pdf
[4] http://www.health.gov.au/internet/main/publishing.nsf/Content/National+Medicines+Policy-1
[5] Full Product Information – Norgesic; eMIMS
[6] Australia's health 2010; AIHW; www.aihw.gov.au
[7] ibid
[8] Benny Katz; Pharmacological management of pain in older people; Journal of Pharmacy Practice and Research Vol 37, No.1, 2007
[9] How to treat chronic non-malignant pain; Australian Doctor 21 March 2008; www.australiandoctor.com.au
[10] Chou R, Peterson K, Helfand M; Comparative efficacy and safety of skeletal muscle relaxants for spasticity and musculoskeletal conditions: a systematic review; Journal of pain and Symptom management; Vol 28 Iss 2:140-175; Aug 2004
[11] Hunskaar S, Donnell D; Clinical and pharmacological review of the efficacy of orphenadrine and its combination with paracetamol in painful conditions; 1991; PubMed
[12] Op cit – eMIMS (Norgesic)
[13] Drugs and breastfeeding; Pharmacy Department, Royal Women's Hospital, Melbourne; 2004
[14] Guidelines on practice-specific issues; http://www.pharmacyboard.gov.au/Codes-and-Guidelines.aspx
[15] http://en.wikipedia.org/wiki/Diphenhydramine
[16] QCPP: T2C – Supplying Pharmacy Medicines and Pharmacist Only Medicines Checklist
[17] www.projectstop.com.au

[redacted]

13 May 2011

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Re: Proposed amendments to the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) as they relate to rescheduling of orphenadrine from Schedule 4 to Schedule 3 when combined with paracetamol and with certain conditions for supply.

Dear Secretary,

In response to the invitation for public comment regarding the above proposed amendments to the SUSMP, [redacted] provides the following public submission.

The proposed amended entry is,

2.4. - Orphenadrine - proposal to reschedule orphenadrine from Schedule 4 to Schedule 3 when combined with paracetamol with certain conditions. These conditions could include:

- limited orphenadrine content per dosage unit, such as 35 mg or less;
- a limited pack size, such as 24 dosage units or less; and/or
- a restricted indication, such as when used for the relief of pain associated with skeletal muscle spasm in adults and children over 12 years of age,

Since publication of the request for public comment, [redacted] have received over 200 letters from Australian pharmacists addressing matters in Section 52E, *Therapeutic Goods Act 1989*

- the risks and benefits associated with the use of a substance,
- the need for access to a substance, taking into account its toxicity compared with other substances available for a similar purpose,
- and taking account of the labelling, packaging and presentation of a substance.

The pharmacist letters express the opinion that the orphenadrine/paracetamol combination, with the criteria proposed for a Schedule 3 medicine, should be accessible to pharmacists as an alternative OTC option for painful musculoskeletal conditions, which can support quality use of medicines given these benefits:

- the only OTC product containing a skeletal muscle relaxant AND
- codeine and opioid free AND
- non-steroidal anti inflammatory drug (NSAID) free AND
- an alternative option to benzodiazepines.

The letters state that the orphenadrine/paracetamol combination will help pharmacists to better support individuals presenting with lower back pain, tension headache and other various acute and traumatic painful musculoskeletal conditions.

Regarding the potential for risk, the pharmacists note that as the supply of Schedule 3 products requires intervention by the pharmacist, they are well equipped to assess the benefits and risks of this combination and make recommendations for its appropriate use as a Pharmacist Only Medicine. Therefore it is appropriate the combination be rescheduled to an S3 medicine.

For your reference, the pharmacist letters accompany this public comment submission.

[redacted] is committed to working with the Pharmaceutical Society of Australia - the professional body representing pharmacists - to ensure thorough education and pharmacy protocols for supplying and recommending the orphenadrine/paracetamol combination are in place if the schedule 3 classification is approved. Under these circumstances pharmacists would be frontline providers of the combination. Importantly, the enclosed letters demonstrate their commitment to patients, to providing responsible care for those patients and to the quality use of medicines.

In your assessment of the rescheduling application, [redacted] asks that you duly consider the collective sentiment expressed by these frontline healthcare professionals and medicines experts.

Yours sincerely

[redacted]

[redacted]

2.1.3 Orphenadrine+paracetamol - submission 3 of 3
Example pharmacists form letter.

The Secretary
Medicines & Poisons Scheduling
Office of Chemical Safety and Environmental Health (MDP 88)
GPO Box 9848
Canberra ACT 2601
Australia

To whom it may concern,

Re: Invitation for public comment - ACMS meeting, June 2011- Orphenadrine / paracetamol combination

I am informed that the Advisory Committee for Medicines Scheduling (ACMS) is considering an application to reschedule orphenadrine / paracetamol combination from Schedule 4 Prescription Only Medicine status to Schedule 3 Pharmacist Only Medicine according to these criteria:

- orphenadrine content is 35 mg or less per dosage unit and
- pack size is limited to 24 dosage units or less and/or
- there is a restricted indication, such as when used for the relief of pain associated with skeletal muscle spasm in adults and children over 12 years of age.

In my professional capacity, I believe the orphenadrine / paracetamol combination fulfils all the above criteria as a Schedule 3 medicine and should be accessible to pharmacists as an alternative over the counter therapy option that supports quality use of medicines.

The orphenadrine / paracetamol combination may help pharmacists to support patients and consumers who present with lower back pain, tension headache and other various acute and traumatic painful musculoskeletal conditions.

Given the supply of a Schedule 3 product requires professional intervention by the pharmacist to assess the benefits and risks of this combination and make recommendations for its appropriate use as a Pharmacist Only Medicine, I support the rescheduling application.

Yours sincerely,

[redacted]

Pharmacist's name: [redacted]

Pharmacy address: [redacted]

2.1.4 Cough and cold preparations - submission 1 of 9.

[redacted]

11 May 2011

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Email: SMP@health.gov.au

INVITATION FOR COMMENT
Regulation 42ZCZK of the Therapeutic Goods Regulations 1990
Cough and cold Preparations – Item 2.1 – ACMS Meeting June 2011

Introduction

Thank you for the opportunity to comment on the proposal for rescheduling of a number of OTC cough and cold medicines. Item 2.1 of the ACMS Agenda refers to a proposal to reschedule five substances currently available in unscheduled cough and cold preparations to Schedule 2. The substances affected by this proposal are:

- Carbapentane
- Guaiphenesin
- Ipecacuanha
- Phenylephrine
- Senega.

In previous meetings of the NDPSC / ACMS (e.g. at the June 2010 NDPSC meeting), scheduling based on age was being considered. The current invitation for comment for the June 2011 meeting however states that the TGA proposes to address the use of cough and cold medicines by different age groups separately through product registration and labelling, implying that age based scheduling will not be considered.

[redacted] of a number of OTC cough and cold medicines and the proposal to reschedule the list of five actives will have an impact on the business. We contend that the existing scheduling arrangements are appropriate and should be retained and that some modifications based on age can be made to the existing scheduling in order to better satisfy the issues relating to use and safety in children.

[redacted]

Background

The TGA commissioned an extensive review of safety and efficacy of cough and cold medicines in children, which was transparent and published for all stakeholders to review. Comments were also sought. [redacted] submitted comments to the previous ACMS meeting, February 2011, as well as to the June 2010 NDPSC meeting. Detailed data on efficacy and safety of cough and cold medicines in children will therefore not be provided or repeated for the purposes of this submission.

[redacted] concerns relating to current proposal

1. Lack of transparency of the delegate's further advice

Previous items on the NDPSC and ACMS agenda addressed the proposed scheduling changes in terms of use and safety in children, as a response to the review commissioned by the TGA. The entire issue of use and scheduling of particular actives was within that framework. There now appears to be a departure from that position, possibly following further advice to the delegate that has not been published and has not been made available to stakeholders, as supported by the following statement in the proposal:

"Following consideration of advice from a number of expert sources including the Advisory Committee on Medicines Scheduling, the delegate refers the following revised proposal regarding cough and cold preparations to the ACMS for further advice"

[redacted] is concerned about the lack of transparency in relation to this item of the ACMS agenda and requests that the delegate should make public the information that has led to the conclusion that age based scheduling is not feasible and that the mainly adult (and children over 12) unscheduled cough and cold preparations should be restricted to sale only in the pharmacy environment.

2. Lack of clarity relating to the other 15 cough and cold actives

There were a number of other actives that were considered by the Committee at the previous meeting (February 2011). The Record of Reasons from that meeting states that *"This matter is still under consideration and no comment is solicited. The delegate is considering the Committee's recommendations and discussion in context of the current regulatory framework and has requested further advice from the ACMS prior to making an interim decision. A revised delegate's proposal inviting public comment will be published in the pre-meeting public notice for matters referred to the June 2011 ACMS meeting."*

No information has been provided that explains how the February 2011 meeting proposal to reschedule on the basis of age for 15 actives then changed to rescheduling of 5 actives, without any reference to age.

The following issues are of concern to [redacted]

- Sponsors have no information on the rationale for changing the scheduling proposal so significantly from the February 2011 meeting to the June 2011 meeting
- Sponsors have no information on whether the existing scheduling for the other 15 actives is to be retained

3. No evidence that restriction of unscheduled cough & cold products currently in grocery indicated for adults and children over 12 is needed

The TGA review focused on safety in children, predominantly under 6s. Phenylephrine and guaiphenesin when in combination with paracetamol are unscheduled only when available on small pack sizes and indicated for children over 12 years and adults. It is unclear how rescheduling of these products to schedule 2 will make any difference to safety in children, since these products are not used by children.

Other countries such as the UK, USA, New Zealand and Canada have not tightened the scheduling of products which are indicated for adults and children over 12, particularly those products that have adult dosage dorms such as tablets and capsules.

4. Paracetamol and ibuprofen products indicated for cold and flu

"Cold and flu" are allowable indications for paracetamol and ibuprofen products, as per ARGOM. There are some unscheduled specific cold and flu products that are marketed in the grocery environment that contain only paracetamol and are marketed under brand names that include the words "cold & flu". We are concerned that potentially, the only unscheduled products that can be marketed with a cold and flu indication will contain only analgesics. This would also seem to imply that paracetamol has a better safety profile compared to phenylephrine and guaiphenesin, when it is well known that analgesics do not have a better safety profile compared to these actives.

Appropriateness of existing scheduling

Many active ingredients on the TGA's list of actives are already scheduled S2 or higher in some cases (e.g. antihistamines, codeine, pseudoephedrine). These are:

Brompheniramine, chlorpheniramine, codeine, dexchlorpheniramine, dextromethorphan, dihydrocodeine, diphenhydramine, doxylamine, oxymetazoline, pheniramine, pholcodine, promethazine, pseudoephedrine, triprolidine, xylometazoline.

[redacted] believes that the above scheduling regime is appropriate for these products. The following entries are allowable exclusions in the SUSMP, and these types of products are unscheduled:

1. Paracetamol in combination with phenylephrine, with or without guaiphenesin

The scheduling entries in the SUSMP under paracetamol in combination with phenylephrine with or without guaiphenesin were finalised very recently after consideration by the NDPSC. The conclusion was reached that the safety profile of these

substances was such that the availability as unscheduled medicines carried little risk. The NDPSC Resolution 2010/58-21 states that the Committee decided to extend the exemption for certain paracetamol + phenylephrine combinations to also include combinations containing guaiphenesin.

The Record of Reasons of the February 2010 meeting indicates that the committee considered data and deliberated carefully over this decision. The delegate is therefore seeking to overturn a recently made decision but has not provided a rationale to sponsors explaining why it is now necessary to reschedule this combination of actives.

It is noted that these exclusions from the SUSMP are shown under the paracetamol entry and also have age based criteria. The exclusion from the schedules does not apply to products labelled for use in children under 12 years.

2. Guaiphenesin and phenylephrine schedules

[redacted] believes that it is possible to implement age based exclusions in the SUSMP for guaiphenesin and phenylephrine, much in the same way as what has already been done for these actives when in combination with paracetamol.

As an example, the existing entry for phenylephrine in S2 that shows the appropriate concentration and dose limits allowed for excluded unscheduled products, could be modified by adding the additional statement “when not labelled for children under 12 years”. This is similar to the situation that exists currently for the paracetamol and paracetamol + phenylephrine +/- guaiphenesin entries, which could be adopted for the phenylephrine entry.

The S4 entry for guaiphenesin can also be modified to effect age based scheduling. The schedule currently exempts oral liquid preparations containing 2% or less of guaiphenesin or divided preparations containing 200mg or less of guaiphenesin per dosage unit. A separate entry in schedule 2 could be included to cover guaiphenesin when labelled for children under 12 years; the Schedule 4 entry could be modified to refer to the Schedule 2 entry. Therefore, guaiphenesin products labelled for use in children under 12 would be captured under Schedule 2 and the remaining guaiphenesin products would retain their existing scheduling, being either S4 or unscheduled.

Age based scheduling is preferable as it affects only the products that are labelled for use in children, i.e. its impact is restricted to the population directly identified in the reviews commissioned by the TGA. There are some entries in the SUSMP that already specify age as part of the schedule. Examples are the paracetamol entry in Schedule 2, where the exclusions include age based criteria; and the ibuprofen entry in Schedule 2, which also includes age based criteria in the exclusions. The age based schedules could be implemented in addition to TGA controlling use in children via administrative decisions relating to labelling and registration.

Harmonisation – Australia / New Zealand

We request that every effort be made to harmonise the scheduling of cough and cold products with New Zealand. The majority of products or formulations being supplied are trans-Tasman, and the costs to sponsors can be controlled when Australia and New Zealand are able to be supplied a product in identical labels and pack sizes. Non-harmonised scheduling means that countries will require their own unique labelling, resulting in lower volumes to each country together with the comparative increase in costs of running smaller production batches or packing/labelling runs.

Overseas Experience

Safety of cough and cold medicines in children has been an issue in many countries with similar regulatory standards to Australia.

In the UK, age based classifications were implemented in March 2010 and the following classification or scheduling applies for these actives:

- phenylephrine is GSL (unscheduled) for use by adults and children over 12 years. Maximum dose is equivalent to 10mg phenylephrine.
- guaiphenesin are allowable as GSL (unscheduled medicines) for adults and children over 12 years. Maximum dose is 200mg.

In Canada, guaiphenesin is GSL and phenylephrine is GSL when in low concentrations. Use in children was managed mainly via labelling.

Implementation Timelines

[redacted] wishes to make the ACMS aware that changes to scheduling will result in changes required for labelling and packaging, and that these changes have lead times for implementation due to the need to design artwork, obtain approvals, order and manufacture components and plan for manufacturing.

In addition, some sponsors may also wish or need to make concurrent changes, since changes to scheduling may affect the overall positioning and look of the product and may therefore require other changes which are regarded by TGA as variations. These types of changes may have an additional 4-6 month evaluation time prior to ordering of packaging and labelling materials and scheduling into the manufacturing plan.

It would be of assistance to sponsors if the ACMS took these limitations into consideration when gazetting possible changes to schedules. We request an implementation of 2013.

