Dear Committee Members,

The proposed classification of isopropyl nitrite as prescription only and amyl nitrite ("poppers") as restricted has consequences for gay and bisexual men in New Zealand.

- Some men rely on poppers as a sex aid and are unable to have anal intercourse without its analgesic and muscle-relaxing effects.
- Requiring a prescription will require some men to effectively 'out themselves' to their doctor/pharmacist. This may lead to prejudice, in particular in small communities, that may result in danger to gay/bisexual men.
- Restricted control of supply is open to 'gatekeeping'. Some doctors/pharmacists may restrict supply to some men because of misunderstanding/prejudice (similar to cases of women being denied emergency contraception) and/or only stocking some brands.
- Ease of supply during periods of high-volume (e.g. Pride) may prevent some men from having their preferred type of gay sex. This could also cause congestion for other pharmacy users in terms of the pharmacist's time.
- Physical and online adult shops are open much longer hours than pharmacies and demand for poppers is often outside business hours.

Although potentially hazardous when taken incorrectly or in excess, the potential negative effects of poppers can be mitigated through warning labels, safety-cap requirements and education.

There are risks with the consumption of poppers, about which the LGBTQI+ community is aware. There are also significant benefits; such as being able to enjoy anal sex when you choose. Members of this community should not be required to talk to someone about an aspect of their sex life when a straight person is not required to do so. The proposed legislation is in effect regulating sex for many of NZ's gay and bisexual men.

Amyl Nitrate Poppers generally have a low-level risk from harm or long term use (especially when compared with Isopropyl Nitrite) and should be freely available to buy in physical and online sex shops. Warnings and education on use should be enhanced instead of restrictions imposed.

The social context of the proposed changes is poorly understood and the current proposal is unreasonable and disproportionate. Harmonisation of rules with Australia is not a good enough reason to restrict, expose, and regulate the sex lives of an already historically persecuted group of New Zealanders.

Regards,

March 16, 2020.

Submission - Agenda Item 5.3 Alkyl Nitrites, 64th Meeting of Medicines Classification Committee

Introduction

[Biographical details redacted].

Comments

There are two points I wish to make.

1. The Committee is considering steps that would amount to an intervention in a well-established sexual culture. The culture is important to the lives of its participants. The use of poppers within that culture is widespread, long-standing, and valued.

Moreover, that use of poppers has been de facto permitted by the state for several decades. The steps the Committee is considering do not appear motivated by any fresh official desire in New Zealand to end poppers use for its own sake.

Given that backdrop many gay and bisexual men would not regard as having been justified or necessarily respect, any decision which prevented the use of poppers either by formal prohibition or via a regulatory regime tantamount to prohibiting them. Such a decision would risk creating a black market in a product for which there is still demand.

2. I urge the Committee to adopt the recommendations made by the New Zealand Drugs Foundation and the New Zealand Aids Foundation in their joint submission to the Committee's 63rd meeting. As I follow them, they would:

allow the least harmful amyl nitrite to become the reigning poppers chemical and be sold through the current channels rather than through the likely near-prohibitive routes of prescription and pharmacy-only access, and

tighten the regulation of the most harmful alkyl nitrites.

I hope the Committee finds that such an outcome would satisfy its purposes as well as be legitimate in the eyes of an affected group and prevent the harms of illegal sale.

Thank you for your consideration.

19 March 2020

My submission with respect to Agenda Item 5.3 alkyl nitrates.

I am a gay man who has been using this product since 1980; I am now 62. I am in good health and have suffered none of the ailments that feature prominently in the apparent safety issues raised in Medsafe's arguments. I find myself questioning the value of this submission and the authenticity of the process. Medsafe have undermined this meeting by adding alkyl nitrates, a substance with no therapeutic or medicinal use, to the Medicines List prior to submissions being made or consideration by the Committee. I have felt intimidated and deterred from making this submission by Medsafe's aggressive strategy.

One of the arguments I have heard put forward has been for NZ to move in line with Australia. I find this assertion dubious. Until the Australian changes, Medsafe always deferred to the UK (and selectively still does) for decisions and guidance. The UK's stance is curiously absent here simply because alkyl nitrates are not considered a medicine in the UK for good reason – it is not a medicine, it has no therapeutic use.

The proposal to make the product a pharmacy only medication is tantamount to a ban. No reputable doctor or pharmacy would prescribe or dispense the product. This, I know, will very quickly lead to 'backyard production' as it has before. The original product called poppers was amyl nitrate, a product that does have medicinal use. When amyl nitrate was effectively banned in the early 1980's and prior to the industry manufacturers adapting to a non-medicinal product, there was a period where a range of backyard products using 'Kiwi resourcefulness and ingenuity' became widely available. The quality and constitution of these products was unknown, packaging invariably problematic with leakage commonplace. Once the industry adapted to new regulation, with a significantly diluted and weakened product, these issues were resolved and marketing through saunas and adult shops became successfully self regulated, as it has remained until today.

I do wonder why Medsafe are so determined to consign this product to the annals of history. To the best of my knowledge, this product is only a problem to Medsafe. I have heard of no issues raised by the Police, no issues raised by Emergency Departments, no issues raised by the Ministry of Education, in fact any branch of Government at all. Safety concerns have been leveled at this product in particular only because it is the predominant product in the market. The issues raised can only factor after sustained and excessive use which is highly unlikely, unrealistic and not in line with the short term, brief manner the product is anecdotally used as well as in my personal experience.

The effective removal of this product from the market would have a significant impact on my personal life. It is one of the few pleasures I have left sexually. For me to ask a doctor for a

prescription and to collect from a pharmacy would be not only highly unlikely but would be an undignified and embarrassing process to undertake.

The current situation works for everyone other than Medsafe. It works for those who chose to use the product, it works for those who sell it and their employee's, it works for the United Kingdom and many other countries. The status quo is working and has done for over 40 years since it first became available in the late 1970's.

I respectfully request the Committee to maintain the status quo.

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Harmonisation of the New Zealand and Australian schedules for alkyl nitrites

Thank you for the opportunity to submit feedback to the 64th meeting of Medicines Classification Committee in May 2020 agenda item around the classification of alkyl nitrites. This issue is of great importance to the LGBT+ community in particular, but additionally has broad health implications for the public.

Medsafe is looking to harmonize the New Zealand and Australian Schedule with respect to Alkyl nitrites. On Feb 1 2020 the updates to the Australian schedule came into effect regarding alkyl Nitrites. Amyl Nitrite is now Schedule 3 (restricted) when in preparations for human therapeutic use and packaged in containers with child-resistant closures - meaning they can be purchased from behind the counter at a pharmacist pending appropriate packaging.

Isoamyl nitrite, butyl nitrite, isobutyl nitrite and octyl nitrite remain on schedule 4 — effectively restricting them to 'prescription only' access.

Isopropyl nitrite & n-propyl nitrite are classified as Schedule 10 - prohibiting them from sale, supply, and use due to the potential health risks of temporary or permanent retinal maculopathy.

The product currently available in Australia through adult stores is butyl nitrite which remains unchanged as schedule 4 – Prescription only.

While this means amyl nitrite may eventually be available through pharmacies, there are no products currently on the market for this purpose in Australia. Adult shops and sex venues sell "aromas" and "leather cleaners". They have always been illegal to sell without prescription, but state and territory police have overlooked that law. There is potential for enforcement to crack down with raids as happened in Canada when legislation changed. Enforcement actions could include stop sales, recalls, voluntary forfeitures detention or disposal or 2 months imprisonment for a first offence. Some Australian adult venues have stopped selling or moved products under the counter to avoid litigation.

If you import, buy, possess, or use poppers in Australia without a prescription, you are now liable for prosecution. This is a particular risk if you bring poppers into areas and events where police regularly harass queer people and people who use drugs, such as lines to enter venues, dance parties and festivals. Arrests have recently been recorded. Likewise, using a bottle of poppers on the dance floor and sharing it with another person could be a supply offence.

Since the February implementation of the change, some vendors have stopped selling poppers while others have moved to selling them under the counter.

There is no timeline for when an amyl nitrite will be approved for supply through pharmacies and there is a lengthy and costly approval process to gain approval. The most likely scenario is that people will self import the same product they are currently purchasing but from overseas suppliers such as buypoppers.net via the self importation guidelines if they can access a prescription.

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Other solutions will be for the black market to take hold with home grown products or people shifting to alternative solution such as GHB/GBL or huffing Ethyl Chloride and other volatile aromas which are readily available and already in use.

This is consistent with the findings from Canada (schwartz, 2022) which identified roughly 40 percent of participants had used within the last year buying poppers online from the US, dating apps or from friends who made their own. A separate survey of popper use by Vancouver's Community Based Research Centre (CBRC) before the ban in 2013 found between 20 and 30 per cent of sexual minority men used it and this has stayed consistent in 2020.

This is not the time for New Zealand to harmonize our regulations with Australia.

In New Zealand the accessibility of nitrites has meant that consumers can enjoy easier and healthier sexual intercourse but has also meant that the there is no black market for these substances. Commercially available poppers are significantly safer than the possibility of 'home-brewed' alkyl nitrites or currently available alternatives.

The cat-and-mouse game between producers of alkyl nitrites and international regulators has undercut markets that are more dangerous and may account for the relatively limited examples of irreversible harms and mortality. Moving alkyl nitrites to prescription only risks reversing this trend and encouraging a harmful black market. Historically New Zealand has moved from amyl to butyl and most recently to propyl nitrite as the product of choice. This has happened in other countries as demand has caused the market to find alternates.

A blanket restriction on all alkyl nitrites has the potential to force people move to other substances to meet their need. Ethyl Chloride has been promoted as an aerosol popper and is readily available over the counter and is in use in New Zealand.. This may lead to increased harm as people access unsafe products with little to know information on best use eg Sniff don't drink.

Secondly, it is important to recognise that New Zealand suppliers have taken into consideration potential harms and proactively ensured that labelling is correct and measures such as child proof caps are in place. This is reinforced by the context of alkyl nitrite sales, which usually occurs in adult stores or sex on premises venues, where staff may engage in harm prevention strategies through peer education. The adult nature of the places use of sale has also served to prevent minors access to alkyl nitrites.

The primary use of alkyl nitrites is for their analgesic and muscle relaxant effects. When inhaled, alkyl nitrites relax smooth muscle in the body which facilitates easier and safer sex, particularly receptive anal sex. Difficulties with penetrative sex, particularly anal sex among men who have sex with men, can cause discomfort, pain and tearing in the anal mucosa. Alkyl nitrites have a crucial therapeutic use in enabling comfortable and enjoyable receptive intercourse and reducing the probability of pain, anal tears or fissures.

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In this context, it is crucial to note that alkyl nitrite use is higher than average among gay and bisexual men, with 32-37% of the FLUX study cohort reporting recent use in the last six month period. The majority of consumers use an alkyl nitrite monthly or less.

For these reasons, moving alkyl nitrites to prescription only would disproportionally risk the health of people in the LGBTIQ community, particularly gay and bisexual men, by leaving them without therapeutic recourse, promoting marginalisation, or by fostering a harmful black market. It also sends the message that there sexual activity is deemed deviant and criminal harkening back to the days before homosexual law reform. This will reduce the willingness of community members to discuss poppers with health care workers and goes against the model of harm reduction through increased education. Australia has moved Amyl to schedule 3 as it is unlikely that physicians would actually prescribe alkyl nitrites for easier receptive anal sex. It is unlikely that the Medsafe datasheet will list receptive anal intercourse as an approved use. The patient is unlikely to broach the conversation and will instead turn to other sources.

Advisories issued by Health Canada provide possible harms such as potentially life threatening low blood pressure, difficulty breathing, muscle weakness, loss of consciousness (fainting or passing out), respiratory depression, and damage to the liver or kidney. This is inconsistent with the Merck Manual of Diagnosis and Therapy which states that there is little evidence of significant hazard associated with inhalation of alkyl nitrites. Although the ACMD report, dated March 16, 2016, identifies some potential harm associated with poppers, the most common after-effect is head-ache. The report's conclusion on harms is that "Poppers …. is not seen capable of having harmful effects sufficient to constitute a social problem." This conclusion was first reached in a 2011 report by the council and re-iterated in the 2016 report. In 2009, the Conseil d'Etat in France lifted a ban on the commercialization of poppers because it was excessive and disproportionate to any possible harm to the users of the products.

Cameron Schwartz reports that there were 250 million recreational doses consumed in the US and there have been no known deaths from inhalation. Similar data were reported by Thomas P. Lowry, M.D., in the Journal of Psychoactive Drugs; Jan-Jun, 1982; Vol. 14(2): 77-79. Few over-the-counter medications have similar safety data.

The reports of poppers link to maculopathy are disquieting. The medical literature has conflicting reports concerning the duration of any link between the inhalation of alkyl nitrites and vision. More is unknown than known about poppers and vision disturbance. What is certain is that only a small number of individuals have been affected. The most significant uncertainty is the lack of a mechanism linking vision impairment to the inhalation of poppers. Other medical reports implicate certain poppers based on isopropyl nitrites but not the traditional poppers. It is possible that some impurity is the issue and not the alkyl nitrite. Then there are the questions of pre-existing eye disorders and dosage. Anecdotal stories or empirical findings are not a replacement for scientific evidence. This is reminiscent of the stories claiming that poppers caused suppression of the immune system and AIDS. Rigorous science showed these claims to be untrue. Rigorous Scientific examination should be followed to examine risk of maculopathy before moving to ban a substance which has shown no local harm.

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While harmonizing with the Australian schedules appears attractive, the appropriate pathways are not yet in place to transition people to the proposed prescription based model. The Australian market has moved to a state of chaos as providers and the public fear litigation for accessing a product that has been available for decades with little recorded harm. Rather than putting New Zealand in the same situation through harmonization this decision should be delayed until an appropriate solution is provided in Australia that can be analysed and adapted to the New Zealand context. Australia has down scheduled Amyl Nitrite to schedule 3 and available without a prescription. During harmonization, this would need to be adopted in New Zealand to ensure a product was approved and available in appropriate locations.

Rather than banning or restricting sale a measured approach which would mitigate many of the disadvantages of both the current situation and the proposed restrictions could be:

> Amyl, Butyl,Pent lNitrite and their isomers be removed from their current schedule and an entry is placed in the schedule indicating that these compounds are unscheduled under certain conditions.
>
> Proposed conditions would include:

- Maximum package volume of 30ml.
- Child proof packaging
- Prohibition of sale to children
- Restriction of sale to premises which only allow adults.
- Prohibition of advertising.
- Mandatory labelling requirements indicating safe usage, hazards and contraindications.
- Marking of product expiry date.

We trust that the committee will consider the community concern regarding this proposed change and take an informed and considered approach to their decision. We wish to minimize societal harm rather than creating a situation where harm is increased through change and the introduction of unknown substances.

Sincerely

Body Positive

Our submission wishes to address the effects on our business and upon men, who have sex with men of the Australian TGA guidelines. Where On February 1st, 2020, the Australian Therapeutic Goods Administration (TGA) passed new guidelines for the rescheduling of alkyl nitrites to largely prescription only medications, with one exception to pharmacy only medication which New Zealand has also proposed to adopt.

Our business is concerned with providing a safe space for men who have sex with men to engage with each other in an environment which they feel comfortable in.
In addition to providing a safe space we also provide our clients with counselling in safe sex practises distributing NZAF information and Home HIV test kits and condoms and of course the sale of alkyl nitrites.

Over 70% of our customer base are men who identify as straight or bisexual. Our establishment is the one place (that these men tell us) they feel secure asking questions that they dare not ask their own health professionals and to purchase products like alkyl nitrites (poppers), condoms and HIV test kits.

Since the new guidelines have become publicly known our customers have expressed their concern that should alkyl nitrites become a pharmacy only product, they could not bring themselves to visit their doctor to obtain a prescription that would enable them to purchase from a pharmacy. Even were they not required to obtain a prescription they feel that they can't expose that part of themselves to a pharmacist in the greater outside world.

As I'm sure you will have become aware over the course of your deliberations, alkyl nitrites are used primarily by men to relax muscles and allow them to engage in pain free sexual activity.
Our customers tell us they feel they are being unfairly penalised by the loss of these products that they have safely used for decades for having sex with other men because a a few very isolated incidents over many years worldwide.

As a business we know that we are best placed to give these men the advice and the products that they need to be fulfilled as human beings because our customers perceive us to be discreet and offer them the anonymity they desperately seek.

For these reasons we would submit that existing supply channels of sex on site venues and sex shops, in addtion to pharmacies are best placed to safely distribute currently used commercially available alkyl nitrites.

We are R18 only establishments
We sell European regulated products, with appropriate safety labels and child proof caps.
We offer an environment where the product can be used in a controlled setting with advice and information readily at hand.
Our staff are trained in the proper use and handling of the product and are best placed to disseminate information on safe use.
We are trusted by men who have sex with men.

We would also like to draw your attention to the effect on our business should the proposed guidelines be implemented.
Like many businesses of our type, we are a small organisation that has to fight to survive to service our community.

We make enough to get by, and employ 3 staff who themselves have families and themselves to look after.

[redacted]

Without this income we are unlikely to be able to exist as a small business serving our community.

We submit that it would be hasty to rapidly follow in the footsteps of the Australian TGA without more thoroughly addressing the damaging effects on those most affected by the proposed changes. At the very least further consultation from those affected should be sought.

Regards

Rob Morgan
Gavin Sloane Enterprises Limited Trading as Guyz Bathhouse.

Introduction

On February 1st, 2020, the Australian Therapeutic Goods Administration (TGA) passed new guidelines for the rescheduling of alkyl nitrites to largely prescription-only medications, with one exception to pharmacy-only medication. Despite community counselling to reach the decision, the ruling impacts a large number of the men who have sex with men (MSM) population, and limits their ability to engage in safer, easier interactions with their partners. In this submission, I would like to address the history/epidemiology of poppers, how they are used, why the above ruling has taken place, and the impact it has subsequently had on the community. I would also like to offer and explore possible pathways forward to empower all parties involved.

What are they/How are they used?

'Poppers' is the common name given to a group of alkyl nitrites (including propyl, isopropyl, butyl, isobutyl, amyl (aka pentyl), isoamyl (aka isopentyl), and octyl nitrites[1]) used recreationally by 36.7% of homosexual and bisexual-identifying individuals in New Zealand in the past 6 months [2] (note that 'poppers' will be used interchangeably with 'alkyl nitrites' throughout this submission). The alkyl nitrite group, when the vapour is inhaled, relaxes smooth muscle and allows for more comfortable penetrative sex for the receptive partner, reducing the likelihood of fissures and haemorrhoids. With alkyl nitrite use dating back to the 1970s, it has engrained itself in queer culture with risks and interactions being well understood by consumers who in NZ consume at least 40,000 bottles per year. The use of poppers is not associated with an increased risk of HIV, or addiction.

Why has the Scheduling changed?

A summation of the final decision by the TGA declared that:

- isopropyl nitrite and n-propyl nitrite be rescheduled to Schedule 10 (Substances of such danger to health as to warrant prohibition of sale, supply and use), given the limited evidence of therapeutic use and stronger evidence of retinal maculopathy
- isoamyl nitrite, butyl nitrite, isobutyl nitrite and octyl nitrite remain Schedule 4 (Prescription-Only Medicine), given associated toxicity/hospitalisations and paediatric exposures, as well as risk associated with concurrent use of certain medications (e.g Viagra, Cialis) and with the added benefit of a medical practitioner overseeing initial and ongoing safe usage
- amyl nitrate down-scheduling to Schedule 3 (Pharmacist Only Medicine) given they are considered generally more safe and have a well-established risk profile [3]

In making the above decision, the Australian TGA did not take into account labelling and packaging, or education and training of pharmacists and/or medical practitioners, as there currently does not exist a product on the market for dispensing at a pharmacy. It also deemed that a public education campaign would be insufficient to appropriately address concerns raised by their assessment.

Looking to the case data/reports available, whilst there still remains a possibility of toxicity (which presents itself in the form of methaemoglobinemia - a rare medical phenomenon

characterised by an oxidized form of haemoglobin that is unable to carry oxygen, resulting in hypoxaemia and possibly death) there was only one case of this presented in Australia, wherein a three-year-old was admitted when they ingested an unknown quantity from a 9ML bottle. The other primary cause of concern stems from rare cases of non-dose dependent retinal maculopathy, though all cases of toxicity can be associated with inappropriate use of the product, and usually associated with poorly stored products.

One of the key differentiating factors between Australia and New Zealand alkyl nitrite supplies is that the only legal popper (isopropyl nitrite) obtainable in New Zealand comes from Europe, where dangerous goods require a childproof cap. Unintentional misuse tends to occur with intoxication or unfamiliarity. Again, this is another aspect that is covered by New Zealand's European-sourced poppers with warning labels and images. New Zealand has experienced 25 calls over 10 years to the National Poisons Centre compared with Australia experiencing 196 calls over 3 years with one of the main differences being packaging.

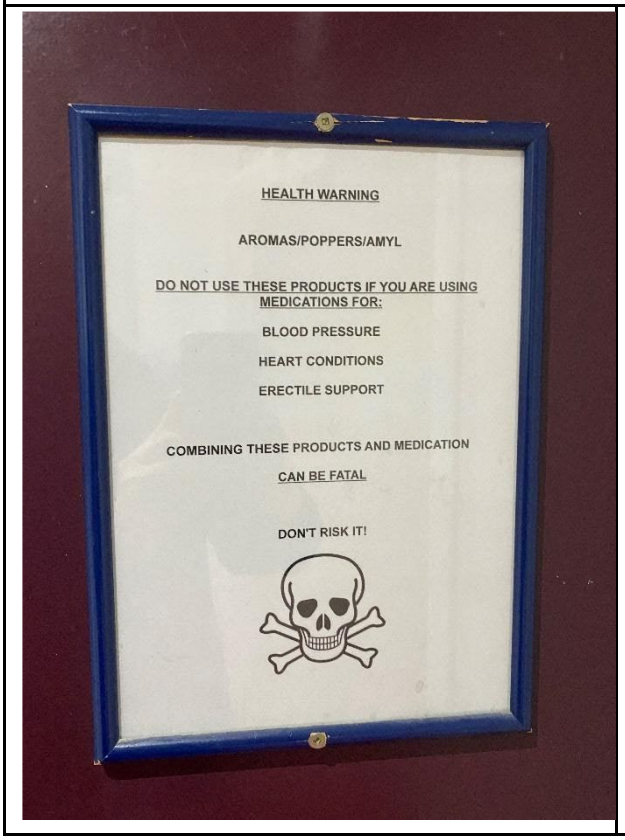
Common Australian Popper

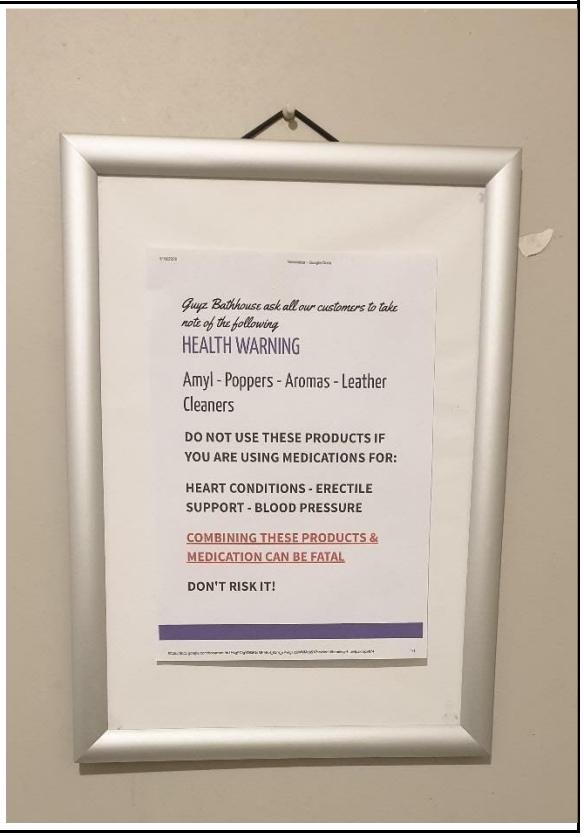
Common New Zealand popper

It is worth stressing again that the product does not have any psychoactive properties, with its largest consumers (being gay and bisexual men) considering the product to be therapeutic.

