From: [redacted]
To: Medicines Scheduling
Subject: [redacted] re ACMS invitation for comment re Benzydamine [SEC=UNCLASSIFIED]
Date: Wednesday, 10 September 2014 9:58:38 AM

Dear Medicines Scheduling Secretariat Team,

Please take this as feedback from [redacted] If you can please lodge it for consideration at the November meeting that would be great.

With respect to the Benzydamine proposal below:

- [redacted] notes that "[t]he secretariat is not able to provide details or rationale of the proposal, as information provided by the applicant may contain confidential information." That said, [redacted] finds the invitation for public comment on particular proposals at upcoming Advisory Committee on Medicines Scheduling (ACMS) and Joint Advisory Committee on Chemicals Scheduling (ACCS)/ACMS meetings lack disclosure of the original detail or rationale underpinning these proposals lodged by the original submitter. It is difficult for the public to make fully informed comment on any proposals without understanding the background underpinning why the proposal was lodged in the first place. [redacted] suggests that the ACCS/ACMS reconsider this part of the consultation process.

- Therefore, at the suggestion of the secretariat, [redacted] requests that it reserves the right to provide additional comments at the time of interim decision. [redacted] is making this request because we may wish to provide comment but would like further information, We trust that we will be kept abreast of developments.

Regards

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]
Sent: Thursday, 14 August 2014 3:06 PM
To: Medicines Scheduling
Subject: ACMS invitation for comment re Benzydamine

Hi Medicines Scheduling,

I've noted that there is an invitation for public comment on ACMS meeting November 2014 (http://www.tga.gov.au/newsroom/consult-scheduling-acmcs-1411.htm#.U-xDF_mSyCk)

I'm interested in the consideration of the substance and proposal below.

Proposed amendments to the poisons standard referred by the delegate for scheduling advice

2. Proposed amendments referred by the delegate for scheduling advice for consideration by the ACMS.

Substance	Proposal
Benzydamine	Proposal to exempt from scheduling benzydamine in preparations for topical use containing 3 mg or less of benzydamine in divided oral preparations and 3 mg/ml or less in undivided oral preparations in a pack of 50 ml or less.

However I cannot seem to access the proposal in detail nor its rationale.

Are you able to send to me? [redacted] may put in a response.

[redacted]

[redacted]

Purpose

[redacted] makes this submission in relation to proposed amendments to the *Poisons standard* referred by the delegate for scheduling advice for consideration by the Advisory Committee on Medicines Scheduling (ACMS) at the November 2014 meeting.

[redacted] comments relate to the proposed amendments to: benzydamine, naproxen, pantoprazole, and paracetamol in combination (individually) with caffeine, ibuprofen and phenylephrine.

[redacted]

[redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]

[redacted]

- [redacted]

[redacted]

Recommendations

Benzydamine

[redacted] *does not support the proposal to exempt topical oral preparations from scheduling.*

Naproxen

[redacted] *opposes any amendment to the S2 entry for naproxen which would result in naproxen being exempted from scheduling.*

[redacted] *supports the inclusion of naproxen in Appendix H on condition that the pharmacy profession is consulted (separate to any consultation that may be conducted as part of the regulatory requirements) and able to have input into the development of any advertisement or promotional material.*

Pantoprazole

[redacted] *believes that a 7-day pack of pantoprazole does not accommodate the general dose recommendations for optimal therapy and may in some cases limit the benefits for consumers or add to the cost of therapy.*

If the current S3 entry for pantoprazole is retained, [redacted] *believes it is possible to consider an Appendix H listing.* [redacted] *requests engagement with the pharmacy profession on the development of any advertisement or promotional material.*

Paracetamol in combination with caffeine

[redacted] *is firmly opposed to the proposal to exempt paracetamol from scheduling when compounded with caffeine.*

Paracetamol in combination with ibuprofen

If Appendix H listing is granted, [redacted] *seeks the involvement of the pharmacy profession in the development of any advertisement or promotional material.*

Paracetamol in combination with phenylephrine

[redacted] *supports, in principle, the rescheduling as proposed. However further consideration of the potential impact of the rescheduling on community pharmacists, the pharmaceutical industry and consumers is warranted. In addition, we request information on the clinical effects of the significant increase in effective dose which has been reported in the new study.*

[redacted]

Benzydamine

Proposal to exempt from scheduling benzydamine in preparations for topical use containing 3 mg or less of benzydamine in divided oral preparations and 3 mg/ml or less in undivided oral preparations in a pack of 50 ml or less.

Benzydamine is a non-steroidal anti-inflammatory drug (NSAID) with analgesic, antipyretic and anti-inflammatory actions. A range of over-the-counter (OTC) products containing benzydamine is readily available in Australia. Different presentations for topical oral use are available for the relief of pain and inflammation associated with a sore throat due to minor mouth infections or following dental procedures or oral surgery.

Most OTC benzydamine products are currently in Schedule 2 (S2) of the *Poisons standard*. While we are not aware of any new safety concerns with benzydamine, we firmly believe its safety profile warrants that it remain in S2. One example is that, the safety of its use in pregnancy has not been established.[2]

A sore throat may often be associated with self-limiting conditions such as a minor infection or an allergy (e.g. hay fever), however it may also present as a symptom of a more serious condition or as a side effect to the use of certain medicines. [redacted] have cited real life cases where oral discomfort or a sore throat, upon referral to a GP and subsequent follow-up with a specialist, was found to be due to a cancerous lump on the tongue or throat cancer. While such serious cases are not encountered frequently, they are indeed a possibility and therefore reinforce the importance of availability of professional pharmacist oversight and opportunity for early intervention at the time of supply of these medicines.

For people who are at risk of complications, particular attention is required since untreated or inappropriately treated sore throats have the potential to lead to significant negative health outcomes. For example, if a sore throat is not treated appropriately, conditions such as acute rheumatic fever (ARF) can develop. Even though AFR is rare in most developed countries, the rate of AFR among Aboriginal and Torres Strait Islander people is among the highest in the world[3] and therefore of relevance to the Australian health care system. Where AFR is not managed or treated appropriately, it can cause permanent cardiovascular damage i.e. rheumatic heart disease.

It is noted that some OTC products for the treatment of a sore throat are currently exempt from scheduling, for example, oral lozenges containing lignocaine. However, as stated above [redacted] focus is that consumers should be encouraged to seek advice from a pharmacist or pharmacy staff so that early intervention and referral can be initiated if required. Adding benzydamine products to the unregulated environment may only perpetuate the misconception to consumers that it is appropriate to continue to self-treat a sore throat which has not resolved within a reasonable period of time.

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[2] Sansom LN, ed. Australian pharmaceutical formulary and handbook. 22nd edn. Canberra: Pharmaceutical Society of Australia; 2012. p. 531.