[redacted]

2.1.4 Cough and cold preparations - submission 2 of 9.

Friday, 13th May 2011
Encl.

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA
ACT 2601

e-mail: SMP@health.gov.au

Dear Sir/Madam

Re: Item 2.1 Cough and Cold Preparations

[redacted] appreciates the opportunity to provide comment on item 2.1 in relation to Cough and Cold preparations.

Item 2.1 Cough and Cold Preparations

Following consideration of advice from a number of expert sources including the Advisory Committee on Medicines Scheduling (ACMS), the delegate refers the following revised proposal regarding cough and cold preparations to the ACMS for further advice:

Cough and cold preparations – proposal to schedule five substances used in currently unscheduled cough and cold preparations to Schedule 2. The delegate proposes that this rescheduling apply to the following substances for use in cough and cold products only where it will not result in less restrictive scheduling:

- Carbetapentane (pentoxyverine)
- Guaiphenesin (guaifenesin)
- Ipecacuanha (cephaelis acuminata and cephaelis ipecacuanha)
- Phenylephrine
- Senega

The TGA proposes to address the use of cough and cold medicines by different age groups separately through product registration and labelling processes.

Additional information for stakeholders on the TGA review of cough and cold medicines is available at Labelling and packaging of cough and cold medicines – proposed changes to requirements

[redacted] would like to formally and strenuously object to the proposal to reschedule:

- Guaiphenesin (guaifenesin) and
- Phenylephrine

This objection to the proposed resch eduling of guaiphenesin and phen ylephrine is primaril y b ased upon the fact that there has been no new data to suggest that there are any safety concerns since these compounds were initiall y reviewed b y the T GA and subsequentl y the NDPSC and ACM S. Additionally, there has been no increased risk to public health or history of abuse for these products containing these compounds.

[redacted] has no objections to the proposal to reschedule the substances listed below

- Carbetapentane (pentoxyverine)
- Ipecacuanha (cephaelis acuminata and cephaelis ipecacuanha) and
- Senega

A full position statement has b een provided over leaf. On behalf of [redacted], I would like to r equest t hat the committee mem bers at the J une 2011 meeting of the Advisor y Committee on Me dicines Sc heduling c arefully consider the points ra ised in the position sta tement before ma king a ny recommendation to the de legate on the resc heduling of guaiphenesin an d phenylephrine.

In the interest of privacy, I would like to request that my name, and contact details are redacted from the correspondence/information that is to become a publically available.

Yours sincerely,

[redacted]

1 Table of Contents

2 Preface

The review of paediatric cough and cold products have been a recurring item on the NDPSC and ACMS agendas in recent times. Once again this item is presented to the ACMS, albeit with an extended focus. Comprehensive data relating to the safety of the active pharmaceutical ingredients in the cough and cold products have been reviewed on each occasion, and on each occasion the advice/recommendations that have been made are consistent. It is apparent that there are no new data to suggest that any of the active ingredients previously reviewed or those recommended for rescheduling at the June 2011 meeting of the ACMS. For these reasons, it is believed that the re-examination of the material previously provided to the expert committees would be an unproductive exercise.

[redacted] through this submission, would like to highlight the pertinent issues that are still unresolved, as well as address the proposed rescheduling of phenylephrine and guaiphenesin.

Finally, given that there are no new safety data for the active ingredients in the cough and cold products, [redacted] calls for the adoption of the recommendation made by the ACMS for the 19 ingredients at the December 2010 meeting – this being

- Schedule 4 for use in children less than 2 years of age.
- Schedule 3 for use in children aged from 2 to 6 years of age.
- Schedule 2 for use in children and adults above 6 years of age.

3 Introduction

Cough and cold preparations are for short-term, symptomatic relief of coughs and colds - self-limiting conditions. The potential safety concerns of cough and cold medicines in general relate to use in children where there currently exists an apparent lack of strong efficacy data.

The review of paediatric cough and cold products has been a recurring item on the NDPSC and ACMS agendas. Again this item is presented to the ACMS, albeit with an extended focus. [redacted] has some grave concerns with the delegate's revised proposal regarding cough and cold preparations. These concerns include, but are not limited to:

- The rationale behind the proposal is not specified. The proposal states "*Following consideration of advice from a number of expert sources including the Advisory Committee on Medicines Scheduling (ACMS)".* In the interest of transparency, the delegate should make all the "advice" available to the public and to the Committee in order to allow a full consideration of the issues and to allow them to be properly addressed. As it currently stands, a thorough and balanced review by the public or the committee cannot be made.
- It is apparent that there is an objection to the proposed age based scheduling. Aged based scheduling is currently utilised for a number of ingredients and is also a practice that is used in the scheduling of ingredients by other regulators. The complexities surrounding the scheduling by age is not sufficient grounds for this approach not to be employed for cough and cold preparations.
- Clarification on the current scheduling of the following substances (below) remains ambiguous and clarification is required.
    - Brompheniramine
    - Chlorpheniramine
    - Codeine
    - Dexchlorpheniramine
    - Dextromethorphan
    - Dihydrocodeine
    - Diphenhydramine
    - Doxylamine
    - Oxymetazoline
    - Pheniramine
    - Pholcodine
    - Promethazine
    - Triprolidine
    - Xylometazoline
- The proposed rescheduling of phenylephrine and guaiphenesin is considerably different to the position that has been adopted by other regulatory agencies. Additionally the initial review conducted by the TGA had the scope of **paediatric** indicated products only i.e. products for **children under 12 years of age**. It is not clear as to why the scope of the review has been expanded to include products indicated for adults and children over 12 years of age.
- Should a decision be made that phenylephrine and guaiphenesin are to be rescheduled, there will be a profound impact for consumers in that consumers will only be able to purchase registered OTC cough and cold products only through pharmacy retailers. This means that only complementary products would be available through non-pharmacy retailers. The question needs to be asked "*Is this proposal really being made in the interest of public health?"*

A proposal to reschedule 19 substances used in registered cough and cold medicines was considered by the ACMS in December 2010. The delegate's Interim Decision noted that:

"*This matter is still under consideration and no comment is solicited. The delegate is considering the Committee's recommendations and discussion in context of the current regulatory framework and has requested further advice from the ACMS prior to making an interim decision.*

A revised delegate's proposal inviting public comment will be published in the pre-meeting public notice for matters referred to the June 2011 ACMS meeting."

The revised proposal contains 5 substances, 4 of which were included in the December 2010 proposal. There has been a decision made by the Delegate in relation to scheduling for the other 15 substances previously considered by the expert committees (ACMS & NDPSC).

[redacted] strenuously objects to the delegate's proposal for the rescheduling of

- Guaiphenesin
- Phenylephrine

This objection is based upon the facts that:

- there has been no additional data or evidence presented to suggest that the safety profile of these compounds has changed since last reviewed by the expert committees,
- the rescheduling of these compounds is outside the scope of the initial review which prompted the proposal (i.e. review of safety in paediatric populations)
- it is inconsistent with the decisions made by regulators in other countries that effectively reviewed the same data

There is no objection to the rescheduling of

- Carbetapentane (pentoxyverine)
- Ipecacuanha and
- Senega

The scheduling of these substances should be such that they ensure safety of cough and cold products for Australian consumers, but also convey benefit for public health. [redacted] calls for the adoption of the recommendation made by the ACMS for the 19 ingredients at the December 2010 meeting – this being

- Schedule 4 for use in children less than 2 years of age.
- Schedule 3 for use in children aged from 2 to 6 years of age.
- Schedule 2 for use in children and adults above 6 years of age.

4 Relevant matters under section 52E of the ACT

As defined under section 52E of the *Therapeutic Goods Act 1989* the following relevant matters will be addressed:

1. Risks and benefits;
2. Purposes for use and extent of use;
3. Toxicity;
4. Labelling, packaging and presentation; and
5. Potential for abuse

4.1 Risks and benefits

Cough and cold products are used for the temporary relief of symptoms associated with self limiting coughs and colds. They have a very long history of safe use in Australia in both adults and children. Some of products currently available have been safely used for more than 30 years.

As part of the review process, the TGA engaged two experts to conduct an external review of the available safety and efficacy data for registered OTC cough and cold medicines for children marketed in Australia. The External Report considered data about poisonings in Australia and stated that "*death or serious injury from children's cough and cold medicines is vanishingly rare*". It noted that, although there are substantial numbers of calls to Poisons Centres in regard to these medicines, very few are considered to be serious enough to refer for assessment and treatment.

[redacted] has conducted a literature review relating to the safety of cough and cold products from the period when TGA conducted the review of paediatric cough and cold medicines in 2009. No relevant publications were indentified. Consequently, it is believed that there is no new safety data of these substances in paediatric populations.

With particular reference to Phenylephrine and Guaiphenesin, the NDPSC recently considered the scheduling of phenylephrine and guaiphenesin when in combination with paracetamol. The outcome of this scheduling review was that phenylephrine when in combination with paracetamol was down scheduled to being exempt from scheduling (June 2007).

The justification for this decision was that the committee decided that the safety profile of these substances was such that allowing a fixed combination to be unscheduled was reasonable. The committee also felt that there was sufficient Australian market experience to support its decision. The primary benefit of this decision was that consumers could purchase a medication for the symptomatic relief of pain and congestion from a non-pharmacy retailer.

In February 2010, the NDPSC made the decision to make paracetamol, phenylephrine and guaiphenesin combinations exempt from scheduling. Again the committee concluded that the risk from this combination was unlikely to be significantly different to that of the currently unscheduled paracetamol + phenylephrine preparations. It also was noted that paracetamol was the most toxic single active ingredient in the combination and as such the addition of guaiphenesin was unlikely to exacerbate this toxicity.

4.2 Purposes for use and extent of use

Cough and cold products are used for the temporary relief of symptoms associated with self limiting coughs and colds.

Guaiphenesin is an expectorant. According the Australian Register of Therapeutic Goods, there are 58 products registered with Guaiphenesin as the active ingredient.

Phenylephine is a nasal decongestant. According the Australian Register of Therapeutic Goods, there are 231 products registered with phenylephrine as the active ingredient. Phenylephrine has uses other than just a nasal decongestant, so this figure may not accurately represent cough and cold products.

Some products containing these active ingredients are unscheduled (available from non-pharmacy retailers). These products may be used for the symptomatic relief of coughs and colds. Their availability from non-pharmacy retailers allows for easy access for consumers to these safe medicines.

4.3 Toxicity

From the report prepared during the external independent review of paediatric cough and cold medicines, it was concluded that it was possible to make definite conclusions about the safety of cough and cold medicines in children. Some of the statements pertaining to the safety of these products are provided below:

- *Generally, these medicines are very unlikely to be harmful in label dosages, and in non-intentional overdose in the typical 1-2 year old age group, serious poisoning is rarely seen.*
- *A recent study in the United States demonstrated that OTC cough and cold preparations were only present in toxicology screens in 5% of life-threatening poisonings in children.*
- *This may not apply to some drugs in adult doses in solid form, but this is not going to be influenced by any changes that might be made in the nature or availability of cough and cold medicines for children.*
- *Overseas reports of serious poisoning including deaths from cough and cold medicines are generally not reflected in current Australian experience. Documentation of such deaths is often confounded by co-existing severe illness, multiple drug administration, solid drug forms, the possibility of homicide and other factors.*

The TGA internal panel report on the safety, efficacy and use of cough and cold medicines in the treatment of children aged 2-12 years noted that:

- *Cough and cold preparations have a relatively safe history of use in children exposed to cough and cold medicines in Australia with only 99 ADRs reported since 1981 for children aged 12 years or under. However, 14 serious reactions (1 probable, 10 possible, 3 unclear) occurred during this period, and so the risks of cough and cold preparations administered to children cannot be considered negligible.*

Of the 14 'serious' ADRs mentioned for the period 1981-2010, Phenylephrine was linked to one serious ADR, however as it was a combination product, causality could not be determined. No serious ADRs were reported for guaiphenesin.

There are a number of substances with different safety profiles, such as paracetamol, that are available to consumers as unscheduled medicines in non-pharmacy outlets. We find it difficult to comprehend that there is adequate justification to reschedule these active ingredients as proposed by the delegate.

4.4 Labelling, packaging and presentation

Irrespective of their scheduling, these registered cough and cold products are reviewed by the evaluators in the OTC medicine section of Office of Medicines Authorisation in the TGA. As such the evaluators will review the dosage form to ensure the presentation does not breach Section 3(5) of the *Therapeutic Goods Act 1989* relating to presentation. The evaluators also review product labels for compliance to

- Section 3(5) of the *Therapeutic Goods Act 1989*
- TGO 69 – General requirements for labels for medicines
- Required advisory statements for medicine labels (RASML)
- MEC Guidelines in the Australian Regulatory Guidelines for OTC Medicines (ARGOM)
- TGO 80 – Child-resistant packaging requirements for medicines

4.5 Potential for abuse

There is no evidence in the Australian market suggesting patterns of misuse, either intentional or accidental.

Those products that could potentially be abused are only available in pharmacy which provides a level of restriction on availability, along with access to advice from a health care professional. Given the absence of any evidence of abuse or misuse, it is unlikely that the proposed restrictions will have any impact on the potential for misuse.

We would like to express our concerns over the proposed scheduling of all substances initially reviewed by the TGA in the review of cough and cold products for paediatric populations. As

mentioned above, some of the products have been available in the market for more than 30 years and have a history of safe use. This history of safe use is attributable to the clear dosing instruction on the product labels. A number of prominent brands are considered heritage brands for generations of consumers. As such, consumers may have used them in children in the past and could be tempted to use them in children again.

By making these products unavailable to children under 6, there is an increased risk that carers will "*guess*" the dose for a child under 6, based on the dosage instructions on a package for children older than 6 years of age. This is what has been observed in the USA.

Therefore, the likelihood of overdose is considerably higher, than if the products were made available, with the advice of a healthcare professional.

Again it should be reiterated that the scheduling of these substances should be such that they ensure safety of cough and cold products for Australian consumers, but also convey benefit for public health. With the potential for an increase in inappropriate dosing of children under 6, it is believed that the Australian public would be better served by having these products available for children under 6, albeit through a more measured means with accurate dosing instructions. The potential risk for overdose is too great if dosage instructions are not available to children between the ages of 2-6. Again, [redacted] calls for the adoption of the recommendation made by the ACMS for the 19 ingredients at the December 2010 meeting – this being

- Schedule 4 for use in children less than 2 years of age.
- Schedule 3 for use in children aged from 2 to 6 years of age.
- Schedule 2 for use in children and adults above 6 years of age.

5 Conclusion

Studies of 8 cough and cold substances representing about 95% of the cough and cold paediatric market are being undertaken in the US to generate data on safety and efficacy in children, and are expected to be completed in 2012-2013. [redacted] recommends that the information from these studies should be considered in Australia when they become available before any further restrictions are imposed. Failing to wait for the results of these studies, is likely to result in this issue again being presented to the ACMS.