Though the concurrent use of Sildenafil (Viagra) and Taldalafil (Cialise) and alkyl nitrites can potentially cause profound hypotension, research currently shows no evidence of this occurring in New Zealand or elsewhere. New Zealand retailers already take steps in order to prevent this occurring with venues posting this information in common areas.

Warnings currently placed in different venues





At the time of sale, this information is also available to the purchaser and is usually offered. I do believe more can be done in this area by providing an information sheet with each sale, perhaps developed by NZDF or Medsafe. This approach would allow both in-store and online consumers to be receiving targeted, useful information regarding proper use, signs and symptoms of toxicity, and what to do in case of accidental misuse/if concerned.

There are no documented interactions between drugs used to treat HIV and Alkyl Nitrites.

Implications of rescheduling

At present, there are no products that anecdotally confer similar efficacy in ease of penetrative anal sex as the alkyl nitrites do - though specific trials and evidence is lacking. An anaesthetic based lubricant has been suggested, however the use of such a product does not prevent injury.

With this product being so popular amongst the queer community, a ban or scheduling of the substance without an alternative ready would lead to an overnight black market. This has been the case already for Canada, Australia and now New Zealand recently due to the rescheduling. Canada over a 5 year period experienced a marginal drop with 30% of gay and

bisexual men now sourcing them from dealers, online and bringing them across the border[4]. The Australian market has seen no comparable change in sale with retailers just moving to under the counter sales or purchase through a dealer. New Zealand will not differ in this regard. It opens the idea of lack of respect for the law and introduces more health issues. As MP Crispin Blunt pointed out, this idea simply serves to bring the law into disrepute and all warnings contained within paragraph 43[5] of the select committee report, particularly those from the Gay Men's Health Collective (GMHC) saying that it results in increased Class A and B drug use and increased transmission of sexually transmitted infections.[6]

New Zealand stores serve to offer a safe space as community outreach Centre's for NZAF and body positive. These agencies have been providing free condoms, counselling, onsite testing and training store staff to help with sexual health related questions. A large portion of these stores income is generated by poppers and the loss of this minimal harm product could lead to the closure of these community help outposts; a loss the already at-risk New Zealand queer community cannot afford.

It remains a simple fact that people operate better under their own decisions in this regard. Doctors are not responsible for policing a person's activities when they are not entirely related to a medical issue. At most, a doctor can provide information and access to resources if a person should require it, but the overwhelming majority of the population have been safely using alkyl nitrites for decades. This process would only serve to put strain on New Zealand's health care system when simple education material would combat further issues.

French case that affected Europe's popper supply and sale

Since 2007, poppers containing only isopropyl nitrite have been sold. The use of isobutyl nitrite was prohibited. In 2007, the French government moved to place a blanket ban on all alkyl nitrites, but this was overruled after litigation and investigation instigated by a conglomerate of adult store owners demonstrated limited evidence for justification of the proposed changes. According to the courts , risks mentioned relating to rare accidents often followed abnormal usage and instead justified compulsory warning on the packaging.

This is a direct translation from French website legifrance.gouv.fr. Legifrance is the French government entity responsible for publishing legal texts online.

"… it appears from the documents in the file that the substances in question have a low toxicity at the usual inhaled doses; that if the toxic effects observed can sometimes be serious when the disputed products are associated with certain drugs of frequent use, these effects are relatively rare and poorly measured; whereas most of the accidents reported, few in number over a long period, on the basis of incomplete or heterogeneous statistics, generally result from abnormal use of the products considered, ingested or consumed in combination with other products; that no scientific study or investigation is produced or cited which would make it possible to establish that, with regard to the dangers observed, only the measure of a total ban on all products containing nitrites in whatever form would meet them; that thus, by deciding to prohibit in a general way the manufacture, the

importation, the exportation, the offer, the detention with a view to the sale or the distribution free of charge, the offer for sale, the sale or the distribution free of charge of products containing these substances, while the provisions of article L. 221-3 also make it possible to regulate, in particular, the labeling, packaging or the method of use of these products, including adopting partial or temporary restrictions, the Prime Minister, in the state of the information in the file."[7]

Possible pathways moving forward

In an attempt to reach a more favourable outcome for the affected community, with little to no impact on the maintenance of positive public health outcomes, below are some suggestions/considerations for the upcoming decision-making process (note that these are not separate/mutually exclusive, but multiple can potentially all co-exist in the future):

1) **Consideration to revisit the Scheduling/unscheduling of alkyl nitrites**
   One of the many problems currently faced in the Australian system is an increased limitation on access to poppers. Now that access through adult stores and sex-on-premises venues is no longer possible, the pathway forward lies only through gaining a prescription from a medical practitioner and sources from online/overseas through the Personal Import Scheme, given that no product is currently registered to be sold in pharmacies in Australia. Multiple issues arise from this, including but not limited to: access to GP's/medical practitioners with a sound knowledge of the substance and its use/risk profile, stigma/concern around discussing access to alkyl nitrites with medical professionals (as compared to adult store workers), many years and a large sum of money required for a product to be registered with the TGA, and poorer or absent regulation of online or overseas sources as compared to what is currently available.
   The pathways/ameliorating measures that would be required to circumvent the above issues all take a combination of time, money and/or resources that have not been allocated prior to the rescheduling decision already being passed in Australia. By allowing further time and community consultation prior to a subsequent decision being made in New Zealand, we can ensure that the safest and most favourable outcome is reached for all involved.
2) **Focusing on labelling and packaging of poppers products**
   The predominant concerns surrounding unrestricted access to alkyl nitrites seems to largely be linked to cases of toxicity, misuse and the potential for accidental ingestion by children, despite very few cases of the latter documented. By focusing on the product packaging and information, these issues can largely be addressed and remove the perceived need to consider the rescheduling of poppers. Having clear packaging with poisons information and accurate detailing of alkyl nitrites contained within the product, alongside childproof safety lids, this should address the main issues raised in the Australian TGA assessment.
   In saying this, this above will result in a large loss of time, money and product for companies currently trading, and there is minimal evidence at best that a child safety

lid is a requirement to improve health outcomes in the population accessing alkyl nitrites

3) **Education for pharmacist/medical practitioners as part of ongoing professional development and mandatory training**
   In Australia, there has been no recommendation or guidelines set in place for the appropriate education of pharmacists or medical practitioners for the prescription and dispensing of amyl/alkyl nitrite products, which is a barrier to consumers approaching the aforementioned for a prescription. In order for the improved health outcomes to be conveyed as they have been described in the final TGA decision in Australia, there should be some form of learning module or training available to medical practitioners such that they can prescribe appropriately. A proxy of this should also subsequently be made available to pharmacy technicians and workers, if and when the product becomes available in pharmacies. (This section assumes that harmonisation with Australia occurs and unscheduling of poppers is not considered.)

4) **Education for current wholesalers of alkyl nitrites such that the above can be circumvented**
   It may also be appropriate to consider the education and empowerment of those currently supplying alkyl nitrites to the community through a similar education module - the equivalent of a 'Responsible Service of Alcohol' - to allow for more informed purchasing and usage of the product. This would allow for stronger community engagement and promote safer sex, ease of access to the product, and reduce the stigma around alykl nitrite usage. An education module in this lens could surely be easily and readily available within a short period of time, and even be made available to interested members of the public such that all involved can be as informed as possible and reduce negative health outcomes associated with the use of alkyl nitrites.

Conclusion

Despite what appears to be extensive community discussion prior to the conclusion reached by the TGA, it appears that the Schedule changes passed February 1st 2020 have been done without due consideration for the issues subsequently raised without proposed solutions. While the Schedule change is an issue that can potentially be reviewed, it would be hasty to rapidly follow in the footsteps of the Australian TGA without more thoroughly addressing the issues of access, education and product labelling and packaging. Ultimately, the use of alkyl nitrites affects an entire community, and at the very least further consultation from those affected should be sought.

References

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4) Community-Based Research Centre. Dec 13, 2018. The poppers headache [video file] retrieved from https://www.youtube.com/watch?v=wC26ZSSeGfI
5) UK Parliament Home Affairs. 2015. Psychoactive Substances - Section 5 - Concept of Harm; Subsection 43. Alkyl nitrites. Available at: https://publications.parliament.uk/pa/cm201516/cmselect/cmhaff/361/36107.htm
6) Crispin blunt video Perraudin, Francis – 21 January 2016 – Tory MP Crispin Blunt: 'I out myself as popper user' – The Guardian – Retrieved from https://www.theguardian.com/politics/2016/jan/20/tory-mp-crispin-blunt-poppers-drug-policy
7) French law Legifrance.gouv.fr – Council of state, 10th and 9th subsections together – 05/15/2009 – [online] available at <https://www.legifrance.gouv.fr/affichJuriAdmin.do?oldAction=rechJuriAdmin&idTexte=CETATEXT000020868995>

New Zealand AIDS Foundation
Te Tūāpapa Mate Āraikore o Aotearoa

The Medicines Classification Committee
Medsafe
PO Box 5013
Wellington 6140

19 March 2020

Decision to add a group entry for Alkyl Nitrites to the New Zealand Medicines Schedule

We would like to comment on alkyl nitrites noted in the Agenda Item 5.3 for the 64th Meeting of the Medicines Classification Committee.

The New Zealand AIDS Foundation (NZAF) is a registered charity and non-governmental organisation funded through contracts with the Ministry of Health and independent fundraising to provide a range of HIV and AIDS related services, including: HIV prevention and health promotion, HIV testing, counselling and support, research, policy, and information services.

We are extremely disappointed that the recommendation made at the 63rd meeting of the Medicines Classification Committee, to add a group entry for alkyl nitrites to the New Zealand Schedule as a prescription medicine, has been approved. The recommendation has been made without community consultation and a thorough understanding of poppers use and the poppers market in New Zealand. Our previous submission raised concerns around introducing changes to the classification, but these were not addressed at the MCC meeting.

We strongly recommend that the New Zealand classification for alkyl nitrites is reversed and enforcement delayed until a legal and viable alternative is made available. We also recommend community consultation is sought to understand poppers use and the market in New Zealand and develop a New Zealand specific approach. The decision to partially follow Australia's recent classification of alkyl nitrates has removed the opportunity to learn from the Australian experience over time and address the specific needs of affected LGBTQI communities in New Zealand. There are also key differences in the alkyl nitrites markets in Australia and New Zealand that will not be addressed through harmonisation and require further investigation.

This decision to add a group classification for alkyl nitrites (known informally as poppers) has effectively criminalised their use, disproportionally impacting LGBTQI communities and increasing the likelihood of harm. It is an extreme response to a drug which has had low levels of harm in New Zealand. Adding a group entry which restricts the sale of alkyl nitrites as a prescription medicine means there is no legal viable alternative to alkyl nitrites available in New Zealand that can help reduce discomfort during receptive anal sex.

We are also concerned at the lack of consultation and the difficulties we have experienced engaging in the classification process. As a community organisation with limited experience providing feedback to the Medicines Classification Committee, it has been difficult to understand the nature of the decisions being made by the Committee, the timeframes and stages within a decision making process,

and how to meaningfully engage in consultation. It remains unclear from the minutes and agenda exactly what information is being discussed and provided at the 64th meeting of the Medicines Classification Committee. This makes it difficult for us to provide relevant feedback. In this instance, the inclusion of alkyl nitrites in the 64th MCC meeting agenda, implied to us that this issue will be further discussed before any enforceable decisions are made.

Alkyl nitrites

Alkyl nitrites are used to improve the comfort levels during penetrative anal sex. When inhaled, they cause a non-specific smooth muscle relaxation, including in the sphincter of the anus. This effect facilitates anal penetration and may prevent rectal injury.

Research in New Zealand has shown poppers are most often used within a sexual setting, are socially acceptable and non-habit forming. A 2019 local cohort study found 53% of the 836 men surveyed had used poppers once or more in their lifetime and 33% had used them recently within the past 6 months.[1] This corresponds with the NZAF 2017 Ending HIV survey results for gay and bisexual men which found that 37.3% of respondents who were sexually active had used poppers in the past 6 months.[2] The group classification of alkyl nitrites criminalises a large proportion of the community who use poppers.

International studies show that many men who have sex with men (MSM) experience high levels of discomfort associated with painful receptive anal intercourse, often referred to as anodyspareunia. In a US survey, 14% of gay and bisexual respondents reported frequent and severe pain when engaging in receptive anal sex.[3] That study reported that poppers non-use was strongly associated with greater severity of painful receptive intercourse.

Harmonisation will fail to minimise harm and impact on health promotion efforts

This is a missed opportunity for health promotion and harm minimisation. We are concerned that harmonising the classification of alkyl nitrites with Australia will negatively impact and further marginalise affected communities in New Zealand. There is currently no legally obtainable or viable alternative to alkyl nitrites available in New Zealand or Australia. Restricting the availability of alkyl nitrites products before ensuring a legal viable alternative encourages criminal behaviour and a shift to the increasingly unpredictable black market.

There is also a concern that people will shift to misusing much more dangerous volatile substances or using other illicit drugs. This is of significant concern with reports of ethyl chloride (chloroethane) being substituted for alkyl nitrates in New Zealand and overseas. Ethyl chloride is found in over the counter sprays for sport injuries and provides a head rush when inhaled without the muscle relaxation effect of poppers. This increases the risk of harm in sexual encounters as well as harm from 'huffing', including the risk of sudden sniffing death. Other substances that may substitute for poppers include

[1] Flux NZ 2019 baseline preliminary findings (unpublished)
[2] New Zealand AIDS Foundation (2017) Ending HIV survey (unpublished)
[3] Damon, W., & Rosser, B. R. (2005). Anodyspareunia in men who have sex with men: prevalence, predictors, consequences and the development of DSM diagnostic criteria. J Sex Marital Ther, 31(2), 129-141.

gamma-hydroxybutyric acid (GHB) and related compounds that act as depressants and are associated with a significant risk of fatal overdose.

The decision to have amyl nitrates as prescription-only medicine also creates barriers for people to access the compound. Research shows that half of gay and bisexual men in New Zealand are not open with their GP about their sexual orientation or behaviour.[4] These barriers were greater among non-European ethnicities, due to issues in accessing and navigating healthcare. While down-scheduling amyl nitrate to be a pharmacist-only medicine, conditional on the availability of the product, addresses some of these issues, many people may still struggle to discuss their sexual activity in the open context of a pharmacy. There is also no available product that meets these requirements and has been approved for use, which effectively means changing classification becomes a ban of any use.

A public health approach focussed on harm minimisation is a more effective approach for LGBTQI communities who are already disproportionately affected by poorer health and justice outcomes. Criminalising drug use can instead lead to greater harm. We support education and behaviour change initiatives alongside manufacturing regulations to minimise harm amongst LGBTQI communities.

The poppers market in New Zealand is not aligned with Australia.

There are key differences between the New Zealand and Australian markets. In Australia the active ingredient in poppers was isobutyl nitrate. However, in New Zealand it is isopropyl nitrate, more closely resembling the poppers market in the United Kingdom. Our current understanding from suppliers in New Zealand is that products sold in New Zealand are made for the European market. Due to this they meet UK packaging requirements and must have a childproof cap and warning labels, which was not the case in Australia.

It is also not clear at this stage whether a pharmaceutical-grade product yet to be developed for the Australian market, based on amyl nitrate, would be available in New Zealand. As far as we are aware, to date, there have been no products in development to meet the legislative thresholds for registration as medicine. This further negates the intent of the classification, that amyl nitrate products are available on prescription, and establishes an effective ban on poppers in New Zealand.

We acknowledge there have been concerns raised internationally about the effects of isopropyl nitrate. However, the UK Advisory Council on the Misuse of Drugs (2016) advised not to restrict or classify access to 'poppers' (isopropyl nitrate) as the harm is rare.[5] Data available from the New Zealand Poisons Centre show that in the last ten years there were 25 calls made concerning alkyl

[4] Ludlam A, Saxton P, Dickson N, Hughes A. General practitioner awareness of sexual orientation among a community and internet sample of gay and bisexual men in New Zealand. Journal of Primary Health Care. 2015;7(3):204-12

[5] Advisory Council on the Misuse of Drugs (2016) ACMD review of alkyl nitrites ("poppers"). Accessed from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/508179/Poppersadvice.pdf

nitrates.[6] While most of these calls were referred for medical advice, further data is not collected and it is not clear what the outcomes may have been.

The decision to apply a group entry for alkyl nitrites effectively criminalises poppers use and is a disproportionate response to the known low-level harms seen from poppers in New Zealand. It directly affects LGBTQI communities who already face greater discrimination and poorer health outcomes. We believe a targeted public health approach focussing on education and behaviour change would be more effective at minimising harm within these communities.

Thank you again for the opportunity to feed back. Please don't hesitate to contact our Senior Policy Officer, Kate Macpherson at kate.macpherson@nzaf.org.nz should you require clarification on any of the points made.

Warm regards,

Jason Myers
Chief Executive

[6] Data received from New Zealand Poisons Centre for calls made during the period 1 January 2010 to 31 December 2019 regarding amyl nitrite, butyl nitrite, isoamyl nitrite, isobutyl nitrite, octyl nitrite, n-propyl nitrite, isopentyl nitrite, propyl nitrite, cyclohexane nitrite, amyl nitrite, alkyl nitrite, OR popper(s).

To Medicines Classification Committee 20th March 2020

New Zealand Drug Foundation comment to the 64th Medicines Classification Committee agenda item 5.3 (9b) alkyl nitrites and decision to add a group entry for alkyl nitrites.

The Drug Foundation is a registered charitable entity under the Charities Act 2005 (No. CC27025). Our work is supported by government funding, grants and donations. We have been at the forefront of major alcohol and other drug policy debates for almost 30 years, advocating for policies and practices based on the best evidence available. We recognise drugs, legal and illegal, are a part of everyday life experience, so we are safety focused and take a harm reduction approach in all our work.

We are concerned that the recommendation for a group classification of alkyl nitrites at the 63rd Medicines Classification Committee was rushed and will result in harm. **We are advocating for the group classification to be reversed and implementation of this recommendation to be paused until meaningful consultation is undertaken and clear recommendations can be made around the group *and* individual classification of alkyl nitrites**.

This comment follows from our previously submitted comment to agenda item 8.2.1a at the 63rd meeting of the Medicines Classification Committee where we outlined potential regulatory options to mitigate the risk of harm from alkyl nitrite use in New Zealand. We were surprised that a recommendation was made at this initial meeting. Also, it was not made clear that this recommendation would immediately be enforced before the request for information from MEDSAFE had been met. We believe this was an inappropriate recommendation as:

1. No consultation was undertaken with the population most affected by this decision
2. Prohibiting alkyl nitrites criminalises part of the LGBTQI population and will likely result in significantly more harmful substance use
3. Australia had a different market to New Zealand and has only partial implemented the regulatory framework making any decision around harmonisation inaccurate and premature

After brief consultation with the gay community and further research which is detailed below, we believe the prescription-only group classification of alkyl nitrites needs to be reconsidered.

1. *No consultation was undertaken before the recommendation was made*

Alkyl nitrite use is common among men who have sex with men[1] and likely the wider LGBTQI community within New Zealand. Use of alkyl nitrites was socially acceptable, non-habit forming and used in sexual setting to decrease discomfort and potentially reduce injury.[2] Use of these products as a harm minimisation technique was also found. One respondent wrote "I only use poppers with

[1] A local cohort study, FLUX, conducted in 2019 found 53% of the 836 men surveyed had used poppers once or more in their lifetime and 33% had used them recently (within the past 6 months). Most of this recent use was infrequent with 48% having only used poppers once or twice in the six-month period. Only 0.5% of those who had recently used poppers were using them daily.

[2] When inhaled alkyl nitrites cause a non-specific smooth muscle relaxation, including in the sphincter of the anus. This effect facilitates anal penetration and may prevent rectal injury as well as decreases discomfort

the boyfriend in low doses when I'm a bit tight". There was also evidence that this use was alongside other safe sex practices with the comment "I use poppers during receptive sex (always protected with condoms) and usually only once at the start for the muscle relaxing effect rather than a 'High'."[3]

This is the key population affected by these decision as noted in the minutes of the 63rd meeting with the committee "not sure if the LGBTQI community was aware that these substances were being considered for reclassification and suggested feedback from them should be sought"[4]. Despite awareness of the affected community and the need to consult the group classification for alkyl nitrites was made without any action to hear these voices.

In Australia the Therapeutic Goods Agency (TGA) undertook community consultation in the form of workshops and online submissions to ensure the voice of the LGBTQI population was heard.[5] There was high community engagement and the decision was of better quality because of this. A similar level of consultation should be conducted in New Zealand before any further classification decisions are made to appropriately understand the local market and how any decision may impact behaviour, health and well-being for this community. This would also be an opportunity to provide education around safer use of alkyl nitrites and warnings around black market products.

2. *Prohibiting alkyl nitrites will result in additional harm*

The recommendation for a group classification of alkyl nitrites is in effect a ban and substitution to other substances is expected. This will increase the risk and experience of harm as well as contribute to the criminalisation of this already marginalised population.

Use of deadly volatile substances will likely increase

No therapeutic agents are registered with the indication to enable anal sex for individuals who suffer from painful anal intercourse. Anecdotal evidence suggests some MSM use local numbing creams for anaesthetic effects – their use is not recommended due to loss of sensation of pain without muscle relaxation, that may increase the risk of injury.

More concerning is the potential misuse of ethyl chloride, a volatile substance, that has been linked to prohibition of alkyl nitrites.[6] When this pharmacy-only medication (intended for healing muscle sprains) is sprayed onto cloth and inhaled or 'huffed' it provides a headrush. This can lead to the assumption it is the same as alkyl nitrites yet volatile substances do not provide non-specific smooth muscle relaxation negating the intention of use and there is a risk of sudden sniffing death.[7] Deaths have been linked to this substance in Canada when it was contained in black market alkyl nitrites.[8] Anecdotal reports suggest the substitution of ethyl chloride is currently rare in New Zealand but can expect to be increased following international learnings where this became the 'new poppers'.

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[3] FLUX (2019) responses to question "Would you like to tell us in your own words how you try to keep yourself safe when using or injecting drugs?" (unpublished)

[4] https://www.medsafe.govt.nz/profs/class/Minutes/2016-2020/mccMin10Oct2019.htm

[5] https://www.tga.gov.au/public-meeting-communique-regulatory-options-appropriate-access-and-safety-controls-alkyl-nitrites

[6] https://link.springer.com/article/10.1186/s41935-019-0136-4

[7] https://www.researchgate.net/publication/12672498_Death_Due_to_Inhalation_of_Ethyl_Chloride

[8] https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2019/69916a-eng.php.