[3] Australian Institute of Health and Welfare. Rheumatic heart disease and acute rheumatic fever in Australia: 1996–2012. Cardiovascular disease series. Cat. No. CVD 60. Canberra: AIHW; 2013. At: www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=60129542747

Benzydamine in topical oral preparations can also be combined with other active ingredients, including substances such as lignocaine. Thus there is a range of products available which we believe would be best managed through a pharmacy environment where the opportunity for professional advice and intervention is available.

In summary, [redacted] does not support the proposal to exempt benzydamine topical oral preparations from scheduling.

Naproxen

Proposal to amend the Schedule 2 naproxen entry to exclude naproxen in a dosage form of 200 mg or less of naproxen per dosage unit in packs of 12 or less dosage units with a maximum recommended daily dose of not more than 600 mg of naproxen, and when not labelled for the treatment of children 12 years of age or less.

Proposal to include naproxen in Appendix H.

Naproxen is widely available in many countries as an OTC NSAID and its uses include: headache, sinus pain, cold and flu symptoms, acute and chronic inflammatory pain, dysmenorrhoea, gout, acute migraine, rheumatoid arthritis, ankylosing spondylitis and osteoarthritis.

The use of NSAIDs for short term relief of pain, inflammation and fever is well established. Just as well known are the risks associated with NSAID use and the need to exercise caution particularly for people over 65 years of age, those at risk of stomach and heart problems, or those with asthma. It should be noted that NSAIDs are "more likely than paracetamol to cause side effects", especially for the elderly as well as people with conditions including: arthritis pain, chronic pain, high blood pressure, asthma, heart failure, impaired kidney or liver function and inflammatory bowel disease.[4]

It is of significance that NSAIDs are considered to be one of several groups of medicines known to be associated with the most severe adverse events and accounting for a large percentage of fatal and non-fatal events.[5] Analgesics, including NSAIDs, were reportedly responsible for around 17% of over 37,000 hospital admissions attributed to adverse drug reactions.[6] Among the NSAIDs, naproxen is regarded as having a medium to high risk of upper gastrointestinal bleeding or perforation.[7] Compared with ibuprofen, for example, naproxen is more than twice as likely to

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[4] NPS MedicineWise. Nonsteroidal anti-inflammatory drugs (NSAIDs). At: **www.nps.org.au/conditions/nervous-system-problems/pain/for-individuals/medicines-treatments-for-pain/nsaids_pain_relievers**

[5] NPS MedicineWise. High-risk medicines: how to avoid errors. 9 Jul 2014. At: **www.nps.org.au/publications/health-professional/health-news-evidence/2014/high-risk-medicines**

[6] NPS MedicineWise. Medicines to avoid in older people. At: **www.nps.org.au/topics/ages-life-stages/for-individuals/older-people-and-medicines/for-health-professionals/inappropriate-prescribing/medicines-to-avoid**

[7] Massó González EL, Patrignani P, Tacconelli S, et al. Variability among nonsteroidal anti-inflammatory drugs in risk of upper gastrointestinal bleeding. Arthritis Rheum 2010;62(6):1592–1601.

[redacted]

cause upper gastrointestinal bleeding or perforation.[8] It is also acknowledged that naproxen may be risk-neutral with regard to cardiovascular events.[9]

Clearly there are a wide range of issues impacting on the safe and optimal use of naproxen and all NSAIDs. Pain management and analgesia through self-medication are legitimate needs for many Australian consumers. To facilitate this in a manner that supports public health and patient safety, responsible consideration and appropriate risk assessment of many factors are necessary. There is no question that the pharmacy profession has a fundamental role in this regard to balance risks and benefits for each person, tailor general advice and medicine information, prevent medication misadventure, promote optimal therapy and support consumers to improve health literacy. These are not considerations that can be fulfilled at outlets where professional oversight or input in the supply of therapeutic goods is not available.

Overall with these substantial concerns and precautions, [redacted] is opposed to the proposal to amend the S2 entry to exempt naproxen from scheduling in any dose or dosage form.

Appendix H. In relation to the proposal to include naproxen in Appendix H of the *Poisons standard*, we believe this could be regarded favourably.

As outlined above, many similar NSAID products are readily available, the ageing population is growing, and many consumers are being encouraged or choosing to self-medicate. Greater interaction between consumers and pharmacists with regards to their medication management generally, but with Schedule 3 (S3) naproxen in particular, is likely to be beneficial. We recognise that Appendix H listing of naproxen is one way to facilitate the professional interaction opportunity, provided the advertising to consumers is conducted in a responsible manner with a focus on quality use of medicines.

To achieve this, however, we would strongly advocate for any promotional material or advertisement developed to meet standards which exceed the minimum regulatory requirements such as those outlined in the *Therapeutic goods advertising code*.[10] In addition, we would strongly encourage sponsors to fully consult with pharmacy professional organisations during the development process to address any prior concerns from a professional practice perspective and to ensure key messages to be disseminated are rigorous and acceptable to pharmacists.

[redacted] therefore supports the proposal to list naproxen in Appendix H with the inclusion of a requirement to engage with professional pharmacy bodies in the development of any promotional materials or advertisements.

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[8] Castellsague J, Riera-Guardia N, Calingaert B, et al. Individual NSAIDs and upper gastrointestinal complications: a systematic review and meta-analysis of observational studies (the SOS project). Drug Saf 2012;35(12):1127–46.

[9] Peterson K, McDonagh M, Thakurta S, et al. Drug class review: nonsteroidal anti-inflammatory drugs (NSAIDs). Final update 4 report. Portland: Oregon Health & Science University; 2010, Nov.

[10] Therapeutic goods advertising code 2007. At: www.tgacc.com.au/code_gloss_files/F2007L00576TherapeuticGoodsAdvertisingCode2007.pdf

[redacted]

Pantoprazole

A new Schedule 2 entry for pantoprazole when supplied in oral preparations containing 20 mg or less of pantoprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 7 days of supply.

Proton pump inhibitors, such as pantoprazole, are used widely as OTC medicines for gastro-oesophageal reflux disease (GORD). A number of submissions have been made previously by [redacted] on pantoprazole over recent years. The most recent was in 2012 when we opposed a proposal to increase the maximum allowable pack size for S3 from 14 to 28 dosage units.

Our position then reflected consideration of a number of factors including:

- the general dose recommendation for optimal therapy is accommodated by the 14-day pack size;
- the need to assess the consumer's response to treatment can be supported by the pharmacist;
- when the pharmacist should refer the consumer for further investigation (e.g. if two weeks of continuous therapy has failed to adequately control symptoms);
- reports of adverse outcomes.

Overall, [redacted] believes that the current S3 entry for pantoprazole remains appropriate since this best supports the likely therapeutic needs of most consumers who may benefit from pantoprazole therapy.

While a 7-day pack size of pantoprazole may be regarded to be inherently safe, [redacted] believes it may not provide optimal support around the overall benefits of pantoprazole therapy at the recommended indications and dosage regimen. A 7-day pack size may also be more costly for consumers.