[redacted] objects to the current proposal to reschedule:

- Guaiphenesin (guaifenesin)
- Phenylephrine

Our objections to the proposal are primarily based upon:

- The rationale behind the proposal is not specified. Additionally, the "advice" available to the public and to the Committee in order to allow a full consideration of the issues and to allow them to be properly addressed has not been disclosed.
- It is apparent that there is a good rationale for age based scheduling. Aged based scheduling is currently utilised for a number of ingredients and is also a practice that is used in the scheduling of ingredients by other regulators.
- The proposed rescheduling of phenylephrine and guaiphenesin is considerably different to the position that has been adopted by other regulatory agencies and contradicts previous NDPSC safety evaluation that led to its decision to exempt these ingredients from scheduling
- The scope of the initial review was for **paediatric** populations. There is no apparent reason as to why the scope of the review has been expanded to include the adult and children over 12 populations.

[redacted] has no objections to the rescheduling of

- Carbetapentane (pentoxyverine)
- Ipecacuanha (cephaelis acuminata and cephaelis ipecacuanha) and
- Senega

Additionally, [redacted] calls for the adoption of the recommendation made by the ACMS for the 19 ingredients at the December 2010 meeting – this being

- Schedule 4 for use in children less than 2 years of age.
- Schedule 3 for use in children aged from 2 to 6 years of age.
- Schedule 2 for use in children and adults above 6 years of age

[redacted]

[redacted]

2.1.4 Cough and cold preparations - submission 3 of 9.

13 May 2011

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Email: SMP@health.gov.au

INVITATION FOR COMMENT

Item 2.1 - Cough and cold preparations:

> Following consideration of advice from a number of expert sources including the Advisory Committee on Medicines Scheduling (ACMS), the delegate refers the following revised proposal regarding cough and cold preparations to the CAMS for further advice:
>
> Cough and cold preparations – proposal to schedule five substances used in currently unscheduled cough and cold preparations to Schedule 2. The delegate proposes that this rescheduling apply to the following substances for use in cough and cold products only where it will not result in less restrictive scheduling:
>
> - Carbetapentane (pentoxyverine)
> - Guaiphenesin (guaifenesin)
> - Ipecacuanha (cephaelis acuminata and cephaelis ipecacuanha)
> - Phenylephrine
> - Senega
>
> The TGA proposes to address the use of cough and cold medicines by different age groups separately through product registration and labelling processes.
>
> Additional information for stakeholders on the TGA review of cough and cold medicines is available at Labelling and packaging of cough and cold medicines – proposed changes to requirements

GENERAL COMMENTS ON THE PROPOSAL

Scheduling of paediatric cough and cold products has been a recurring item on the NDPSC and ACMS agendas recently.

It was last considered at the December 2010 ACMS meeting, at which 19 substances were considered. The *Interim Decisions & Reasons for Decisions by the Delegate of the Secretary t the Department of Health and Ageing* from that meeting noted that:

[redacted]

"This matter is still under consideration and no comment is solicited. The delegate is considering the Committee's recommendations and discussion in context of the current regulatory framework and has requested further advice from the ACMS prior to making an interim decision.

A revised delegate's proposal inviting public comment will be published in the pre-meeting public notice for matters referred to the June 2011 ACMS meeting."

The revised proposal contains 5 substances, 4 of which were included in the December 2010 proposal.

[redacted] does not support the revised proposal to reschedule these 5 substances to Schedule 2.

[redacted] contends that this proposal is outside the scope of the original TGA review of paediatric cough and cold medicines, is not justified on the basis of the evidence available, and will have unintended effects on the scheduling of products labelled for use in adults.

The proposal notes that "the TGA proposes to address the use of cough and cold medicines by different age groups separately through product registration and labelling processes."

As the TGA will be managing all labelling issues, including warning statements and appropriate use by age groups, [redacted] contends that the current scheduling of these substances ought to be maintained to enable adult access to simple cough and cold medicines.

INTRODUCTION

[redacted] has a number of concerns with the above proposal:

- The proposal is to restrict access to products containing these ingredients and no justification for such a radical regulatory intervention has been provided and therefore appears to be entirely baseless
- It is unclear why age based scheduling (as employed for other ingredients and in other jurisdictions) cannot be employed for cough and cold preparations.
- The disposition of the 15 substances previously considered (which are not separately identified in the above proposal) remains ambiguous. It is unclear whether
  a) the current scheduling of the other cough and cold substances is to be retained;
  b) the recommendations of the previous Committee are to be implemented;
  c) the scheduling proposals in the TGA's 2009 review are to be implemented or;
  d) some combination of these three possibilities is to be implemented.
- The proposal is out of step with the approaches adopted by other regulators and markets, which have relied on essentially the same information.
- The proposal again extends beyond the scope of the initial TGA review which examined paediatric products, i.e. products for children under 12 years of age. For reasons that have not been adequately stated, the focus of this proposal has now been widened to include products that are recommended for use by adults and children over 12 years of age
- This proposal again will have a significant impact on the products available to consumers. In effect the proposed change will remove all registered OTC and one listed cough and cold products from non-pharmacy retailers. It has to be questioned whether this proposal is a public health benefit.
- This matter has already been addressed in other jurisdictions by age based scheduling. Australia is not only lagging behind these other markets, but is also looking at a different approach entirely.

[redacted] questions why the TGA has referred this for a scheduling decision when the TGA has administrative powers to amend the conditions of market entry to remove paediatric instructions on the label if required without necessitating any scheduling changes, and thereby supporting their position that scheduling should not be age-based. **In fact this has been done before.**

Cough and cold preparations are for short-term use in self-limiting conditions. The potential safety concerns of cough and cold medicines in general relate to use in children where a lack of strong efficacy data is accompanied by some increased risks, in particular in cases where the recommended use and dosage have not been followed.

In relation to this proposal, the substances are all currently exempt from scheduling with certain caveats. In addition, two of the ingredients, phenylephrine and guaiphenesin, were only recently considered to be appropriate to exempt from scheduling. [redacted] is therefore perplexed by the proposal, which provides no transparency of rationale.

[redacted] rejects the proposal to reschedule the substances listed above to Schedule 2. There is no evidence of market failure which would warrant restricting access through rescheduling. As well, this proposal is outside the scope of the TGA review which prompted the proposal in the first place and will have an unacceptable impact on products labelled for use in adults.

[redacted] contends that in the absence of evidence based concerns about public health and safety the proposed changes are totally inappropriate.

[redacted] believes very strongly that the current scheduling of these substances is still appropriate and should therefore be retained for the benefit of Australian consumers who have been using these products safely for decades. This would be consistent with the principles of minimum effective regulation and harmonisation, with New Zealand in this instance. Any age-based considerations can be effectively dealt with by the TGA.

MOTIVATION FOR THIS PARTICULAR PROPOSAL

The delegate indicates that the referral to the Committee follows “consideration of advice from a number of expert sources including the ACMS”.

In the interest of transparency and to facilitate full public consultation and informed responses, all the “advice” available to the delegate should also be provided to the public and to the Committee in order to ensure a comprehensive consideration of the issues and the best possible solutions to identified and agreed issues..

In the absence of all the facts it is impossible to provide a fully informed response and alternative proposals.

SECTION 52E

[redacted] appreciates the opportunity to provide comment in relation to this issue. We wish to address relevant matters under section 52E of the Therapeutic Goods Act 1989 as these apply to the substances mentioned above:

(a) risks and benefits;
(b) purposes for use and extent of use;
(c) toxicity;
(d) labelling, packaging and presentation; and
(e) potential for abuse.

Risks and benefits

Cough and cold products have a very long history of safe use in Australia in both adults and children. Many products on the market today have been available and used safely for more than 30 years. Mild, reversible side effects of cough and cold medicines are well known, well described and the incidence has remained stable at very low levels.

No new safety data has come to light since the TGA's 2009/2010 review of paediatric cough and cold medicines which would justify the proposal to restrict access to products containing these substances.

Purposes for use and extent of use

These substances are indicated for short-term use in self-limiting conditions.

Toxicity

The summary of the TGA independent review of paediatric cough and cold medicines noted that:

- *Generally, these medicines are very unlikely to be harmful in label dosages, and in non-intentional overdose in the typical 1-2 year old age group, serious poisoning is rarely seen.*
- *Overseas reports of serious poisoning including deaths from cough and cold medicines are generally not reflected in current Australian experience. Documentation of such deaths is often confounded by co-existing severe illness, multiple drug administration, solid drug forms, the possibility of homicide and other factors.*

The *TGA internal panel report on the safety, efficacy and use of cough and cold medicines in the treatment of children aged 2-12 years* noted that:

- *Cough and cold preparations have a relatively safe history of use in children exposed to cough and cold medicines in Australia with only 99 ADRs reported since 1981 for children aged 12 years or under. However, 14 serious reactions (1 probable, 10 possible, 3 unclear) occurred during this period, and so the risks of cough and cold preparations administered to children cannot be considered negligible.*

Of the 14 'serious' ADRs mentioned for the period 1981-2010, only one was associated with ipecacuanha. Phenylephrine was linked to another serous ADR, however as it was a combination product, causality could not be determined. No serious ADRs were reported for guaiphenesin, pentoxyverine or senega & ammonia.

It should also be noted that these products already use child-resistant packaging, which adds another level of safety for these medicines.

A number of substances with different safety profiles, such as simple analgesics, are available to consumers as unscheduled medicines in non-pharmacy outlets. [redacted] contends that the 5 substances that are the subject of this proposal have a favourable safety profile when compared with some of these other ingredients.

We therefore contend that there is no justification to reschedule to Schedule 2.

Labelling, packaging and presentation

As noted, these substances are only indicated for short-term use in self-limiting conditions.

Section 3(5) of the *Therapeutic Goods Act 1989* requires that the presentation of therapeutic goods should not be 'unacceptable'. Included in the label include advisory statements if so required.

Prior to approving a product for inclusion on the Australian Register of Therapeutic Goods (ARTG) the TGA evaluates compliance with labelling and packaging of medicines must comply with a number of instruments, including:

- TGO 69 – General requirements for labels for medicines
- Required advisory statements for medicine labels (RASML)
- MEC Guidelines in the Australian Regulatory Guidelines for OTC Medicines (ARGOM)
- TGO 80 – Child-resistant packaging requirements for medicines
- Therapeutic Goods Advertising Code (TGAC) (as required)
- Tamper-evident packaging Code of Practice (as required).

Issues relating to labelling and packaging should therefore be directed to the TGA.

Potential for abuse.

There is no evidence of any abuse or misuse in the public domain which would suggest reconsideration of the current access to products containing these substances.

Those products that could potentially be abused are already only available in pharmacy and enable access to advice from a pharmacist. Given the absence of any evidence of abuse/misuse the proposed restrictions cannot be justified.

OTHER POINTS

The five ingredients in this proposal have a long history of safe use in Australia and there is no evidence which could raise concerns about public health and safety.

Carbetapentane (pentoxyverine)

SUSDP No. 1 (1986) included the following Schedule 2 entry for carbetapentane:

CARBETAPENTANE **except** in preparations containing 0.5 per cent or less of carbetapentane

This entry has not been changed since 1986.

[redacted] contends there is no evidence to warrant its up-scheduling.

Ipecacuanha (cephalis acuminate and cephalis ipecacuanha)

These ingredients are listed in Schedule 4 of SUSMP No. 1 **except** in preparations containing 0.2 per cent or less of emetine.

SUSDP No. 1 (1986) included the Schedule 4 entry:

EMETINE **except** in preparations containing 0.2 per cent or less of emetine.

That is, the scheduling has remained unchanged.

[redacted] contends there is no evidence to warrant the up-scheduling of ipecacuanha.

Senega

Senega is an herbal ingredient and has never been 'scheduled' or included in the poisons standard.

The Australian Register of Therapeutic Goods lists *Polygala senega* as an acceptable herbal ingredient, and permits its use as an active ingredient and an excipient in therapeutic goods.

Senega has been used by pharmacists for innumerable years in making extemporaneous preparations such as Senega and Ammonia, the formulation of which continues to be provided in the Australian Pharmaceutical Formulary (APF).

The scheduling of senega will have significant flow on effects for sponsors of these listed medicines, who will need to delist their products and apply to register them as complementary medicines. Should this proposal be endorsed by the committee, consideration will need to be given to an implementation that allows for the availability of the medicine during the long registration period.

[redacted] contends there is no evidence to warrant the up-scheduling of senega.

Guaiphenesin (guaifenesin) and Phenylephrine
The NDPSC recently considered the scheduling of phenylephrine and guaiphenesin when in combination with paracetamol.

Paracetamol combined with phenylephrine was exempted from scheduling in June 2007. The Committee decided that the safety profile of these substances was such that allowing a fixed combination to be unscheduled was reasonable. The Committee also felt that there was sufficient Australian market experience to support its decision.

In February 2010, the NDPSC exempted paracetamol, phenylephrine and guaiphenesin combinations from scheduling. The Committee concluded that the risk from this combination was unlikely to be significantly different to that of the currently unscheduled paracetamol+phenylephrine preparations. It also was noted that paracetamol was the most toxic single active ingredient in the combination and the addition of guaiphenesin was unlikely to exacerbate this toxicity.

The Committee generally agreed that there was sufficient data to justify extending the current scheduling exemption for paracetamol+phenylephrine combinations to also included guaiphenesin, noting the low risks and at least some small benefits from allowing unscheduled access to paracetamol+pheneylephrine+guaiphenesin combination preparations.

At the June 2010 NDPSC meeting, the committee had been advised that in New Zealand, guaiphenesin was contraindicated in children under six; there was little reported risk from use in children six years and older; and that there appeared to be better evidence of efficacy for guaiphenesin with no real safety issues.

The NDPSC had agreed that “guaiphenesin in preparations for treating cough and cold did not need to be rescheduled.”

As no new safety data has been presented in the current proposal to dispute or contradict the previous scheduling determinations, [redacted] does not support the proposal that the substances listed above be rescheduled to Schedule 2.

INTERNATIONAL SITUATION

New Zealand
All 5 substances are available as general sale medicines in New Zealand as follows.

- *Carbetapentane* in medicines containing 0.5% or less
- *Senega* – no additional conditions.

- *Ipecacuanha* in medicines containing less than 40 mcg of ipecacuanha alkaloids per recommended dose for the treatment of the symptoms of cough and cold in children aged 6-12 years
- *Phenylephrine* for adults and children over 12 years of age for oral use in medicines containing 50 mg or less per recommended daily dose and in packs containing 250 mg or less of phenylephrine per pack
- *Guaiphenesin* for adults and children over 6 years of age for oral use in medicines containing 2% or less or 200 mg or less per dose form; for oral use in modified release form with a maximum recommended daily dose of not more than 2.4 grams sold in a pack containing not more than 5 days' supply

Cough/cold labels in New Zealand must also include a warning along the lines of "seek advice from a healthcare professional if taking more than one cough/cold medicine".

UK
New requirements were implemented in March 2010.