Use of harmful illicit drugs will potentially increase

Another potential market shift due to the group classification for alkyl nitrites is the increase in illicit drug use. This shift is most likely to be the increased use of gamma-Hydroxybutyric acid (GHB). GHB is a central nervous system depressant with similar psychoactive effects as alcohol as well as providing smooth muscle relaxation and increased sex drive. GHB is used recreationally within the gay community but currently at a very low level.[9] Shift to wider use of GHB is concerning as this is a very potent substance with a steep dose response curve that makes the risk of fatal overdose high.

The LGBTQI community will be criminalised

As decided by the United Kingdom government, further regulation of alkyl nitrites will increase harm through criminalisation and is not justified for a substance "not seen to be capable of having harmful effects sufficient to constitute a social problem"[10]. Under this new state of prohibition those seeking to continue using alkyl nitrites, or substitutions mentioned above, risk being criminalised. Contact with the criminal justice system is particularly detrimental to the LGBTQI community and this is an extreme mechanism to address a low harm substance. There is anecdote that the LGBTQI community in Australia are facing fines of $450 and other penalties for possessing any alkyl nitrites.

3. *Harmonisation is not valid or needed at this point*

We welcome the Medicine Classification Committee request for more information on the risk of harm of alkyl nitrites and specifically how it interacts with HIV medication. No decisions should have been made until this information had been received and more informed decisions on the individual and group classification could have been made at the same time.

The current New Zealand market for alkyl nitrites is distinct from Australia

From conversations with local importers and retailers of alkyl nitrites, the current market in New Zealand is distinct with isopropyl nitrite being the main substance sold, not isobutyl nitrite. The manufacturing standards of previously available alkyl nitrite products in New Zealand were also high with child proof caps, warning labels around not ingesting the substance and maximum size bottles. This is in contrast to the Australian market with no child proof caps or warning labels and these products still mis-sold as room deodoriser. The difference is based on historical classification in 2000 with New Zealand largely being supplied from the legally permitted market for isopropyl nitrites in the United Kingdom. The need to regulate in Australia was higher than in New Zealand and this should not have been a decision of harmonisation based on these market differences.

Any decision should only be considered with full implementation of Australian model

This decision around a group entry for alkyl nitrites, which is not even in-line with the TGA decision, should only have been contemplated following full implementation of the model. Without an approved alkyl nitrite product (amyl nitrite was classified for this purpose) available for sale in

[9] FLUX 2019 found prevalence of 4.3% in the past six months

[10] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/508179/Poppersadvice.pdf

pharmacies harmonisation should be delayed. Having a legally available alternative was a key justification being the restrictive scheduling decision by the TGA.

In conclusion we believe the process to reach the recommendation for a group classification of alkyl nitrites was premature and devoid of community voice. This needs to be addressed along with a thorough process to determine a long-term regulatory framework (potentially outside of just medicine classification) to reduce the risk of harm from alkyl nitrite use.

If you have any points of clarification, seek further information or want to partner in community consultation please contact [redacted]

Warm regards,

[redacted]

[redacted]

[redacted]
New Zealand Drug Foundation

change.org

Medsafe: Don't Ban Poppers!

842 have signed. Let's get to 1,000!

Body Positive started this petition to Medicines Classification Committee (Medsafe)

Medsafe is seeking to list amyl/poppers and all associated chemical variations as prescription medications and to ban (schedule 10) iso-propyl nitrate which is the only type of poppers available in New Zealand. Details on the interim decision can be found at https://www.medsafe.govt.nz/profs/class/Minutes/2016-2020/mccMin10Oct2019.htm where it is recommended that a group entry for alkyl nitrates should be added to the New Zealand Schedule as a prescription medicine however a final decision may not come until later in 2020. The next meeting scheduled for April and public submissions can be made prior to that meeting once the agenda is published. This petition will be submitted to that meeting.

This change is to harmonize our regulations with Australia who recently reviewed alkyl nitrates and classed them as prescription medications. This was seen as a win as they were not banned but by making them prescription only they can be accessed legally through the medical system which includes doctors and pharmacies. Poppers would no longer be available through saunas and adult stores being restricted to pharmacies and currently no Alkyl Nitrates are currently registered for supply through pharmacies so they will effectively be banned from use and poppers will move to the

black market. There is potential for the police to crack down on the sale of poppers through current venues if they are made prescription – similar to the experience when amyl was originally banned.
For decades, gay men and receptive partners have relied on amyl/poppers to comfortably enjoy sex, and decades of research on the effects of poppers have shown that the negative effects are minimal and contained - amyl/poppers are not a drug of dependence or addiction and result in little harm.
Medsafe has proven capable of regulating Viagra (a comparably dangerous substance) for the benefit of active partners and now considering medicinal cannabis use. We believe that Medsafe should acknowledge the need for poppers and regulate the substance for safe use by receptive partners. Poppers have been used safely for decades - its use should be legitimised not criminalised and the government should not be targeting gay men's sexual practices. The goal should be to guarantee quality and to reduce harm through improved packaging such as correct labelling and child proof containers.
The reasons stated by the Medsafe for this listing do not justify the criminalisation and control of adults engaging in consensual and considered behaviour that is accepted in many other jurisdictions around the world. In 2016 the UK Government attempted to ban amyl/poppers however the bid was unsuccessful when the justifications were put under scrutiny - we believe that the same findings can be made in New Zealand and that common sense may prevail and the listing of these substances as schedule 10 not occur. The UK Government Advisory Body on the Misuse of Drugs found the use of poppers was 'not seen to be capable of having harmful effects sufficient to constitute a societal problem.'[i]
We will update you here once public submissions are open on this topic at Medsafe.
A ban on amyl/poppers and a listing of the substances as a schedule 10 drug will disproportionately affect gay men - overnight an entire class of law-abiding adults will be regarded as criminals.
We ask that Medsafe does not criminalise the sex lives of gay men that seek to have comfortable, consensual sex in the privacy of their own homes with the assistance of amyl/poppers, we ask that Medsafe ceases all action to further restrict the use of or access to amyl/poppers in New Zealand.
[i] Home Affairs Committee, Psychoactive Substances (report), London: Stationery Office, 23 Oct 2015, p. 14 https://publications.parliament.uk/pa/cm201516/cmselect/cmhaff/361/361.pdf
Start a petition of your own

Start a petition of your own

This petition starter stood up and took action. Will you do the same?
Start a petition

Updates

The Petition Remains open
The petition has been submitted to the medicines classification committee for consideration at the May Meeting. A number of other submissions have gone in as well in support of keeping poppers available. We will keep the p...

The Petition Remains open

The petition has been submitted to the medicines classification committee for consideration at the May Meeting. A number of other submissions have gone in as well in support of keeping poppers available. We will keep the petition open until the meeting occurs on the 14th of May. It is possible that he meeting will be postponed as the covid-19 situation develops.

If the meeting goes ahead as scheduled on the 14th May they have seven weeks to publish the minutes (2nd July). We will keep you informed when the minutes become available. Once the minutes are published there is a period of 10 working days for the public to object to any recommendation that has been made.

Submissions to the committee close on the 20th March if you would like to make a personal submission. Instructions on how to do this are in a previous update.

Body Positive
1 day ago
More updates

Reasons for signing

Submission on the prohibition of poppers

Thank you for the opportunity to submit feedback to the 64th meeting of Medicines Classification Committee in May 2020 agenda item around the classification of alkyl nitrites. This issue is of great importance to the LGBT+ community in particular, but additionally has broad health implications for the public.

At the 63rd Meeting on the topic of alkyl nitrites the committee stated "The Committee was also not sure if the LGBTQI community was aware that these substances were being considered by reclassification and suggested that feedback from them should be sought". The community decided to be proactive on this request and gather community input on the topic. We have taken out two editorials in Gay Express magazine to raise awareness and have been distributing posters and flyers through online media, sex on site and adult stores where poppers are available across the country. A petition was created though change.org and to date the petition (tinyurl.com/nzpoppers) has gained 830 signatures since its inception and is attached to this submission. We have encouraged the community to take this opportunity to provide submissions to the committee to ensure their voice is heard.

At the 63rd meeting the Medicines Classification Committee (MCC) made a recommendation to classify all alkyl nitrites (poppers) as prescription only and this was enacted through a gazette notice on March 6th 2020. This is in effect a ban as there are no products currently registered for distribution through pharmacies. We are concerned that this will lead to more harmful substance use and that it unfairly discriminates and criminalizes LGBT+ communities. This does not harmonize with the Australian guidelines as originally proposed at the meeting as all poppers now require a prescription – in Australia amyl is schedule 3 and can be obtained from a pharmacy without a prescription when a product becomes available.

Having amyl as schedule 3 ensured there was a pathway for people to continue to have access in a controlled and managed manner. This is an appropriate harm reduction model to ensure that the community is kept safe by providing an acceptable alternative. This has not happened in New Zealand as we have moved to prohibition.

We believe the group entry was introduced as previous attempts to eliminate nitrites has resulted in the active components being adjusted and for distribution to continue. This has happened numerous times as demand remains constant. The group entry has ensured this does not occur again but will not eliminate the demand. As shown in Canada where poppers were banned in 2013 the usage patterns have remained the same. Products are now being imported, home grown or alternates accessed such as ethyl chloride "aerosol poppers".

Senior Investigators have been in contact with suppliers informing them: "Alkyl nitrites, which includes isopropyl nitrite are now scheduled as prescription medicine. Isopropyl nitrite was commonly used in poppers as an alternative to amyl nitrite, which has been a prescription medicine for many years." Anecdotal reports are that vendors can sell their current stock before the prohibition takes effect. But now suppliers, reatilers and users of amyl are now in fear of litigation.

Why a ban is more harmful

Alkyl nitrites are low harm products with therapeutic benefits for the people engaging in anal sex. When inhaled alkyl nitrites a non-specific smooth muscle relaxation, including in the sphincter of the anus. This effect facilitates anal penetration and may prevent rectal injury. These are also low harm and the British government places alkyl nitrites among the less harmful of recreational drugs[1] and in 2016 decided not to prohibit the sale or use of isopropyl nitrate (which is the same product used in New Zealand).

[1] Nutt D, King LA, Saulsbury W, Blakemore C (March 2007). "Development of a rational scale to assess the harm of drugs of potential misuse". Lancet. 369 (9566): 1047–53.

Following the blanket prescription only classification of alkyl nitrites and banning current use in New Zealand would:

- Criminalise gay and bisexual men of which around 40% currently use poppers
- Contribute to the stigmatisation of the LGBTQI+ community and placing our sexual practices as deviant.
- Increase the availability and use non regulated formulations and substitution to other significantly higher harm products.
- Provide enforcement agencies with the power to arbitrarily target queer community members, especially gay and bisexual men as well as sex workers.
- Reduce the willingness of community members to discuss amyl use with health workers.
- Increase the administrative demands on law enforcement agencies.
- Will not address the harms associated with unintended misuse (i.e. swallowing) as current products have childproof caps and warnings

We are calling on Medsafe to:

1. Remove the group entry of Alkyl Nitrates
2. Defer harmonisation of Alky Nitrites until there is an approved product available in Australia to ensure an appropriate harm reduction pathway
3. Consult with the community through community forums in main cities and online to create a New Zealand Model.

The attached documents include the 830 signatures to date along with their comments. We will keep the petition in operation in the lead up to the May meeting and continue to gather signatures.

We are calling for harm minimization over prohibition.

change.org

Body Positive

Recipient: Medicines Classification Committee

Letter: Greetings,

Medsafe: Don't Ban Poppers!

Comments

Name	Location	Date	Comment
[redacted]	New Zealand	2020-01-13	"I'm an adult and it's my right to use if it suits me to indulge.."
[redacted]	Auckland, New Zealand	2020-01-13	"I want the availability of these products to remain as they are."
[redacted]	Auckland, New Zealand	2020-01-14	"It's good to regulate the market, but definitely not a BAN"
[redacted]	Auckland, New Zealand	2020-01-14	"This is just Draconian. Go do something actually constructive for the community med safe."
[redacted]	Auckland, New Zealand	2020-01-14	"It shouldn’t be banned"
[redacted]	Auckland, New Zealand	2020-01-14	"These shouldn't be banned.... do something more constructive with your time"
[redacted]	Auckland, New Zealand	2020-01-14	"Totally support this! Well done Body Positive."
[redacted]	Auckland, New Zealand	2020-01-14	"Id rather harm minimization or the status quo than poppers becoming a black market drug."
[redacted]	sydney, Australia	2020-01-14	"It seems ridiculous that NZ late to the party would attempt to pass reforms like this when they have been struck down in every modern jurisdiction around the world"
[redacted]	Christchurch, New Zealand	2020-01-14	"This should be individual choice"
[redacted]	auckland, New Zealand	2020-01-14	"they are safe non addictive, short acting"
[redacted]	Melbourne, Australia	2020-01-14	"This is just another way for the government to monitor and restrict activities specific to the queer community. Conservatives should look more closely at what is happening in their circles, and leave us alone. Thanks"
[redacted]	Auckland, New Zealand	2020-01-15	"Popper is not a psycoactive drug, nor will create dependence on it. It is short acting and have no apparent lasting side effects. Don’t make this a black market thing."
[redacted]	Picton, New Zealand	2020-01-15	"Because this is a low risk and enjoyable sexual pleasurable toy."
[redacted]	Auckland, New Zealand	2020-01-15	"Banning a perceived problem will not mitigate the risk. Regulation is the key"

Name	Location	Date	Comment
[redacted]	wellington, New Zealand	2020-01-15	"I believe that this would be a step backwards towards criminalizing homosexual sex, we have the right to marry let us have the right to have sex too"
[redacted]	New Zealand	2020-01-15	"Harm reduction is everyone's goal, which is not achieved by stigmatising users of a previously legal substance and leading to the inevitable rise in black market of unsafe and untested products. Consensual, law-abiding adults who practice consensual sex in a controlled environment are unfairly targetted sweeping, generalised legislation."
[redacted]	Christchurch, New Zealand	2020-01-16	"I am an adult and able to make decisions for myself .."
[redacted]	Auckland, New Zealand	2020-01-16	"This creates more criminals and solves a nok existent problem. It is a waste of money boyh in the process and the administration."
[redacted]	Auckland, New Zealand	2020-01-17	"F*^k off Medsafe"
[redacted]	Auckland, New Zealand	2020-01-17	"Im supporting this"
[redacted]	Wellington, New Zealand	2020-01-18	"Because amyl/poppers is not capable of having harmful effects sufficient to constitute a societal problem so should be left alon"
[redacted]	Wellington, New Zealand	2020-01-19	"If they're going to waste their time trying to ban something harmless like amyl, why don't they go the full Monty and ban tobacco & cigarettes? Surely tobacco has a lot more harmful, detrimental, costly and health effects than amyl ever did."
[redacted]	Wellington, New Zealand	2020-01-24	"This is ridiculous....as they are going to make marijuana legal!! There is nothing wrong with poppers!"
[redacted]	Wellington, New Zealand	2020-01-26	"There is nothing wrong with poppers"
[redacted]	Auckland, New Zealand	2020-01-27	"I believe in the freedom of the individual."
[redacted]	Auckland, New Zealand	2020-01-28	"gay rights"
[redacted]	Auckland, New Zealand	2020-01-28	"Poppers are safe when used correctly. A ban will only encourage a black market wich may cause inferior products to be peddeld. It would be a waste of taxpayer money to dedicate resources to ban a product that doesn't do any real harm."
[redacted]	Auckland, New Zealand	2020-01-28	"So if this happens we have to go see a Dr. Which for me is $35 and the cost of the amyl which is $40 because there is no way that Pharmac is going to subsidize amyl. I've not heard of any one dying of amyl overdose, go back into your

Name	Location	Date	Comment
			thinking hut. How laughable as we vote on making weed legal this year in the 2020 elections."
[redacted]	Auckland, Australia	2020-01-29	"I love them"
[redacted]	Wellington, New Zealand	2020-01-29	"Making things illegal is not going to stop people accessing them prohibition doesn't work it just makes it less safe for the user. don't ban poppers, It will only start an underground blackmarket."
[redacted]	Dargaville, New Zealand	2020-01-30	"POPPERS have no place in the purview of MedSafe. leave alone what you don't need to touch."
[redacted]	Melbourne, Victoria, Australia	2020-02-01	"I am a 'Kiwi' and once again here is an organisation trying to stop peoples right of purchase."
[redacted]	New Zealand	2020-02-01	"In signing because I feel it is unnecessary to ban a recreational substance that has never produced any social or mental health issues. I think medsafe could spend more time looking into other substances that have far more obvious health effects."
[redacted]	Auckland, New Zealand	2020-02-01	"I find it odd trying to ban poppers and yet they want to legalise marijuana.This ban on poppers only create another black market. There's nothing with poppers!"
[redacted]	Auckland, New Zealand	2020-02-01	"I find it odd trying to ban poppers and yet they want to legalise marijuana. This will only create an unnecessary black market,There is nothing wrong with poppers!"
[redacted]	Australia	2020-02-06	"Banning poppers would only create a black market. 65 percent of poppers users in Australia said they would find an alternative this means placing people in dangerous situations where they could be exposed to 'backyard concoctions' or leading to a use of a illicit substances."
[redacted]	Auckland, New Zealand	2020-02-06	"While I don't use them myself (they give me a mild headache) I have never seen any evidence to support a ban. The ban seems to be badly thought out ("because Australia has banned them" is not , in itself, a reason)"
[redacted]	Fitzroy, Melbourne, Victoria, Australia	2020-02-06	"I'm signing because this is a blatant attack on what the conservative far right think is the homosexual lifestyle. There is no sensible reason for this ban. Cigarettes are much more harmful."
[redacted]	Wellington, New Zealand	2020-02-06	"How ridiculous to ban this"
[redacted]	Australia	2020-02-06	"Freedom for our way of life"
[redacted]	Wellington, New Zealand	2020-02-06	"They are great! My fave is liquid gold!!"

Name	Location	Date	Comment
[redacted]	Melbourne, Australia	2020-02-13	"There’s no harm is using these products. Banning them is completely unnecessary."
[redacted]	Levin, New Zealand	2020-02-23	"Why not regulate instead of banning. I feel medsafe has decided that because poppers is used by a small minority it would be more cost effective to do a blanket ban. Thanks medsafe for creating another thing that will damage us from the black market. If medsafe is focused on recreational drugs it should be solely focused on recreational drug testing stations around the country, not focusing on a Victorian era pearl clutching reaction to an ass fucking recreational drug. Given there’s so much research showing no significant long term effects it just looks like straight up institutional homophobia from a profession rife with bullying."
[redacted]	christchurch, New Zealand	2020-03-13	"I actively enjoy anal stretching/fisting which ro me is part of my enjoyment of sex.Withiut the use of amyl/popper I would be unable to have that enjoyment.I have been in recovery from Alcohol and drugs for 23 year with out using any drugs be it legal or illegal. I have used ayml for many years without it setting off my desire to go back to using iusing harder drugs.Removal of ayml could potentially put my recovery at risk as my only option maybe an illicit addictve drug that would allow me to continue the sexual practices I enjoy.Or put my health at risk using ayml which is made by back yards cooks with not regulation, as well as making me a "criminal" because I am using a classified drug."
[redacted]	Timaru, New Zealand	2020-03-14	"This ban makes no sense. Alkyl Nitrites are extremely safe substances (much safer than alcohol, tobacco, and Marijuana) and are widely used in the LGBT community. This ban will drive users to less safe alternatives and will lead to a growing black market. It also disproportionately affects and stigmatises the LGTB community."

Human papillomavirus (HPV) Vaccine Reclassification

March 2020

The submitters: The Cancer Society of New Zealand is a non-profit organisation that is committed to reducing the incidence and impact of cancer and cancer inequities in the community. We work across the cancer continuum with a focus on prevention, supportive care and funding of cancer research.

The issue: Compelling evidence shows HPV vaccination programmes have a significant and substantial impact on reducing HPV related infections and cancers. However, HPV immunisation rates are below target (54%[1]-67%[2]) and sustained vaccination coverage needs to improve to achieve herd immunity and meet the Ministry of Health's minimum target of 75%. Community pharmacists are ideally placed to expand access to vaccination among young people.

Recommendation: The Cancer Society of NZ recommends that community pharmacists provide HPV vaccines to support New Zealand's HPV and cancer elimination goals, and that such an initiative is started as soon as possible.

Background

Vaccination against HPV substantially reduces the **cause** (high risk HPV infection) **and risk** of cervical cancer; other anogenital cancers; oropharyngeal cancers and genital warts [1-3]. In addition, vaccination for young males indirectly provides protection against cervical cancer for future female partners [4].

The funded HPV vaccine is currently available to males and females aged between 9-26 years through participating primary schools and health centres. The immunisation programme is school based, targeting all students in year 7 or 8. Three doses are given, ideally at zero, three and six months [5]. There does not appear to be a reduction in vaccine efficacy if the intervals between doses are longer [6].

[1] Three dose coverage for female cohort born in 1993 [15]
[2] Three dose coverage for female cohort born in 2003 [15]

The optimal age to receive the vaccine is early adolescence, before exposure to HPV through sexual contact. However, the programme funds vaccination up to age 26 to maximise population-level impact [1]. For adolescents and adults aged 13 to 26 years who have not been previously vaccinated or who have not completed the vaccine series, catch-up vaccination is recommended. Vaccination is still recommended in young people within the recommended age range who have evidence of prior HPV infection, as it can still provide protection against infection with HPV vaccine types not already acquired [7].

Clinical trials have found Gardasil, the HPV vaccine offered in NZ, is safe and highly efficacious [8]. Adverse events are usually minor and transient and include pain at injection site, fainting (usually needle-related) and dizziness [9, 10].

Very substantial reductions in the prevalence of vaccine-specific HPV have been demonstrated since the introduction of the HPV immunisation programme over 10 years ago (for females) and in 2017 (for males). In NZ, a 61% reduction in genital warts was observed seven years following programme commencement [11]. In Australia, where 3-dose coverage has surpassed 80% (for females), and (76% for males), a reduction of over 90% of young women with genital warts has been observed [12, 13].

Remarkable declines in high risk HPV are is leading to significant declines in cervical pre-cancers, providing very promising signs that cervical cancer elimination is possible in countries with organised population-based programmes, such as NZ [1, 14]. Provided vaccine coverage is high, equitable and sustained, it is estimated that HPV vaccination has the potential to prevent more than 2300 cases of cervical cancer and cervical pre-cancer per year [15] and reduce cancer inequities [16]. Cervical cancer incidence rates are approximately twice as high in Māori women compared with NZ European women. Increasing vaccine uptake has been identified as one of the most effective strategies to reduce cervical cancer disparities - a cancer control priority in NZ [16, 17].

Pharmacists as HPV vaccination providers: improving access and uptake for young New Zealanders

Increasing the uptake of the HPV vaccination is a key cancer prevention strategy in the New Zealand Cancer Action Plan 2019-2029 [17]. Uptake of required dose coverage needs to increase from 65% to 75% overall and needs to be consistently high (80%) in males and

females for a comprehensive reduction in HPV disease to be achieved at a population-level [18]. The observed three-dose coverage of the HPV vaccine was 61% among girls born in 1997 and 67% for girls born in 2003 (higher rates are observed in Pacific 73%, Asian 71%, Maori 67%, than for European/other 65%) [19].

The uptake rate for boys in New Zealand has been modelled at 53% [16]. As funding was only extended to males recently in 2017, the vast majority of eligible males will not have been vaccinated at school and relatively few will have been vaccinated in general practice. Vaccination rates in young adults, including those in higher risk groups, are much lower than younger cohorts [19].