Further to our current view that S3 is likely to maximise the benefits of pantoprazole therapy, [redacted] also believes it would not be inappropriate to consider the suitability of Appendix H listing for pantoprazole. [redacted] has previously supported[11] Appendix H listing for this substance and commented that other similar or equivalent products used to treat uncomplicated GORD (which are S2 or unscheduled) are already being advertised to the public.

However, as with our comments in relation to naproxen (earlier in this submission), [redacted] support for Appendix H listing is underpinned by our request that any advertisement developed must meet standards which exceed the minimum regulatory requirements. To do this [redacted] would strongly encourage sponsors to fully consult with pharmacy professional organisations during the development process. [redacted] would be pleased to discuss with sponsors any concerns from a professional practice perspective and to assist with the dissemination of key messages in a rigorous and professionally acceptable manner.

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[11] [redacted] submission to the February 2011 meeting of the ACMS.

In summary, [redacted] notes that a 7-day pack of pantoprazole may in some cases limit the overall benefits of pantoprazole therapy for consumers. If the current S3 entry for pantoprazole is retained, it may be possible to consider an Appendix H listing. In this case [redacted] is strongly of the view that the pharmacy profession must have input into the development of any advertisement or promotional materials.

Paracetamol

In combination with caffeine

Proposal to exempt paracetamol when compounded with caffeine, in a powder or granule product containing 1000 mg or less of paracetamol and in tablets or capsules containing 500 mg or less of paracetamol when paracetamol is the only therapeutic active constituent and when supplied in primary packs of not more than 20 tablets/caplets or 10 sachets of powders/granules.

[Note: In relation to this rescheduling proposal, [redacted] has confirmed with the ACMS Secretariat that the caffeine component would be treated as a therapeutic active constituent in addition to the paracetamol.]

Paracetamol and caffeine combination products currently available in Australia are included in S2 and generally consist of 65 mg of caffeine and 500 mg of paracetamol per dosage unit. In [redacted] view these products are being managed appropriately in S2 and offer an alternative analgesic for consumers.

[redacted] has significant concerns with the current proposal which seeks to exempt such products in small pack sizes from scheduling. [redacted] concerns are explained below.

- Caffeine is considered to be safe at recommended doses of the S2 paracetamol combination product. At this dose it is reported that caffeine may supplement the analgesic effect of paracetamol, however any benefit is considered to be small.[12]

- While caffeine toxicity is normally expected at doses above 520 mg to 600 mg, smaller doses (e.g. 50 mg) may result in adverse outcomes depending on an additive effect of caffeine from other sources including other medicines and dietary intake. Tolerance to the effects of caffeine is also variable.[13]

- Oral dose preparations of caffeine are available as unscheduled medicines for the relief of mental fatigue and drowsiness. These are generally presented as 100 mg caffeine per dosage unit with a maximum daily dose of six tablets. The recommended wording for inclusion in the labelling of caffeine preparations to be used as a stimulating or alerting

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[12] NPS MedicineWise. Medicine Update: Panadol Extra (paracetamol and caffeine) for pain. Dec 2010. At: www.nps.org.au/__data/assets/pdf_file/0009/114210/Medicine_Update_Panadol_Extra.pdf

[13] Sansom LN, ed. Australian pharmaceutical formulary and handbook. 22nd edn. Canberra: Pharmaceutical Society of Australia; 2012. p. 269.

[redacted]

agent is[14]: *100 mg per dose maximum, which may be repeated at three hourly intervals. Do not exceed 600 mg in 24 hours.*

- Many vitamin and mineral supplements contain caffeine. Generally the quantity of caffeine per dosage unit in these products are in the low range however there are exceptions, for example, *Berocca Boost* (ARTG ID 218721) contains 72.7 mg of caffeine per tablet and *ThermoBooster* (for the support of weight management; ARTG ID 224691) contains 37.8 mg of caffeine per tablet. Such levels will contribute substantially to the total caffeine intake often without the person realising the additive effect or potential consequences.

- Dietary intake of caffeine can vary between individuals but can reach significant levels through consumption of foods such as tea, coffee (average of 80 mg caffeine per cup), cola, chocolate and energy drinks (e.g. a 250 ml can of *Red Bull* contains 80 mg of caffeine).[15] Many consumers may not be aware of or associate their dietary caffeine intake with the contents of the medicines they are taking.

- Currently, many paracetamol and caffeine combination products are differentiated from paracetamol (only) products by the inclusion in the brand name of words such as "extra". While it may be intended that this alerts consumers to the inclusion of an additional ingredient (the caffeine component), [redacted] believes it has the potential to misguide consumers into thinking that the product is 'better' or 'special'. Therefore we believe consumers may display a preference to use these products as first-line therapy when this may not be warranted.

- It is possible that some consumers may choose the combination product with a preference for the effects of caffeine. In such cases there is considerable risk of paracetamol toxicity through ingestion of multiple tablets even though this may be within a 'safe' dose range for caffeine.

These points highlight [redacted] concerns that the potential for consumers to experience an adverse outcome is greatly increased if combination products of paracetamol and caffeine are made available for general sale where professional intervention, and therefore the opportunity to prevent medication misadventure, is not available.

It is also noted by [redacted] that the appropriate schedule for paracetamol and caffeine in combination has been considered several times in the past. This includes rescheduling from OTC to prescription only status in 1977 (based on a recommendation of the National Health and Medical Research Council) and rescheduling from S4 to S2 in 2007 (as a consequence of considerations under trans-Tasman harmonisation, although the paracetamol and caffeine combination was classified as general sale in New Zealand at the time). We believe these considerations further emphasise the need for caution in contemplating any lessening of restrictions through rescheduling.

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[14] Therapeutic Goods Administration. Australian regulatory guideline for over-the-counter medicines. Appendix 5: guidelines on OTC application for specific substances. Version 1.0. Oct 2012. p. 18. At: **www.tga.gov.au/pdf/otc-argom-app5.pdf**

[15] Australian Beverages Council. Caffeine – the facts. Aug 2013. At: **http://australianbeverages.org/for-consumers/caffeine-facts/**

[redacted] is firmly opposed to the proposal to exempt paracetamol from scheduling when compounded with caffeine.

In combination with ibuprofen

Proposal to include paracetamol when combined with ibuprofen in Appendix H.

The use of paracetamol in combination with ibuprofen is not considered to be first-line therapy for the treatment of mild to moderate pain. As such [redacted] is concerned that an advertisement could misguide consumers who may form a preference for the combination product before considering paracetamol or ibuprofen monotherapy.

More broadly however, an advertisement for an S3 medicine may create the desire for consumers to visit a pharmacy and therefore the opportunity to initiate a conversation and consult the pharmacist. Given the plethora of OTC analgesic products, this could facilitate better use of appropriate OTC analgesics by more consumers and divert people away from more harmful presentations such as ibuprofen and codeine combination products.

If the ACMS approves Appendix H listing for paracetamol in combination with ibuprofen, as outlined in our earlier comments on Appendix H listing requests, [redacted] re-iterates its firm view that the pharmacy profession must be consulted and have the opportunity to input into the development of any advertisement or promotional materials.