- Phenylephrine for internal use by adults and children over the age of 12 years, with a maximum dose equivalent to 10 mg phenylephrine
- Guaiphenesin for use by adults and children over the age of 12 years, with a maximum dose of 200 mg
- Ipecacuanha for use by adults and children over 12 years
- Senega – all medicines are available for general sale

CURRENT AUSTRALIAN UNSCHEDULED PRODUCTS

Attachment 1 provides a list of [redacted] products that will be affected by the rescheduling of the 5 substances in the proposal.

We have also been advised that products containing paracetamol and/or phenylephrine and/or guaiphenesin are either in the process of being evaluated by the TGA or have been approved and are to be launched shortly.

IMPACT

The potential regulatory impact of the proposed rescheduling of these substances is of such a magnitude that a full Regulatory Impact Statement would need to be conducted to satisfy current Government policy guidelines. The potential impact is broader than just implementation and loss of sales in non-pharmacy outlets within Australia and will potentially extend to the viability of cough and cold products in the New Zealand market, as many products are co-marketed in both Australia and New Zealand.

Compelling evidence of gross market failure is required to justify the scale of the impact on consumer access, industry generally and sponsors specifically

SOLUTION

We argue that rescheduling as proposed is not only inappropriate but also unnecessary to give effect to the outcomes of the TGA Review in relation to paediatric use of cough/cold medicines. To be consistent with precedent and previous recommendations of the ACMS, [redacted] proposes the following:

- The unscheduled status of these five ingredients be maintained as at present
- TGA use their administrative powers under the *Therapeutic Goods Act 1989*, s28 to require additional conditions of registration in relation to labelling. This means was employed in 2008 to require removal of any information relating to dosage or use of cough and cold medicines in children under 2 years of age, and to include the statement "Do not use in children under 2 years of age" (or words to the effect) o labels – this did not necessitate any scheduling changes
- Guaiphenesin to be available unscheduled when labelled for adults and children over 6 years of age (as in New Zealand), either as a single ingredient or when in combination with Paracetamol and/or phenylephrine – labelling requirements to be achieved through the regulatory process
- Phenylephrine to be available unscheduled as a single ingredient or in combination with paracetamol and/or guaiphenesin when labelled for adults and children over 12 years of age – labelling requirements to be achieved through the regulatory process
- Current scheduling requirements for carbetapentane, senega and ipecacuanha when labelled for adults and children over 12 years of age – labelling requirements to be achieved through the regulatory process.

TIMING of IMPLEMENTATION

Given the significance of the proposed changes and inherent logistical and manufacturing complexities a minimum of 9 months' lead time will be required to implement any changes arising from consideration of this matter. Our calculations – based on consideration by ACMS, recommendations to the delegate and final decision by the delegate, the seasonality of the products; preparation and submission of applications to the TGA, approval of applications by the TGA; development of reprographics film/plates; ordering of stock (typically from Europe) and freight time– indicate that full implementation will not be possible before the 2013 cough/cold season.

CONCLUSION

[redacted] rejects the blanket rescheduling of the above five substances because we believe it is unjustified and inappropriate given the lack of evidence of market failure and the enormous regulatory impact resulting from rescheduling.

[redacted] contends that this proposal is outside the scope of the TGA Review which prompted the proposal. To give effect to the recommendations of review we proposed the following regulatory measures:

- The unscheduled status of these five ingredients be maintained as at present
- TGA use their administrative powers under the *Therapeutic Goods Act 1989*, s28 to require additional conditions of registration in relation to labelling. This means was employed in 2008 to require removal of any information relating to dosage or use of cough and cold medicines in children under 2 years of age, and to include the statement "Do not use in children under 2 years of age" (or words to the effect) on labels – this did not necessitate any scheduling changes
- Guaiphenesin to be available unscheduled when labelled for adults and children over 6 years of age (as in New Zealand), either as a single ingredient or when in combination with Paracetamol and/or phenylephrine – labelling requirements to be achieved through the regulatory process

- Phenylephrine to be available unscheduled as a single ingredient or in combination with paracetamol and/or guaiphenesin when labelled for adults and children over 12 years of age – labelling requirements to be achieved through the regulatory process
- Current scheduling requirements for carbetapentane, senega and ipecacuanha when labelled for adults and children over 12 years of age – labelling requirements to be achieved through the regulatory process.

[redacted] contends that the current scheduling of these substances is still appropriate and should be retained for the benefit of Australian consumers, to be consistent with the principle of minimum effective regulation, and to maintain harmonisation with New Zealand; and that any age-based considerations be dealt with by the TGA.

We remain committed to working with the TGA to implement appropriate labelling requirements to ensure the continued safe use of these products by Australian consumers.

[redacted] hopes these comments are useful in the Committee's deliberations.

Yours sincerely

[redacted]

Attachment 1: [redacted] Products that will be affected by rescheduling of the 5 substances

Brand name	Ingredients	Current dosage age range
Lemsip Cold & Flu with Decongestant Capsules	Phenylephrine, paracetamol	12 years – Adult
Lemsip Max Cold & Flu with Decongestant Hot Drink Blackcurrant	Phenylephrine, paracetamol	12 years – Adult
Lemsip Max Cold & Flu with Decongestant Hot Drink Lemon	Phenylephrine, paracetamol	12 years – Adult
Lemsip Max Multi Relief Hot Drink Lemon	Phenylephrine, guaiphenesin, paracetamol	12 years – Adult
Lemsip Multi Relief Capsules	Phenylephrine, guaiphenesin, paracetamol	12 years – Adult
Nyal Bronchitis	Polygala senega (as an excipient), ammonium chloride	5 years – Adult
Nyal Chesty Cough Medicine	Guaiphenesin	2 years – Adult
Nyal Cold & Flu Medicine	Phenylephrine	2 years – Adult
Nyal Decongestant Nasal Spray	Phenylephrine	12 years – Adult
Nyal Dry Cough Medicine	Pentoxyverine	4 years – Adult
Panadol Cold & Flu + Decongestant Caplets	Phenylephrine, paracetamol	12 years – Adult
Panadol Cold & Flu Max + Decongestant Hot Lemon drink	Phenylephrine, paracetamol	12 years – Adult
Panadol Sinus Relief PE caplets	Phenylephrine, paracetamol	12 years – Adult
Robitussin Chesty Cough Capsules	Guaiphenesin	6 years – Adult
Robitussin Chesty Cough oral liquid	Guaiphenesin	2 years – Adult *
Robitussin Cold & Chesty Cough oral liquid	Phenylephrine, guaiphenesin	2 years – Adult *
Robitussin Cold & Flu + Decongestant	Phenylephrine, paracetamol	12 years - Adult
Robitussin Cold & Flu Junior oral liquid	Phenylephrine	2 – 12 years *
Robitussin Cold & Flu oral liquid	Phenylephrine	2 years – Adult *
Robitussin Cough & Chest Congestion oral liquid	Phenylephrine, guaiphenesin	2 years – Adult *
Robitussin Head Cold & Sinus tablets	Phenylephrine, paracetamol	12 years - Adult
Robitussin Sinus Relief capsules	Phenylephrine	12 years - Adult
Robitussin Sinus Relief oral liquid	Phenylephrine	2 years – Adult *
Senegar oral liquid	Senega and ammonia	Adults
[redacted]	[redacted]	[redacted]
Vicks Cough Syrup for chesty cough	Guaiphenesin	2 years – Adult
Vicks Honey cough syrup for chesty cough	Guaiphenesin	6 years – Adult

* These labels all include the statement “For children 2 to under 6 years of age, consult a healthcare professional before use.”

[redacted]

[redacted]

2.1.4 Cough and cold preparations - submission 4 of 9.

13 May 2011

The Secretary
Scheduling Secretariat
GPO Box 9848
Canberra, ACT 2601

E-mail: SMP@health.gov.au

Item 2.1: Cough and cold preparations
Response to invitation for comment

This responds to TGA invitation for comment to the proposed rescheduling of certain cough-cold medicine actives to be tabled in the 21-June-2011 ACMS meeting. (Kindly keep the name of the company/applicant confidential in the public record).

Proposed scheduling

Item 2.1 - Cough and cold preparations:

> Following consideration of advice from a number of expert sources including the Advisory Committee on Medicines Scheduling (ACMS), the delegate refers the following revised proposal regarding cough and cold preparations to the CAMS for further advice:
>
> Cough and cold preparations – proposal to schedule five substances used in currently unscheduled cough and cold preparations to Schedule 2. The delegate proposes that this rescheduling apply to the following substances for use in cough and cold products only where it will not result in less restrictive scheduling:
>
> - Carbetapentane (pentoxyverine)
> - Guaiphenesin (guaifenesin)
> - Ipecacuanha (cephaelis acuminata and cephaelis ipecacuanha)
> - Phenylephrine
> - Senega
>
> The TGA proposes to address the use of cough and cold medicines by different age groups separately through product registration and labelling processes.
>
> Additional information for stakeholders on the TGA review of cough and cold medicines is available at Labelling and packaging of cough and cold medicines – proposed changes to requirements

Arguments/Reasons against upscheduling of Guaiphenesin

We believe that the proposed upscheduling of Guaifenesin is not warranted for the following reasons:

1. There is no new safety or efficacy evidence to warrant reversing the recent scheduling decisions made by the NDPSC that maintain unscheduled status for Guaifenesin, either singly or in combination with paracetamol+phenylephrine, as follow:.

    a. "Guaiphenesin combined with Paracetamol and Phenylephrine" was declared to be unscheduled.

    NDPSC 58th meeting (Feb 2010): Based on extensive review of evidence, the Committee "agreed that there was sufficient data at this time to justify extending the current scheduling exemption for paracetamol+phenylephrine combinations to also include guaiphenesin, noting the low risks and at least some small benefits from allowing unscheduled access to certain PPGC preparations."

    b. "Guaiphenesin" remains to be unscheduled.

    NDPSC 59th meeting (June 2010): Based on extensive review of evidence, the Committee agreed that "use of guaiphenesin in preparations for treating cough and cold did not need to be rescheduled."

2. Guaifenesin has low toxicity profile, and has generally proven benefit as an expectorant.

    1. There was little reported risk from use of Guaiphenesin in children aged 6 years and above. Additionally, it appears that Guaiphenesin has a better evidence of efficacy with no real safety issues. In fact, out of the 22 cough-cold actives being reviewed by TGA, Guaiphenesin has the best benefit to risk profile.

    2. Guaiphenesin has long history of safety use in Australia despite being unscheduled since 1998. (At the Feb 1998 meeting, the Committee agreed to exempt Guaiphenesin in oral preparations from Schedule 2 when accompanied by a statement warning against use in children under two years of age.) In fact, no serious ADR's were reported for Guaiphenesin for period 1981 – 2010.

    3. The presentation of cough and cold medicines in Australia is far more stringent than in most countries like US, and this reduces risk of overdose or misuse. This includes the application of child-resistant packaging, supply of dosage cap, and consumer-focused labeling that recommends against use in children under 2 years of age.

    4. Most coughs are self-limiting, and given the low safety risk and efficacy to help relieve chesty cough, there is no reason why Guaiphenesin should have restricted access for consumers.

3. The proposed upscheduling is not in line with that of NZ Medsafe. Trans-tasman harmonization with New Zealand should be considered in order to ensure consistent and viable supply of these cough medicines to both Australia and New Zealand.

    At its 43rd meeting (April 2010), the MCC (Medicines Classification Committee) of NZ Medsafe recommended that the "current unscheduled classification of Guaiphenesin remained appropriate" following extensive review of data and evidence. As it is the same data/evidence

being reviewed by TGA, it is expected that TGA will reach the same conclusion/view and adopt the same approach as other jurisdictions like Medsafe.

We are amenable to enhanced labeling approach similar to measures implemented by Medsafe. This includes contraindicating Guaiphenesin for children below 6 years old and additional warning statements, like "consult a healthcare professional for use in children 6-12 years old" as additional safeguard measures.

Section 52E

We hereby address the relevant matters under Section 52E of the Therapeutic Goods Act 1989 as these apply to Guaiphenesin.

Risks and benefits

The safety risk profile and efficacy benefits of Guaiphenesin have been reviewed extensively by TGA since 2008, when this whole "pediatric cough-cold issue" came about. In fact, this evidence was again reviewed by the Committee in last year's NDPSC meeting (58th and 59th meeting) for related scheduling proposals for Guaiphenesin. In both meetings, it was concluded that the current unscheduled status of Guaiphenesin is appropriate based on extensive review of safety/efficacy data. Since then, there had been no new safety data that would warrant changing that position.

Purposes for use and extent of use

The five actives under consideration are for symptomatic treatment of cough and cold. In particular, Guaiphenesin is an expectorant for relief of chesty cough, and helping to clear phlegm.

Toxicity

Guaiphenesin has low toxicity profile, per TGA's extensive review of all safety data, including Adverse effects reported for Guaiphenesin. In fact, the number of ADR's reported for children 12 and under between 1981 and 2010 for Guaiphenesin is three, and none of these is serious ADR.

Labelling, packaging and presentation

Labelling of Guaiphenesin products contain warning statements, including "not to be used in children under 2" as mandated by Section 28. Packaging includes a child-resistant closure and a dosage cap. These minimize potential risk of misuse and overdose.

Potential for abuse

We are not aware of any abuse/misuse of Guaiphenesin.

Conclusion

We contend that the proposed upscheduling of Guaiphenesin is excessive and not justified on the basis of the evidence available.

While we are fine with contraindicating the use of Guaiphenesin in children under 6 through enhanced labeling, a change to the current unscheduled status of Guaiphenesin is not warranted.

A more appropriate approach is to impose a more enhanced labeling, including: (a) contraindication in children under 6; i.e., do not use in children under 6, and (b) additional warning statements like "consult

with a healthcare professional for use in children 6-12 years old," while retaining its current "unscheduled" status.

Timing and Implementation

As most of [redacted] marketed products are sourced overseas, a leadtime of 18 months would be requested for implementing labeling changes in order to minimize scrapping and avoid unnecessary product retrieval from market.

[redacted]

2.1.4 Cough and cold preparations - submission 5 of 9.

[redacted]

11th May 2011

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Email: SMP@health.gov.au

Ref: Meeting of the ACMS June 2011 Item 2.1 Cough and cold medicines. Consideration of scheduling resulting from a review by the TGA

[redacted] appreciates the opportunity to provide this submission for consideration by the members of the ACMS at their June 2011 meeting.

Item 2.1 of the pre-meeting gazette notice states

'2.1 Cough and Cold preparations:

Following consideration of advice from a number of expert sources including the Advisory Committee on Medicines Schedules (ACMS), the delegate refers the following revised proposal regarding cough and cold preparations to the ACMS for further advice:

Cough and cold preparations – proposal to schedule five substances used in currently unscheduled cough and cold preparations to Schedule 2. The delegate proposes that this rescheduling apply to the following substances for use in cough and cold products only where it will not result in less restrictive scheduling:

Carbetapentane (pentoxyverine)

Guaiphenesin (guaifenesin)

Ipecacuanha (cephaelis acuminata and cephaelis ipecacuanha)

Phenylephrine

Senega

The TGA proposes to address the use of cough and cold medicines by different age groups separately through product registration and labelling processes.