Internationally, coverage among comparable countries has been very mixed – from 30% in USA to 80% in Scotland [20, 21]. Very low uptake in the US has been attributed to the reliance on delivery through medical providers and provider reluctance [22]. Although such obstacles may, in part, be overcome by education campaigns and school-based vaccine provision, it is clear from uptake data that many young people are missing out on this very important cancer prevention intervention. Parental ethical concerns over vaccinating children against a sexually transmitted infection have been identified as a barrier, along with limited access to and use of health care services among young people, and low awareness of HPV and the HPV vaccination [23, 24]

Community pharmacists are accessible health care professionals that are ideally placed to capture young New Zealanders of age of consent. Pharmacies are accessible by public transport and often have extended opening hours. Some meet certain youth-friendly criteria, including a private consultation area where informed consent can be sought [25]. As pharmacies can be found in multiple and convenient locations and may not require an appointment, they are in a good position to prompt walk-ins to consider vaccination. The provision of free services and advice is particularly important for disadvantaged high risk populations – groups that pharmacists have been successful at identifying for preventive health services in the past, including flu and measles vaccinations [26].

Support is strong among surveyed NZ pharmacists to play an expanded immunisation role, although lack of time, a clear reimbursement model and clarification of client vaccine status are some key issues that will need addressing [27]. For equity of access, to ensure the vaccinations reach the most vulnerable group, this service should be enabled as soon as

possible with funding. While we appreciate funding is not a consideration of the Medicines Classification Committee, we wish to highlight the importance of both availability and free availability to all eligible. Furthermore, given the large number of New Zealanders who are not currently vaccinated, and the benefits of vaccinating early to prevent HPV infection and cancer, this initiative should be implemented without delay.

In conclusion, community pharmacists can play an important role in achieving sustained high and equitable coverage of HPV vaccination among young New Zealanders. The Cancer Society supports pharmacist provision of HPV vaccinations to help meet NZ's goal vaccination rates and improve public health.

Helga Wientjes

Acting Chief Executive, Cancer Society of New Zealand

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Comments on Meeting 64th Agenda item 6.1 Reclassification of HPV
Loretta Roberts
to:
committees@health.govt.nz
28/02/2020 12:35 p.m.
Hide Details
From: "Loretta Roberts" <l.roberts@auckland.ac.nz>
To: "committees@health.govt.nz" <committees@health.govt.nz>,
History: This message has been replied to.

To who it may concern

We (IMAC) have no specific objections to the HPV9 vaccine being reclassified for intern and registered pharmacist to administer who has successfully completed a vaccinator training course approved by the Ministry of Health and who is complying with the immunisation standards of the Ministry of Health. However we do feel that this ongoing piece meal approach to reclassification of vaccines is not helpful, uses additional resources and creates system confusion. We advocate for an comprehensive Immunisation Strategy which includes the delivery of vaccines both funded and private purchase through pharmacy that could be considered with a more consistent approach.

Kind regards Loretta

IMMUNISATION ADVISORY CENTRE
THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau

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Immunisation on time every time

HPV in Pharmacy
[redacted]
to:
committees
25/02/2020 05:37 p.m.
Hide Details
From: [redacted]
To: committees@health.govt.nz,
History: This message has been replied to.

As an ex RNZCGP MCC committee member I have no issues with pharmacists providing adult vaccines as long as check lists are satisfied and they are linked in with NIR. The immunization handbook is not undemanding. Severe reactions however are rare.
GPs end up being de facto unpaid data collectors for the NIR which we accept as part of our role in primary care however we expect these vaccinators to also be integrated digitally with NIR.
General practice does not have DHB funded nursing staff so handwritten or faxed notifications are unacceptable and may well be voided.
Digital NIR notifications still require some work - often by the GP in fact not nursing staff - but the data reception and storage is not very onerous and is generally accepted as a part of international standard primary care provision.
ln an age if evolving high standard IT in healthcare, multispecialty service provision should ideally only be approved with suitable Ministry standardized data integration.
[redacted] DipObst DipPharm FRNZCGP

New Zealand AIDS Foundation
Te Tūāpapa Mate Āraikore o Aotearoa

The Medicines Classification Committee
Medsafe
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19 March 2020

Human Papillomavirus (HPV) vaccine – proposed change to the prescription classification statement

Thank you for the opportunity to comment on the Agenda Item 6.1 of the 64th Meeting of the Medicines Classification Committee.

The New Zealand AIDS Foundation (NZAF) is a registered charity and non-governmental organisation funded through contracts with the Ministry of Health and independent fundraising to provide a range of HIV and AIDS related services, including: HIV prevention and health promotion, HIV testing, counselling and support, research, policy, and information services.

We strongly support the application to reclassify the Human Papillomavirus (HPV) Vaccine in New Zealand to allow pharmacists who have successfully completed an approved vaccination course to provide this vaccine without a prescription.

Gay, bisexual and other men who have sex with men (GBM) are a community disproportionately affected by HIV in New Zealand and are a key community that NZAF works closely with. This community experiences a range of health disparities and inequities, of which HPV is one.

The HPV vaccine is an effective, safe, well-established and well-tolerated vaccine that protects against HPV-related cancers and genital warts. We strongly believe that allowing pharmacists to provide the vaccine without a prescription will help to increase awareness and uptake of the vaccine among communities that struggle to access primary healthcare and has the potential to counter some of the HPV-related health inequities experienced by GBM.

GBM are a population group that received little to no benefit from the female-only HPV vaccination programme as their sexual partners included or were exclusively male. Estimated rates of anal cancers among GBM are equivalent to those of cervical cancers prior to the introduction of screening programmes and is continuing to increase over time.[1] [2] Additionally, GBM may not consider HPV vaccination relevant to them as much of the health promotion has historically been focused on cervical cancer among females and more recently to their male partners.

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The current uptake of HPV vaccine is 67% in recent birth cohorts and is below the 75% target for 2017, with uptake amongst boys is similar to that seen among girls. Additionally, there is currently no measure of sexual orientation collected in administrative health databases to monitor uptake among GBM. Targeted cross-sectional surveys can provide an estimate of uptake among GBM and in the 2014 GAPSS and GOSS survey of GBM only 3% of those surveyed reported receiving the vaccine, however this was prior to public funding for males [3]. More recently, a local survey of GBM conducted by NZAF in 2017 reported that 87% had not received the Gardasil [4].

While this possible increase in uptake among GBM in NZ since to introduction of a gender-neutral programme is to be celebrated, uptake remains concerningly low among GBM in Aotearoa NZ and there remains uncertainty as to whether uptake among this group is comparable to their heterosexual peers.

Research data from the same survey in New Zealand shows that awareness of HPV amongst GBM is low, more than 51% were not aware that the Gardasil vaccine is available and helps to protect against HPV-related cancers and warts. Yet in spite of this, acceptability of the vaccine was high, with more than 85% of GBM reporting that they would get the HPV vaccine if it was provided for free.[5]

Extending the ability to provide HPV vaccinations to pharmacists has the potential to raise awareness of the vaccine and aid access for GBM. Pharmacies are well-placed to reduce barriers to accessing the HPV vaccine as they are convenient, community-based and don't require an appointment or enrolment. They also provide an alternative to existing services such as GPs and sexual health services that are already stretched in their capacity.

Research shows that half of GBM in New Zealand are not open with their GP about their sexual orientation or behaviour.[6] This barrier was reported more frequently among non-European ethnicities, likely due to issues in accessing and navigating healthcare as well as socio-cultural differences in stigma relating to non-heterosexual identities. While disclosure of sexual orientation is not necessary for accessing HPV vaccination, these data indicate that GBM experience difficulties accessing healthcare that specifically targets this population through primary care models, resulting in missed opportunities. Pharmacies provide another option for these communities and are often viewed as more accessible than primary care.

Beyond our community of focus, there continues to be a large cohort of males (and females) who have missed out on the school-based programme and should be encouraged to receive the vaccine while still eligible for funding (up to age 26). There is also likely to be 9-12 year olds who are not captured through the current HPV school program. We recommend that there should be no minimum age to ensure the widest coverage of the HPV vaccine. We feel that mixed messaging around the age eligibility of the vaccine may be confusing for parents and those trying to access the

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[4] NZAF (2017) Ending HIV survey (unpublished)

[5] NZAF (2017) Ending HIV survey (unpublished)

[6] Ludlam A, Saxton P, Dickson N, Hughes A. General practitioner awareness of sexual orientation among a community and internet sample of gay and bisexual men in New Zealand. Journal of Primary Health Care. 2015;7(3):204-12

vaccine and should be avoided where possible. This is required to meet the targets New Zealand has set for HPV vaccine uptake and ensure equity of access.

Thank you again for the opportunity to feed back. Please do not hesitate to contact our Senior Policy Officer, Kate Macpherson at kate.macpherson@nzaf.org.nz should you require clarification on any of the points made.

Warm regards,

Jason Myers
Chief Executive

NEW ZEALAND COLLEGE OF
PUBLIC HEALTH MEDICINE

19 January 2020

Submission to the Medicines Classification Committee: Human Papillomavirus Vaccine Reclassification Application

The New Zealand College of Public Health Medicine would like to thank the Medicines Classification Committee for the opportunity to make a submission on item *6.1 Submission for reclassification of the Human Papillomavirus (HPV) vaccine*, from the agenda of the upcoming Medicines Classification Committee meeting on 14 May 2020. [1]

The New Zealand College of Public Health Medicine (the College) is the professional body representing the medical specialty of public health medicine in New Zealand. We have 223 members, all of whom are medical doctors, including 178 fully qualified Public Health Medicine Specialists with the majority of the remainder being registrars training in the specialty of public health medicine.

Public Health Medicine is the branch of medicine concerned with the assessment of population health and health care needs, the development of policy and strategy, health promotion, the control and prevention of disease, and the organisation of services. The NZCPHM partners to achieve health gain and equity for our population, eliminating inequities across socioeconomic and ethnic groups, and promoting environments in which everyone can be healthy.

General Comments

The College supports the proposed changes to the classification statement for the HPV vaccine i.e. to allow pharmacists who have successfully completed an approved vaccination course to provide this vaccine without a prescription.

We believe this reclassification would increase awareness and uptake of the HPV vaccine in older eligible age groups and therefore help attain the 75% vaccination target presumed to achieve herd immunity from the infection.

We assert that increased uptake of the vaccine, as a consequence of the reclassification, will in turn promote better health outcomes such as a decline in genital warts and cancers, critically cervical cancer, caused by HPV.

Making the vaccine available through community pharmacies will reduce access barriers to the HPV vaccine and promote equity of access to the vaccine in high deprivation and rural areas, especially when supplemented with applied funding.

Improved coverage of vaccinations will promote equity in HPV-related cervical cancer outcomes for Māori, Pasifika and Asian groups who are over-represented in the incidence of cervical cancer and under-represented in cervical smear tests.

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The College believes that permitting pharmacists to administer the vaccination is ultimately in the best interest of public health and health equity.

Background

HPV is a very common carcinogenic infection which gives rise to cervical, anal, oropharyngeal and vulvar cancers as well as genital warts.[2, 3] The HPV vaccine is a well-established, effective and well-tolerated vaccine with a key public health role in preventing infection, cancer and genital warts.[4, 5, 6] The HPV vaccine has been funded in NZ since 2008 and is now funded in females and males up to the age of 26 years.[7] The vaccine is generally administered around age 12, in schools or at a General Practice (GP), as it is most effective when given prior to sexual debut (although later provision is also beneficial).[8]

The College is generally supportive of the applicant's submission that sets out the proposed changes to the classification statement for the HPV vaccine.[1] We briefly highlight the public health arguments which support the reclassification of the HPV vaccine below.

Specific Issues

Improved uptake and outcomes

Current uptake of the HPV vaccine in New Zealand sits at 67% in recent birth cohorts (girls born between 1990 and 2003).[9] This falls short of the 75% coverage target, by December 2017, set for all District Health Boards.[10] Herd immunity from the carcinogenic HPV infection is expected at about 75-80%, and increasing coverage is important to provide more individuals with protection from this effective vaccine and reduce the incidence of the infection, genital warts and cancers.[11] In particular, increasing coverage of the HPV vaccine is an important step towards minimising HPV-related cervical cancers. Every year in New Zealand cervical cancer occurs in around 160 women and kills 50 women.[3, 12]

While uptake of the HPV vaccine has been gradually increasing, data shows a levelling off in the last five years for which complete data is available.[9] This is despite a recall system being set up in general practice from 2014. Furthermore, most eligible males are unvaccinated, given their funding and school-based programme only started in 2017.

We also note that 'Increase the uptake of HPV vaccinations' is an action under the goal of 'Prevent cancers related to infection' in the New Zealand Cancer Action Plan 2019-2020.[13] Therefore, there is a need to consider another mechanism, to boost coverage of the HPV vaccine, for instance through pharmacy provision.

Increased accessibility and awareness

Making the HPV vaccine available from pharmacies will help improve accessibility to and awareness of the vaccine and hence increase its uptake in target populations i.e. young people.

Community pharmacists are very accessible health professionals; all pharmacies must have a pharmacist on-site when open, they tend to have longer hours of operation, they are conveniently placed in the community and they do not require appointment or enrolment. Increasing numbers of pharmacists are becoming trained in vaccine administration. The public is becoming increasingly

familiar with vaccinations in pharmacy and consumer satisfaction with pharmacy vaccinations is reportedly high, with appreciation of the convenience and flexibility of hours, particularly for working age individuals and adolescents.[14, 15, 16, 17]

Research shows that adolescent and young adult males are often unaware or misinformed about HPV vaccine recommendations, which is likely affecting their uptake of the vaccine.[18] This is likely to also be true in New Zealand where there is no known figure for overall uptake of HPV in males, but it is expected to be very low. Provision of the HPV vaccine through pharmacies will enable pharmacists to raise the topic of the vaccine opportunistically when patients come in for other reasons.

Equity

Evidence shows that ethnic and socioeconomic inequities exist in the distribution of cervical cancer and cervical smear tests as well as geographical inequities to accessing health services. Provision of the HPV vaccine through pharmacies, if funded, will work to address these disparities and promote equity of access.

Māori, Pacific and Asian women have disproportionately high rates of cervical cancer, compared with their European counterparts. This is primarily because they are under-represented in cervical screening rates (68% for Māori, 66% for Pasifika and 61% for Asian, versus 76% for European/other), which provide an early warning of precancerous lesions.[19] Similarly, when compared by deprivation quintile, the least deprived group in New Zealand sits at 82% coverage contrasted with the most deprived group, which sits at only 57% coverage.[20]

Very few New Zealand women who have been diagnosed with cervical cancer have had the necessary screening according to the New Zealand guidelines, with Māori, Pacific peoples and those living in the most deprived areas, least likely to have done so.[21] Increasing coverage of the HPV vaccine is crucial to minimising HPV-related cervical cancer. Pharmacy provision of the HPV vaccine will aid in protecting the most vulnerable from HPV infection, either directly or through herd immunity and is a step towards achieving equity in New Zealand's cervical cancer rates.

Young New Zealanders living in rural areas are another group who are likely to benefit from being able to receive an HPV vaccine in pharmacies. Those living in rural and remote areas face significant access barriers to attending GP clinics, including transport times, cost of travelling long distances, limited hours of operation of rural clinics and long wait times.[22, 23] In the recent meningococcal W outbreak in Northland, pharmacy was successfully used to aid adolescent uptake of the meningococcal vaccine.[24] Pharmacies delivered a substantial proportion of the total vaccinations given, and it was estimated that the number of vaccinations provided per pharmacy would have been substantially higher than the number delivered by general practice. With a large proportion of Northland teenagers being located in rural locations, it was concluded that quickly implementing pharmacies as an additional location and resource is a logical choice.

We believe that providing the HPV vaccine at community pharmacies, and supplementing this with funding, is equity enhancing and has the potential to increase uptake amongst young New Zealanders.

Thank you for the opportunity for the NZCPHM to submit on the Human Papillomavirus Vaccine Reclassification Application. We hope our feedback is helpful and are happy to provide further clarification on matter covered in this submission.

Sincerely,

Dr Felicity Dumble, President, NZCPHM

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New Zealand Medical Association
Te Hauora mō ngā Iwi Katoa

18 March 2020

Medicines Classification Committee Secretary
By email: committees@health.govt.nz

Agenda for the 64th meeting of the Medicines Classification Committee

Dear Sir/Madam

The New Zealand Medical Association (NZMA) wishes to provide comment to the Medicines Classification Committee (MCC) regarding item 6.1 (Human Papillomavirus (HPV) vaccine) on the agenda for the 64th meeting scheduled for 14 May 2020. We note this item relates to an application for the reclassification of the HPV vaccine to allow pharmacists with approved training to provide this vaccine without a prescription.

While we are not opposed to the proposed reclassification of HPV per se, and support measures to increase the uptake of HPV vaccine, we are concerned by some of the claimed benefits that are being touted to support the reclassification. In particular, as a claimed benefit to the health system, the application identifies pharmacies being able to help out with vaccine stock where a General Practice has run out, with influenza vaccine as an example of where this has occurred.

Vaccine supply issues have been a major concern for General Practice twice over the past year—for MMR during last year's Auckland outbreak, and for the 2019 flu season. We question the extent to which flu vaccination by pharmacies contributed to the interruption of flu vaccine supply to General Practice. Many patients at higher risk of complications and hospitalisation missed out on their flu vaccination last year due to stock and supply issues while fit and well individuals were able to present directly to a pharmacy to pay for, and receive, flu vaccination. It is difficult to accept that this represents a benefit to the health system. We ask the Committee to consider at what point vaccine supply to pharmacies compromises supply to General Practice, and how this gets resolved.

Yours sincerely

K. Baddock

Dr Kate Baddock
NZMA Chair

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THE PAEDIATRIC SOCIETY OF NEW ZEALAND

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Medicines Classification Committee
Medsafe
New Zealand Medicines and Medical Devices Safety Authority
PO Box 5013
Wellington 6145

25 March 2020

Dear Sir/Madam,

HPV Reclassification Application

On behalf of the Pharmacists and Therapeutics Special Interest Group of the Paediatric Society of New Zealand, I would like to comment on the above submission.

We agree with the application to widen access to HPV vaccination to community pharmacists and pharmacy interns. We support option one allowing HPV to be classified as a 'Prescription Medicine, except when administered by a registered pharmacist or registered intern pharmacist who has successfully completed a vaccinator training course approved by the Ministry of Health and who is complying with the immunisation standards of the Ministry of Health'.

This application would widen access especially in communities where access to any and timely GP visits is limited. We acknowledge the data presented from other countries where pharmacists are able to administer HPV vaccines. We are supportive of measures to increase safe access to timely and opportunistic vaccinations.

Yours sincerely,

Louise McDermott
Chairperson,
Pharmacists and Therapeutics SIG
Paediatric Society of NZ

This letter is supported by members of the Pharmacist and Therapeutics Special Interest Group
This letter is supported by Dr Tony Walls, Chair PSNZ Infection and

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists

Excellence in Women's Health

17 March 2020

Medicines Classification Committee
committees@health.govt.nz

Human Papillomavirus (HPV) vaccine
Proposed change to the prescription classification statement
64th Meeting of the Medicines Classification Committee | 14 May 2020

Thank you for the opportunity to provide a submission on the changes to the HPV vaccine classification, proposed by the Pharmaceutical Society of New Zealand, the Pharmacy Guild of New Zealand and Green Cross Health.

About the Royal Australian and New Zealand College of Obstetricians and Gynaecologists

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) is a not-for-profit organisation dedicated to the establishment of high standards of practice in obstetrics and gynaecology and 'excellence in women's health'. The College trains and accredits doctors throughout Australia and New Zealand in the specialties of obstetrics and gynaecology. The College also supports research into women's health and advocates for women's healthcare by forging relationships with individuals, the community, professional organisations and government.

In New Zealand RANZCOG's Te Kāhui Oranga ō Nuku supports College activities, taking into account the context of the New Zealand health system and the needs of women in Aotearoa New Zealand. A particular focus of Te Kāhui Oranga ō Nuku, and its sub-committee He Hono Wāhine, is recognising Māori as tangata whenua and supporting initiatives that will improve equity of outcomes.

Feedback on the proposed reclassification of the HPV vaccine

RANZCOG supports the reclassification of the HPV vaccine to allow pharmacists who have successfully completed an approved vaccination course to provide this vaccine without a prescription. Further we support the proposed Option 1 (or 4) that allows pharmacists to administer at any age in line with the immunisation standards of the Ministry of Health (currently at or above 9 years of age). RANZCOG does not have a view on the suitability of registered intern pharmacists being included or excluded from the change.

Cervical cancer remains a significant cause of cancer morbidity and mortality in women throughout the world. Persistent infection with oncogenic Human Papilloma Virus (HPV) is associated with the development of cervical cancer. Infection with oncogenic HPV types is also implicated in the development of other cancers, including vulva, vagina, anus, penis, as well as some head and neck cancers. Of the

oncogenic HPVs, types 16 and 18 account for about 70% of cervical cancers.[1] Non-oncogenic HPV types 6 and 11 cause genital warts. HPV infection is common with an estimated 70-80% of sexually active women worldwide becoming infected at some stage in their life.[234] The use of HPV vaccines prevents infection with vaccine-related HPV types, and has been shown to reduce the incidence of precursor (pre-malignant) lesions and, potentially, malignant cervical cancer.

In clinical trials Gardasil vaccine demonstrated high efficacy against all included HPV types in both males and females. Many studies have now been completed confirming the high efficacy of Gardasil 9.[56]

In countries with high HPV vaccine coverage, such as Australia and Denmark, there has been a profound reduction in the number of genital wart cases. Data collected by the Victorian Cervical Screening Register indicates a reduction in the incidence histologically confirmed high-grade cervical abnormalities since the introduction of the HPV vaccine in women aged under 20, and 20-24, and that this decrease is becoming manifest in the 25-29 age group. In young women, there has been a decline in incidence of almost 75%.[7]

RANZCOG notes that anaphylaxis after HPV vaccination occurs about 1–3 times in every million vaccine doses. No other serious responses to the vaccine have been identified. Most adverse reactions after vaccination are minor (injection site reactions, fever, headaches, dizziness, muscle pain).

RANZCOG Statement (C-GYN-18) 'Guidelines for HPV vaccine' recommends that *Participation in the HPV Vaccination Program should be encouraged for all eligible boys and girls in the National programs in Australia and New Zealand.*

A key part of encouraging participation in HPV vaccination programmes is ensuring good access to vaccination. RANZCOG notes that New Zealand has an effective school vaccination programme. We believe that a wide variety of options for accessing vaccines is helpful in increasing uptake. International evidence, and New Zealand experience around update of influenza vaccination, indicates that ability to access vaccines through pharmacies increases uptake. We note that trained pharmacists already deliver a number of other vaccines including influenza, Tdap, meningococcal and MMR.

As well as uptake of vaccinations through pharmacies, we believe that ability to be vaccinated in a pharmacy will increase awareness of HPV vaccination, through pharmacy promotion - irrespective of where people chose to actually be vaccinated.

RANZCOG supports a change to the reclassification of the HPV vaccination that does not impose age restrictions, beyond those in the Ministry of Health's immunisation standards, on pharmacy administration. We note that effectiveness of HPV vaccination is optimal when the vaccine is given under 15 years of age, and prior to onset of sexual intercourse. While there is potential for concern about the impact of pharmacies administering the HPV vaccine on the school programme, we support providing broad (safe) access to the vaccine and choice in how the vaccine is accessed.

Other considerations

We note that in Australia there is evidence that participation in the cervical screening programme has declined among women since the introduction of the National HPV Vaccination program. Cervical screening recommendations should be followed regardless of vaccination status. We suggest this means there is a need to promote continued cervical screening, alongside vaccination.