In combination with phenylephrine

Proposal to include the following in Schedule 3:

- *500 mg of paracetamol when combined with more than 2.5 mg phenylephrine per tablet or capsule or caplet*
- *Individually wrapped powders or sachets of granules containing paracetamol 1000 mg and more than 5 mg phenylephrine per dose*

Proposal to include in the following in Schedule 2:

- *500 mg of paracetamol when combined with 2.5 mg phenylephrine or less per tablet or capsule or caplet in packs containing more than 20 tablets or capsules or caplets per pack*
- *Individually wrapped powders or sachets of granules containing paracetamol 1000 mg and 5 mg phenylephrine or less per dose in packs containing more than 10 such powders or sachets*

Proposal to exempt from scheduling the following:

- *500 mg of paracetamol when combined with 2.5 mg phenylephrine or less per tablet or capsule or caplet in packs containing 20 or less tablets or capsules or caplets per pack*
- *Individually wrapped powders or sachets of granules containing paracetamol 1000 mg and 5 mg phenylephrine or less per dose in packs containing 10 or less such powders or sachets.*

[redacted]

[redacted] is aware of a recently published study on the effects of paracetamol co-administered with phenylephrine.[16] The peak plasma concentration of phenylephrine is reportedly quadrupled and plasma exposure doubled when compared to phenylephrine administration alone based on a 'standard' 10 mg dose. The authors also noted that a halving of the phenylephrine dose (from 10 mg to 5 mg) in combination with the same standard paracetamol dose achieved plasma levels of phenylephrine similar to a 10 mg dose administered alone. [redacted] understands these outcomes form the basis for the rescheduling proposal which seeks to translate the findings into a clinical perspective.

[redacted] has no objections in supporting this proposal in principle, as it represents a response to new clinical evidence. However, we believe several issues warrant further consideration as outlined below.

- The number and range of OTC products containing phenylephrine currently available in pharmacies and other retail outlets are significant. Therefore if the proposed rescheduling is implemented in full, there will be substantial impact on community pharmacies and the industry from a logistical point of view.

- Paracetamol and phenylephrine have been used in combination for many years. At the existing 'standard' combination dosages, [redacted] is not aware of any significant reported cases of adverse cardiovascular effects. Therefore we would request information on the clinical effects of the 10 mg dose of phenylephrine in combination with the paracetamol i.e. the extent to which the reported substantial increase in peak plasma concentration and plasma exposure affects blood pressure due to the sympathomimetic effects of phenylephrine.

Submitted by:

[redacted]

Contacts:

[redacted]

[redacted]

10 September 2014

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[16] Atkinson HC, Stanescu I, Anderson BJ. Increased phenylephrine plasma levels with administration of acetaminophen. N Engl J Med 2014;370(12):1171–2.

[redacted]

[redacted]

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Email: SMP@health.gov.au

Dear Sir/Madam

Public Comment Submission to the March 2014 joint meeting of the Advisory Committee on Chemicals Scheduling (ACCS) and the Advisory Committee on Medicines Scheduling (ACMS)

We refer to the notice published on 14 August 2014 inviting public submissions, with respect to certain substances, addressing a matter raised in s.52E of the *Therapeutic Goods Act 1989*.

[redacted] wishes to provide information on **gamma-butyrolactone** for consideration at the November 2014 joint meeting of the ACCS and ACMS.

Please see the attached submission for details.

We thank the Committees and the Secretariat for the extension to provide comments. It is greatly appreciated.

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

We look forward to further advice from the ACCS, ACMS and the Delegate. Should the Committees or the Delegate require any additional information from Accord at this stage please do not hesitate to contact me on [redacted]

Yours faithfully

[redacted]

[redacted]

11 September 2014

[redacted]

ACCS/ACMS joint-meeting: November 2014

Gamma-butyrolactone

While the feedback [redacted] suggests that gamma-butyrolactone is either not used in cosmetics in Australia or its use is very low, according to the International Cosmetic Ingredient Dictionary and Handbook, gamma-butyrolactone (INCI name butyrolactone) can be used as a solvent or fragrance ingredient in nail polish and enamel removers.

Gamma-butyrolactone is also listed as a solvent and masking agent in the EU Cosmetic Ingredients database with no restrictions.

While the reasons behind the scheduling proposal have not been divulged, based on the proposal to consider the addition of gamma-butyrolactone to Schedule 9 we believe that the concern may relate to gamma-butyrolactone being a precursor of gamma-hydroxybutyrate (GHB), a known recreational drug.

If the reason for this consideration is in fact due to the potential misuse of gamma-butyrolactone as a precursor to a recreational drug, we believe that the scheduling controls should only apply to the types of products that could be misused i.e. where gamma-butyrolactone is a major ingredient in the product with no other toxic or unpleasant tasting ingredients, or where gamma-butyrolactone can be easily extracted from the product.

As far as we are aware, individual ingredients in products like nail polish and enamel removers are difficult to extract from the product.

Any scheduling consideration should also restrict the schedule entry to gamma-butyrolactone. As gamma-butyrolactone is a simple molecule, inclusion of derivatives is likely to capture a much wider range of chemicals with unintended consequences (salts of gamma-butyrolactones are not likely to exist).

Many lactones occur naturally and are known to give a “creamy” tone to the fragrance of flowers such as jasmine, tuberose and gardenias. It is our understanding that they also occur in fruits such as peaches, apricots and plums.

Naturally occurring substances found in these plants such as gamma-undecalactone (also known as peach lactone) and gamma-nonalactone (also known as coconut lactone) as well as synthetic lactones such as gamma-methyl decalactone are used as fragrances. While all of these chemicals are derivatives of gamma-butyrolactone, as far as we are aware, their potential for conversion to GHB has not been raised as a concern.

We also understand that many derivatives of gamma-butyrolactone are used as food flavours e.g. gamma-hexalactone (toasted almond, caramel, tomato), gamma-heptalactone (caramel, milk, nut flavours) and gamma-decalactone (cappuccino, custard, beer). Again, as far as we are aware, no concerns have been raised with the potential for these flavours agents to convert to GHB.

[redacted]

Advisory Committee for Medicines Scheduling
Meeting November 2014

Comments by [redacted] to the proposed amendments referred by the delegate for scheduling advice

11 September 2014

Contact person:

[redacted]

[redacted]

[redacted]

Introduction

[redacted] welcomes the opportunity to comment on proposed amendments to the Standard for the Uniform Scheduling of Medicines and poisons (SUSMP) being considered by the Advisory Committee on Medicines Scheduling (ACMS) at its meeting of November 2014.

[redacted]

Further information can be found in Appendix 1.

