[redacted]

PROPOSED AMENDMENTS TO POISONS STANDARD

ACMS Meeting November 2019

Comments by The Pharmacy Guild of Australia on the proposed amendments referred by the delegate for scheduling advice for consideration by the Advisory Committee on Medicines Scheduling

1. **Paracetamol**
2. **Hyoscine butylbromide**
3. **Calcifediol monohydrate**
4. **Lidocaine**
5. **Paracetamol and ibuprofen**

Date 26 September 2019
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[redacted]

1. PARACETAMOL

Proposal

This proposal would modify the Schedule 4 and Schedule 2 entries for paracetamol to limit the concentration and/or the volume and/or the maximum paracetamol mass in Schedule 2 paracetamol liquid preparations.

Overview

We do not object to the intention behind this proposal as it would provide consistency with the maximum for tablets or capsules where the primary pack cannot contain more than 100 tablets or capsules (and by extension 50g).

However, we believe that there has been a drafting error with the proposed wording as it is incomprehensible to state that "*a liquid preparation can be no greater than 50 mg per mL in 100 mL with a maximum of 50 g of paracetamol per container*".

We presume that the suggested amended entry should have read:

> "liquid preparations for oral use containing no greater than 50 g paracetamol per container"

The risks and benefits of the use of a substance

As noted by NPS Medicinewise article on the *"Safe and appropriate use of paracetamol: closing the consumer knowledge gap"*[1]:

> *In Australia, paracetamol is recommended as first-line therapy for mild acute or chronic pain that is not relieved by non-pharmacological approaches such as reassurance, rest, ice or heat packs.*
>
> *The maximum daily oral dosage of paracetamol in adults and children older than 12 years is 500 to 1000 mg every 4 to 6 hours, or 665 to 1330 mg modified-release paracetamol every 6 to 8 hours, with a maximum of 4 g in a 24-hour period.*
>
> *In children aged 1 month to 12 years the optimal oral paracetamol dosage is 15 mg/kg (lean body weight, up to a maximum of 1 g) every 4 to 6 hours with no more than four doses (or a total of < 4 g) in a 24-hour period.*
>
> *Hepatotoxicity has been reported at doses within the therapeutic range of paracetamol (in some cases at doses less than the recommended 4 g/day), although why certain individuals may be at greater risk of toxicity is unclear.*
>
> *Toxicity can be influenced by age, comorbidities, alcohol use, nutritional status (eg, prolonged fasting), concurrent medicine use and genetics.*
>
> *In children with febrile illness the therapeutic margin for paracetamol may be particularly narrow.*
>
> *Approximately half to two-thirds of overdose cases associated with paracetamol use are unintentional.*

[1] https://www.nps.org.au/news/safe-and-appropriate-use-of-paracetamol-closing-the-consumer-knowledge-gap

Descriptive, cross-sectional studies have highlighted deficiencies in patient knowledge about paracetamol use.
These deficiencies centred around:

- *lack of recognition of paracetamol as the active ingredient in a multitude of generic and brand name medicines.*
- *uncertainty surrounding the maximum daily dose*
- *lack of knowledge about the dangers of 'double-dipping' or taking two over-the-counter medicines containing paracetamol*
- *perceived safety of paracetamol due to its over-the-counter status*
- *lack of awareness of the potential for liver damage with misuse.*

Given the fact that paracetamol is one of the most commonly used OTC analgesics but also one that can have a narrow safety margin it would be sensible to have a maximum mass in liquid preparations. We do not believe that there should be a change to the scheduling of the currently available paracetamol registered products.

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

As noted above in the NPS Medicinewise article paracetamol is one of the most commonly used OTC analgesics but also the most commonly misused in Australia in 2013.

Having a maximum quantity would be a sensible option. If the intended wording was supposed to be:

"liquid preparations for oral use containing no greater than 50 g paracetamol per container"

then this would provide a ceiling to liquid presentations of paracetamol but have no scheduling change to any currently ARTG listed product as listed in the invitation.

Strength			Volume in mL	Total in milligrams		Total Mass in Grams	
24	mg	ml	50	1200	mg	1.2	grams
24	mg	ml	100	2400	mg	2.4	grams
24	mg	ml	200	4800	mg	4.8	grams
24	mg	ml	500	12000	mg	12	grams
48	mg	ml	50	2400	mg	2.4	grams
48	mg	ml	100	4800	mg	4.8	grams
48	mg	ml	200	9600	mg	9.6	grams
48	mg	ml	500	24000	mg	24	grams
50	mg	mL	60	3000	mg	3	grams
50	mg	mL	100	5000	mg	5	grams
50	mg	mL	200	10000	mg	10	grams
50	mg	mL	1000	50000	mg	50	grams
100	mg	mL	5	500	mg	0.5	grams
100	mg	mL	20	2000	mg	2	grams

32.5	mg	mL	120	3900	mg	3.9	grams
32.5	mg	mL	240	7800	mg	7.8	grams
32.5	mg	mL	360	11700	mg	11.7	grams

The toxicity of a substance

As noted in the NPS article above paracetamol has a narrow safety margin with hepatotoxicity being reported at doses within the therapeutic range.