If you need further information on any of the comments above please contact me through Catherine Cooper, RANZCOG New Zealand Manager at ccooper@ranzcog.org.nz.

Ngā mihi

Dr Celia Devenish
Chair, Te Kāhui Oranga ō Nuku

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24 March 2020 Our ref: KV20-079

Jessica Lo
Medicines Classification Committee (MCC) Secretary
Ministry of Health

via email: committees@health.govt.nz

Kia ora Jessica

Agenda for the 64th meeting of the Medicines Classification Committee (MCC) to be held on 14 May 2020

Thank you for giving The Royal New Zealand College of General Practitioners the opportunity to comment on the Agenda for the 64th meeting of the Medicines Classification Committee (MCC).

The Royal New Zealand College of General Practitioners is the largest medical college in New Zealand. Our membership of 5,400 general practitioners comprise almost 40 percent of New Zealand's specialist medical workforce. Our kaupapa is to set and maintain education and quality standards for general practice, and to support our members to provide competent and equitable patient care.

Submission

The College wishes to comment on Agenda item 6.1 Human Papillomavirus Vaccine. This is a submission from the Pharmaceutical Society of New Zealand, the Pharmacy Guild of New Zealand and Green Cross Health proposing changes to the classification statement for human papillomavirus vaccine. The current classification of human papillomavirus vaccine is prescription. These organisations are requesting a reclassification of the Human Papillomavirus Vaccine in New Zealand to allow pharmacists who have successfully completed an approved vaccination course to provide this vaccine without a prescription.

HPV vaccination

HPV vaccination has the potential to reduce the incidence of cervical cancer, head and neck cancers and genital warts. Cervical cancer rates among Māori are considerably higher than among non-Māori. The age standardised registration rate for cervical cancer in 2016 was 10.9 per 100,000 Māori women compared to 5.8 per 100,000 among non-Māori women.[1] Increasing the coverage of HPV vaccine can be expected to reduce the ethnic disparity in cervical cancer incidence in addition to reducing the overall incidence of cervical cancer.

Delivery of vaccinations by pharmacists.

Currently pharmacists who have completed the appropriate training and are working in sites with appropriate equipment can deliver several vaccines without a prescription being needed. While the College supports moves to increase the coverage of HPV vaccination, members expressed some concern at the proposal to add HPV to the list of vaccines that can be delivered by appropriately trained and equipped pharmacists. Our members alerted us to several issues that they are experiencing with other pharmacist vaccinations. As a

[1] https://www.health.govt.nz/publication/selected-cancers-2015-2016-2017 accessed 20/3/2020

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result of experiencing these issues members are less supportive of the proposal than they might otherwise have been. These issues are outlined later in the submission.

In addition, the following factors related to the HPV vaccine are of particular concern:

- The implications of a multi dose vaccine
- The implications for sexual health.

Implications of a multi dose vaccine

Two doses of vaccine, or in the case of people aged 15 and over three doses, are required to complete vaccination against HPV. As almost all other immunisations delivered by pharmacists require only one dose of vaccine, this is a new situation for pharmacists. Recall of young people will be challenging as they are often mobile. General practice is already accustomed to recalls. Recalls can be resource intensive however and practices will be reluctant to devote scarce resources to contacting patients who have not returned for further doses if they believe the person has had the vaccination elsewhere. With multiple providers and poor communications, GP practices will be disincentivised to devote resources to follow up and unsure whose responsibility it is to follow up a patient who is not recorded as having completed the full course of injections.

Implications for sexual health

HPV immunisation can be an important segway into sexual health and contraceptive discussions. Young people are usually well so often not familiar with accessing general practice. HPV protects against an infection that is usually sexually transmitted, so HPV vaccination provides an opportunity to open conversations with young people around sexual health, and contraception. Conversations around substance harm minimisation, mental health, sexual and domestic violence can also develop.

These are consultations that general practitioners are trained for. General practitioners are familiar with support services and management and can make appropriate referrals if needed. These consultations are appropriate in general practice but not in pharmacies. The pre vaccination checklist and consent form does not screen for sexual health and related concerns either, and in a pharmacy environment this is probably not appropriate.

Despite the desire to see good uptake of HPV, GPs consider that the potential loss of this opportunity to address health issues in younger people needs to be considered by the Medicines Classification Committee when they make their recommendation.

Reported issues with pharmacist vaccinations

We sought to understand the perspectives of members on this issue and surveyed members on their experiences. Forty percent of the 62 respondents to our survey stated that they or their practice had experienced problems associated with pharmacist vaccinations.

Lack of communication between GPs and Pharmacists was the most frequently reported issue. GPs reported not knowing whether patients have received vaccines from pharmacist. There were reports of vaccinations being repeated when practices were unaware the vaccine had already been given by a pharmacist. Even when the vaccine was recorded on the National Immunisation Record (NIR) this information did not appear to flow through to the practice management system. On some occasions, it was necessary to query the NIR to obtain this information and it took one to two days before these queries were resolved.

Members also reported clinical concerns. In one case a vaccination was reportedly given in the wrong tissue plane and wrong muscle., Members also cited frequent reports from patients that they have been allowed to leave very soon after the vaccine is given.

In another instance, there was a report of a local pharmacy which experienced a power cut having no cold chain failure policy, nor alternative storage and no external temperature monitor. There were also accounts of general practice being called upon to urgently manage adverse reactions including anaphylaxis following pharmacist administered vaccines. The current requirements seem to clearly require pharmacies to have cold chain accreditation or compliance and all vaccinators need to be able to administer intramuscular adrenaline in the event of an anaphylactic reaction to an immunisation event. [2] [3] It is possible that some of the incidents reported may have predated this requirement but the public needs to have confidence that standards are being adhered to.

A further concern relates to the vaccination event being an opportunity to sell extras such as vitamins that are unnecessary. There was a general concern expressed that pharmacists were not adhering to the frameworks around UTI and erectile dysfunction medications. This led to a loss of confidence that the pharmacy sector was adhering to the guidance provided. A Ministry of Health (MOH) audit reported in 2018 also suggests that guidance has not been followed.[4] Since that time the MOH has strengthened its auditing process and it is suggested that this has resulted in some improvements. [5]

Conclusion

The College considers that there is a role for pharmacist provision of HPV vaccine in those aged 16 and over. This change should be implemented however only after the renewed NIR becomes operational to allow adequate communication and effective recall to occur.

We hope that you find our submission helpful. If you have any questions, or would like more information, please email us at policy@rnzcgp.org.nz

Nāku noa, nā

Karen Vaughan
Head of Stakeholder Relations

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[4] https://www.pharmacytoday.co.nz/article/news/audits-highlight-issues-around-correct-supply-sildenafil Accessed 16/3/2020
[5] https://www.medsafe.govt.nz/profs/PUArticles/September2019/Pharmacy-quality-audits.htm

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19 March 2020

The Secretary, Medicines Classification Committee
Medsafe
PO Box 5013
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New Zealand

Sent by email: committees@moh.govt.nz

Dear Sir/Madam,

Re: Response to public consultation for the Medicines Classification Committee Agenda for 64th meeting – Item 6.3 Pholcodine

Thank you for the opportunity to comment on the agenda for the 64th meeting of the MCC. Consumer Healthcare Products Australia would like to provide some comment on item 6.3 of the agenda on the proposed reclassification of pholcodine from Pharmacy Medicine to Restricted Medicine.

CHP Australia is the leading voice and industry body for manufacturers and distributors of consumer healthcare products, which includes non-prescription medicines. We strive to advance consumer health through responsible Self Care and were previously known as the Australian Self Medication Industry (ASMI). Our key priorities for the industry include improving health literacy, growing the consumer healthcare products industry and increasing access to medicines where appropriate.

Most sponsors that market pholcodine products in Australia also market these same products in New Zealand and are members of both CHP Australia and NZSMI. Most of these products are currently harmonised across both markets as pharmacy medicines, with the same finished product characteristics as well as labelling where possible. The ability to market harmonised products is very important given that both Australia and New Zealand are relatively small markets individually. Some sponsors choose not to market unique Australian or New Zealand products, due to the detrimental impact on the cost of goods and the increased cost burden on consumers. A single product harmonised across both markets is important for economic viability for both countries.

Medsafe and the MCC acknowledge the importance of harmonisation and we refer in this context to the MCC's statement on general principles of Trans-Tasman Scheduling Harmonisation here.

We also refer the MCC to the submission made by NZSMI (New Zealand Self Medication Industry) and would like to make the MCC aware that any change to the classification of pholcodine in New Zealand may have an impact in Australia.

In summary, CHP Australia's position is that:

- The classification of pholcodine should not be changed
- There is no evidence of concerns regarding misuse or abuse in Australia or New Zealand
- Regarding the hypothetical association between pholcodine use and anaphylactic reactions to neuromuscular blocking agents (NMBAs) during surgery, there are many uncertainties and inconsistencies and a causative effect has not been demonstrated
- Pholcodine products have been marketed for decades in Australia, New Zealand, the UK and many other European countries, and there have been no new or emerging clear safety signals regarding cross sensitivity with neuromuscular blocking agents
- There are many other products that feature the molecular structure thought to be responsible for the reactions (quaternary ammonium ions, QAI) – these products include personal care items, cosmetics, disinfectants and many more and there is no certainty that pholcodine is the causative factor.
- The EMA has reviewed the evidence and determined that no changes to access of pholcodine is needed due to the many uncertainties and inconsistencies in the available evidence
- More research is needed to understand the inter-relationship between pholcodine, other compounds that feature a QAI as part of the molecular structure, and NMBAs and anaphylaxis.
- Any decision to reclassify pholcodine before an accurate understanding of this complex issue is premature
- Based on the data provided by Medsafe, reclassification is a disproportionate regulatory action

CHP Australia does not support the proposal to reclassify pholcodine. The majority of consumers use pholcodine products safely and responsibly and there is no new evidence of safety concerns, to change the existing benefit/risk balance.

Any change to the classification in New Zealand would have consequences for Australia as it would significantly impact the ability of sponsors to supply harmonised products across both markets.

Thank you for considering this submission.

Yours sincerely,

Julie Viatos

Quality Use of Medicines Manager

Medicines Classification Committee Agenda for 64th meeting – Item 6.3 Pholcodine

Consumer safety is of paramount concern to CHP Australia and our members, however we do not believe that the submission put forward by the MCC and Medsafe justifies re-classification of pholcodine to Restricted Medicine.

Like all medicines, pholcodine has risks and benefits. Labelling requirements and supply from a pharmacy can mitigate risk and pharmacists and pharmacy assistants also play an important role in educating consumers about risk. However, medicines also have benefits – and consumers should be able to easily access medicines in order to relieve minor ailments that are recognisable and able to be self-managed by the consumer.

CHP Australia believes that the proposal to reclassify pholcodine to Restricted Medicine is not consistent with the evidence provided in the submission and is disproportionate to the known risks.

Need for OTC access of cough medicines as part of self-care

Acute cough is a prevalent condition, especially as it relates to the common cold. It is one of the most common reasons for visiting a pharmacy or self-selecting an OTC medicine. The majority of New Zealanders and Australians choose an OTC cough medicine to relieve cough; indeed self-care for symptoms of viral coughs and colds has been recommended in order to decrease utilisation of antibiotics (See NICE https://www.nice.org.uk/guidance/GID-NG10116/documents/draft-guideline).

Acute cough is regarded as a minor symptom and tends to be trivialised, but availability of cough relief is important because people's daily routines can be impaired. In conditions such as temporary post-viral inflammatory cough, the cough can be troublesome and persistent but not necessarily contagious, and access to effective OTC cough products can alleviate some of the discomfort. Consumers are familiar with navigating and self-selecting in the pharmacy cough and cold category.

One of the consequences of reclassification to Restricted Medicine is that there will be no options for dry cough available as Pharmacy Medicines at the front of counter. With dextromethorphan now a Restricted Medicine and the commercial viability of some unique New Zealand labelled dextromethorphan products now being questionable, consumers' options for relief of dry cough will be very limited should pholcodine also be reclassified, forcing sponsors to re-examine the volumes and commercial viability of their product ranges.

Another possible consequence is that consumers may instead select other, possibly unsuitable options, e.g. "chesty cough" products for dry cough, or products that have a very poor evidence base such as homeopathic products.

An unintended consequence of this may be the inappropriate increased pressure on busy pharmacists, who will in the coming winter months be facing increased workload. GPs are also under-resourced and making appointments in a timely manner can sometimes be difficult. Making changes to further restrict access to familiar well-established products that have a history of safe use could result in increased pressures and costs on the healthcare system.

In Australia, all OTC medicines containing pholcodine are Schedule 2 (Pharmacy Medicines). As such, these products must be kept close to the pharmacy professional area, so that consumers can self-select under supervision from pharmacy assistants, but without the need for the pharmacist to be involved with every purchase. Pharmacists are available for advice if needed. All of the important information required for safe use is on the label.

The information provided by MARC and Medsafe as part of the risk/benefit review (here) raises the following concerns leading to their conclusion that reclassification is the only appropriate course of action:

- Pholcodine is an old medicine – there is a lack of safety and efficacy data
- Possible association between pholcodine use and anaphylactic reactions to neuromuscular blocking agents (NMBAs) during surgery
- The requirement for patient information
- There is "marginal" benefit compared to risk

CHP Australia believes that Medsafe's recommendation that reclassification is appropriate is disproportionate to the level of risk, and that consumers should be able to continue to access pholcodine as a Pharmacy Medicine, with advice available at the point of sale as needed.

We will address each of the above points separately.

Safety and Efficacy – Pholcodine is an old medicine

Pholcodine was developed in the 1950s. It is a grandfathered medicine. CHP Australia acknowledges that the clinical studies are not well designed and controlled in comparison to recently developed medicines using modern standards. However, we do not agree with Medsafe's conclusion that because it is an old medicine, it has "assumed efficacy" and that consumers who use pholcodine experience "unproven widely perceived benefit" (p 51, MARC report, 5th December 2019). There are many grandfathered medicines that continue to be used and the long history of use is reassuring from a safety point of view.

We acknowledge that the lack of demonstrated efficacy of pholcodine is a factor of the age of the medicine and this can make it difficult to ascertain benefit in comparison to risk (p. 2 Medsafe summary). However we also believe that consumers who do not benefit from a medicine will not continue to purchase and use it.

Pholcodine has a long history of use and a well-established, favourable safety profile. A search of the TGA Database of Adverse Event Notifications (DAEN) was conducted, for the period 1971 until December 2019. Some key points from the results of this search are:

- The search covered 23 products, some of which included combinations that are no longer available and products that have been discontinued
- Over this period, there were 189 adverse event reports, with 146 being reports from a single suspected medicine
- There were no reports of intentional product misuse
- There were no reports of drug dependence
- There were no reports of intentional or unintentional overdose
- There were three reported deaths, and these were classed under various MeDRA adverse reaction classification terms, that include thyroid cancer, drug interactions, cardiac disorders, cardiomegaly, toxicity to various agents, lower respiratory tract infection and tracheo-oesophageal fistula
- The most commonly reported adverse events involved general disorders, gastrointestinal disorders, nervous system and psychiatric, skin disorders, respiratory disorders
- Some reports of allergy and anaphylaxis were reported
- There were no observed patterns of misuse, abuse or other adverse event trends

Considering the very high volume of products used over the past three to four decades, the Australian DAEN reports do not indicate any new safety concerns or trends that ought to trigger any change to the classification of the medicine.

CHP Australia does not believe that there are any new or emerging safety signals for pholcodine.

<u>The Pholcodine Hypothesis: Pholcodine and anaphylactic reactions to Neuromuscular Blocking Agents</u>

The Medsafe and MARC submission papers refer to the hypothetical association between rare, severe allergic reactions to neuromuscular blocking agents during surgery and previous pholcodine exposure, providing summaries of some of the studies and data on this issue.

The concerns are based on observations performed over several years by a Swedish / Norwegian team of researchers who found that withdrawal of a particular pholcodine containing product (Tuxi) in Sweden and Norway resulted in an apparent decrease in reports of NMBA related anaphylaxis.

The European Medicines Agency published an assessment report for pholcodine in 2012[1], reviewing the safety and efficacy of pholcodine as well as the pholcodine-NMBA anaphylaxis hypothesis.

The key findings of this review were that:

"*the evidence in support of an association between pholcodine and NMBA related anaphylaxis is circumstantial, not entirely consistent and does not support the conclusion that there is a significant risk of cross-sensitisation to NMBAs and subsequent development of anaphylaxis during surgery. Further data needs to be generated to clarify the possibility of an association between pholcodine use and NMBA-related anaphylaxis*."

The report concluded that the benefit/risk balance of pholcodine-containing products in the treatment of non-productive cough is positive under normal conditions of use, and that no changes to access were required. Regarding the hypothetical association between pholcodine and anaphylaxis to NMBAs, the EMA believes that further research is required as there are inconsistencies that do not support the association.

There are some uncertainties and inconsistencies that are difficult to reconcile with the pholcodine / NMBA anaphylaxis hypothesis.

There is strong evidence that quaternary ammonium ions (QAI) are the allergic determinants in NMBAs. These molecules are present in many other drugs as well as foods, cosmetics, disinfectants, and industrial materials. It is possible that predisposed individuals may be sensitised to undetermined QAIs and thus potentially be at risk. The possible causative factor(s) are uncertain, and the possibility remains that unrecognised environmental factors may also play a role. There is a wide range of possible sources for sensitisation to NMBAs[2].

There are some additional concerns with the pholcodine hypothesis. The gender difference between males to females (from 2:1 to 4:1) is unexplained; it is possible that there are other factors involved such as an environmental trigger (e.g. cosmetic use).

In a study investigating the prevalence of specific IgE to quaternary ammonium ions in two populations professionally exposed to quaternary ammonium compounds in north-eastern France, it was found that exposure to hairdressing professional occupational factors, such as quaternary ammonium ion hairdressing products, increased IgE-sensitization to NMBAs compared to bakers and a control group, indicating that occupational and environmental exposure to these compounds may be a factor[3].

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[1] EMA/78398/2012 Assessment report for Pholcodine containing medicinal products. February 2012. http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Pholcodine_31/WC500124716.pdf

[2] Mertes PM et al. Hypersensitivity reactions to neuromuscular blocking agents. Curr Pharm Des. 2008;14(27):199-211

[3] Dong S et al. Prevalence of IgE against neuromuscular blocking agents in hairdressers and bakers. Clin Exp Allergy. 2013 Nov;43(11):1256-62

In a multicentre study that examined the pholcodine hypothesis[4], the consumption of pholcodine containing cough medicines was compared to the prevalence of IgE antibodies to pholcodine, morphine and suxamethonium (a NMBA). The findings showed some inconsistencies, in that the Netherlands and the USA that do not have pholcodine products on the market, had some high figures of IgE sensitisation. The USA, where no pholcodine is consumed, showed similar levels of IgE sensitivity as the UK, where pholcodine is readily available and widely used as an OTC cough suppressant. Of the four countries with antibodies to suxamethonium, two (the USA and Germany) have no pholcodine consumption.

Further uncertainty on the association between pholcodine use and NMBA anaphylaxis is cast by the observation that despite the absence of pholcodine from the US market, 2% of the sera from US samples had positive IgE antibodies to pholcodine. This result is unexpected and raises questions about either the test accuracy and specificity or the validity of exposure data (p. 39, MARC report 5th Dec 2019).

The incidence of anaphylaxis in surgery is extremely low. Some studies based in Australia and France have estimated the overall incidence to be between 1 in 10,000 and 20,000 procedures. The low number of reports can present difficulties in studying the effects of individual drugs.

The EMA, in its 2012 review, concluded that the existing evidence for risk is weak and that the benefits of pholcodine continue to outweigh its risks. The EMA did not recommend reclassification in 2012, and since the time of publication of the EMA review no new evidence has come to light that would change that conclusion. The MARC/Medsafe have not provided any new evidence as part of the reclassification submission. Without new evidence to displace the EMA conclusions it is difficult to see how the MCC can reasonably come to a different conclusion to the EU.

Much of the research surrounding the pholcodine hypothesis was conducted between 2005 and 2011, i.e. around 10 – 15 years ago, however the most recently published data do not strengthen the evidence of a causal relationship between pholcodine use and NMBA-induced anaphylaxis. The finding that hairdressers and baker's apprentices demonstrated a higher frequency of positive IgE against QAIs suggests that exposure to other environmental agents may contribute to sensitisation.

Given the availability of pholcodine as a Pharmacy Medicine for many decades in both Australia and New Zealand, we are concerned that very little evidence regarding incidence of anaphylaxis with NMBAs has been provided in the Medsafe reviews. Given the volumes of product supplied over time, it is reasonable to expect more robust data would have been generated, taking into account the rarity of these adverse events.

CHP Australia therefore believes that although NMBA anaphylaxis is a serious concern, reclassification of a medicine based on a hypothetical association and ignoring the possibility that other environmental agents may be a factor, is a disproportionate regulatory action. CHP Australia believes that the evidence base does not support the

[4] Johansson et al. National pholcodine consumption and prevalence of IgE-sensitization: a multicentre study. Allergy 2010 Apr;65(4):498-502

reclassification of pholcodine to Pharmacist Only medicine. We query whether focussing on pholcodine as the causative factor in anaphylaxis with NMBA agents is a potentially risky strategy in giving a false sense that this serious issue is somehow being proactively addressed.

Requirement for patient information

CHP Australia supports the provision of timely, easily accessible and accurate information to enable consumers to use their medicines safely.

However, on the issue of pholcodine specifically, CHP Australia believes that the current labelling on the product provides all the necessary information for safe use of the product. Additional warning statements are difficult to word in a simple, accurate and consumer friendly way. The issue of the hypothetical association of pholcodine with anaphylaxis to NMBA is complex and difficult to condense into a concise and effective consumer statement, whether for the label or the Consumer Medicine Information (CMI).

We are aware that in the UK some Patient Information Leaflets (PILs) include wording to the effect of "*Tell your doctor or pharmacist if you or your child are having surgery, as muscle relaxants used may react with this medicine*". While consumer awareness is important, these statements do not provide consumers with context and certainty and may serve to confuse. For example, how long after taking the medicine should a consumer report that they are taking the medicine? Most consumers will act upon that warning statement while they are taking the medicine.

Although pharmacists are required to counsel consumers when supplying Restricted Medicines, they generally do not provide CMI for Restricted Medicines and there is uncertainty and variability as to whether and how individual pharmacists will convey information on this hypothetical association, and whether consumers will understand this information.

Anaphylaxis during surgery is a serious concern. Patients can experience anaphylaxis in response to other drugs used during surgery, e.g. antibiotics, opiates as well as NMBAs. The data sheets for NMBAs already contain warnings regarding anaphylactic reactions and anaesthetists and staff routinely question patients regarding the medicines they use. These healthcare professionals are best placed to interpret this complex issue and advise patients accordingly.

CHP Australia cautions against taking a simplistic approach to this issue and drawing unsupportable conclusions regarding cross-sensitisation with pholcodine, which cannot be supported by the evidence to date.

Overall benefit vs. risk

As stated above, the age of pholcodine means that it is impossible to quantify its efficacy benefit using current standards and clinical trial designs. However, the long history of use as a Pharmacy Medicine shows that when used for its intended purpose of symptomatic relief of dry cough, pholcodine has a well-established safety profile consistent with an over the counter medicine.

Regarding the pholcodine hypothesis, the review conducted by the EMA as well as MARC and Medsafe indicates that there is no evidence of a causal relationship between pholcodine use and cross sensitivity to NMBAs.

It is therefore impossible to objectively characterise benefit vs risk due to the uncertainty in both domains.