Comments on Proposed Amendments

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

2.1- Benzydamine schedule exemption
2.2- Naproxen-Schedule exemption
2.3- Proposal to include Naproxen on Appendix H
2.4- Pantoprazole- New Schedule 2 entry
2.5- Paracetamol when compounded with caffeine-schedule exemption
2.6- Proposal to include paracetamol when combined with ibuprofen in Appendix H.
2.7- Paracetamol in combination with Phenylephrine- Schedule 2, 3 and exemption amendments

Proposal 2.1 Benzydamine-Schedule exemption

(Proposal to exempt from scheduling benzydamine in preparations for topical use containing 3 mg or less of benzydamine in divided oral preparations and 3 mg/ml or less in undivided oral preparations in a pack of 50 ml or less.)

[redacted] does not support this proposal as we believe benzydamine should remain in a pharmacy setting so consumers have access to health professionals who can determine the nature and cause of the condition being treated (sore throat) and determine a more suitable treatment or referral to a doctor if required.

[redacted]

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

Although most sore throats are not serious, certain demographic groups are more at risk of developing complications from a sore throat and may need to see their doctor. These groups include[2] :

- 2–25 years old living in Aboriginal and Torres Strait Islander communities who are at high risk of rheumatic fever (e.g. in central and northern Australia)
- with heart problems caused by rheumatic fever
- with scarlet fever
- with a weakened immune system due to an illness such as HIV or leukaemia
- who are taking medicines that suppress the immune system (e.g. after an organ transplant, chemotherapy for cancer, or for rheumatoid arthritis)
- who have no spleen or whose spleen doesn't work properly
- with anaemia
- who are taking anti-thyroid medicines for an overactive thyroid gland (e.g. carbimazole). Carbimazole can decrease the number of white blood cells (leucopenia), which reduces the body's ability to fight infection.

In the more general population, it is important to determine whether sore throat symptoms are caused by a bacterial infection (such as Streptococcus pyogenes) or by a virus such as the common cold or influenza.[3] Other symptoms associated with a bacterial infection may include fever, swollen glands and tonsillitis[4] and could be indicative of a more serious infection which warrants further medical attention.

General safety precautions

Precaution should be exercised with local anaesthetics when used in the mouth or throat as it may impair swallowing and increase the risk of aspiration.[5] Consumers should also exercise caution if consuming hot food or drinks after a local anaesthetic, as the perception of heat may be dulled, increasing the risk of scalds and burns. The numbing effect of local anaesthetics could also lead to inadvertent biting of the internal walls of the mouth, the tongue or lip in children and/or the elderly.[6] While the risks are relatively minor, they can cause discomfort to consumers and these risks are best managed when the product is sold in a pharmacy setting.

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[1] Section 52E(1A)- *Therapeutic Goods Act 1989*
[2] NPS Medicines Wise- What are the symptoms of a throat infection? LINK
[3] NPS Medicines Wise- What Causes a throat infection? LINK
[4] NPS Medicines Wise- How is a throat infection diagnosed LINK
[5] MIMS online- Difflam Anaesthetic, Antibacterial and Anti-inflammatory Lozenges
[6] IBID

[redacted]

Specific risk factor-pregnancy and breastfeeding

Benzydamine has a B2 classification in relation to pregnancy and the product information states the use of Difflam® lozenges during pregnancy is not recommended.[7] Allowing unscheduled and unsupervised sale of these benzydamine products in a non-pharmacy setting could pose an unnecessary and preventable risk to this demographic group.

Recommendation

[redacted] does not support the proposal and believes the current scheduling remains appropriate.

Making benzydamine a non-scheduled medicine would mean consumers could access this medicine from non-pharmacy outlets without any recourse to healthcare professional advice, intervention or appropriate diagnosis of symptoms which poses a risk to public health and safety.

Proposal 2.2 Naproxen- amend schedule 2 entry

(Proposal to amend the Schedule 2 naproxen entry to exclude naproxen in a dosage form of 200 mg or less of naproxen per dosage unit in packs of 12 or less dosage units with a maximum recommended daily dose of not more than 600 mg of naproxen, and when not labelled for the treatment of children 12 years of age or less.)

[redacted] does not support this proposal as we believe it poses a risk to public health.

Risks and benefits of the use of a substance[8]

This proposal would make this naproxen product a non-scheduled medicine, meaning consumers could access the product from non-pharmacy outlets without any recourse to healthcare professional advice or intervention.

NSAID Guidelines[9] state:

- NSAIDs or selective cyclooxygenase-2 (COX-2) inhibitors should be used at the lowest effective dose for the shortest possible time; as needed rather than regularly;
- Proton Pump Inhibitors should be used in combination to prevent side-effects;

[7] MIMS online- Difflam Anaesthetic, Antibacterial and Anti-inflammatory Lozenges
[8] Section 52E(1A)- *Therapeutic Goods Act 1989*
[9] Gnjidic, D., Blyth, F. M., Le Couteur, D. G., Cumming, R. G., McLachlan, A. J., Handelsman, D. J., ... & Naganathan, V. (2014). Nonsteroidal anti-inflammatory drugs (NSAIDs) in older consumers: Prescribing patterns according to pain prevalence and adherence to clinical guidelines. *PAIN®*.

- All older consumers should be monitored for side effects, drug interactions and drug-disease interactions.

[redacted] argues these guidelines are more likely to be followed if naproxen remains exclusively available in a pharmacy setting with access to health professionals.

All NSAIDs have a similar capacity to cause renal impairment, congestive heart failure, hypertension and oedema.[10]

Chronic sustained systemic exposure to NSAIDs, particularly in consumers over 65 years of age is of concern owing to documented increased risk of gastrointestinal and cardiovascular events.[11]

Elderly consumers are more at risk of NSAID-related adverse effects and their need for NSAID therapy should be assessed carefully.[12] The choice of a short-acting drug is especially important in consumers with impaired renal function. Guidelines for prescribing indicate only one non-aspirin NSAID should be used at any time.[13] The elderly may be particularly at risk of non-adherence to these guidelines, due to the prevalence of osteoarthritis in this age group, there is a strong likelihood that they may use topical NSAID preparations as well as oral NSAIDs owing to targeted marketing campaigns.

Concomitant administration of naproxen with other oral or topical NSAIDs or aspirin may result in increased adverse NSAID effects.[14] With the availability of aspirin, ibuprofen and diclofenac gel outside a pharmacy setting, there is a potential for consumers to combine the use of these products without health professional advice, increasing the risk of systemic adverse effects.