Of all accidental poisonings by pharmaceuticals resulting in hospital admissions reported in Australia during 2009–2010, around 3% occurred in children aged 0–4 years and were attributable to non-opioid analgesics, antipyretics and antirheumatics. Of these most were due to paracetamol, and non-steroidal anti-inflammatory medicines.

Knowledge gaps in carers of young children may contribute to unintentional misuse and overdose of paracetamol. In a cross-sectional study performed in the USA, only 38% of participants correctly selected and measured the appropriate paracetamol dose for infants or children.

Knowledge gaps with respect to paracetamol use in children included:

- *the perception that paracetamol is a safe medicine*
- *an uncertainty around appropriate indications*
- *a lack of awareness of strengths and formulations*
- *the methods used to measure the correct dose.*

Multivariate analysis demonstrated that limited literacy was a significant independent predictor of paracetamol overdose. Therefore, in addition to simple and effective package labelling, education on the appropriate and safe use of paracetamol in adults and children is an important contributor to safe use.

A maximum mass in a liquid product of paracetamol would be a sensible safety option which would be consistent with solid dosage forms. As suggested above we believe the appropriate wording should be:

"liquid preparations for oral use containing no greater than 50 g paracetamol per container"

The dosage, formulation, labelling, packaging and presentation of a substance

Paracetamol comes in a number of formulations with different strengths, colours, flavours and brands which are sold alongside other preparations which include other active ingredients such as ibuprofen. As noted above the knowledge gaps with respect to paracetamol use in children could lead to inadvertent overdose. We agree that having a maximum mass in bottles of liquid paracetamol will help to address some of these concerns and be consistent with the maximum for tablets and capsules.

The potential for abuse of a substance

There is a potential for paracetamol to be misused but this is often inadvertent rather than intentional especially with liquid presentations used for children. By having a maximum mass it may prevent misadventure with this substance.

Summary

We agree that the change is an appropriate safety measure for this substance to ensure that paracetamol products are sold in preparations that have a ceiling on the paracetamol mass in the container. However, the suggested wording would, depending on interpretation, mean that the 100mg/mL formulation in 20 mL (eg [redacted] would become a Schedule 4 Prescription Only Medicine.

We suggest the following wording would be more appropriate than that suggested in the invitation for consultation:

> "liquid preparations for oral use containing no greater than 50 g paracetamol per container"

2. HYOSCINE BUTYLBROMIDE

Proposal

This proposal would modify the Schedule 2 entry to allow for the (undivided) oral liquid dose form for preparations containing 20 mg or less per dose unit in a pack containing 200 mg or less hyoscine butylbromide from a 'Prescription Only' (Schedule 4) to a 'Pharmacy Only' (Schedule 2) medicine.

Overview

Given the recommendation made in an article in the Australian Prescriber[2] *"Dosing errors with* [redacted] *"* that the product be withdrawn from the market we do not agree with this proposal. Whilst this particular product was a mixture of anticholinergic compounds hyoscyamine, atropine and hyoscine do not see a compelling reason for hyoscine butylbromide to be downscheduled from Prescription Only. Presumably the sponsor of this application intends to market a product with hyoscine butylbromide in a liquid form and given the previous experience in the market with a similar product we believe the current scheduling remains appropriate.

The risks and benefits of the use of a substance

Risks

Hyoscine butylbromide is the active ingredient in [redacted] tablets which are indicated for use in spasm of the gastrointestinal tract. According to the TGA-approved Product Information[3] hyoscine butylbromide is contraindicated in patients with:

- mechanical stenosis in the gastrointestinal tract;
- achalasia;
- paralytic or obstructive ileus;
- intestinal atony;
- prostatic hypertrophy with urinary retention;
- myasthenia gravis;
- glaucoma;
- pathological tachyarrhythmias;
- megacolon.

In severe cases, unexplained abdominal pain persists or worsens, or occurs together with symptoms like fever, nausea, vomiting, changes in bowel movements, abdominal tenderness, decreased blood pressure, fainting or blood in stool, medical advice should immediately be sought.