Medsafe has proposed reclassification despite this uncertainty, citing additional reasons around the need for consumer information to be delivered by the pharmacist. However, CHP Australia believes that more research is needed, together with increased vigilance by healthcare professionals and sponsors, who are best placed to provide raw data on the incidence of anaphylaxis to NMBA, whether affected patients had a history of consuming pholcodine, together with an analysis of the kinds of cosmetics and personal care products these patients used. Sponsors have an obligation to comply with pharmacovigilance reporting requirements.

CHP Australia therefore believes that there is no strong case for reclassification and it is not the appropriate measure to address concerns regarding uncertain benefit and hypothetical risk of cross sensitivity to NMBAs. It is disproportionate, has an impact on pharmacy practice, on consumer choice, as well as on the commercial viability of these products in both Australia and New Zealand. No recent events have occurred, that would otherwise prompt reclassification and no new evidence of risk has been presented that would support reclassification. We can see no obvious pressing concerns for which reclassification is the only or most appropriate solution.

20 March 2020

The Secretary
Medicines Classification Committee
Medsafe
P.O. Box 5013
WELLINGTON 6145

Sent by email: committees@moh.govt.nz

Re: Public Comment - Agenda for the 64th Meeting of the Medicines Classification Committee

Item 6.3: Proposal for reclassification of pholcodine from a pharmacy medicine to a restricted medicine

Executive Summary

iNova Pharmaceuticals (iNova) does not support the proposal to reclassify pholcodine to restricted medicine status.

Pholcodine has been the standard of care for dry non-productive cough since the 1950s. Any consideration of the available pholcodine efficacy data must therefore be made within the context of its longevity of use. Patients continue to return to pholcodine-containing products when suffering from a dry cough, which strongly advocates for their efficacy, as acute cough is an obvious and irritating symptom and a person can quickly ascertain following self-medication whether their cough improves or not. This position agrees with that of the EMA following a thorough review of pholcodine safety and efficacy which was published in 2012 (1):

> *'….the existing data is consistent and supportive of the efficacy of pholcodine in the treatment of non-productive cough.'*.

From a safety perspective, pholcodine is generally considered to be a well-tolerated molecule which has a predictable adverse event profile (refer to Review of Reported Safety Data Section). Pholcodine usage levels have risen over time, however, as outlined in this document, despite this rise in usage there were no detectable safety signals, trends, or changes in frequency of reporting observed with pholcodine that would be considered to modify its safety profile.

There is limited literature which suggests the potential for allergic cross-reactivity between pholcodine and Neuromuscular Blocking Agents (NMBAs) used in anaesthetic procedures, however, the data gathered is suggestive, not conclusive, as summarised by the European Medicines Agency (EMA) in 2012 (1). Since this publication there have been relatively little new data published (although there have been many reviews of the pre-existing studies). The limited new data that is available has not clarified the issue, instead additional confounding factors have been added e.g. patients showing cross-reactivity to NMBAs who have not been exposed to pholcodine or showing potential cross-reactivity following exposure to common household and/or occupational products (2-6).

Consequently, the current pharmacy-only medicine classification, which has been in place for many years, provides adequate supervision of patients who need advice regarding management of their cough and the appropriate use of cough medicines. Restricting access to products containing pholcodine further reduces the empowerment of patients to manage their minor ailments, will have a negative impact on the availability of pharmacists and physicians, and, accordingly, the New Zealand health system – particularly at a time when it will be under increasing pressure due to the likely demands of COVID-19 infections. This proposal will present greater difficulties for sick patients to readily and quickly access medicines which, due to their longevity of use in an acute indication, can be seen to provide relief from dry cough. Furthermore, the proposal is contradictory to the international movement to downregulate medicines, an area in which New Zealand have previously been a leading proponent (7).

[redacted]

Studies examining the impacts of cough and cold clearly demonstrate the negative economic and health implications of these conditions, further bolstering the argument that it is important to maintain easy access to medicines which may be used to alleviate them (9, 10).

The Medicines Classification Committee has a history of being rigorous and evidence-based in their decision making and seeking clear data and conclusions. The evidence to support an allergic cross-reactivity between pholcodine and NMBAs is uncertain and must be carefully considered within the context of the value pholcodine has provided to patients over many years for dry cough relief. Should there be lingering concerns with respect to a possible, unproven, link to cross-reactive anaphylaxis with NMBAs, then it would be most appropriate, at least in the first instance, for this to be addressed by the addition of warning statements into the corresponding NMBA product datasheets, the provision of appropriate physician education and materials, and/or an increase in active pharmacovigilance measures.

Introduction

iNova wishes to comment on the NZ Medicines Classification Committee (MCC) agenda item 6.3 – the proposed reclassification from a pharmacy-only medicine to a restricted medicine for pholcodine.

Pholcodine is a cough suppressant that acts primarily on the central nervous system (CNS) causing depression of the cough reflex, partly by a direct effect on the cough centre in the medulla. Pholcodine has a mild sedative effect, with little or no analgesic action (11).

Pholcodine is structurally related to morphine, however, therapeutic doses of pholcodine do not cause depression of respiration, CNS excitation, or other side effects associated with narcotics. Pholcodine has a selective effect on the cough centre without affecting the respiratory centre (11).

Pholcodine is not euphorigenic and there is no evidence of physical dependence after prolonged administration of pholcodine, consequently it is not proposed to be habit forming (11). Indeed, the Medicines Classification Committee recommended up-scheduling morphine for cough (Gee's linctus) to prescription medicine on this basis in 2018 but were not concerned about this for pholcodine.

[redacted]

The Medsafe Proposal and Pholcodine

The current proposal for reclassification of pholcodine to a restricted medicine has been prompted by the Medicines Adverse Reactions Committee (MARC), who undertook a review of the efficacy and safety data available to support pholcodine at their 180th meeting on the 5th of December 2019. The MARC consider that the evidence for pholcodine efficacy is weak, whilst also acknowledging that adequate safety studies for pholcodine are similarly lacking. The MARC posit that post-marketing adverse reaction reporting data from the Centre for Adverse Reactions Monitoring (CARM) indicates that the main risk is allergic-type reactions to pholcodine, including anaphylaxis. Furthermore, the MARC indicate that there is some ecological evidence 'that suggests (but does not confirm) an association between pholcodine and anaphylaxis to NMBAs' (12).

The quantity and quality of published efficacy studies available to support the use of this molecule in the treatment of dry cough would be mirrored by almost all 'grandfathered' type active ingredients in their corresponding indications, as current requirements for supportive clinical efficacy and safety studies were not in place when this product was initially developed and marketed. However, the limited studies that are available do support a mechanistic role for pholcodine in the treatment of dry cough (13-19).

It should also be noted that, if a similarly high bar were applied to all 'grandfathered' products currently available then there would be a dramatic reduction in the number of older, but valuable, products in the pharmacist's and physician's armamentarium. Think, for example, of lithium for bipolar disorder.

The safety argument mounted against the pharmacy-only availability of pholcodine, even in the documents submitted by the MARC, is hypothetical, being based primarily on a range of small studies conducted by a single research group in the European Union between 2005 and 2011 (12). It is critical to note that the EMA undertook a full review of the available information in 2012, which concluded that, at that time, the benefit risk balance for the active ingredient was appropriate and that no amendments to scheduling or availability were required (1).

At the time of writing the EMA's position has not changed.

Subsequent to the EMA review, few further studies have been published in this area, and those that have been published have not further clarified the relationship between pholcodine and NMBAs, as it would seem that 'pholcodine' antibodies can be present in subjects who have not been exposed to pholcodine and that cross-reactivity to NMBA's may be equally hypothetically initiated by a range of readily available household materials (2-6).

Impact on Affected Products

[redacted]

[redacted]

Reclassifying pholcodine as a restricted medicine would require a significant volume of product to be stored behind the counter and create additional workload for pharmacists. Given the absence of convincing reported or published evidence to support the proposition that pholcodine definitively causes cross-reactivity to NMBAs, as acknowledged in the MARC proposal, the benefit of reclassification to both public health and the individual patient is dubious and does not outweigh the negative impact on pharmacy management and patient inconvenience. As pharmacy-only medicines these products already have some degree of oversight from a healthcare professional, which helps ensure that the products are safely, effectively and appropriately used. As outlined in forthcoming sections of this document there are a range of activities which would be more appropriate, and likely effective, in containing/understanding this hypothetical risk.

Review of Efficacy Publications

iNova undertook a systematic literature search to accumulate data relating to the efficacy of pholcodine for use as a cough suppressant for the temporary relief of non-productive dry cough.

The literature sources identified in this search are presented in Table 2.

Table 2. Clinical Efficacy Literature – Adults				
Author, API	**Study Design**	**No Subjects (n)**	**Dose**	**Outcome**
Snell, E. Armitage P. (1957) (13) Diamorphine Pholcodine	Randomised placebo controlled trial	n = 45; Adult patients with chronic bronchitis, pulmonary new growth, bronchiectasis, mitral stenosis and chronic pulmonary tuberculosis	Diamorphine - 1.6 mg/mL, approximately 7 mL/24 hr Pholcodine – 4 mg in 7 mL/24 hr	Diamorphine and pholcodine were considered equally effective. Both were deemed more effective than placebo.
Bickerman, HA. Itkin, SE. (1960) (14) Pholcodine	Double blind, randomised, placebo controlled trial	n = 16; Healthy adult subjects. (Induced cough)	Homarylamine (10-40 mg) Pholcodine (10 mg) Benzonatrate (40 mg) Dihydrocodeinone (5 mg) Methadone (2.5 mg) 4964U (30 -60 mg) 9558U (7.5 mg)	A 10 mg pholcodine dose showed significant cough suppression over the 4 hour test period.
Mulinos, MG. Nair, KGS. Epstein, EG. (1962) (15) Codeine phosphate Pholcodine	Observational Placebo controlled trial	n = 28; Adult patients with chronic cough due to asthma or upper respiratory tract infection. n = 49 Adult patients with chronic cough	10 mg pholcodine (6 times daily, tablet) 10 to 20 mg pholcodine or codeine phosphate (2 – 6 times daily) in one group of 23 patients. In a second group each dose was administered once per day, in the evening.	26 subjects showed marked improvement, with relief being assessed as better than achieved with placebo. Clinical superiority of pholcodine and codeine over placebo was evident. Pholcodine was preferred over codeine by subjects. No patients preferred placebo treatment.

Rose, JR 1967 (16) Pholcodine Pseudoephedrine	Double blind crossover comparison	n = 45; (35 Male, 10 Female) with chronic respiratory disease causing breathlessness and cough	Pholcodine 15 mg + pseudoephedrine Codeine phosphate 15 mg	Trial preparation was effective in relieving cough and breathlessness in more patients than the control and produced significantly greater overall clinical improvement.
Edwards, GF. Lewis, HE. Stafford, D 1977 (17), Pholcodine Phenyltoloxamine	Double blind Randomised controlled trial	n = 24; Adult patients with chronic bronchitis	Pholcodine 30 mg / 24h (15mg bid – Syrup) Phenyltoloxamine 20 mg / 24 h (10 mg bid Syrup)	Pholcodine plus phenyltoloxamine together reduced cough (as measured by frequency of cough in 24 hours) by more than 50%. Pholcodine alone did not impact cough.
Belcher, N. Rees PJ. 1986 (18) Pholcodine Salbutamol	Randomised, placebo controlled, double blind trial	n = 10; Healthy adult subjects (induced cough)	Pholcodine 1 mg/mL / 24 hr Salbutamol 0.4 mg/mL /24 hr	Pholcodine significantly increased the cough threshold when given alone ($p < 0.05$)
Equinozzi, R. Robuschi, M. 2006 (19) Pholcodine Dextromethorphan	Randomised, double blind, parallel group, multicentre trial	n = 129; Adult subjects with acute, frequent, non-productive cough	Pholcodine 19.65 mg, or Dextromethorphan bromidrate 19.95 mg In a syrup formulation (tid for 72 hours)	A reduction of 1.4 and 1.3 points in the mean daytime cough frequency at Day 3 was seen in the pholcodine and dextromethorphan groups, respectively, in the per-protocol population. The reduction in mean night-time cough was 1.3 for both groups. Cough intensity reduction was 0.7 for pholcodine and 0.8 for dextromethorphan

The studies presented in Table 2 demonstrate the centrally-acting cough suppressant properties of opiates, and show that pholcodine has been used in this indication since the 1950's. As a 'grandfathered' molecule, the methodology used in most of these efficacy studies may be considered of low quality by modern standards. Most studies were not adequately controlled, either with active or placebo medications, and some were performed using combination products, which makes it difficult to isolate and measure the efficacy of the single component pholcodine. No study has been performed on the long-term effects of pholcodine, although it should be noted that pholcodine is generally indicated for the temporary relief of non-productive cough, a self-limiting condition, and thus long-term data would not be expected to be available.

These concerns should be tempered by the fact that all studies which were conducted with appropriate populations and in relevant, acute, indications demonstrated efficacy of pholcodine, in several cases over placebo. Furthermore, there are no available well-designed studies that would suggest that pholcodine is not effective in the approved indication.

Consequently, it seems likely that pholcodine is effective. This is further supported by fact that this active ingredient has high usage for cough in New Zealand and Australia. Acute cough is an obvious and irritating symptom and a person can quickly ascertain following self-medication whether the cough improves or not.

This position agrees with that published by the EMA in 2012 (1):

> *'….the existing data is consistent and supportive of the efficacy of pholcodine in the treatment of non-productive cough.'*

Review of Reported Safety Data

[redacted]

Consequently, from the evidence available, it is difficult to extrapolate this information to a safety issue with pholcodine, or, more specifically, to the proposed reaction between pholcodine and NMBAs.

Should there be additional data pointing to a reaction between pholcodine and NMBAs, this should have been reported to CARM and be represented in the reported data.

For context and additional information, iNova undertook a search of the Medsafe Centre for Adverse Reactions Monitoring (CARM) reports for NMBAs, via the Suspected Medicine Adverse Reaction Search (SMARS). The resulting report shows the adverse event profile of serious reactions reported with NMBAs over the period 1st January 2000 and 19th February 2020. NMBAs are considered to be the trigger medication in the 'Pholcodine Hypothesis', and, from the data reported, show a generally high level of adverse reactions, particularly immunological or anaphylactic in nature. From the information reported no linkage to pholcodine is evident.

At this time, and based on the available data, no other action on safety grounds is warranted, beyond the drug safety activities proposed below.

Proposal for Action

iNova recommend that, prior to making significant changes to the classification of pholcodine, based on limited adverse event data for New Zealand, more should be done to proactively examine the safety of the molecule in the form of:

- enhanced pharmacovigilance activities, such as the generation of three-yearly PSUR documents,
- proactive seeking and provision of related published data to the authorities,
- enhanced review and evaluation of adverse events by CARM via M2 Medicines Monitoring.

Review of Safety Data from Published Literature

Pages 3 to 6 of the summary document submitted by MARC provide a summary of the 7 key papers available to support the 'Pholcodine Hypothesis'. Summarised in this MARC documentation are the key findings from each of the publications, and, critically, the issues, and challenges with each (12).

In the original study in 2005, Florvaag *et al.*, (20) suggested that consumption of pholcodine-containing syrups may be linked to the occurrence of anaphylactic reactions to the depolarizing NMBA, suxamethonium. It was observed that the occurrence of anaphylactic reactions to NMBAs was 6 times more common in Norway than in Sweden. Comparison was made to the prevalence of specific IgE to suxamethonium, pholcodine, and morphine in samples of patients from both

Sweden and Norway with suspected allergies, 500 blood donors from both countries and 65 Norwegian patients with documented anaphylaxis to NMBA.

The study demonstrated that in Norway 0.4% of the blood donors, 3.7% of allergy sufferers and 38.5% of patients suffering from anaphylaxis were sensitised to suxamethonium, and 5.0%, 10% and 66.7%, respectively, to morphine. No serum sample from Sweden was positive. It was established that several household chemicals present in the homes of study subjects demonstrated suxamethonium and/or morphine activity, but the only difference identified between Norway and Sweden was the existence in Norway of a cough syrup containing pholcodine. IgE antibodies to pholcodine were present in 6.0% of blood donors from Norway and in no serum from Sweden. Of the anaphylaxis sufferers, 65-68% were sensitised to morphine or pholcodine but only 39% to suxamethonium (20).

At no point does this study, or any of the subsequent work, definitively demonstrate that the presence of IgE antibodies to pholcodine has resulted in hypersensitivity reactions in the presence of NMBAs. Furthermore, it is important to note that, as is outlined in the datasheet for all currently available NMBAs and demonstrated in the adverse event data provided in Appendix 1, these molecules have a well-documented history of allergic reaction.

Much of the subsequent evidence purported to support an association between pholcodine and NMBA-related anaphylaxis derives from studies conducted by a single research team, and related groups, relying on spontaneously reported adverse reactions to NMBAs (which are, by their nature, reported at an extremely low level, some studies suggesting a level of 1 in 10,000, or 20,000 procedures).

The EMA published a thorough assessment for pholcodine in 2012 (1). This document undertook a full review of the safety and efficacy of pholcodine, whilst considering the available evidence for the 'Pholcodine Hypothesis'. The conclusions of this study were as follows:

> *..the evidence in support of an association between pholcodine and NMBA-related anaphylaxis is circumstantial, not entirely consistent and does not support the conclusion that there is a significant risk of cross-sensitisation to NMBAs and subsequent development of anaphylaxis during surgery.*

At this time the EMA proposed that the benefit-risk ratio for pholcodine was positive and that no changes in schedule or access were required.

There is evidence that quaternary ammonium ions (QAI) are the molecular component of NMBAs which cause the relatively high level of allergic reactions noted with these anaesthetic agents in normal practice. This molecular structure is also found in a range of drugs, foods, cosmetics, disinfectants and industrial materials – hence it is very possible that patients may become sensitized to this structural element via a range of occupational and household exposure routes (2).

In a recent study examining the prevalence of specific IgE to QAI in hairdressers and bakers in France it was determined that exposure to common occupational chemicals found in hairdressing products appeared to increase IgE sensitization to NMBAs, above the levels seen in both bakers and a control group (3). Interestingly, this appears to tie in with an additional apparent gender skew in cases, where females more commonly suffer from this kind of reaction than males.

This study also demonstrated that molecules other than pholcodine, which contain the QAI structure, can also raise the levels of IgE present in serum samples. Consequently, care clearly

needs to be applied prior to assuming that IgE antibodies found following allergic reactions are specific for only pholcodine.

In a multicentre study (4) that set out to examine the 'Pholcodine Hypothesis', the consumption of pholcodine-containing cough medicines was compared to the prevalence of IgE antibodies to pholcodine, morphine and the NMBA, suxamethonium. The findings of this study showed interesting inconsistencies, as patients from the Netherlands and USA showed high levels of IgE sensitization, despite not having pholcodine-containing products available in these countries. Study subjects from the United States also showed similar levels of IgE sensitivity to those from the UK, where pholcodine is available as an OTC product. Furthermore, of the four countries which demonstrated the presence of antibodies to suxamethonium, two (USA and Germany) have no pholcodine products available.

Katelaris *et al*., (5) also demonstrated that IgE to 'pholcodine' could be found in 1% of the samples tested in Japan and Korea where no pholcodine-containing products were available on the market.

It is also noted that in Norway, although there were a lower number of anaphylaxis reports after pholcodine was withdrawn, the severity of the reactions reported has not changed. Class II and III reactions still represent the majority of reported cases, exactly as when pholcodine was still marketed (1).

Furthermore, the absence of any report of IgE-mediated anaphylactic reaction to NMBAs in Sweden since 1990 raises further questions on the reliability of the data, as regardless of pholcodine use, NMBAs would still be expected to cause anaphylactic reactions and the Swedish data does not appear to reflect this expected background rate (1).

In countries with small populations, such as Norway and Sweden, where the original studies were conducted, confounding factors such as a change in anaesthetic procedures, type of products used in anaesthesia (including materials used in operations, such as latex and surface cleaners, povidone-iodine containing products [6]), differences in community use of products containing QAIs, and overall use of NMBAs could play a role in explaining the results obtained.

In conclusion with respect to the safety of pholcodine, there are no safety concerns with iNova pholcodine-containing products, either as a single active ingredient or as combination with other actives. This finding is in accordance with the cumulative experience and reference safety information for the respective products. No signs or signals of major safety concerns have emerged from reports or published literature describing the use as unfavorable or negative. No new safety findings have been identified through ongoing pharmacovigilance activities that have an impact on the overall safety profile of any iNova pholcodine products.

<u>Proposal for Action</u>

- Given the type and timing of the hypothetical interaction between pholcodine and NMBAs, iNova expects that physicians will be asking about a history of any allergy to medicines before administering anaesthetics, and if there is history of an allergy the physicians will be cautious. iNova contends that it may be logical to add an appropriate warning to the existing NMBA datasheets – alerting physicians of the theoretical possibility of cross-sensitivity and advising them to appropriately question and counsel patients prior to anaesthesia.
- This simple step could be easily coupled, if deemed required, with a note that suspected interactions should be reported to CARM and a campaign of physician education activities to ensure that appropriate dialogue and questioning was conducted at key points prior to treatment with NMBAs.

Health Economic Impacts – Patients and Pharmacists

Patients

A cough is inconvenient, and irritating. The Ministry of Health in NZ states that viral coughs can last for several weeks and often get worse at night (21). A cough can affect sleep for the sufferer and rest of the household. It can cause urine leakage in those prone to this problem. Very importantly, coughs can transmit infections.

People want to avoid coughing, and society benefits if they can stop or reduce coughs through reduced disease transmission, via fewer infected droplets being present in the air, on hands, and on surfaces. If people find that cough suppressants work for them, they should have reasonable access to them without excessive burden or cost. Cost to consumers is likely to increase for a restricted medicine given the additional work in recording patient details and need to involve the pharmacist for every purchase. Given a recession is likely, this will most affect those with the least money, reducing equity of access.

Several studies have been conducted which show the potential financial burden of cough and cold on society and demonstrate the need for symptomatic treatment to lessen the economic impacts on patient productivity and improve quality of life.

In 2015, Dicpinigaitis *et al*., published the results of a survey examining the impact of cough and common cold on productivity, absenteeism, and daily life in the United States (9). The study was designed as a 36-question online survey. In October 2012, 3333 study subjects were recruited into the study, of which 2505 were randomised as the primary analysis pool. Demographics and impact of cough/cold were reported using means, frequencies, and percentages.

Of those study subjects who responded, most (84.7%) had suffered from at least one cold in the previous year. Fifty-two percent indicated that the cough and/or cold had impacted upon their daily life, whilst other key measures included a reported reduction in productivity by a mean of 26.4%, whilst 44.5% indicated that the cough/cold had caused 1-2 days out of the office or school.

Such levels of absence from the workplace do have a significant financial impact. A study undertaken to quantify the cost of respiratory tract infections in the USA found that when survey results of 4,051 respondents who experienced cough in the past year were extrapolated to the population, the total economic burden approached $40 billion annually. This included $22.5 billion in indirect costs (productivity losses), per year (10). Although these results were obtained in the United States it could reasonably be assumed that the data obtained may be extrapolated to countries such as New Zealand, where it would equate to costs of over $500 million per year.

Ninety three percent of survey participants reported some sleep difficulty during a cough/cold, whilst 57% reported cough or nasal congestion as the symptoms making sleep difficult. The authors acknowledged that a higher frequency of colds, more cold symptoms, difficulty sleeping, and worse overall health status correlated with greater impact on productivity, absenteeism, and daily life (9). Consumer research conducted by iNova has demonstrated that of all of the symptoms associated with winter illness, consumers are most debilitated by cough and feel this has a high negative impact on daily life (22).