The dosage, formulation, labelling, packaging and presentation of a substance [15]

Under this proposal consumer safety would rely entirely on labelling advisories and consumers reading and understanding these advisories. Although advisory labels would inform consumers of some of the risks relating to the product, [redacted] has consistently argued that risk cannot be addressed by warning labels

[10] NPS RADAR August 2005; Elevated cardiovascular risk with NSAIDs
[11] Safety of diclofenac topical solution compared with oral diclofenac for treatment of osteoarthritis of the knee in consumers aged ≥65 years; 30th Annual Scientific Meeting of the American Pain Society; 19 May 2011
[12] ETG online – Diclofeanc http://online.tg.org.au/complete/desktop/index.htm
[13] ETG online – Diclofeanc http://online.tg.org.au/complete/desktop/index.htm
[14] Voltaren gel Prescribing Information; September 2009; http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm193047.htm
[15] Section 52E(1D)- *Therapeutic Goods Act 1989*

alone. A survey of 1000 consumers conducted in Northern Ireland identified only 80% of participants always or often read the instructions on non-prescription medicine packages and that 3.4% rarely or never read the information. Coupled with participants that only sometimes read the manufacturer's information, 10% of the consumers would be at risk of misusing these medicines.[16] As such, [redacted] believes, pharmacist oversight is essential in ensuring this product is suitable for individual consumers, increase patient education regarding the key differences with varying strengths of diclofenac and hence increase the likelihood the medicine will be taken correctly and safely.

Recommendation

[redacted] believes the current scheduling remains appropriate.

Naproxen and other commonly available NSAIDs are associated with increased cardiovascular risks with elderly consumers being particularly at risk. This risk is magnified with concomitant use with oral and topical NSAIDs or aspirin which are currently available from a non-pharmacy setting. These risk are best mitigated if these products remain exclusively in a pharmacy setting.

Proposal 2.3 Naproxen- Listing on Appendix H

(Proposal to include Naproxen on Appendix H)

[redacted] supports this proposal on the condition that any consumer awareness messages related to naproxen emphasises the essential (mandatory) role of pharmacists in the supply of Schedule 3 medicines and recommend consumers consult with their pharmacist to determine if naproxen is appropriate for them.

Risks and benefits of the use of a substance[17]

[redacted] believes listing naproxen on Appendix H would increase consumer awareness of a specific therapeutic product that may be more suitable, simpler to take, available without a prescription and encourages consumers to seek advice from a pharmacist. We believe this proposal if adopted will lead to consumers being better informed about products that are available without a prescription and the role of the pharmacist in determining whether those products are appropriate.

We note that diclofenac, another non-steroidal anti-inflammatory medicine which has similar pharmacological properties and risk profile has been listed on Appendix H since August 2001. As outlined in the committee report at the time, the decision to list diclofenac on Appendix H was based on the following the reasons:

- long history of safe use;

[16] M Wazaify, E Shields, CM Hughes et al; Societal perspectives on OTC medicines; Family Practice 2005; 22:170-176

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

- well characterised adverse effects; and
- increasing consumer awareness of the range of over-the-counter NSAIDS that are available[18]

Owing to the broad similarities between naproxen and diclofenac, we believe these factors are equally pertinent to this proposal.

Recommendation

[redacted] supports the proposal to include naproxen on Appendix H. We believe this proposal will better inform consumers of products that available without a prescription and encourage consumers to seek counseling and advice from a pharmacist. Naproxen also has broadly similar pharmacological properties to diclofenac which has been listed on Appendix H for over 10 years.

Proposal 2.4 Pantoprazole- New Schedule 2 entry

(A new Schedule 2 entry for pantoprazole when supplied in oral preparations containing 20mg or less of pantoprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 7 days of supply.)

[redacted] believes pantoprazole is best kept as a Schedule 3 medicine, requiring pharmacist intervention to ensure safe and appropriate use.

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

[redacted] believes there are some public risks which warrants pantoprazole and other PPIs to remain as a Schedule 3 medicine.

A Danish review advises that PPIs seem to be associated with increased risk for adverse cardiovascular outcomes.[20]

A recent study has indicated long-term PPI therapy was associated with increased risk of falls and fracture-related hospitalizations. Consequently the long term use of these products need to be carefully managed.[21]

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[18] National Drugs and Poisons Schedule Committee Record of Reasons 32nd Meeting 21-23 August 2001, 26

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

[20] M Charlot, O Ahlehoff, M Lykke Norgaard et al; Proton-Pump inhibitors are associated with increased cardiovascular risk independent of clopidogrel use; Ann Intern Med. 2010; 153:378-386

[21] Lewis, J. R., Barre, D., Zhu, K., Ivey, K. L., Lim, E. E., Hughes, J., & Prince, R. L. (2014). Long-Term Proton Pump Inhibitor Therapy and Falls and Fractures in Elderly Women: A Prospective Cohort Study. *Journal of Bone and Mineral Research*.

There have been long-standing suspicions that acid-suppressive therapy increases the risk of small intestinal bacterial overgrowth, though it has been uncertain whether this risk is restricted to certain patient groups such as the elderly, those infected with H.pylori or those with irritable bowel syndrome.[22]

Inhibition of gastric secretion of acid and gastric enzymes could affect the absorption of nutrients such as calcium, iron and vitamin B12.[23]

Evidence from large case-control studies suggests an association between current PPI use and community-acquired pneumonia, the risk being greatest in consumers commencing therapy within the previous 7 days.[24]

In early 2011, the US Food and Drug Administration (FDA) concluded that fracture risk with short-term, low dose non-prescription PPI use was unlikely as the products are marketed at low doses and only intended for a 14 day treatment course up to 3 times per year. Interestingly though, the FDA also acknowledged that consumers may take the products contrary to the instructions on the label.[25]

Acknowledging the seriousness of these risks, PPIs have been available for several years as a Schedule 3 medicine without undue adverse health outcomes. Pharmacists supply non-prescription PPIs according to a professional protocol[26] with referral to the GP for more serious issues and identified concerns.

[redacted] acknowledges that Nycomed, the sponsor of Somac®, has continued to work collaboratively with pharmacy in developing protocols and training to support the professional supply of pantoprazole with consideration of patient safety. With this in mind, [redacted] continues to support listing pantoprazole and other PPIs within Appendix H of the SUSMP, allowing direct-to-consumer advertising as well as the ability to provide pharmacy assistants with information to enhance their capacity in responding to direct product requests for these medicines.

It is also anticipated that with the implementation of electronic patient records, consideration will be given to the inclusion of non-prescription medicines on a person's medication history. It would be reasonable to expect that Schedule 3 medicines would be considered for inclusion and [redacted] believes there would

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[22] M Charlot, et al; Proton-Pump inhibitors are associated with increased cardiovascular risk independent of clopidogrel use; Ann Intern Med. 2010;
[23] ibid
[24] NPS Prescribing Practice Review for Primary Care; May 2009; Proton pump inhibitors
[25] http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforConsumersandProviders/ucm213206.htm
[26] http://www.psa.org.au/archives/5347

be benefit in recording the incidence and treatment of reflux as part of a person's health records.

The purpose for which a substance is to be used and the extent of use of a substance[27]

[redacted] notes a very similar proposal was assessed by the committee at its February 2012 meeting and a key reason at the time for retaining pantoprazole as a Schedule 3 medicine was are follows

"Members suggested that the very effectiveness of pantoprazole might also be a reason to retain pantoprazole in Schedule 3. Members noted that retention in Schedule 3 would enhance the likelihood that a pharmacist would detect a patient who was repeatedly accessing pantoprazole, allowing the pharmacist to advise that unresolved GORD symptoms when using pantoprazole were a reason to consult with a GP."[28]

[redacted] believes this remains a key reason for why pantoprazole should remain a Schedule 3 medicine.