Additional information for stakeholders on the TGA review of cough and cold medicines is available at Labelling and packaging of cough and cold medicines - proposed changes to requirements'

Background

Paediatric cough and cold products has been a recurring item on the NDPSC and ACMS agendas recently. The above proposal is significantly different to that first put forward for discussion even though there is no new data which is relevant to the Committee's deliberations. [redacted] believes that this proposal extends beyond the scope of the initial review of these substances when indicated for children. [redacted] questions whether this was the intention of the committee to include adult medicines in this proposed change and believes that - this is not supported by current use

When this matter was discussed at the June 2010 meeting of the NDPSC it was initially relating to the proposal to increase scheduling of 19 substances used in cough & cold preparations in children under 12 years of age. This meeting recommended the increased scheduling for these 19 substances when indicated in adults & children.

[redacted]

[redacted]

[redacted]

It is now proposed to reschedule 5 substances, including Guaiphenesin, which was not previously under consideration. It is not clear what is proposed for the other 15 substances no longer under consideration.Or what new safety concerns have arisen in relation to Guaiphenisin to warrant it being added to this list.

The delegate indicates that the referral to the Committee follows "consideration of advice from a number of expert sources including the ACMS". All the "advice" should be made available to the public and to the Committee in order to allow a full consideration of the issues and to allow them to be properly addressed.

[redacted] disagrees with the proposal to increase the scheduling of the 5 substances to schedule 2 when used in over-the-counter cough and cold medicines as detailed above. We recommend for the current scheduling of cough and cold products to be broadly retained, but with some refinements to scheduling being based on age.

TGA Review

The actives listed for consideration do not appear to have safety issues according to the data analaysed by the TGA's External Reviewers (April 2009) nor form the TGA's Internal Panel report (May 2009). No new safety data has been released and no additional safety concerns have be raised since this proposal was original put to the NDPSC.

The "TGA internal panel report on the safety, efficicay and use of cough and cold medicines in the treatment of children 2-12 years, May 2009" (Internal Report) shows that many of the actives under consideration for scheduling changes have few if any ADR's. We would seek a reconsideraton of the need to include these actives for consideration for upscheduling. It seems this group has little if any risk and may be inappropriately grouped with those actives that have shown a greater number of ADR's.

The summary of the TGA independent review of paediatric cough and cold medicines noted that:

- Generally, these medicines are very unlikely to be harmful in label dosages, and in non-intentional overdose in the typical 1-2 year old age group, serious poisoning is rarely seen.
- Overseas reports of serious poisoning including deaths from cough and cold medicines are generally not reflected in current Australian experience. Documentation of such deaths is often confounded by co-existing severe illness, multiple drug administration, solid drug forms, the possibility of homicide and other factors.

The TGA internal panel report on the safety, efficacy and use of cough and cold medicines in the treatment of children aged 2-12 years noted that:

- Cough and cold preparations have a relatively safe history of use in children exposed to cough and cold medicines Australia with only 99 ADRs reported since 1981 for children aged 12 years or under. However, 14 serious reactions (1 probable, 10 possible, 3 unclear) occurred during this period, and so the risks of cough and cold preparations administered to children cannot be considered negligible.

Of the 14 'serious' ADRs mentioned for the period 1981-2010, only one was associated with ipecacuanha. Phenylephrine was linked to another serous ADR, however as it was a combination product, causality could not be determined. No serious ADRs were reported for guaiphenesin, pentoxyverine or senega & ammonia.

It should also be noted that these products use child-resistant packaging, which adds another level of safety for these medicines.

We therefore contend that there is no justification to reschedule to Schedule 2.

Recent Scheduling Decisions

The NDPSC recently considered the scheduling of phenylephrine and guaiphenesin when in combination with paracetamol.

Paracetamol combined with phenylephrine was exempted from scheduling in June 2007. The Committee decided that the safety profile of these substances was such that allowing a fixed

combination to be unscheduled was reasonable. The Committee also felt that there was sufficient Australian market experience to support its decision.

In February 2010, the NDPSC exempted paracetamol, phenylephrine and guaiphenesin combinations from scheduling. The Committee concluded that the risk from this combination was unlikely to be significantly different to that of the currently unscheduled paracetamol and phenylephrine preparations. It also was noted that paracetamol was the most toxic single active ingredient in the combination and the addition of guaiphenesin was unlikely to exacerbate this toxicity.

The Committee generally agreed that there was sufficient data to justify extending the current scheduling exemption for paracetamol and phenylephrine combinations to also included guaiphenesin, noting the low risks and at least some small benefits from allowing unscheduled access to paracetamol, phenylephrine and guaiphenesin combination preparations.

As no new safety data has been presented in the current proposal to dispute or contradict the previous scheduling determinations, [redacted] **does not support the proposal that the substances listed above be rescheduled to Schedule 2.**

International Recommendations

Analysis of the safety data from Australia, New Zealand the UK, USA and Canada all show that the actives responsible for most reports of adverse events are the sedating antihistamines and pseudoephedrine; these are already scheduled as Pharmacy Only or higher. Accidental childhood ingestion followed by overdose, present the highest risk factors for Australia. The restricted availability of C&C medicines via Pharmacy (antihistamines and pseudoephedrine) does not provide an effective solution for this problem as the events occur after purchase and in the home. Hence, upscheduling any other actives would seem to be of little benefit in preventing ADR's given it has not stopped events with medicines that are already Pharmacy Only.

In 2009 the MCC did a similar review of cough and cold preparations and the findings showed no change to the safety profile these substances. The decision was made that the scheduling would remain unchanged and that Cough/cold labels in New Zealand must also include a warning to "seek advice from a healthcare professional if taking more than one cough/cold medicine".

All 5 substances currently under discussion are available for general sale when indication for children over 12 in the UK, New Zealand and Canada. The classification changes proposed seem to be an unprecedented regulatory measure greater than that taken in any other country to date and [redacted] questions the rationale for this. The proposal is out of step with the approaches adopted in other markets, which have relied on essentially the same information.

Market Impact

Increasing scheduling of these products will have a major financial impact on the industry. If this proposal was to go ahead millions of dollars in sales will be lost in the first year alone. There would also be a major resource required to implement this change, with pack changes required to be implemented for many SKUs. Write off of any stock currently in the grocery supply chain and component for planned productions will also incur a significant cost.

A move to a Pharmacy Only classification will have significant availability implications for all Australians; in particular availability will be severely affected in rural areas. We also feel this is against the governments Self Care initiative and is further increasing the burden on pharmacists and the health care system.

It is anticipated that this will have a significant affect on grocery outlets currently stocking these cold & flu preparations and that pharmacy would not be able to manage the same volumes that are currently being sold. This could possibly lead to discontinuation of certain products in the Australian market. Addition of Pharmacy signal headings to pack will also affect harmonisation with New Zealand which would force separate SKUs and possible discontinuation in their market.

[redacted]

Other Comments

- The rationale behind such a drastic change to the initial proposal is not specified.
- The proposal for the 15 substances previously considered which are not mentioned in the above proposal remains ambiguous. It is unclear whether the current scheduling of the other cough and cold substances is to be retained or if previous recommendations are to come in to effect.
- It is unclear why age based scheduling (as employed for other ingredients and in other jurisdictions) cannot be employed for cough and cold preparations.
- This proposal will have a very significant impact on the products available to consumers. In effect the proposed change will remove all registered OTC cough and cold products from non-pharmacy retailers, with only complementary products being accessible through these outlets
- This matter has been already been addressed in other jurisdictions by age based scheduling. Australia is not only far behind these other markets, but is also looking at a different approach entirely.
- The TGA mention in their proposal that they 'propose to address the use of cough and cold medicines by different age groups separately through product registration and labelling processes'. If this is the case, they are able to make administrative decisions and amend the conditions of market entry to remove paediatric instructions on the label if required without necessitating any scheduling changes.

[redacted] is aware that [redacted] industry groups have made submission to the ACMS; in this regard [redacted] strongly supports the submission made by [redacted], both of which seek no change to the classifications at this time.

[redacted] is very interested in the outcome of the ACMS's June 2011 meeting and seeks to be included in any further developments.

Yours sincerely

[redacted]

[redacted]

2.1.4 Cough and cold preparations - submission 6 of 9.

[redacted]

13-May-11

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601
e-mail: SMP@health.gov.au
Facsimile: 02-6289 2500

Re: Public submission under Regulation 42ZCZK of the Therapeutic Goods Regulations 1990

Advisory Committee on Medicines Scheduling (ACMS)

2.1 Cough and Cold preparations:

Following consideration of advice from a number of expert sources including the Advisory Committee on Medicines Schedules (ACMS), the delegate refers the following revised proposal regarding cough and cold preparations to the ACMS for further advice:

Cough and cold preparations - proposal to schedule five substances used in currently unscheduled cough and cold preparations to Schedule 2. The delegate proposes that this rescheduling apply to the following substances for use in cough and cold products only where it will not result in less restrictive scheduling:

- Carbetapentane (pentoxyverine)
- Guaiphenesin (guaifenesin)
- Ipecacuanha (cephaelis acuminata and cephaelis ipecacuanha)
- Phenylephrine
- Senega

The TGA proposes to address the use of cough and cold medicines by different age groups separately through product registration and labelling processes.

Additional information for stakeholders on the TGA review of cough and cold medicines is available at Labelling and packaging of cough and cold medicines – proposed changes to requirements

[redacted]

[redacted]

[redacted] wishes to address relevant matters under section 52E of the Therapeutic Goods Act 1989 (a) risks and benefits; (b) purposes for use and extent of use; (c) toxicity; (d) labelling; (e) potential for abuse.

Risks and benefits

[redacted] in Australia which includes cough liquids containing three of those actives referred to the ACMS; Carbetapentane (pentoxyverine), Guaiphenesin (guaifenesin) and Phenylephrine which have been sold almost exclusively through the grocery channel since the early 1980's.

These products have shown as demonstrated in our previous submission to pose little to no risk as currently scheduled with a safety profile that far exceeds many other substances which currently remain unscheduled.

To be almost exclusively sold through the grocery channel since the 1980s and remain viable in a highly competitive market place it is clear that there is a benefit to provide the products to the consumer through an unscheduled setting. The products have provided convenient access to the consumer to ease the symptoms of self limiting conditions for approximately 30 years with sales of [redacted].These symptoms are easily identifiable by the average person and choice of symptomatic relief containing these actives does not require the intervention of a pharmacist.

It is [redacted]' position that the risk benefit remains unchanged for these products and does not warrant any change to the current scheduling requirements. [redacted] believes that any concerns regarding use in paediatric populations which was the original intent of the review can be adequately addressed by age related labelling rather than a reschedule to a pharmacy only setting which would be an excessive and unjustified response.

[redacted]

[redacted]

[redacted]

Purposes for use and extent of use

[redacted] affected by this review have extensive pattern of use as noted above with approximately [redacted] units sold [redacted] almost exclusively through the grocery (unscheduled) channel. This demonstrates the extensive use of the product and is an indication of the access to symptomatic relief for mild and self limiting conditions that these products and the grocery channel provide.

The products are not marketed to pediatric populations while they do have in some cases dose ranges for children under 12. [redacted] believe that the products meet a large need in the community for ease of access to effective medicines for the relief of symptoms in self limiting conditions. This need will remain unchanged due to the changing purchasing habits of the consumer and will ultimately be met by complementary medicines should the proposed scheduling change occur.

Toxicity

Below is the TGA independent review of paediatric cough and cold medicines which provides an overview of toxicity concerns:

- *Generally, these medicines are very unlikely to be harmful in label dosages, and in non-intentional overdose in the typical 1-2 year old age group, serious poisoning is rarely seen.*
- *Overseas reports of serious poisoning including deaths from cough and cold medicines are generally not reflected in current Australian experience. Documentation of such deaths is often confounded by co-existing severe illness, multiple drug administration, solid drug forms, the possibility of homicide and other factors.*

The TGA internal panel report on the safety, efficacy and use of cough and cold medicines in the treatment of children aged 2-12 years noted that:

- *Cough and cold preparations have a relatively safe history of use in children exposed to cough and cold medicines Australia with only 99 ADRs reported since 1981 for children aged 12 years or under. However, 14 serious reactions (1 probable, 10 possible, 3 unclear) occurred during this period, and so the risks of cough and cold preparations administered to children cannot be considered negligible.*

Phenylephrine, an active contained in some [redacted] products was linked to a serious Adverse Drug Reaction (ADR), however as it was a combination product, causality could not be determined. The [redacted] products contain Phenylephrine only, not in combination.

No serious ADRs were reported for guaiphenesin, pentoxyverine or senegas which are also contained in [redacted].

[redacted]

[redacted] has received no serious ADR's for any products containing the ingredients which are the subject of this review.

[redacted] products containing the actives subject to this review are all contained in child resistant packaging adding further protection from inadvertent overdose by the paediatric population.

The toxicity profile of the products does not warrant any change in scheduling and is far better than other active ingredients which are currently unscheduled.

Labelling

[redacted] believes that any concerns in use in paediatric populations should be addressed through labelling. The current proposal for review does not allow for this and greatly restricts the availability of adults to access products for symptomatic relief for mild and self limiting conditions that products in the grocery channel provide.

Potential for abuse.

[redacted] is unaware of any abuse/misuse of products containing these substances, either intentional or accidental. A scheduling change would have no impact on this potential and would only serve to reduce availability to the adult population.

Conclusion

[redacted] does not believe that the proposed recommendations for review will have any positive impact on the area of concern of the initial review which was use in pediatric populations. The proposal is not in line with original intent; it greatly exceeds any justified response and it will have little if any beneficial effect on the public.

The proposed changes do not take into account the changing purchasing patterns of the public who are increasingly relying on the grocery channel to provide symptomatic relief of self limiting conditions, if implemented it would mean that these consumers would be increasingly reliant on complementary medicines.

[redacted]

[redacted] almost exclusively provides [redacted] to consumers through the grocery channel. The brand has a history of providing high quality and efficacious medicines to the Australian public since [redacted], the proposed scheduling changes endangers the future of this brand in the Australian market place due to their excessive and unjustified nature.

[redacted] appreciates the opportunity to provide a response to the proposals and believes that the [redacted] recommendations above are in line with the National Medicines Policy on Access to Medicines and are of a balanced nature.

[redacted] are happy to provide more information should it be warranted.

Best Regards

[redacted]

[redacted]

[redacted]

[redacted]

2.1.4 Cough and cold preparations - submission 7 of 9.

13 May 2011

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Email: SMP@health.gov.au

RE: Invitation for Public Comment - Scheduling of Cough and Cold Preparations

[redacted] welcomes the opportunity to provide comment on the proposal to schedule five substances that are currently unscheduled cough and cold preparations to Schedule 2. [redacted] understands that the substances to be rescheduled include Carbetapentane (pentoxyverine), Guaiphenesin (guaifenesin), Ipecacuanha (cephaelis acuminata and cephaelis ipecacuanha), Phenylephrine and Senega.