Thus, it can be concluded that it is to the benefit of patients with cough and colds and the greater economy to have ready access to short-term treatments to alleviate cough symptoms.

Pharmacists

At the present time products containing pholcodine are scheduled as pharmacy-only. This means that pharmacists and their staff already have interaction with, and oversight of, patients seeking cough medications.

[redacted]

Based on the above, it is hard to see what additional consumer protection could be achieved by the proposed up-scheduling of pholcodine without placing undue stress on limited pharmacist resources (both space and time).

Conclusion

iNova contend that the current proposal to amend the scheduling of pholcodine to a restricted medicine is not rational based on the evidence available at the present time.

Despite an increase in the level of pholcodine usage in the New Zealand market over time, there is no suggestion that the benefit-risk ratio of pholcodine has changed in recent years and the hypothetical risk of cross-reactivity to NMBAs has not been conclusively demonstrated. Conversely, since the EMA performed their review in 2012 the relationship between pholcodine and NMBA cross-reactivity has only become more confused.

Furthermore, with the recent emergence of COVID-19, and increased levels of pressure on health resources worldwide, iNova questions whether it is an appropriate juncture to even consider reducing self-select patient options for dry cough treatments. At this time, permitting patients access to medicines to address their own, mild, cough symptoms could only be of benefit to a health system which will be under increasing pressure in coming months.

iNova proposes that, should there be remaining concerns regarding the hypothetical interaction between NMBAs and Pholcodine, there are steps that it would be more rational to undertake prior to rescheduling and removing consumer access to one of the few cough products which remains in the front of shop environment. The proposed actions are as follows:

- Perform enhanced pharmacovigilance activities, such as the generation of three-yearly PSUR documents,
- Proactively seek and provide related published data to the authorities,
- Undertake enhanced review and evaluation of adverse events by CARM via inclusion on the M2 Medicines Monitoring.
- Add an appropriate specific warning to the existing NMBA datasheets – alerting physicians to the proposed hypothetical interaction and advising that questioning and counselling of patients should be undertaken prior to anaesthesia.
- Conducting physician education activities to ensure that appropriate dialogue is conducted at key points prior to treatment with NMBAs.

Based on the information available at present, the current pharmacy-only classification provides an appropriate degree of patient oversight to ensure responsible use of pholcodine. iNova recommends rejection of the proposal to reclassify pholcodine to a restricted medicine and retention of the status quo.

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Appendix 1 – Contextual Safety Data Obtained from CARM

NMBAs

for Rocuronium between 1 Jan 2000 and 19 February 2020

Number of reports for Rocuronium: 323

Number reports where death was reported: 3

Number of reactions: 623

System Organ Class	MedDRA Reaction Term
Cardiac disorders	Bradycardia
	Cardiac arrest
	Myocardial infarction
	Supraventricular tachycardia
	Tachycardia
	Ventricular fibrillation
Eye disorders	Periorbital oedema
Gastrointestinal disorders	Abdominal pain
	Gastrointestinal necrosis
	Gastrooesophageal reflux disease
	Salivary hypersecretion
	Tongue oedema
General disorders and administration site conditions	Drug interaction
	Infusion site rash
	Therapeutic response decreased
Immune system disorders	Anaphylactic reaction
	Anaphylactic shock
	Anaphylactoid reaction
Investigations	Allergy test positive
	Drug specific antibody present
	Oxygen saturation decreased
	Skin test negative
	Skin test positive
Musculoskeletal and connective tissue disorders	Myalgia
Nervous system disorders	Brain hypoxia
	Cerebrovascular accident
	Depressed level of consciousness
	Dizziness
	Generalised tonic-clonic seizure
	Memory impairment
Respiratory, thoracic and mediastinal disorders	Apnoea
	Bronchospasm
	Cough
	Dyspnoea
	Laryngeal oedema
	Laryngotracheal oedema
	Pulmonary embolism
	Respiratory depression

for Suxamethonium between 1 Jan 2000 and 19 February 2020

Number of reports for Suxamethonium: 191

Number reports where death was reported: 3

Number of reactions: 342

System Organ Class	MedDRA Reaction Term
Cardiac disorders	Bradycardia
	Cardiac arrest
	Myocardial infarction
	Myocardial ischaemia
	Tachycardia
Gastrointestinal disorders	Oedema mouth
Immune system disorders	Anaphylactic reaction
	Anaphylactic shock
	Anaphylactoid reaction
Investigations	Allergy test positive
	Blood creatine phosphokinase increased
	Blood immunoglobulin E abnormal
	Drug specific antibody present
	Hepatic enzyme increased
	Oxygen saturation decreased
	Skin test negative
	Skin test positive
Musculoskeletal and connective tissue disorders	Rhabdomyolysis
Nervous system disorders	Amnesia
Respiratory, thoracic and mediastinal disorders	Apnoea
	Bronchospasm
	Hypoxia

Johnson & Johnson Pacific

20th March 2020

Medicines Classification Committee
Medsafe
PO Box 5013
Wellington 6145

Dear Sir/Madam,

Re: Agenda for the 64th meeting.
Item 6.3 Pholcodine - reclassification from a Pharmacy Medicine to a Restricted Medicine (Medsafe)

Johnson & Johnson (New Zealand) Limited (JJNZ) appreciates the opportunity to provide comment on agenda item 6.3 Pholcodine, which is a Medsafe submission proposing to reclassify Pholcodine from a Pharmacy Medicine to a Restricted Medicine.

JJNZ does not support the reclassification proposal for Pholcodine to a Restricted Medicine as there is no new evidence and the body of evidence has **not changed** since the Medicines Classification Committee (MCC) made the decision at the 61st meeting of the MCC that the pholcodine classification **remained appropriate,** (November 2018).

At this meeting, the MCC reviewed the classification of pholcodine and other opiate-related cough and cold medicines due abuse potential. They also considered pholcodine and its potential association with cross-sensitivity with neuromuscular blocking agents (NMBAs). The MCC confirmed that pholcodine has limited potential for abuse and limited potential with the rare but fatal association with anaphylaxis and NMBA's. The MCC concluded that pholcodine had minimal safety concerns and that the current classification of Pharmacy Medicine remained appropriate. However, Medsafe was requested to review the risk-benefit profile as well as efficacy of pholcodine, because it is a grandfathered medicine.

Classification is based on a risk-benefit profile, and either the benefit or the risk would need to shift in order to deem the profile to be unfavourable. It is important to note that the review conducted by

Medsafe and MARC did not identify any new evidence either from an efficacy or safety perspective to shift the risk-benefit profile since the MCC decision in November 2018 that deemed pholcodine to have appropriate classification.

The MARC discussed the ecological evidence for an association between pholcodine exposure and an increased risk of anaphylaxis to NMBAs and agreed that it is suggestive but not conclusive. They considered that the evidence of an unfavourable risk-benefit profile balance is currently insufficient to warrant withdrawal of pholcodine from the New Zealand market, but raise the following issues, which are not evidenced based, to justify the conclusion that reclassification is an appropriate action:

- Possible association between pholcodine use and anaphylactic reactions to NMBAs during surgery
- Pholcodine is an old medicine – there is a lack of safety and efficacy data
- Requirement for pharmacist intervention necessary

<u>Possible association between pholcodine use and anaphylactic reactions to neuromuscular blocking agents (NMBAs) during surgery</u>

Based on available literature (also included in the Medsafe submission), it is suspected that primary IgE sensitization could occur in substances carrying a quaternary ammonium ion epitope structure (other than NMBA). Therefore cross-reactivity appears to be the quaternary ammonium ion epitope that is also found in pholcodine and is thought to potentially increase the risk of NMBA-induced anaphylaxis. However, the quaternary ammonium ion epitope is also found in many other compounds such as antihistamines, anti-anxiety agents, anti-hypertensives, parasympathomimetics, and narcotics. It is therefore clear that there are still unknown factors which needs to be explored before any reclassification decisions can be made. This position is very well acknowledged in literature, by health authorities such as the European Medicines Agency (EMA), TGA as well as Medsafe and previously, the MCC.

As previously discussed by the MCC, and included in the Medsafe submission, the EMA scientific discussion and conclusion, which formed the basis to make no regulatory changes, was because it put into question the findings from Johansson SGO et al. 2009 and 2010 studies (which is also included in Medsafe submission) where a team of researchers in Norway raise the possibility that high consumption of cough mixtures was related to increased prevalence of IgE antibodies to pholcodine, morphine and suxamethonium, and ultimately higher incidence of IgE-mediated anaphylactic reactions to NMBAs. Researchers concluding that withdrawal of pholcodine from the market in Norway significantly lowered within 1-2 years levels of IgE and IgE antibodies to pholcodine and within 3 years, the frequency of NMBA suspected anaphylaxis. Data from Sweden where pholcodine has not been marketed since the 1980's is indicative, like in Norway, that the level of IgE-sensitisation to pholcodine had been decreasing over time in parallel to a decrease in the number of NMBA-related anaphylaxis cases[1].

However, the EMA raise questions about these studies, as the observed decrease in reporting does not actually reflect lower occurrence. It is also noted that in Norway that although there is a lower number of anaphylaxis reports since pholcodine was withdrawn, the severity of the reactions has not changed, therefore possible that the observed decrease in reporting does not actually reflect lower occurrence. A broad range of other agents may also be responsible such as household products, the EMA note that this could explain why data from countries such as the USA or the Netherlands does not fit with the pholcodine 'hypothesis' as in these countries pholcodine is not marketed, and still prevalence of IgE to pholcodine was found to be high.

An ad-hoc expert group composed mainly of immunologists and anaesthesiologists was consulted to provide advice to CHMP on this issue. The group had split views about the strength of the evidence of an association between pholcodine exposure and allergic reactions to NMBAs, although it was agreed that this is an issue that warrants further investigation. The EMA review concluded:

"the evidence in support of an association between pholcodine and NMBAs related anaphylaxis is circumstantial, not entirely consistent and does not support the conclusion that there is a significant risk of cross-sensitisation to NMBAs and subsequent development of anaphylaxis during surgery. Further data needs to be generated to clarify the possibility of an association between pholcodine use and NMBA-related anaphylaxis."

There are some additional concerns with the pholcodine hypothesis. The gender difference between males to females (from 2:1 to 4:1) is unexplained; it is possible that there are other factors involved such as an environmental for instance - cosmetic use.

In a study investigating the prevalence of specific IgE to quaternary ammonium ions in two populations professionally exposed to quaternary ammonium compounds in north-eastern France, it was found that exposure to hairdressing professional occupational factors, such as quaternary ammonium ion hairdressing products, increased IgE-sensitization to NMBAs compared to bakers and a control group, indicating that occupational and environmental exposure to these compounds may be a factor[2].

The possible causative factor(s) are uncertain, and the possibility remains that unrecognised environmental factors may also play a role. There is a wide range of possible sources for sensitisation to NMBAs[3].

In Australia the above issue was also discussed, and the TGA shared EMAs view that further data is needed to establish the link between pholcodine and NMBA related anaphylaxis. Therefore JJNZ believes that any reclassification decision is premature and not based on new compelling evidence that would shift the risk-benefit profile of pholcodine. Considering the high volume of products used over the past decades, the Australian DAEN reports do not indicate any new safety concerns or trends that warrants the change to the classification of the medicine. Pholcodine has had many years of safe use in New Zealand and Australia which is also reflected in the Company Adverse Events reporting.

While the MARC agreed that the link is suggestive but not conclusive, they agreed that the possibility of an association between pholcodine and anaesthetic anaphylaxis warranted regulatory action in order to limit unnecessary exposure to the medicine. However, this approach is heavy handed, it will not necessarily address the route problem and a disproportionate regulatory action. A more suitable regulatory approach would be to ensure consumer education through labelling means. The risk of anaesthetic anaphylaxis due to pholcodine cross sensitisation is rare therefore should not have a regulatory approach above what is required for other contraindications and precautions where label warnings are considered a suitable measure.

JJNZ believes that NMBA anaphylaxis is a serious concern, however labelling options should be considered before reclassification given the evidence has not changed, and that there is the possibility of other environmental substances that may be a factor. No new evidence has been provided to the MCC to change the MCC decision from the 61st meeting in 2018.

Efficacy

The MARC consider the fact that that pholcodine is a "grandfathered" medicine is a reason to warrant the reclassification to Restricted Medicine, to ensure it is only used by those who may potentially benefit from its use. This position assumes that only a small population base benefit from pholcodine which is unfounded and not consistent with the available evidence, especially given the restriction on cough suppressants in New Zealand. Just because it is an old medicine, doesn't mean it has "assumed efficacy" and that consumers who use pholcodine experience "unproven widely perceived benefit" (p 51, MARC report, 5th December 2019).

Although Pholcodine was developed in the 1950s it has a long history of safe use and there are many clinical studies to support this. In fact, there are many medicines that are grandfathered that continue to be safely used and have a long history of safe use. Further, there is no new evidence regarding pholcodine's efficacy to suggest the benefits should be put into question shifting the risk-benefit profile.

JJNZ maintains that as discussed above, the decades of established efficacy and safe use is indicative of the benefits pholcodine provides.

Other options before reclassification

Given the risk-benefit profile has not changed since the MCC decision in 2018, which concluded the classification of pholcodine remained appropriate, the MCC needs to consider whether reclassifying pholcodine to a Restricted Medicine is justified, evidence based and addresses the potential problem.

NMBA anaphylaxis is a serious concern, however there are still a lot of uncertainties. Therefore, to address the plausible link to pholcodine, the MCC should consider the option of additional label warnings to alert consumers to the possible link with cross-sensitivity with NMBA's. This empowers the consumer to be more aware of the concerns (much like other serious contraindications and warnings included on a label) before use of the product. The label is the most logical place, as unlike a leaflet or datasheet, the information always remains on the label whenever the product is used. Further, given the problem manifests prior to surgery, there may also be more opportunities to ensure clinicians ask patients about the use of cough suppressants or other over the counter medications/ cosmetics known to have the quaternary ammonium ion epitope, prior to surgery.

Another important consideration for the MCC to be aware of is that reclassifying pholcodine to Restricted Medicine will almost remove the dry cough option from the New Zealand over the counter marketplace. While Medsafe suggest that the Restricted Medicine classification will allow consultation with a pharmacist at the time of sale, the reality is that most of these products will be discontinued altogether if reclassification occurs.

If the same decision is made with pholcodine, contrary to the MCC position that there are other cough and cold products available, the New Zealand consumer will have almost no dry cough offering over the counter. This could have unintended consequences that the MCC needs to be mindful of. Restricting access to safe and effective pholcodine cough products is likely to eliminate dry cough products from over the counter access. It can drive consumers with dry cough into general practice and increase access to prescription products and this could have negative impact on the

public health system and the health budget at a time when over-utilisation of medical services is very difficult to control, and it may potentially drive the inappropriate prescribing and use of antibiotics. It can also drive people to use incorrect products (e.g. salbutamol or a wet cough products) simply because consumers cannot find a dry cough product, causing safety concerns.

Based on the above, JJNZ believes that in the absence of new evidence a reclassification decision is premature and not aligned with the approach taken by other similar regulatory agencies such as the EMA and TGA. The review conducted by Medsafe has not uncovered anything new to demonstrate a confirmed relationship between pholcodine use and cross sensitivity to NMBAs. This together with the fact that there is no new evidence that puts the efficacy of pholcodine into question, confirms that there has not been a shift in the risk-benefit balance since the MCC November 2018 decision to warrant such extreme regulatory action.

A reclassification decision also has the potential to impact on pharmacy practice, on consumer options adding additional risks. Pholcodine products have been safely used for decades for the self-limiting condition of dry cough. Other options such as additional labelling, [redacted] should be considered as a suitable regulatory approach.

[redacted]

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New Zealand
Self-Medication Industry
Association Inc.

The Secretary, Medicines Classification Committee Medsafe
PO Box 5013
Wellington 6145

New Zealand
Sent by email: committees@moh.govt.nz

From:

New Zealand Self Medication Industry Association Inc.
P O Box 6473
Auckland
New Zealand

Dear Sir/Madam,

Re: Response to public consultation for the Medicines Classification Committee Agenda for 64th meeting – Item 6.3 Pholcodine

The New Zealand Self-Medication Industry Association Inc (NZSMI) is the national trade association representing importers, manufacturers, marketers and distributors of a wide range of products, generally available "over-the-counter" (OTC) and mainly for use in self-medication by New Zealand consumers. NZSMI's mission is to promote better health through responsible self-care. This means ensuring that safe and effective self-care products are readily available to all New Zealanders at a reasonable cost. SMI works to encourage responsible use by consumers and an increasing role for cost-effective self-medication products as part of the broad national health strategy.

We appreciate this opportunity to provide feedback on this upcoming agenda item.

NZSMI will order its comments based on a view of the past, current and future treatment of this ingredient.

Old Medicine

It appears that one of the driving factors behind the current review of Pholcodine efficacy and safety is because of its age. Having been developed in the 1950's it is a grand-fathered ingredient and has been accepted as useful and safe for OTC supply by the regulator, to date. This is based on the very low incidence of side effects in relation to the hundreds of millions of doses consumed by patients who have either been prescribed or purchased Pholcodine.

By today's standards the research data on Pholcodine from forty and fifty years is frail. Much of it does not have placebo comparison or double blind implementation. Much of it was conducted with products containing combination active ingredients making it difficult to accurately define cause and effect to Pholcodine alone. And there is none since 2000. No single study measures up as definitive.

However, when read as a body of work there are valid conclusions. All conclude cough suppressant activity – none conclude ineffectiveness. Only products in combination recorded adverse effects; the rest either did not comment on any adverse effects or recorded no adverse effects. It is acknowledged that many of these studies have small samples, often poor recording techniques and were often working to hypotheses of efficacy in comparison to other suppressants.

That said, this ingredient has been on the commercial market for seventy years. NZSMI can think of no other ingredient that has stood the test of that sort of time frame without falling from favour because of risk or poor performance or no perceived value.

Reclassification because of age is, in our opinion, not reasonable. And the use of the phrase "assumed efficacy" also lacks reason and qualification and should be dismissed. Pholcodine does not have efficacy as proven by modern day research but does have efficacy proven by aged research and seventy years survival as a commercial product.

Old Arguments

The primary argument for a change of classification springs from the potential connection of Pholcodine use to an anaphylactic response. This started twenty years ago with a hypothesis that a quaternary ammonium ion component in Pholcodine reacted with certain neuromuscular blocking agents used in general anaesthesia to cause anaphylaxis.

Subsequent studies over the next decade aimed to substantiate the hypothesis but in all cases there was no definitive conclusion able to be made. Many of these studies involved serum samples (in some case 40 year old samples). Reasons for this ranged from unexplained anomalies that showed positive response to IgE antibodies in countries where Pholcodine had never been available, to gender discrepancies of 100% in other studies, and still others that strongly indicate environmental factors are more significant than Pholcodine consumption when measuring the potential for an anaphylactic response, often referred to as the "hairdresser's and baker's" analysis. This came about because many other foods, drugs, cosmetics, disinfectants and industrial compounds contain QAI's that could have caused sensitisation.

Again, like the arguments for not changing classification just because of age, NZSMI contends that all of these studies have failed to show a definitive causative relationship but should instead be looked at as a body of work. There may be some relationship between pholcodine and an anaphylactic reaction but given the millions of doses consumed it is an extremely tenuous one. NZSMI contends the solution to this concern, if it exists, is not helped at all by a change in classification.

Probably as a result of these numerous non-definitive studies the EMA reviewed the evidence for a link between pholcodine and NMBA-induced anaphylaxis in 2011. They considered the evidence available at the time to be circumstantial, not entirely consistent, and insufficient to support the conclusion that there is a significant risk of cross-sensitisation to NMBAs. NZSMI supports this conclusion but also notes and acknowledges their other comment, that more data is required.

It is understood that about this time a group of New Zealand anaesthetists lobbied the regulator to ban the sale of Pholcodine. Given the lack of weight in the evidence at that time, the regulator declined. The lobbying for this action has, however, not stopped and it re-appears from time to time albeit without any additional argument, new data or sound reasoning. NZSMI does not agree that this course of behaviour warrants a change in classification.

Perhaps, however, as a result of this lobbying the MCC reviewed the classification of a number of cough medicines in 2018 primarily due to concerns about their potential for abuse. It was unusual that Pholcodine was included here because there is no evidence over its seventy years of use that Pholcodine attracts abuse as do many other medicines. The MCC then re-endorsed the Pharmacy Only classification of Pholcodine. NZSMI supports this finding.

The Current Situation

Since the upscheduling of dextromethorphan containing cough mixtures in 2019 there are few remaining efficacious remedies available in retail pharmacy or general sale. This is particularly concerning for dry cough symptoms. When upscheduling dextromethorphan the MCC commented that other safer treatments were available to the public. NZSMI can find no other cough suppressants (apart from Pholcodine) available for dry cough that have anything like the quality of research the MCC is seeking to validate benefit claims.

The New Zealand market has a plethora of natural remedies and alternative healthcare products that seek to satisfy a market for dry cough relief. These products are not registered as medicines and have little or no clinical study back-up.

There is a real danger that the removal of Pholcodine from pharmacy store shelves to behind the counter and only available from a Pharmacist will lead to inappropriate purchase of cough relief product simply due to lack of choice and that patients are unaware of the "Pharmacy Only" category. This has been quantitatively proven by the almost total loss of sales for Dextromethorphan containing products from the middle of last year to now. New Zealand's advertising regulations make informing the public of this category difficult. NZSMI believes the regulator is responsible for creating the environment where safe and effective medicines are available to the wider public and that restricting choice via the Pharmacist Only classification is unwarranted and counter-productive to good primary healthcare.

It is also important to note the relatively small market that dry cough presents to New Zealand suppliers. If an upscheduling was to occur product would no longer be harmonised with Australian suppliers due to a disparity in schedules and there is a VERY high likelihood that product would be withdrawn from New Zealand shelves. NZSMI contends this is a highly undesirable outcome given the data around the reasons for change.

The Future

Where to from here? The MARC agreed the link of Pholcodine causing hypersensitivity is suggestive rather than conclusive but also sought regulatory action to limit unnecessary exposure to the medicine alongside general anaesthesia using NMBA's. NZSMI does not believe that action should be upscheduling to Pharmacist Only as this will likely not solve the perceived problem.

Pharmacists would have to be trained to appropriately interrogate patients about the likelihood of them having a general anaesthetic in the future and advising them of the risks of receiving NMBA's in any future general anaesthesia. This is not appropriate or realistic primary healthcare.

It raises questions about how long after taking pholcodine is a patient potentially at risk, does this risk apply to all patients, is the risk cumulative, is the risk permanent or transient and a plethora of other unanswerable questions.

Similarly, warning labels on product with language of, or like, "Cross-sensitivity to neuromuscular blocking agents may lead to anaphylactic reactions" does little, in our opinion, to appropriately and realistically educate patients.

A far more sensible approach is to direct the warning advice to the cohort most likely to be affected – those receiving NMBA's. And this advice should be delivered by the health professionals administering the NMBA's; the anaesthetists. There are already substantial protocols used prior to anaesthesia and these already include questions about immediate prior use of all medications and should include pholcodine. Given the suggestive nature of some of the research these questions could also include questions around exposure to other QAI epitopes also found in many other compounds such as antihistamines, anti-anxiety agents, anti-hypertensives, parasympathomimetics, and narcotics.