Any other matters that the Secretary considers necessary to protect public health[29]

[redacted] is also concerned with the potential availability of pantoprazole as a Schedule 2 product through licensed non-pharmacy retail outlets in rural/remote areas. Jurisdictions license non-pharmacy outlets to supply Schedule 2 medicines in locations in which there is no pharmacy within a specified distance (from 10km in Tasmania[30] to 40km in the Northern Territory[31]). In such circumstances, there is no training for any of the retail staff and there is no access to health professional advice. Given that consumers living in rural and remote areas have generally older populations, higher levels of health risk and higher rates of chronic disease,[32,33] the risks described above may be increased. Even though the population may be small, the safety of consumers in these locations still remains an important priority. Although consumers in rural/remote areas may be disadvantaged to a small extent with regards to access to PPIs for the treatment of oesophageal reflux, other effective treatments such as ranitidine remain readily available.

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

[28] Interim Decision & Reasons for Decisions by delegates of the Secretary to the Department of Health and Ageing- April 2012, 121

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

[30] Tasmanian Poisons Act 1971 (s.27)

[31] Northern Territory Poisons and Dangerous Drugs Act (s.24)

[32] National Rural Health Alliance; Fact Sheet 2 – The way forward for rural health; May 2011; www.ruralhealth.org.au

[33] AIHW – Rural Health; http://www.aihw.gov.au/rural-health/

[redacted]

Recommendation

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

Proposal 2.5 Paracetamol when compounded with caffeine- Schedule Exemption

(Proposal to exempt paracetamol when compounded with caffeine, in a powder or granule product containing 1000mg or less of paracetamol and in tablets or capsules containing 500mg or less of paracetamol when paracetamol is the only therapeutic active constituent and when supplied in primary packs of not more than 20 tablets/caplets or 10 sachets of powders/granules.)

[redacted] does not support this proposal as it poses a risk to public health.

This proposal would enable consumers to purchase these medicines from non-pharmacy outlets without any recourse to professional advice or intervention. The risks in relation to inadvertent excessive intake of caffeine are magnified in these non-pharmacy settings with no increased benefit to consumers.

Risks and benefits of the use of a substance[34]

A detailed breakdown of the benefits and risks of paracetamol compounded with caffeine is presented on the NPS Medicine Wise website[35]

Caffeine is claimed to enhance the efficacy of paracetamol. However, peak plasma levels and extent of absorption are similar for paracetamol with caffeine and paracetamol alone. Compared with paracetamol alone, a person taking the combination of paracetamol with caffeine may be more likely to experience adverse effects than to get improved analgesia.

The amount of caffeine that can be ingested per day from paracetamol with caffeine is between 65 mg (1 tablet) and 520 mg (8 tablets).Even a small dose of 50 mg caffeine can cause tachycardia, anxiety and ectopic beats. Toxicity is normally seen at doses > 500 mg, but this depends on tolerance.

Take into account dietary and other sources of caffeine: consumers may not be aware from the brand name that a particular preparation contains caffeine. Consider whether paracetamol with caffeine is necessary: it cannot be assumed that it will be tolerated in the same way as paracetamol alone.

[34] Section 52E(1A)- *Therapeutic Goods Act 1989*
[35] NPS Medicine Wise- brief item- paracetamol in combination with caffeine

Frequent and prolonged use may result in medication-overuse headache

Medication-overuse (rebound) headache may occur with prolonged and frequent use of medicines used for headache, including those containing paracetamol and caffeine.

Medication-overuse headache is the most prominent sign of withdrawal and over time may lead to an imperceptible dependence on analgesic drugs. It can be diagnosed only after abstinence from the drug for a week or more.

Excessive consumption of caffeine

Caffeine is present in a variety of foods and beverages as well as in herbal, prescription and over-the-counter medicines.

Consequently, consumers should be advised about dietary and other sources of caffeine if paracetamol compounded with caffeine is being taken so that they do not inadvertently consume more than the recommended maximum of 520 mg caffeine per day.[36] This will not occur if this medicine can be purchased from a non-pharmacy outlet.

Specific risk factor pregnancy and breastfeeding

Pregnant women should not consume more than 200 mg caffeine per day, as this may increase the risk of spontaneous miscarriage. Consuming more than 300 mg per day may also increase the risk of preterm delivery and foetal growth retardation. [37]

Caffeine is readily transferred to breast milk and young infants are poor metabolisers of caffeine. Infants who are breastfed by mothers consuming more than 300 mg caffeine per day may become jittery and restless, and may experience sleep difficulties. If the product is available outside of pharmacies, a mother's caffeine intake (from medicines as well as food and drink) cannot be monitored; hence they could be at risk of inadvertently consuming an excessive amount of caffeine.

the dosage, formulation, labelling, packaging and presentation of a substance[38]

Paracetamol in combination with caffeine is sold under the brand name Panadol Extra®. Advertisements for this product generally avoid placing emphasis on the fact this product contains caffeine, rather it is mentioned in general terms such as 'contains a second active ingredient that amplifies the analgesic effects of

[36] NPS Medicine Wise- brief item- paracetamol in combination with caffeine
[37] IBID
[38] Section 52E(1A)- *Therapeutic Goods Act 1989*

paracetmol [39]' or 'clinically proven combination of ingredients.'[40].Owing to the name of the product combined with its marketing campaign is could be argued that many consumers will make the assumption that Panadol Extra® is a 'better' or 'more powerful' product than regular Panadol®. Therefore, [redacted] asserts that a significant proportion of consumers will automatically self-select the Panadol Extra product, but may not necessarily be aware that the product contains 65 mg of caffeine, nor the potential additional side effects and risks of using this combination product as opposed to regular paracetamol.

This presents a significant risk of adverse medical events if paracetamol in combination with caffeine were available from a general retail setting, without access to a health professional.

Recommendation

[redacted] does not support the proposal and believes the current scheduling remains appropriate.

The proposal to exempt from scheduling would mean consumers could purchase the product from non-pharmacy outlets without any recourse to healthcare professional advice or intervention. As such the risks of the product particularly in relation to excessive intake of caffeine by consumers are magnified.

Proposal 2.6 Paracetamol in combination with ibuprofen – Appendix H listing

(Proposal to include paracetamol when combined with ibuprofen in Appendix H)

[redacted] is not opposed to this proposal, however we have some concerns that should be taken into consideration and be mitigated where possible.