From a customer perspective, the products to be affected by this scheduling include a number of popular cold and cough syrups that are currently available from a range of retailers including [redacted] – this includes a range of Lemsip products, Nyall, Robitussin and Vicks branded cough syrups as well as Panadol cold, flu and sinus treatments. As a result of this rescheduling, these products would no longer be available from retailers such as supermarkets – being only available to customers from pharmacists. This is despite the fact that such products have been sold in supermarkets for a number of years with, we understand, little evidence of misuse.

[redacted] provides customers with a range of cough and cold medications as part of our health and beauty [redacted]. In our experience, customers look to [redacted] when purchasing these cough and cold medications for themselves and their families for a range of reasons including the fact tha[redacted] stores are generally open longer than pharmacies and other stores (with the majority of [redacted] stores trading from early in the morning to late at night on weekdays and across the weekend). In a number of regional communities [redacted] stores are often the only store open for extended hours at night and on weekends. This convenience is particularly important when customers are suffering from, and wish to alleviate, the effects of a cold or cough (which can emerge at any time of the day across the week or weekend). It is also valuable where customers do not want to travel long distances to purchase products to alleviate these symptoms.

[redacted]

[redacted] appreciates the role that scheduling plays in helping to protect the health and safety of consumers, and would not support any measure that would result in consumers being exposed to unacceptable safety risks. [redacted] is also committed to complying with any changes to the requirements around the sale of these products. [redacted] does, however, believe that it is important for the TGA to consider as part of its analysis, the significant customer benefit that having the abovementioned cough and cold treatments available from supermarkets provides – being that customers are more able to purchase these products at a time when they need them and from an outlet that provides them with value.

[redacted] would therefore be concerned for our customers if these products were forced to be removed from sale in [redacted] (or other non-pharmacy outlets) without clear evidence that there was a material risk of potential harm from their sale. This would particularly be so if any potential risks could be adequately and effectively addressed via other means without unintended consequences for the vast majority of customers – for example, through mandating changes to on-pack labelling regarding the appropriate use of the product (including in relation to how these products should be used (if at all) by children under the age of 12).

[redacted] trust that information in this letter assists the Advisory Committee with its consideration of this proposal. Should the Committee require any further information or have any questions please do not hesitate to contact me on [redacted].

Yours Sincerely

[redacted]

2.1.4 Cough and cold preparations - submission 8 of 9.

[redacted]

13/04/2011 01:12 PM

To <smp@health.gov.au>
cc
bcc
Subject s2 proposal for cough mixtures. [SEC=No Protective Marking]

History: This message has been replied to.

DOCUMENT NOT YET CLASSIFIED

I protest strongly against the proposal to add phenylephrine,senega and other simple drugs to S2 listing. We are now completely,over the top with regulations regarding all simple medicine.I have been a pharmacist for [redacted] years and have seen what were simple.effective and inexpensive remedies now removed and replaced by literal over kill of accessibility.

These products are tried and true remedies and need to left accessible AND INEXPENSIVE for the general public who cannnot afford the increase that will occur once these products become restricted from being purchased freely. .

People do far more harm smoking,drinking alcohol and over eating than being cross examined when they wish to purchase a bottle of cough mixture or cold tablets.

These products are safe, proven , reliable and useful.Please do not walk furthur down the path over this constant over regulation.Remember the great majority of people are reliable and intelligent.You do not only have to be an academic to be intelligent. and make decisions about cold medication

[redacted]

DOCUMENT NOT YET CLASSIFIED

[redacted]

2.1.4 Cough and cold preparations - submission 9 of 9.

13 May 2011

Comments by [redacted] to the Advisory Committee for Medicines Scheduling – Meeting of 22-23 June 2011

Proposal

2.1 Cough and Cold preparations

Following consideration of advice from a number of expert sources including the Advisory Committee on Medicines Schedules (ACMS), the delegate refers the following revised proposal regarding cough and cold preparations to the ACMS for further advice:

Cough and cold preparations - proposal to schedule five substances used in currently unscheduled cough and cold preparations to Schedule 2. The delegate proposes that this rescheduling apply to the following substances for use in cough and cold products only where it will not result in less restrictive scheduling:

- Carbetapentane (pentoxyverine)
- Guaiphenesin (guaifenesin)
- Ipecacuanha (cephaelis acuminata and cephaelis ipecacuanha)
- Phenylephrine
- Senega

[redacted] position

[redacted] supports the proposal for cough and cold products to have a minimum Schedule 2 listing.

Contact person:

[redacted]

[redacted]

[redacted]

Background

A large number of cough and cold medicines are available in Australia for adults and children over two years of age. Many of these products have been available for many years for indications that were accepted with much lower levels of evidence than now required. These products have not previously been required to demonstrate their efficacy for registration on the Australian Register of Therapeutic Goods (ARTG) due to their grandfathering onto the register.

Cough and cold products are available in a variety of formulations such as dispersible sachets, tablets or capsules, oral liquids (mixtures or syrups), nasal sprays or throat lozenges. Some products are registered solely for use in adults and children over 12 years of age.

Australia has one of the most effective scheduling systems for medicines in the world, having two non-prescription schedules that either require consultation with a pharmacist (Pharmacist Only Medicine/Schedule 3) or the opportunity to consult a pharmacist (Pharmacy Medicine/Schedule 2). The majority of cough and cold medicines in Australia are either Schedule 2 or Schedule 3, although there are some which are only available only on prescription (Prescription Only Medicines/Schedule 4) and some that are exempt from scheduling and are available through the grocery sector without any opportunity for health professional intervention.

For the most part, the medicines being considered with this proposal are available in cough and cold preparations that would be classified as either Schedule 2 under the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) or would be exempt from scheduling.

Quality Use of Medicines

Quality Use of Medicines (QUM) is one of the central objectives of Australia's National Medicines Policy[1]. [redacted] believes that QUM is best supported by the supply of medicines through a pharmacy with access to specialised professional support and advice from a pharmacist. As such, we have traditionally opposed exempting medicines from scheduling because we have been concerned that the proposed arrangements may facilitate use of the medicines in a manner that does not align with QUM principles. There are no controls or quality assurance processes in place for the supply of medicines through the grocery channel and grocery customers can purchase one or one hundred packs of medicines exempt from scheduling without any question asked about the condition, the patient history or the use of the medicine.

Key Points

1. Significant safety concerns for combination cold products containing paracetamol
2. Misdiagnosis and product misuse is associated with considerable risk – important to protect the most vulnerable patient groups, particularly the young, elderly, debilitated and people whose first language is not English

3. The inclusion of warnings and directions on packs does not surmount the issues associated with poor consumer health literacy without the opportunity for counselling
4. Access through the pharmacy sector is more than adequate and provides access to health professional advice to support QUM objectives

Comments

[redacted] has considered the proposal to remove the scheduling exemption for the identified range of cough and cold medicines with particular reference to the following subsections of the *Therapeutic Goods Act 1989 – Section 52E (1)*:

(a) the risks and benefits of the use of a substance

- [redacted] is particularly concerned with combination cough and cold products that contain paracetamol and the risk of accidental paracetamol overdose that may lead to liver damage because people are unaware that they may be duplicating paracetamol doses by taking products for different indications.

  Paracetamol is one of the most frequently used drugs in Australia and is used in many forms either alone or in combination with other drugs. It is available in many non-prescription analgesic and cough and cold products, as well as in some of the stronger prescription analgesics such as Panadeine Forte® and Digesic®. Many non-prescription analgesic and cough and cold products in pack sizes of up to 24 units are exempt from scheduling and available through the grocery sector.

  Paracetamol is the most common means of drug overdose in the United Kingdom[2] and it is not unreasonable to assume that it has a similar profile in Australia. No doubt many cases of overdosage will reflect self-poisoning which is of concern considering how easy it is to access paracetamol. But for this proposal, [redacted] is particularly concerned for those people who inadvertently overdose because they take several different medicines containing paracetamol without being aware that they are doing so or the risk they face. An Irish report[3] observes that the proportion of intentional paracetamol overdoses rose from 54.4% in 1993 to 72.3% in 1999 and that for accidental paracetamol poisoning, children under the age of 5 years accounted for approximately 20% of admissions. This report identified that the incidence of paracetamol poisoning is related to its ease of access.

  The US Food and Drug Administration (FDA) has been concerned about the public health problem of liver injury related to the use of both non-prescription and prescription paracetamol (acetaminophen) products and coordinated a meeting[4] of an advisory committee in June 2009 to consider the matter. Background information for this meeting advised that nearly half of the paracetamol overdose cases in the USA are due to accidental overdose and identified the following as contributing factors:

  - consumers attempting to treat different conditions or symptoms with multiple choices among products containing paracetamol, not realising that paracetamol was an ingredient common to each

- the association between paracetamol and liver injury is not common knowledge

- extensive retail availability may contribute to the perception that the ingredient is unlikely to be harmful.

(b) the purposes for which a substance is to be used and the extent of use of a substance

- The National Medicines Policy identifies that 'to achieve optimum use of medicines, consumers and health practitioners should have timely access to accurate information and education about medicines and their use'. Many cough and cold medicines have been 'grandfathered' onto the ARTG without having provided evidence to demonstrate efficacy. Pharmacists are the most highly trained health professional group with regards to medicines, and with the appropriate support, are ideally placed to provide consumers with the most current information about cough and cold medicines and which products would best meet their needs.

- The common cold is usually caused by a viral infection and begins with rhinorrhoea and sneezing accompanied by nasal congestion. Cough and sore throat may or may not be present. Systemic signs and symptoms, such as malaise and headache, are mild or absent and fever is unusual. Symptoms last for 4 to 9 days and generally resolve spontaneously without sequelae. Cough may persist for 14 days or more.[5]

- As the common cold is a self-limiting, non-life-threatening condition, the benefits of treatment are limited to symptomatic relief. However, at-risk populations need to be identified with consideration given to:

    - situations requiring referral
    - drug-disease interactions
    - drug-drug interactions.[6]

- Particular attention should be paid to drug usage and product choice in the young, elderly and those with renal and hepatic impairment.

- There are significant risks attached with misdiagnosis or misuse of cough and cold products. While mild symptoms may be a nuisance, depending on their cause, they may be symptomatic of more serious conditions. A pharmacist has the capacity to assist people with cough and cold symptoms without complications and to refer complicated cases to the doctor for further investigation. With the availability of cough and cold products through grocery outlets, there is no professional support and advice available and there can be significant consequences from delayed referral for complicated cases.

(c) the toxicity of a substance

- Phenylephrine is an oral decongestant which has the potential to impact on the control of diabetes, heart disease, hypertension, prostatic hypertrophy, glaucoma and hyperthyroidism. It may also interact with monoamine oxidase inhibitors and other sympathomimetic drugs.[7]

- Phenylephrine is categorised as B2 regarding risk during pregnancy[8], which means that there is limited data available. It is excreted in breast milk but absorption from the gastrointestinal tract is erratic. As such, it is recommended to avoid the use of oral preparations when breast feeding.[9]

- Drug-disease precautions for expectorants such as guaiphenesin, senega and ipecacuanha include hepatic impairment, renal impairment and gastrointestinal ulceration.[10]

(d) the dosage, formulation, labelling, packaging and presentation of a substance

- We note that applications for medicines to be exempted from scheduling typically assert that the key to safe and efficacious use of medicines that are exempt from scheduling is responsible labelling that addresses the known areas of potential concern. However, health literacy is a serious issue and we are concerned that not only do people not read the labels, but when they do, they often don't understand what they are reading.

- A survey[11] conducted by the Australian Bureau of Statistics (ABS) identified 46% of Australians aged 15 to 74 years as not having sufficient literacy skills to meet the complex demands of everyday work and life, and that on the health scale, 60% attained scores below the minimum requirement to meet everyday needs.

- The ABS survey also identified that only 36% and 38% of people whose language was not english attained scores at or above the level that demonstrated sufficient prose and document literacy respectively to meet everyday needs.

- As such, [redacted] has concerns that any medicine available through the grocery sector has increased risks of being inadvertently misused by people who do not understand the directions or the precautions. There would be a risk of administration to children or the elderly, or use for extended periods without consulting a health professional.

(e) the potential for abuse of a substance

- [redacted] believes there is more a risk of inappropriate use than abuse associated with unrestricted access to the cough and cold medicines under consideration.

(f) other matters in public health interest

- One of the most common arguments for proposing medicines to be exempt from scheduling is that availability through the grocery channel provides greater after-hours access. With the wide distribution of pharmacies and the ever

increasing number that operate 7 days a week with extended trading hours, this argument now lacks base. In fact, in country areas, pharmacists provide after-hours patient access for urgent cases and in some jurisdictions, regulations for store trading hours mean that after-hours pharmacy access is as good as or better than that through the grocery sector.

As an example, a recent analysis of access in metropolitan areas showed:

- In Western Australia, pharmacy has no restricted trading hours as it is a 'specialty retail store'. There is a majority of pharmacies operating 7 days a week and 2 pharmacies open for 24 hours a day. In contrast, supermarkets have restricted trading hours and can open until 9pm Monday to Friday, until 6pm on Saturday, and cannot trade on Sunday.

- In Brisbane, there are no pharmacies or supermarkets that open for 24 hours a day. There are 3 pharmacies that open until 11pm and the majority operate 7 days a week. There are restrictions on trading hours for supermarkets which can open on weekdays until 9pm and till 6pm on weekends.

- In Adelaide, there are no 24 hour pharmacies, however there are 2 pharmacies that open to midnight each day. Because of trade restrictions in South Australia, supermarkets can only open until 9pm on weekdays, and till 5pm on weekends. They also cannot open on public holidays.

- In Melbourne, there are 2 pharmacies that are open for 24 hours a day and the majority operate 7 days a week. By comparison, there is only 4 Coles and no Woolworths supermarkets that are open for 24 hours a day.

- Having people with cold symptoms present to pharmacy in order to obtain cold and flu medicines also facilitates the opportunity to check on a person's immunisation status for influenza and pertussis. This can be useful when targeting at-risk population groups, particularly when attempting to address outbreaks as with the recent pertussis outbreak in many Australian jurisdictions.

- Exempting medicines from scheduling for access through the grocery sector does not meet QUM principles if there is no quality assurance processes to restrict the number of packs that can be purchased at a single time or to manage consumers who may be using the medicines inappropriately or who have a condition requiring medical intervention. With access through the grocery sector, multiple packs can be bought in a single transaction without question.

  Within the pharmacy sector, pharmacy assistants are trained to ask clinically relevant questions and facilitate consultation with a pharmacist if appropriate. They are also trained to note 'red flags' for referral to the pharmacist, such as requests for multiple packs or repeat purchases, pregnancy, breast-feeding or people taking other medicines or presenting with other symptoms such as fever or asthma.

  Pharmacists are also experienced in triaging people with cold and flu symptoms with referral to the doctor when warranted.

- Pharmacists are able to advise consumers on effective and cost-effective therapies for the symptomatic relief of colds and flu.