The Product Information notes that "Hyoscine may cause drowsiness: patients so affected should not drive or operate machinery" although it is not listed in Appendix K *"Drugs Required to be Labelled with a Sedation Warning".*

Patients should abstain from alcohol. However, as a quaternary ammonium compound with low lipid solubility, hyoscine butylbromide cannot cross the blood/brain barrier easily and only rarely causes the central nervous system side effects associated with atropine and hyoscine.

Elevation of intraocular pressure may be produced by the administration of anticholinergic agents such as hyoscine butylbromide in patients with undiagnosed and therefore untreated narrow-angle glaucoma.

[2] https://www.nps.org.au/australian-prescriber/articles/dosing-errors-with-donnalix-infant-drops
[3] https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2018-PI-01383-1&d=201909161016933

Because of the potential risk of anticholinergic complications, caution should be used in patients prone to narrow angle glaucoma as well as in patients susceptible to intestinal or urinary outlet obstructions and in those inclined to tachyarrhythmia.

Benefits

Hyoscine butylbromide is a quaternary ammonium compound which, as an anticholinergic agent, has a ganglion blocking component. Due to its anticholinergic action, hyoscine butylbromide reduces the tone and peristalsis of smooth muscle in hollow organs with parasympathetic innervation.

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

The TGA-approved Indications for the currently marketed products that contain hyoscine butylbromide is for the treatment of spasm of the gastrointestinal tract.

The dose for adults and children over 6 years of age is two tablets (2 x 10 mg) four times daily.

The tablets are not recommended for children under 6 years of age.

The currently marketed product containing the substance states that the tablets are not recommend for children under 6 years of age. We would question why then a liquid presentation containing this substance would be necessary.

The toxicity of a substance

As noted in the TGA-approved PI for hyoscine butylbromide serious signs of poisoning have not been observed in man. In case of overdose, anticholinergic symptoms such as urinary retention, dry mouth, reddening of the skin, inhibition of gastrointestinal motility, tachycardia, drowsiness and transient visual disorders may occur.

Toxicity data from studies in animals after parenteral administration suggest that the following may be possible:

- shock,
- Cheyne-Stokes respiration,
- respiratory paralysis,
- clonic spasms,
- paralysis of striated muscle,
- coma,
- paralytic ileus,
- bladder atony.

The approved PI suggests the following management for oral overdose:

> induce emesis, gastric lavage, activated charcoal followed by magnesium sulfate (15%). Supportive measures if necessary should be instituted. Symptoms of overdosage may respond to parasympathomimetics. Ophthalmological advice should be sought urgently in cases of glaucoma. Pilocarpine may be administered locally in patients with glaucoma. Sympathomimetics may be used for circulatory support. For mental excitation, diazepam.

> Cardiovascular complications as a result of using this medicine should be treated according to usual therapeutic principles. In case of respiratory paralysis, intubation and assisted respiration. Catheterisation may be required for urinary retention. In addition, appropriate supportive measures should be used as required.

Given that consumers will assume that a liquid presentation is especially formulated for children we do not believe that it would be appropriate for this product to be Schedule 2 given the experience with another product with similar ingredients as outlined in the National Prescriber article where there were a number of cases of misadventure. The authors recommending that the product be withdrawn from the market.

The dosage, formulation, labelling, packaging and presentation of a substance

There is currently no product registered on the ARTG that is a liquid containing hyoscine butylbromide and we would question why such a product would be necessary given that the Australian Prescriber[4] article stated that "[redacted] *(containing the anticholinergic compounds hyoscyamine, atropine and hyoscine) is used to relieve infant colic although evidence supporting its effectiveness is lacking."*

Given that there is no product currently available and we question why a product would be developed we believe that the current scheduling remains appropriate.

The potential for abuse of a substance

There is probably little potential for abuse of this substance but there may be a potential for inadvertent misuse as was seen with the infant colic drops which were the subject of the Australian Prescriber article.

Summary

We believe that the current scheduling remains appropriate.

[4] https://www.nps.org.au/australian-prescriber/articles/dosing-errors-with-[redacted]

3. CALCIFEDIOL MONOHYDRATE

Proposal

This proposal would create a new entry in Schedule 4 for calcifediol monohydrate to restrict the daily dosage to less than 10 micrograms per day unless medically prescribed.

Overview

We believe that this proposal is unnecessary as a Schedule 3 entry would be appropriate to restrict the daily dosage to less than 10 micrograms per day.

Pharmacists currently provide products such as colecalciferol 175 mcg (equiv vit D3 7000 IU) ([redacted] as a Schedule 3 product and provide advice on the correct dosage for this particular product.