- Advertising these products runs the risk that consumers will want to use combination ibuprofen/paracetamol products as a first line treatment for relieving all types of pain when ideally they should start with products containing a single active ingredient (assuming medication is the most suitable treatment option) and moving to a combination product only if required.
- Furthermore, we believe there is limited evidence to suggest that combination ibuprofen/paracetamol products are appropriate for first line treatment of pain relief, perhaps with the exception of dental pain where studies have indicated combination products are more effective than stand-alone paracetamol or ibuprofen products.
- In circumstances where consumers are allergic to paracetamol or ibuprofen but are unaware of it, taking a combination product as first line treatment may make

[39] Panadol Extra 2010 Advertismentr- http://www.youtube.com/watch?v=hzrbkYaTlXU
[40] Panadol Extra with Optizorb Australia Advertisment- http://www.youtube.com/watch?v=4OFmFEf6ZZY

it more difficult to identify which active ingredient was the cause of the adverse event.

- We believe the views of gastroenterologists and pain management specialists should be sought as part of the decision making process.

Recommendation

While [redacted] does not oppose this proposal, we believe there are some risks that need to be taken into consideration and mitigated where possible prior to listing on Appendix H being approved.

Proposal 2.7 Paracetamol in combination with phenylephrine –Scheduling Changes

Paracetamol in combination with Phenylephrine

Proposal to include the following in Schedule 3:
500 mg of paracetamol when combined with more than 2.5 mg phenylephrine per tablet or capsule or caplet. Individually wrapped powders or sachets of granules containing paracetamol 1000 mg and more than 5 mg phenylephrine per dose

Proposal to include in the following in Schedule 2:
500 mg of paracetamol when combined with 2.5 mg phenylephrine or less per tablet or capsule or caplet in packs containing more than 20 tablets or capsules or caplets per pack. Individually wrapped powders or sachets of granules containing paracetamol 1000 mg and 5 mg phenylephrine or less per dose in packs containing more than 10 such powders or sachets
Proposal to exempt from scheduling the following:
500 mg of paracetamol when combined with 2.5 mg phenylephrine or less per tablet or capsule or caplet in packs containing 20 or less tablets or capsules or caplets per pack Individually wrapped powders or sachets of granules containing paracetamol 1000 mg and 5 mg phenylephrine or less per dose in packs containing 10 or less such powders or sachets.

[redacted] supports this proposal as it places parameters for scheduling classification not only on the amount of paracetamol, but also the amount of phenylephrine contained in these products.

Risks and benefits of the use of a substance[41]

A recent study has highlighted the risks for consumers when consuming higher doses of phenylephrine in combination with paracetamol. The results showed an unexpected pharmacokinetic interaction among the three drugs: the administration of phenylephrine (at a dose of 10 mg) in combination with acetaminophen aka paracetamol (1000 mg) and ibuprofen (300 mg), as compared with the administration of 10 mg of phenylephrine alone, resulted in nearly a

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

quadrupling in the maximal plasma concentration.[42] Ibuprofen was subsequently shown not to contribute to this increase.

The plasma exposure of phenylephrine combined with acetaminophen doubled, increasing exposure beyond levels that were previously deemed to be safe and effective. Elevated phenylephrine plasma concentrations is related to an increase in systolic and diastolic blood pressure, thus increasing the potential risk of adverse events, particularly in older consumers.[43]

Recommendation

[redacted] supports the proposed amendments to the scheduling of paracetamol in combination with phenylephrine. New evidence has indicated risks associated with paracetamol products in combination with higher doses of phenylephrine. These risks can be minimised by restricting the availability of higher strength products to pharmacy where consumers have access to the advice of health professionals.

[42] Atkinson, H. C., Stanescu, I., & Anderson, B. J. (2014). Increased Phenylephrine Plasma Levels with Administration of Acetaminophen. *New England Journal of Medicine*, *370*(12), 1171-1172.
[43] IBID

[redacted]

Appendix 1

Quality Use of Medicines

Quality Use of Medicines (QUM) is one of the central objectives of Australia's National Medicines Policy[44]. [redacted] believes that QUM is best supported by the supply of medicines through a pharmacy where there is access to professional support and advice from a pharmacist, with assistance provided from trained pharmacy assistants.

It should be noted that community pharmacy maintains a high standard of patient care with the Quality Care Pharmacy Program (QCPP) which is recognised as the Australian Standard[45] for service provision within the community pharmacy sector. By contrast, there are no controls or quality assurance processes in place for the supply of medicines outside of the pharmacy sector.

The QCPP is a quality assurance program aimed at raising the standards of pharmacy services, ensuring community pharmacies provide a uniform approach when delivering professional services and customer care. QCPP accreditation has been shown to support continuous improvement in the supply of medicines.[46]

As of 1 September 2014, approximately 93 per cent of Australian community pharmacies are QCPP accredited. As part of QCPP, it is a requirement that all pharmacy assistants involved in the supply of non-prescription medicines must be appropriately trained by an external training provider. This training includes initial and refresher training in supplying non-prescription medicines and teaches the use of protocols such as 'Ask, Assess, Advise'[47] in order to triage patient requests and refer to the pharmacist when appropriate.

Consumer access and advice

Medicines are not normal products of commerce, having the potential to do significant harm if used incorrectly or inappropriately. Consumers need and want advice on the correct and proper use of medicines and this is best achieved with supply through the pharmacy sector.

The use of and access to medicines in Australia is changing, with the population ageing and consumers contributing more and more to the cost of medicines.[48] It is essential to protect the most vulnerable consumer groups, particularly children, the elderly, those from poorer socio-economic backgrounds or those who do not speak or understand English well. Providing consumer access to information via hand-outs or labelling is not

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[44] http://www.health.gov.au/internet/main/publishing.nsf/Content/National+Medicines+Policy-1

[45] Australian Standard® AS 85000-2011 Quality care Pharmacy Standard – quality management system for pharmacies in Australia

[46] Chapman J, An Evaluation of the Quality Care Pharmacy Program Part 5; Pharmacy Guild of Australia; 2005

[47] http://www.guild.org.au/Guild_Training/Pharmacy+Assistants+Training/A+Career+in+Pharmacy/Ask+Assess+Advise.page

[48] Australians paying for medicines – new research; AHHA 13/09/2011; http://ahha.asn.au/news/australians-paying-more-medicines-new-research

enough. Facilitating access to professional advice for the prescribing and supply of medicines is the best way to maintain safe and cost-effective access to medicines.

The high incidence of polypharmacy warrants health professional advice on the use of medicines. A recent random cross-sectional survey of Australians aged 50 years and over reports that 87% of the respondents used a medicine in the previous 24 hours, with a mean of 4.6 medicines per participant. Over 43 per cent of participants reported use of five or more medicines in the previous 24 hours and almost 11 per cent reported using ten or more medicines.[49]

With regards to non-prescription medicines, a research project[50] from the Fourth Community Pharmacy Agreement demonstrated that 80% of the interviewed consumers wanted advice to always be available at the time of purchase and the majority of consumers do not have issues with accessing non-prescription medicines from community pharmacies.

[49] Morgan TK, Williamson M, Pirotta M; A national census of medicines use: a 24-hour snapshot of Australians aged 50 years and older; MJA 2012; 196(1):50-53

[50] Consumer perception on supply of and access to Pharmacy Medicines; Healthcare Management Advisors; March 2010