Conclusion

[redacted] believes the recent review of cough and cold medicines has provided an opportunity to re-consider the availability of these products in line with QUM principles. [redacted] supports the proposal for a minimum Schedule 2 listing for cough and cold products.

Reference Sources:

[1] http://www.health.gov.au/internet/main/publishing.nsf/Content/National+Medicines+Policy-1
[2] Emergency medicine Journal 2008;25:140-143; Survey of cases of paracetamol overdoses in the UK referred to NPIS consultants
[3] Paracetamol availability and overdose in Ireland; Department of Public Health, Eastern Regional Health Authority
[4] June 29-30, 2009: Joint meeting of the Drug Safety and Risk management Advisory Committee with the Anesthetic and Life Support Drugs Advisory Committee and the Nonprescription Drugs Advisory Committee; www.fda.gov
[5] http://www.nps.org.au/__data/assets/pdf_file/0018/17082/pharmacyletterno5.pdf
[6] Ibid NPS
[7] Ibid NPS
[8] www.tga.org.au
[9] Drugs and Breastfeeding, Pharmacy Department, Royal Women's Hospital, Melbourne
[10] Op cit NPS
[11] ABS 4228.0 – Adult Literacy and life Skills Survey, Summary Results, Australia, 2006 (Reissue); www.abs.org.au

[redacted] [redacted]

2.2.1 Rabeprazole - submission 1 of 2.

13 May 2011

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Email: SMP@health.gov.au

Invitation for public comment – ACMS meeting 22 June 2011

2.5 Rabeprazole – Proposal to create a new entry for rabeprazole 10 mg or less in Appendix H

[redacted] appreciates the opportunity to provide comment in relation to this issue. We wish to address relevant matters under section 52E of the Therapeutic Goods Act 1989 as these apply to the substance mentioned above: (a) risks and benefits; (b) substance purpose; (c) toxicity; (e) potential for abuse.

The current Schedule 3 entry for Rabeprazole is as follows:

> *"RABEPRAZOLE in oral preparations containing 10 mg or less of rabeprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 14 days' supply."*

The question for the ACMS is whether the availability of such a product ought to be brought to the attention of consumers through advertising directed to them.

For the reasons outlined below, [redacted] contends that consumers ought to be made aware of such products and supports the inclusion of Rabeprazole in Appendix H.

NCCTG Guidelines on Schedule 3 Advertising

The NCCTG has published guidelines describing the process for determining whether a substance in Schedule 3 may be advertised[1].

It is [redacted] position that these guidelines have been met in relation to Rabeprazole and offers the following comments in relation to each of the guidelines:

Potential public benefit
[redacted] contends that advertising will prompt consumers to seek advice from a pharmacist and that such advice may result in more effective treatment or earlier identification of consumers who require medical intervention.

[1] http://www.tga.gov.au/ndpsc/ndpsc3a.htm

[redacted]

Additionally, [redacted] suggests that inclusion in Appendix H will provide a public benefit through potential reduction in unnecessary visits to GPs. Any such reduction would be strengthening the role of Schedule 3 medicines in removing the need for a prescription in order to access them. Where a consumer becomes aware of Rabeprazole through advertising and obtains the product after a consultation with the pharmacist, then he or she will be in a similar position as if they were provided with a prescription from their GP. However, they will have obtained the product (and the advice) without occupying the GP's time. This reduction in the burden on GP's will be of public benefit.

As Rabeprazole is in Schedule 3, the pharmacist will continue to act as a final safeguard between the consumer and the product. No matter what the effect of advertising, the consumer cannot purchase the product except with the intervention of the pharmacist. This ought to be kept in mind when weighing the benefits of inclusion in Appendix H against any potential risk that advertising may inappropriately influence demand.

Availability of Rabeprazole in Schedule 3 does not necessarily translate to consumer awareness of its availability from pharmacists without a prescription. The ability to advertise will highlight this availability, while at the same time directing consumers to talk to a health professional about effective treatments for gastro-oesophageal reflux disease.

Likelihood of advertising leading to inappropriate patterns of use

[redacted] has seen no evidence and can envisage no arguments to suggest that the advertising of Schedule 3 Rabeprazole products will result in inappropriate use.

The wider regulatory system

All advertising to consumers must comply with the *Therapeutic Goods Act*, the *Therapeutic Goods Regulations* and the Therapeutic Goods Advertising Code. Inclusion of Rabeprazole in Appendix H will not affect the various requirements imposed by these instruments.

Among other things, any Rabeprazole advertising to consumers must be consistent with the registered indications, must comply with a range of general principles, must comply with the requirements for prohibited and restricted representations and must contain certain information (including the statement "Your Pharmacist's Advice Is Required").

The responsibility of Pharmacists to be involved

Educational tools and treatment protocols for Proton Pump Inhibitors (PPIs) have been prepared in order to ensure that pharmacists are able to provide appropriate professional advice.

Availability of Consumer Medicine Information (CMI)

A CMI for Rabeprazole is available to assist pharmacists when counselling consumers.

Desire for consumers to manage their own medication

In general, there is no doubting the interest that consumers have in accessing medical and pharmaceutical information and in taking control of their medication and treatment.

In particular, the growth of the gastrointestinal category in supermarket products shows the willingness of consumers in this category to manage their own medication.

52E(1)(a) Risks and benefits

Rabeprazole was switched to Schedule 3, effective 1 January 2010. It has a favourable safety profile.

The risks of misuse of rabeprazole are low and the safety of PPIs as a group is equivalent to that of H2 receptor antagonists, which are unscheduled and therefore able to be advertised directly to consumers.

[redacted] contends that advertising will prompt consumers to seek advice from a pharmacist and such advice may result in more effective treatment or earlier identification of consumers who require medical intervention.

It should be noted that medicine advertisements directed to consumers must comply with a range of regulatory requirements and be formally approved if they are to be shown in "specified media". This includes TV, radio, mainstream newspapers and magazines, cinema and public display e.g. billboards, posters, public transport.

52E(1)(b) Purpose

The purpose of the product is for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease. This purpose is capable of being communicated to consumers via advertising.

52E(1)(c) Toxicity

Rabeprazole has a well documented safety profile.

52E(1)(e) Potential for abuse

[redacted] is unaware of any evidence that Rabeprazole is associated with dependence, abuse or illicit use.

Summary

Rabeprazole ought to be included in Appendix H, for the various reasons outlined above.

We believe that the safety profile; history of safe use; indication for short-term use; the ability of pharmacists to provide professional advice to ensure the quality use of medicines; the preparation of pharmacy through education and information provision; and, the potential public health benefit resulting from increased awareness of all available treatments all combine to provide a sound justification for products containing this substance (as Schedule 3) to be advertised.

We trust that the Committee will consider the merit of this submission for the inclusion of Rabeprazole in Appendix H in terms of the efficacy and safety of this substance compared to others that are currently available and able to be advertised. We believe that consumers stand to benefit immensely through awareness of the options available to them, supported through mandatory intervention by pharmacists.

We look forward to hearing the outcomes of the Committee's deliberations on this issue.

Yours faithfully,

[redacted] **pre-mtg comment**

[redacted]

2.2.1 Rabeprazole - submission 2 of 2.

13 May 2011

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Dear Secretary

RE: **Public Comment on the Agenda for ACMS Meeting June 2011 Agenda item: 2.5 Rabeprazole – proposal to create a new entry for rabeprazole 10mg or less in Appendix H**

[redacted] welcomes the opportunity to comment on the above agenda item relating to the amendment of the appendices to enable rabeprazole 10 mg to be listed in Appendix H.

Pursuant to the February 2011 meeting of the ACMS, the Delegate's interim decision was to retain the current scheduling for pantoprazole 20mg, Schedule 3 with no appendix H listing. At the time of writing [redacted] awaits the outcome of the Delegate's final determination on that issue.

Presently, pantoprazole 20mg is the only Schedule 3 listed PPI in Australia with significant in-market experience (which is now in excess of 2.5 years). Moreover, SOMAC® Heartburn Relief is the only PPI listed in Schedule 3 that has published data directly demonstrating appropriate supply in the Australian setting.[1]

[redacted] does not oppose the application for Appendix H listing of rabeprazole in principle, provided that a consistent approach is taken with respect to requirements for demonstration of adequate Australian OTC data with individual PPIs before Appendix H listing is granted. Precedent has already been set in this respect, with the prior rejection of the Appendix H listing for pantoprazole 20 mg in February 2010, despite having 16 months in-market use at that time.

Rabeprazole 10mg was launched as a Schedule 3 product, under the brand name **Pariet 10,** in January of this year. As such there are very limited relevant in-use data with which

[redacted]

[redacted]

to inform the Committee with regard to risks and benefits, potential hazards, extent and pattern of use and other relevant matters in the context of advertising and public health benefit.

[redacted] therefore proposes that the Appendix H listing of rabeprazole 10 mg should only be granted at a time in the future when sufficient in-market use and Pharmacist experience with this particular medicine has been obtained.

In the event that the Delegate determines that rabeprazole 10mg is suitable for inclusion in Appendix H, [redacted] requests that this decision also be conferred to pantoprazole 20mg. The rationale being that pantoprazole 20mg has significantly greater in-market use and has already demonstrated the potential for public benefit that would result from direct to consumer advertising of this medicine in the community.

I trust that the above is of value. Should you require any further information, please do not hesitate to contact me on telephone [redacted] or via email [redacted]

Yours faithfully,

[redacted]

Reference s

(1) Bell J, Katelaris P, Krassas G. An Australian pharmacy audit of the management of heartburn and the role of over-the-counter proton pump inhibitors. *Aust Pharmacist* 2010;29(6):526-528.

Bell 2010

An Australian pharmacy audit of the management of heartburn and the role of over-the-counter proton pump inhibitors

By John Bell, Associate Professor Peter H Katelaris, George Krassas

Introduction

Heartburn affects one in five adults regularly[1] and is predominantly self-managed.[2] It is typically described as a feeling of discomfort, burning or pain rising upward from the epigastrium or lower chest,[3] and varies in intensity from occasional mild symptoms to frequent heartburn that adversely impacts the sufferer's quality of life.[4] Proton pump inhibitors (PPIs) are the most effective therapy for the relief of heartburn irrespective of severity[5] and are the most effective treatment for patients with frequent heartburn.[6]

The first over-the-counter (OTC) PPI, *Somac Heartburn Relief* (pantoprazole 20 mg), was introduced in Australia as a *Pharmacist Only Medicine* in 2008. After taking this formulation, 20% of patients are free of heartburn symptoms on day 1; this increases to 74% on day 7 and 84% on day 14.[7] Twelve months after its introduction we conducted a pharmacy audit to assess pharmacy management of this new category of heartburn therapy, to better understand the needs of heartburn patients presenting to pharmacy and to assess the role of OTC PPI treatment.

Method

A prospective, fixed-time audit was conducted to evaluate the OTC management of heartburn within Australian community pharmacy. A wide geographic spread of pharmacies was recruited into the audit. Participating pharmacists were given brief instructions relating to the audit process and were asked to audit up to 10 adult people who entered the pharmacy seeking relief of their heartburn or acid-related symptoms. Recruitment of people into the audit was to be capped at 150 respondents.

All people aged 18 years or older presenting to the pharmacist seeking to treat heartburn with an OTC heartburn therapy were eligible for inclusion in the audit. People who were currently using or had previously used prescription therapies for their heartburn or reflux were not automatically excluded from the audit. However, they were only eligible to participate if they were currently seeking advice about the OTC management of their condition.

Consenting people completed a questionnaire about their heartburn. They were then asked to review the information on the back of the *Somac Heartburn Relief* pack to self-assess whether *Somac Heartburn Relief* was suitable for them. In addition, label comprehension as to the correct use of the product was assessed. The pharmacist then conducted their normal consultation and discussed suitable treatment options with the customer. After completing the normal consultation, the pharmacist completed the pharmacist questionnaire before the consumer left the pharmacy. Pharmacists were instructed to fulfill their normal duty of care and that participation in the audit was not to influence therapy recommendation or sale. Participating pharmacies were reimbursed for their time in conducting this audit.

Results

The audit involved 20 pharmacies located throughout Sydney NSW. They contributed 153 completed surveys. The mean number of surveys completed per pharmacy was 7.65. The demographics of the audited respondents are summarised in Table 1.

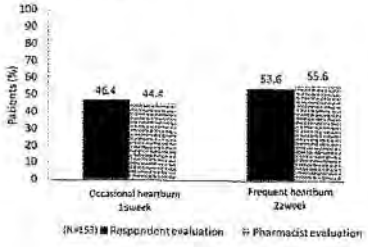
More than half of the respondents presented with frequent heartburn symptoms, occurring two or more times per week (Figure 1).

Half of the respondents rated their heartburn symptoms as moderate or severe (43.8% and 10.5%, respectively) (Figure 2). Despite this profile, the most frequently used previous therapy was antacids

Table 1. Demographic profile of respondents

	N	%
Gender		
Male	66	43.1%
Female	87	56.9%
Age		
<18 years	0	0.0%
18–30 years	48	31.4%
31–54 years	63	41.2%
55 years or older	42	27.4%
Previously seen a doctor for their heartburn		
Yes	83	54.2%
No	70	45.8%

Figure 1. Respondent and pharmacist-assessed frequency of heartburn symptoms

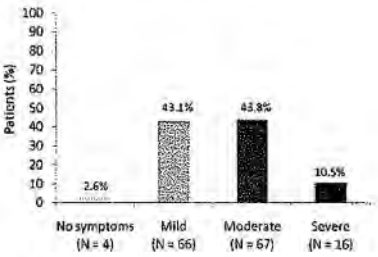


John Bell, *Principal Adviser, Pharmacy Self Care, Pharmaceutical Society of Australia.*
Associate Professor Peter H Katelaris, *Gastroenterology Department, Concord Hospital, University of Sydney, NSW.*
George Krassas, *Scius Solutions Pty Ltd, Mosman, Sydney NSW.*

Table 2. Previously used heartburn treatments

	N	%
Antacid	81	52.9%
OTC ranitidine	66	43.1%
Somac Heartburn Relief	23	15.0%
Prescription product	41	26.8%
Other	0	0.0%
No product	12	7.8%

Figure 2. Severity of heartburn symptoms



(52.9%), followed by ranitidine (43.1%), with only 15% having previously used *Somac Heartburn Relief* (Table 2).

Pharmacist evaluation

Results from the pharmacist evaluations indicated that almost all (91.5%; 140/153) respondents seeking OTC heartburn treatment experienced typical heartburn symptoms. Upon completing their assessment, pharmacists determined that *Somac Heartburn Relief* would be suitable therapy for 76.5% (117/153) of the respondents. This was marginally lower than the respondent's self assessment (79.7%; 122/153). Mild symptoms or occasional heartburn were the two most common reasons for the product being considered unsuitable for a particular respondent.