Also needing to be considered is the action patients will take when self-care treatment is not easily accessible. As earlier stated by NZSMI and proven by patient behaviour seen after other products are up-scheduled, changing supply classification to Pharmacist Only severely curtails access.

Published results of recent independent research commissioned by NZSMI states :

The NZSMI survey revealed that if faced with the unavailability of an OTC product, 27 – 73% of consumers would visit their GP for treatment depending on their medical conditions. This would result in GP's shouldering an increased burden and add to the growing overcrowding in waiting rooms in both GP clinics and our hospitals. Other options were to use a homemade remedy or not treat the ailment at all.[ii]

Another course of action likely to occur is the self-selection of inappropriate or ineffective treatment due to lack of choice. This will likely lead to extended discomfort at best to exacerbated illness and the need for secondary treatment at worst.

Conclusion

NZSMI does not believe any change in scheduling is either necessary or helpful.

We also strongly believe harmonised scheduling with Australia is important in promoting continued access for patients to "small market" products like Pholcodine.

And that patient education of possible sensitisation to NMBA's by Pholcodine is best addressed by those administering these products rather than product labelling changes that cannot adequately explain the potential issue and scope of the pholcodine hypothesis.

As always, we are appreciative of the opportunity to have input into these discussions.

Scott Milne – Executive Director

For: New Zealand Self Medication Industry Association

PHARMACEUTICAL SOCIETY
of New Zealand Incorporated

11 March 2020

Medicines Classification Committee Secretary
Medsafe
PO Box 5013
Wellington 6145
via email: committees@moh.govt.nz

Dear Jessica,

MEDICINES CLASSIFICATION COMMITTEE (MCC)
COMMENTS TO THE 64th MEETING AGENDA Thursday 14th May 2020

Thank you for the opportunity to submit comments on the Agenda for the 64th meeting of the Medicines Classification Committee.

The Pharmaceutical Society of New Zealand Inc. (the Society) is the professional association representing over 3,700 pharmacists, from all sectors of pharmacy practice. We provide to pharmacists professional support and representation, training for continuing professional development, and assistance to enable them to deliver to all New Zealanders the best pharmaceutical practice and professional services in relation to medicines. The Society focuses on the important role pharmacists have in medicines management and in the safe and quality use of medicines.

Regarding the agenda items for the above meeting of the Medicines Classification Committee, the Pharmaceutical Society would like to note the following comments for consideration:

6.3 Pholcodine- reclassification from a pharmacy medicine to a restricted medicine

The Society **does not** support the application to reclassify pholcodine. The Medicines Adverse Reactions Committee (MARC) Secretariat developed a comprehensive review paper, which was discussed by MARC in December 2019 and was used to inform the Medicines Classification Committee (MCC) proposal. However, the Society have several comments that MCC may wish to consideration during their discussions.

Clinical efficacy of the product

The MARC paper has captured and evaluated a large number of studies related to pholcodine. The European Medicines Agency (EMA) state that "due to the age of the product most of the methodology used in most efficacy studies would be considered poor by modern standards".[1] This is reflected to a degree in the assessment by the MARC team.

However, EMA have recommended that existing data is also consistent and supportive of the efficacy of pholcodine in the treatment of acute non-productive cough.

The MARC paper describes outcomes of a study from 2006 (Equinozzi and Robuschi), which compared pholcodine and dextromethorphan.[2] The commentary in the MARC paper included limitations with the study and suggested that it was not possible to draw the conclusions described by the authors. However, the authors of the MARC paper have not reviewed the full published article and only accessed the abstract and published clinical trial report. Springer who published the original research are "a leading global scientific, technical and medical portfolio, providing researchers in academia, scientific institutions and corporate R&D departments with quality content through innovative information, products and services".[3] It is also likely that the original research by Equinozzi and Robuschi was peer reviewed. If the Equinozzi paper is going to be critiqued by MARC and potential limitations

assumed regarding the research, then the full primary reference should ideally be reviewed before a recommendation is made to both MARC and MCC.
Based on the current balance of the evidence available, the Society supports the EMA summary that existing data is consistent and supportive of the efficacy of pholcodine in the treatment of acute non-productive cough.

Safety of the product
Various formulations of pholcodine have been available on the New Zealand market since 1969.[4] The CARM data in the MARC report (Table 9) lists all the case reports for pholcodine since product launch.
To ensure the evidence is balanced, please can the committee remove the three cases linked to children (002896, 004285, 035772) because pholcodine is not currently used in children under 6 years old. It would also be beneficial if the committee could exclude the cases where pholcodine is not the sole ingredient, because the other suspected medicines may have caused the adverse reaction (006822, 024434, 043027, 084894, 086809).
Anaphylaxis is defined as a severe and potentially life-threatening reaction to a trigger such as an allergy.[5] The CARM data contains some reports of a potential allergic response to pholcodine but only two reports of anaphylaxis since the product was brought to market (114715, 118693). It is not clear from the information if these outcomes were confounded by the presence of other risk factors or clinical conditions. Please can the committee also consider the context and sizes of these reactions in relation all other anaphylaxis reports captured by CARM for the other pharmacy only and general sale list medicines that are currently available.

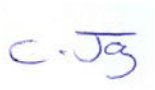
Anaphylaxis to neuromuscular blocking agents (NMBAs)
The MARC paper and MCC document provide a good summary of the information relating to anaphylaxis and NMBAs. However, the evidence presented to potentially link pholcodine and anaphylaxis to NMBAs is described as weak, is mainly ecologically defined to one population (Norway and Sweden) and later to some IgE studies in Australia. The IgE reaction has not been described wider, despite the product being freely available across multiple countries.
The authors of the MARC and MCC papers provide evidence that the "allergenic epitope responsible for IgE-mediated anaphylaxis to NMBAs is the quaternary ammonium ion which is widely available in the human environment". An alternative hypothesis to the pholcodine hypothesis is proposed which states that "sensitisation to NMBAs may therefore occur from environmental exposure to a cross-reacting substance rather than the pholcodine".
The EMA have stated that "the evidence in support of an association between pholcodine and NMBA-related anaphylaxis is circumstantial, not entirely consistent and does not support the conclusion that there is a significant risk of cross-sensitisation to NMBAs and subsequent development of anaphylaxis during surgery. Further data needs to be generated to clarify the possibility of an association between pholcodine use and NMBA-related anaphylaxis".[1] Currently no additional data has been published.

Review of proposed upscheduling
It appears that there is insufficient conclusive evidence linking pholcodine and anaphylaxis to NMBAs in New Zealand. This was confirmed by MARC. Any reclassification would require the sponsor to supply a data sheet which includes adverse effects. This may be beneficial for the patient. However, with the development of the Therapeutic Products Bill this requirement could be delivered without a change of classification.
Pharmacists provide advice to patients regarding appropriate treatments, including those presentations with coughs and colds. However, it is unlikely that any health professional providing or prescribing pholcodine to a patient will know if they are likely to undergo surgery in the future or potentially trigger the theoretical increase in IgE which may cause analphylaxis with NMBAs. It may be more appropriate to mitigate any risks by ensuring the patient is asked about their medicines (including pholcodine) at their pre-assessment clinic or prior to surgery.

This will provide real time information and also ensure all health professionals can provide optimal care for their patients.

Thank you for consideration of this submission. I would be happy to discuss any aspect of this submission further, if required.

Yours sincerely,



Chris Jay
Manager Practice and Policy
p: 04 802 0036

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Dear Jessica

Thank you for your response to my letter to Andy Shirtcliffe addressing my concerns over the reclassification of gees linctus and pholcodine linctus. I have included a copy of that letter as a follow on from this one. It covers my concerns for those two specific medicines. However I have a more fundamental concern for the processes of the Medicines Classification Committee.

Drawing from my extensive experience as national President of the Pharmaceutical Society of New Zealand, a Director of PHARMAC and a member of a variety of medicines -related committees, my concern is that there is a drift in the Medicines Classification Committee towards an overly restrictive approach to the classification of medicines. The two medicines mentioned here were those that finally piqued me to convey my concerns to the MCC.

1/ Designating a medicine to be Prescription Only may at times simply result in the public being denied that medicine because the average General Practitioner is unlikely to be familiar with it and they may well say to the patient with a minor ailment such as a cough "you can get something from the pharmacy for that".

2/ Doctors generally are familiar with a limited range of medicines which they prescribe for the bulk of patients they see. They are universally not familiar with the proprietary medicines traditionally available from pharmacies. Such medicines are not promoted to doctors by medical representatives and they don't appear in medical literature which doctors regularly see.
3/ There is a knock-on effect to the supplier. When the product is relegated to Prescription Only status by the MCC, usage of that medicine collapses then the supplier identifying that it is little used, ceases to source the medicine and it is no longer available to anybody.
4/Some years ago pharmacy services were the subject of a major review in which I played a part. It was recognised that the process of seeing a doctor was a barrier to healthcare and that the needs of many people could be dealt with by the pharmacist and the strong thrust of that review was that the pharmacist could exercise supply discretion via the Pharmacist Only (restricted medicine) classification. It was also seen as a way of relieving pressure on doctors time, energy and cost. I personally worked through much of this planning with the then Associate Minister of Health The Right Honourable Peter Dunne.

Sadly much of the planning and lessons learned then have been forgotten over time and decisions on medicine classification are again made on the experiences, attitudes and biases of the current members of MCC.
There seems to be an UNDER consideration of the interests of the thousands of people who will benefit from a medicine and an OVER consideration of the few who will inevitably suffer some form of side effects. Such over caution seems to be an affliction of our current society and I'm quite convinced that New Zealand would not have developed in the manner it has if the early pioneers and statesman of this nation had adopted this level of fear and caution. Some people are more simplistic in their expression of this concept and use the term "Nanny State". I could not possibly comment!!

I don't make a habit of reading the proceedings of the MCC but I retain an interested overview of my profession and the way in which it serves the public in this country. Serving the public inevitably leads to some difficult decisions. Making them in a balanced and wise manner will always with require wisdom and courage.

Thank you for your attention

Christopher Budgen
Former President of the Pharmaceutical Society of New Zealand

Pholcodine & Gee's Linctus Reclassification Submission

I was dismayed over a recent decision to make "Gee's Linctus" a prescription only medicine, effectively denying it to the public. Now I understand that pholcodine is to be reviewed. I'm sure the current generation of younger doctors would have no idea what these preparations are, let alone prescribe them.

A 'cough mixture' of the type referred to here has five beneficial modes of action, <u>efficacy</u> being only one of them. Others include: -

(a) a soothing feel to the mouth and throat (though not the bronchi!) due to its thick 'syrupy' nature;

(b) a dose adequate to produce a suppressant effect on the 'Cough Centre' of the CNS

(c) a calming effect on the child due to the very nature of the attention received.

(d) a calming effect on the mother, gratified and relieved that she can 'do something' for her child to relieve the condition

I have my doubts that striving for a medicine which selectively targets 'The Cough Centre' will be successful. Do we know that a 'Cough Centre' actually exists? Has it been anatomically isolated? And if it is so intimately embedded in the CNS, wouldn't its suppression likely suppress the whole CNS? Therefore; are cough suppressants actually mild hypnotics? In which case; are all effective cough suppressants really only mild hypnotics and are we misguided in our efforts to categorise them as '*Cough Suppressants'*?

There is a deal of inconsistent (and non-scientific?) thinking around this issue. I recall that during last year one of the reasons given by the committee for reclassifying Gees Linctus was that it was a 'relic' of a bygone age. What has the term 'relic' got to do with a review of the pharmacological action and classification of medicine? Might not the reason for it remaining in use for so many years be due to the fact that several generations of the public found it helpful in the treatment of an irritating non-productive cough, especially for children?

A further point around any classification decision is surely the fact that Gee's Linctus (Opiate Squill Linctus)and pholcodeine both elicit their action via the '<u>*Opioid receptor*</u>' in the CNS in which case they should surely be regarded as 'parallel' medicines in their action and classified in a similar manner.

BOTH of these medicines have value for the reasons stated above and the public should not be denied them for inconsistent and comparatively minor shortcomings. They do however require a degree of oversight in their use and the 'Pharmacist Only' classification is ideally suited for this purpose.

I therefore respectfully request (to the MCC) that <u>BOTH</u> of these medicines be reclassified to be available to the public as <u>'Pharmacist Only Medicines'.</u>

PHARMACY GUILD OF NEW ZEALAND

20 March 2020

Medicines Classification Committee Secretary
Medsafe
Wellington

Sent via email to: committees@moh.govt.nz

Dear Committee Members

RE: Agenda for the 64th meeting of the Medicines Classification Committee

Thank you for the opportunity to provide feedback on the agenda for the 64th meeting of the Medicines Classification Committee (MCC), to be held on 14 May 2020.

The Pharmacy Guild of New Zealand (Inc.) (the Guild) is a national membership organisation representing the majority of community pharmacy owners. We provide leadership on all issues affecting the sector.

Our feedback covers two agenda items. These are:

- Agenda item: *6.2: Cetirizine – proposed change to the pack size limit (AFT Pharmaceuticals Limited)*
- Agenda item: *6.3: Pholcodine – reclassification from a pharmacy medicine to a restricted medicine (Medsafe)*

Each of these agenda items are discussed below.

Agenda item 6.2: Cetirizine – proposed change to the pack size limit (AFT Pharmaceuticals Limited)

The Guild **does not** support AFT Pharmaceuticals Limited submission proposing to change the general sale restrictions of cetirizine hydrochloride from five days' supply to ten tablets.

The proposal to change the general sale restrictions of cetirizine hydrochloride underestimates the value of the important role that community pharmacy plays in ensuring medicines safety in the primary care setting. Medicines when supplied by a pharmacy have the oversight of a pharmacist who has significant clinical expertise and where needed, patients can be provided with medicines information, advice and verbal reinforcement.

We have concerns that changing the general sale restrictions will encourage the public to put off or prolong the time before engaging with a health care professional. Seasonal allergic rhinitis is commonly confused with a range of other diagnoses, such as a simple cold, a sinus infection, conjunctivitis, and serious eye conditions. Due to the prevalence of misdiagnosis, there is potential risk to deterioration of a person's health due to inappropriate treatment.

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When purchasing cetirizine in quantities of more than five days, the public should have access to health care advice to determine whether it is the most appropriate treatment for their condition. In some cases, people may need to be referred to another health provider for further diagnosis to achieve the best patient outcome.

Agenda item 6.3: Pholcodine – reclassification from a pharmacy medicine to a restricted medicine (Medsafe)

The Guild **does not** support the proposed reclassification of pholcodine from a pharmacy medicine to a restricted medicine. We have concerns over the lack of conclusive evidence to make such a significant change and believe that the proposed changes will not be effective in mitigating the risks that have been raised by the Medicines Adverse Reactions Committee (MARC).

We note that the European Medicines Agency (EMA) has recommended that existing data is consistent and supportive of the efficacy of pholcodine in the treatment of acute non-productive cough.

The data available from CARM has only reported that there have been two reported cases of anaphylaxis linked to pholcodine since the product was brought to market in NZ. Pholcodine has been available in New Zealand since 1969 and we request due consideration be given to the size of the risk in comparison to the volume of pholcodine used in the market.

The EMA has stated that the evidence supporting an association between pholcodine and NMBA related anaphylaxis is circumstantial, not consistent and does not conclude that there is a significant risk of cross-sensitisation of NMBAs.

MARC has recommended that the MCC changes the classification of pholcodine from a pharmacy medicine to a restricted medicine to limit unnecessary exposure. We would like to highlight that there are existing processes in place in community pharmacy to appropriately manage the unnecessary sale and supply of medicines. Is there any evidence demonstrating the unnecessary supply of pholcodine containing medicines?

Pharmacists are required under the Pharmacy Council Code of Ethics to only provide a treatment that is necessary for a patient's needs. This also applies to all pharmacy staff as their activities in a pharmacy fall under the supervision and responsibility of the charge pharmacist.

Pharmacy staff are trained to identify uncomplicated dry cough and to provide appropriate treatment options to patients. They are also trained to refer on to the pharmacist when further assessment is necessary.

We note the consultation states that "MARC considered that changing the classification to prescription could overwhelm primary healthcare providers with patients seeking symptomatic relief". Although we support this statement, we believe the proposal to reclassify pholcodine to a restricted medicine will also put unnecessary burden on the pharmacist for a process that is already managed appropriately in a pharmacy.

We would also like to highlight that it would not be likely that a pharmacist or a prescriber will be able to manage the risk for a patient who may be required to have surgery at some point in the future.

To effectively mitigate any risks, it would be more appropriate for the sponsor to include within the packaging a data sheet which includes known adverse effects and for surgeons to ensure that the patient has their medicine history checked at their pre-assessment appointment prior to surgery. It will be at the pre-assessment appointment that any risks about pholcodine can be managed appropriately.

Based on the evidence we request that the classification remains as a pharmacy-only medicine. We believe that the proposed change will not be effective in managing the risk identified by MARC.

Thank you for your consideration of our response. If you have any questions about our feedback, please contact our Professional Services Pharmacist, Alastair Shum, at alastair@pgnz.org.nz or on 04 802 8209.

Yours sincerely,

Nicole Rickman
General Manager – Membership and Professional Services

ANZCA
FPM

April 7, 2020

Medicines Classification Committee
Medsafe
Ministry of Health
PO Box 5013
Wellington 6140

By email: committees@health.govt.nz

Tēnā koutou,

Reclassification of pholcodine to restricted medicine

The Australian and New Zealand College of Anaesthetists (ANZCA) is responsible for training and examining anaesthetists and specialist pain medicine physicians, and for setting clinical standards in New Zealand and Australia. ANZCA's mission is to serve the community by fostering safe, high quality patient care in anaesthesia, perioperative medicine, and pain medicine.

ANZCA notes that the above item is included on the agenda for the 64th meeting of the Medicines Classification Committee, scheduled for May. ANZCA has had previous contact with Medsafe, highlighting that there is strong evidence that pholcodine consumption sensitises users to quarternary ammonium ions in neuromuscular blocking agents (NMBA) that are required for anaesthesia. This increases the risk of death and serious morbidity due to anaphylaxis to these agents. This issue is critical for anaesthetists and for patients undergoing surgery, as anaphylaxis is the leading cause of direct anaesthesia-related mortality in New Zealand and Australia, causing more deaths than airway failures, aspiration, or cardiac arrest (1, 2).

ANZCA's New Zealand National Committee has reviewed the Medicines Adverse Reactions Committee's (MARC) proposal to reclassify pholcodine as a pharmacist only (restricted) medicine to ensure pharmacists inform patients of the risk of harm with pholcodine and to mandate the provision of a data sheet. MARC has outlined that "the possibility of an association between pholcodine and anaesthetic anaphylaxis warranted regulatory action to limit unnecessary exposure to the medicine." ANZCA strongly supports MARC's proposal to reclassify pholcodine as a pharmacist only (restricted) medicine.

ANZCA would support even stronger measures though, such as reclassifying pholcodine as a prescription medicine, or prohibiting inclusion of pholcodine in cough medicines altogether. ANZCA takes this position based on the lack of efficacy for pholcodine as a cough suppressant, and the strong evidence that pholcodine poses serious risk for patients undergoing anaesthesia. ANZCA notes that the MARC refrained from recommending pholcodine become prescription only based on concerns this would risk overwhelming primary health care providers with patients seeking symptomatic relief. Although a valid concern, ANZCA disagrees with this assessment, as other products for symptom relief that do not contain pholcodine would still be available to consumers. Also, ANZCA considers any preventable risk of death or serious morbidity to patients to be unacceptable.

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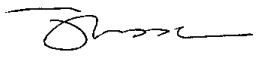
New Zealand data supports ANZCA's position. The Centre for Adverse Reactions Monitoring (CARM) has received 353 reports of neuromuscular blocking agent (NMBA) anaphylaxis over the past 12 years. Laboratory testing for pholcodine specific IgE has not been universally available in New Zealand but in a review of 62 reports of NMBA anaphylaxis submitted to CARM between January 2017 and June 2019, pholcodine specific IgE was measured in 37 (60%) of cases and found to be elevated in 20 (54%) of cases.

Overall, ANZCA will support any moves to limit patient exposure to pholcodine, including the current proposal to reclassify pholcodine as a pharmacist only (restricted) medicine. ANZCA will continue to work with stakeholders to encourage stronger measures for limiting exposure to pholcodine, and notes that removal of pholcodine from the market in Norway resulted in a reduction in anaphylaxis to muscle relaxants, and a decline in the prevalence of elevated pholcodine-specific IgE in the general population (3).

Thank you for the opportunity to comment on the above agenda item. We look forward to hearing the Medicines Classification Committee's decision on the issue. If you have any queries about this submission, or would like further information, please contact Virginia Mills (Senior Policy Advisor) at vmills@anzca.org.nz in the first instance.

Ngā mihi nui,



Dr Jennifer Woods

Chair, New Zealand National Committee

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Andi Shirtcliffe

Chief Advisor Pharmacist

Community Health Service Improvement

Ministry of Health

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Dear Andi Shirtcliffe

I note that Medsafe is asking the Medicines Classification Committee to recommend that the cough suppressant pholcodeine be reclassified as a Pharmacist-Only medicine based on concerns over possible lack of efficacy and possible health risks.

Whilst no longer involved in any of the medicine decision making processes via my earlier roles with the Pharmaceutical Society and Pharmac, I continue to take an interest in the processes and the outcomes from the public wellbeing perspective.

I was dismayed over a recent decision to make "Gee's Linctus" a prescription only medicine, effectively denying it to the public as the current generation of younger doctors would have no idea what it is, let alone prescribe it.

A 'cough mixture' of the type referred to here has five beneficial modes of action, efficacy being only one of them. Others include: -

(a) a soothing feel to the mouth and throat (though not the bronchi!) due to its thick 'syrupy' nature;

(b) a dose adequate to produce a suppressant effect on the 'Cough Centre' of the CNS

(c) a calming effect on the child due to the very nature of the attention he or she is receiving and

(d) a calming effect on the mother, gratified and relieved that she can 'do something' for her child to relieve the condition. All of which raises the likelihood that those concerned will enjoy calm for a period and get back to sleep before dawn.

I have my doubts that striving for a medicine which selectively targets 'The Cough Centre' will be successful. Do we know that a 'Cough Centre' actually exists? Has it been anatomically isolated? And if it is so intimately embedded in the CNS, wouldn't its suppression likely suppress the whole CNS? Therefore; are cough suppressants actually mild hypnotics? In which case; are all effective cough suppressants really only mild hypnotics and are we misguided in our efforts to categorise them as '*Cough Suppressants'*?

There is a deal of inconsistent (and non-scientific?) thinking around this issue. I recall that during last year one of the reasons given by the committee for reclassifying Gees Linctus was that it was a 'relic' of a bygone age. What has the term 'relic' got to do with a review of the pharmacological action and classification of medicine? Might not the reason for it remaining in use for so many years be due to the fact that several generations of the public found it helpful in the treatment of an irritating non-productive cough, especially for children?

A further point around any classification decision is surely the fact that Gee's Linctus (Opiate Squill Linctus)and pholcodeine both elicit their action via the '*Opioid receptor*' in the CNS in which case they should surely be regarded as 'parallel' medicines in their action and classified in a similar manner.

BOTH of these medicines have value for the reasons stated above and the public should not be denied them for inconsistent and comparatively minor shortcomings. They do however require a degree of oversight in their use and the 'Pharmacist Only' classification is ideally suited for this purpose.

I therefore respectfully request (to the MCC) that BOTH of these medicines be reclassified to be available to the public as 'Pharmacist Only Medicines'.

I remain Ma'am

Your respectful and admiring colleague

Christopher J Budgen