From a safety perspective, pharmacists identified the presence of suspected red flag symptoms in 12.8% (18/153) of respondents. Seven of these were referred to their doctor for further medical assessment. Red flags were specified in eight cases, with the presence of atypical symptoms, the need for continuous therapy for more than four weeks, chest pain, sharp pains, nausea, fatigue, vomiting and symptoms worsening despite treatment being correctly reported as red flag symptoms. Additional analysis of pharmacist action in these cases saw five of these people being referred to a doctor for further investigation. Of the remaining three cases, one received no product and two were sold ranitidine (one case of worsening symptoms and one case of chest pain). Of the 10 unspecified red flags, only one case of doctor referral was noted. Five respondents were pregnant and none of these was offered *Somac Heartburn Relief* which is consistent with the product information.

Pharmacists identified that concomitant medications may have been contributing to the reflux symptoms in 15.0% (23/153) of respondents. Non-steroidal ant-inflammatory drugs (NSAIDs) were the most common agents (N = 16), of which 57% (9/16) were OTC NSAIDs (ibuprofen or diclofenac). In addition, on three occasions where red flags were identified, NSAIDs were also considered to be contributing to the respondent's reflux symptoms.

Of the 117 (77%) subjects that pharmacists determined were suitable for Somac Heartburn Relief, they recommended the product to 105 (69%) and 88 (58%) purchased the product (Figure 3).

Label comprehension

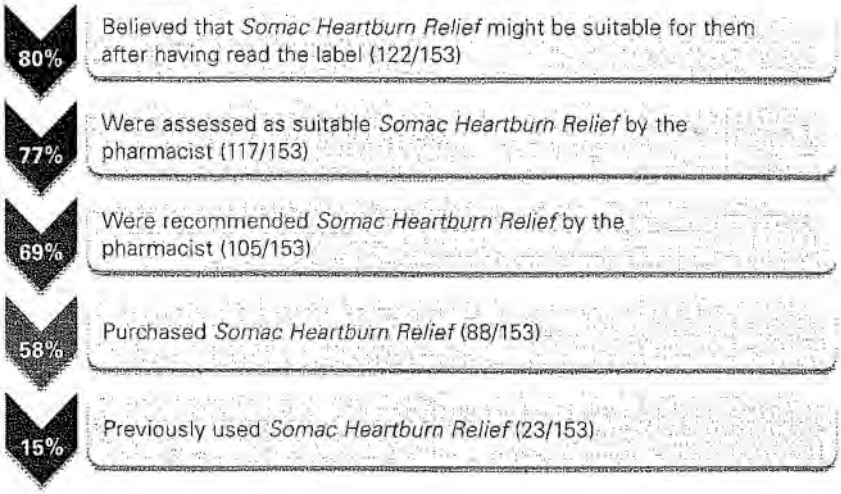
After reading the information on the back of the *Somac Heartburn Relief* packaging, the vast majority of respondents (92.2%, 141/153) were able to correctly identify that the dosing regimen was one tablet per day.

When asked about duration of *Somac Heartburn Relief* therapy before seeking medical advice, 86.3% (132/153) of respondents were able to provide the correct answer. Nine respondents indicated that duration of therapy was one month and 12 answered indefinitely.

Discussion

In this audit, over half (55.6%, 85/153) of the people coming into the pharmacy seeking treatment for heartburn experienced frequent heartburn (occurring on two or more days per week). The prevalence of frequent heartburn is likely to be an underestimate as 11% (17/153) of subjects reporting only occasional heartburn were either taking or had taken prescription PPIs for their condition. To our knowledge this is the first research to determine the profile of people with heartburn seeking treatment within pharmacy in Australia. As PPIs are recognised as the most effective therapy for frequent heartburn,[1,4–6] there is potential to improve the management of heartburn by pharmacist intervention and recommendation of non-prescription PPIs. The prior use of OTC PPIs in our audit was modest, at only 15% (23/153). This result is not entirely unexpected given that at the time of the audit only one PPI was available OTC and its scheduling had not permitted direct-to-consumer advertising. However, the identified disparity between the number of consumers with frequent heartburn and the number being treated with an OTC PPI indicates that there is a significant opportunity to improve the

Figure 3. The relationship between product suitability and purchasing



pharmacy management of heartburn. This observation is further supported by the fact that when the respondents in our audit discussed their heartburn with the pharmacist, the purchase of *Somac Heartburn Relief* increased to 58% (88/153).

The audit results have demonstrated that pharmacists can appropriately assess and manage people presenting with frequent heartburn. Pharmacists' recommendations were consistent with the product information and a treatment algorithm specifically developed to facilitate the appropriate supply of *Somac Heartburn Relief* (Figure 4). The majority (91.5%, 140/153) of people presented with typical heartburn symptoms and were free of signs or symptoms (red flags) that would necessitate further medical review before commencing short-term symptomatic treatment. When red flags were identified and specified, most people were referred to their doctor for further investigation. A limitation of this audit was that when red flags were identified, information on pharmacist referral to a doctor was collected via voluntary comment rather than in direct response to a specific question. This was done to avoid biasing the findings of the audit, however it may have resulted in the under-reporting of doctor referral rates, especially amongst those cases where the nature of the red flag was not specified. In all cases where red flags are suspected it is essential that the pharmacist refers the person on for medical review.[8] Pregnant women were managed appropriately and none was offered PPI therapy.

Although this audit did not assess the use of *Somac Heartburn Relief* by customers who purchased the product, we investigated label comprehension as a surrogate marker as to whether usage would be as instructed. Comprehension of the label was excellent, with 92% (141/153) of respondents correctly determining the daily dosage and 86% (132/153) correctly determining that the maximum duration of use was 14 days. For those consumers who deviated from the labelled instructions, the majority had previously used prescription PPIs and hence their previous experience (which allows longer duration of therapy and at higher doses) may have influenced their responses. Even though *Somac Heartburn Relief* is a *Pharmacist Only* medicine and consumers cannot self select the product, it was reassuring that the customer's assessment of product suitability was in agreement with the pharmacist's assessment in 86% (132/153) of cases.

Figure 4. *Somac Heartburn Relief* treatment algorithm

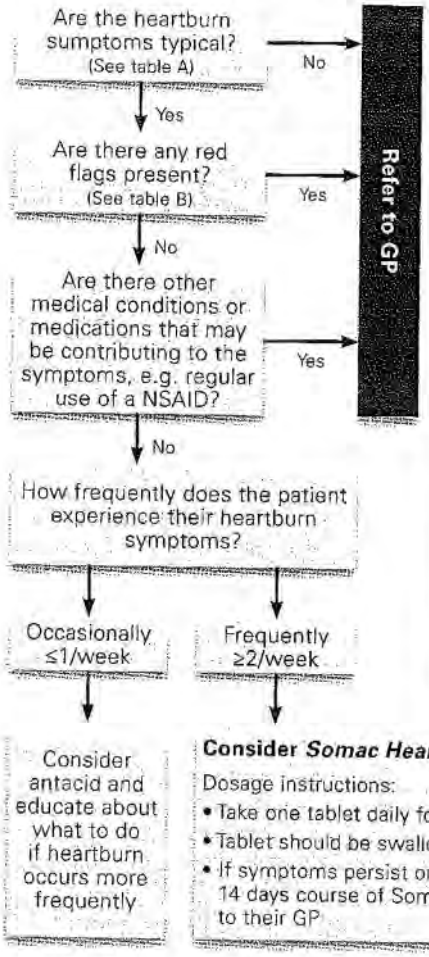


Table A. Typical symptoms

- **Heartburn** (a burning feeling rising from the stomach and lower chest up towards the neck)
- **Acid regurgitation**

Table B. Red flags – refer to GP if present

- Unintentional weight loss
- Anaemia
- Gastrointestinal bleeding (haematemesis/ malaena)
- Difficult/painful swallowing
- Vomiting
- Choking attacks, especially at night
- Age ≥55 years with either
  - first-time reflux symptoms **or**
  - longstanding, frequent and troublesome reflux symptoms
- Previously taken heartburn medication continuously for 4 or more weeks
- Jaundice or severe hepatic impairment
- Gastric ulcer or previous gastrointestinal surgery
- Suspected agina or heart attack
- Patient appears very unwell

Conclusion

Heartburn is a common, predominantly self-managed, condition with many consumers self-selecting products that are available outside the pharmacy. In our audit more than half of the subjects suffered frequent heartburn, for which PPIs are an effective first-line therapy, but only 15% had previously used Somac Heartburn Relief. In addition, approximately one in 20 consultations with the pharmacist resulted in a doctor referral. This opportunity for medical intervention is missed amongst those consumers who currently do not seek pharmacist advice for their heartburn. The results of this audit demonstrate that pharmacists seem able to manage the use of *Somac Heartburn Relief* appropriately, in a manner consistent with the product labelling. From a wider public health perspective, the results also suggest that benefit may be gained from increased consumer awareness of the availability of OTC PPIs and of the pharmacist as a source of advice.

References

1. Shenfield G, et al. Therapeutic Guidelines Gastrointestinal (4th ed). Therapeutic Guidelines, 2006.
2. Sayer GP, Britt H, Horn F, et al. Measures of health and healthcare delivery in general practice in Australia SAND supplementary analysis of nominated data 1998–99. Australian Institute of Health and Welfare, 2000. Report No.: General Practice Series 3.
3. Digestive Health Foundation. Facts about ... Heartburn oesophageal reflux (3rd ed). 2007.
4. Gastroenterological Society of Australia. Gastro-oesophageal reflux disease in adults Guidelines for clinicians (3rd ed). 2001. At: www.gesa.org.au/pdf/RefluxDisease1Ed07.pdf [accessed Mar 5, 2008].
5. Australian Medicines Handbook. Adelaide: AMH, 2008.
6. Inadomi JM, Fendrick AM. PPI use in the OTC era: who to treat, with what, and for how long? Clin Gastroenterol Hepatol 2005 Mar;3(3):208–15.
7. Gatz G. Comparison of the efficacy and tolerability of pantoprazole (20mg/day) and lansoprazole (15mg/day) in patients with mild gastroesophageal reflux disease (stages 0 and 1 according to Savary/Miller). Research Report 301/98. 1999.
8. Haag S, Andrews JM, Katelaris PH, et al. Management of reflux symptoms with over-the-counter proton pump inhibitors: issues and proposed guidelines. Digestion 2009;80(4):226–34.

[redacted]

SUBMISSION TO THE JUNE 2011 MEETING OF THE ADVISORY COMMITTEE ON MEDICINES SCHEDULING

PURPOSE

1. [redacted] makes this submission in relation to items referred by the Delegate to the June 2011 meeting of the Advisory Committee on Medicines Scheduling (ACMS) for scheduling advice.

RECOMMENDATIONS

2. [redacted] provides the following recommendations to the ACMS:

a. **Cough and cold preparations.** [redacted] supports the proposal to schedule the five substances listed in the public notice currently used in unscheduled cough and cold preparations to Schedule 2 provided this does not result in less restrictive scheduling.

b. **Loperamide.** [redacted] does not support the proposal to reschedule packs of eight dosage units currently in Schedule 2 to unscheduled. Further details are outlined below in this submission.

c. **Nicotine.** [redacted] does not object to the proposal to amend the Schedule 4 entry to exempt from scheduling, when used as an aid in withdrawal from tobacco smoking, nicotine oromucosal film and nicotine inhalation cartridges for oromucosal use.

d. **Orphenadrine.** In the event that orphenadrine is rescheduled from Schedule 4 to Schedule 3 when combined with paracetamol with the conditions listed in the public notice, the applicant must work with [redacted] to develop best practice resources to support the implementation of a revised schedule. Further details are outlined below in this submission.

e. **Rabeprazole.** [redacted] supports the proposal to create a new entry for rabeprazole 10 mg or less in Appendix H.

LOPERAMIDE

3. [redacted] notes that in June 2010, an applicant's request to exempt loperamide from scheduling when in a maximum pack size of eight dosage units was considered by the National Drugs and Poisons Schedule Committee. The Record of Reasons shows that while acknowledging that "consumers experience a degree of urgency when seeking access to loperamide", a committee member asserted "it was important for consumers to be able to obtain advice and information for loperamide and that scheduling would ensure that this was available". The Record also summarises that committee members generally agreed that "on balance, it was not appropriate for loperamide to be available as unscheduled".

4. [redacted] submission in June 2010 opposed any proposal to exempt loperamide from scheduling. Diarrhoea can be life-threatening if not managed appropriately or if supportive treatment is not instituted. Timely access to loperamide must occur from an environment where pharmacist intervention is available so that precautions are exercised, medication use and patient health outcomes can be monitored or taken into consideration, and referral to a medical practitioner occurs if the consumer's condition has not improved or resolved as expected.

5. [redacted] current position on the scheduling of loperamide remains unchanged and therefore, we do not support the proposal listed in the public notice even with the inclusion of the words “up to a maximum of one days’ supply”.

ORPHENADRINE

6. The item in the public notice on orphenadrine lists a number of conditions that would be attached to its rescheduling to Schedule 3 (S3). Based on a product containing orphenadrine citrate 35 mg and paracetamol 450 mg per dosage unit with a dosage regimen of two tablets three times a day, the maximum pack proposed would contain four days’ supply under S3. A current entry in the Australian Register of Therapeutic Goods matching this description (156623) lists the approved indications as “tension headache, occipital headaches associated with spasm of skeletal muscles in the region of the head and neck” and “acute and traumatic conditions of the limbs and trunk: sprains, strains, whiplash injuries, acute torticollis, prolapsed intervertebral disc”.

7. [redacted] notes that should this rescheduling application be approved, the product would represent a new type of non-prescription combination analgesic available through community pharmacy. This option may be beneficial for consumers who do not respond to codeine-based products or those who cannot take non-steroidal anti-inflammatory drugs due to possible interactions or side effects.

8. [redacted] notes, however, that orphenadrine is toxic in overdose primarily due to its anticholinergic effects. Further, the United States National Library of Medicine (and other sources) reports that “orphenadrine has been chronically abused for its euphoric effects” and that “the mood elevating effects may occur at therapeutic doses”.

9. The orphenadrine and paracetamol combination product is currently available as a Prescription Only Medicine and as such, pharmacists are familiar with clinical and therapeutic information, including expected benefits and potential risks associated with the medicine. However, in order to appropriately support pharmacists in the provision of this medicine as a Pharmacist Only Medicine (S3), [redacted] would need to implement resources such as a pharmacist protocol (which has been produced for other substances when rescheduled from S4 to S3) and associated education/training.

10. In relation to rescheduling applications, [redacted] has previously stated its view that it should be mandatory for applicants to:

a. include information in their application about the likely impact the new schedule will have on health professionals and consumers;

b. propose an education program for health professionals and consumers to facilitate appropriate use, quality use and minimise any possible misuse of the product; and

c. demonstrate an ongoing commitment to work with relevant stakeholders.

11. [redacted]

12. In summary, if the committee approves the proposal to reschedule orphenadrine from S4 to S3 when combined with paracetamol with the conditions listed in the public notice, [redacted] believes the applicant must work in partnership with [redacted] to develop resources to support best practice in the implementation of the outcome.

Submitted by:

[redacted]

13 May 2011