The risks and benefits of the use of a substance

Risks

There is a risk of vitamin D toxicity and this is usually because of inadvertent or improper intake of extremely high doses of pharmacological preparations of vitamin D[5]. As noted in the Therapeutic Guidelines[6] hypercalcaemia can be caused by vitamin D toxicity, usually from an exogenous source (ie calcitriol or high-dose colecalciferol therapy).

The Database of Adverse Event Notifications (DAEN)[7] shows only 33 cases for 'vitamin d' but none listed 'hypercalcaemia" as an adverse event and there were no reports of death.

Benefits

The Therapeutic Guidelines state that vitamin D supplementation is recommended for people who:

- have uncomplicated moderate or severe vitamin D deficiency (serum 25-hydroxyvitamin D concentration lower than 30 nanomol/L), particularly if symptomatic
- are starting drug therapy for osteoporosis and have a serum 25-hydroxyvitamin D concentration lower than 50 nanomol/L (see also Vitamin D and osteoporosis)
- have osteomalacia or rickets.

In patients with mild vitamin D deficiency without symptoms or complications (ie not associated with rickets, osteomalacia or hyperparathyroidism), evidence that vitamin D supplementation improves outcomes is limited and inconsistent. Lifestyle changes to improve sun exposure are usually sufficient; however, supplementation for mild deficiency is also reasonable and unlikely to cause harm.

Healthy people with a serum 25-hydroxyvitamin D concentration above 50 nanomol/L are not deficient, and there is no evidence that vitamin D supplements prevent long-term disease in these people.

Like most substances there are risks and benefits and we believe that the risks associated with calcifediol can be managed by the pharmacist as they do with the high dose "once-a-week" preparations of vitamin D currently on the market. We do not believe that it is appropriate for or necessary for this substance to be Schedule 4.

[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6158375/

[6] https://tgldcdp.tg.org.au/viewTopic?topicfile=hypercalcaemia&guidelineName=Bone and Metabolism#toc_d1e175

[7] https://apps.tga.gov.au/PROD/DAEN/daen-report.aspx

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

Whilst to our knowledge there is no currently ARTG-registered product containing calcifediol if there was to be such a product registered in the future it would be used as a supplement for the treatment and prevention of vitamin D deficiency in patients as directed by a doctor or pharmacist.

An ABS Feature Article on Vitamin D[8] states that majority of Australian adults had sufficient levels (>50 nmol/L) of Vitamin D in 2011–12. Just under one in four (23%), or 4 million adults, had a Vitamin D deficiency, which comprised 17% with a mild deficiency, 6% with a moderate deficiency and less than 1% with a severe deficiency. Overall, rates of Vitamin D deficiency were very similar for both men and women.

The article also stated that National Health Survey (NHS) component of the Australian Health Survey asked all people about the different types of supplements they were taking, including Vitamin D.
The results showed that one in twenty Australian adults (5%) were taking Vitamin D supplements in 2011–12.

The is no doubt a need for vitamin D supplementation in Australians with a vitamin D deficiency with the groups at greater risk typically being those with limited sun expose.

Access to calcifediol should not require a prescription and if there is a concern about the potency of this particular version of vitamin D then a schedule 3 listing would address these concerns.

The toxicity of a substance

As mentioned above in “Risks” there is a potential for vitamin D toxicity if taken in excessive amounts but we believe that a Schedule 3 listing such as that for the Once A Week dose of colecalciferol would be appropriate.

The dosage, formulation, labelling, packaging and presentation of a substance

We are unaware of any product containing this substance on the market at the time of writing. If there should be a product launched it would, like other Schedule 3 vitamin D products have all the required labelling such as dosage and warnings. A Schedule 3 listing would ensure that the pharmacist was involved in the sale and would reinforce the difference between this substance and other vitamin D preparations available on the market.

The potential for abuse of a substance

There is little potential for abuse of this vitamin substance but some patients may inadvertently overdose on the substance not realising that it is a more potent version of Vitamin D. If it was Schedule 3 the pharmacist would be involved in the sale as they are for the Once a Week preparations and can provide advice and counselling to the patient.

[8] https://www.abs.gov.au/ausstats/abs@.nsf/Lookup/4364.0.55.006Chapter2002011-12

Factors for pharmacist only medicines (schedule 3)[9]

1. The medicine is substantially safe with pharmacist intervention to ensure the quality use of the medicine. There may be potential for harm if used inappropriately. The consumer can identify the ailments or symptoms that may be treated by the medicine but counselling and verification by a pharmacist is required before use. Consumer consultation with a pharmacist is necessary to reinforce and/or expand on aspects of the safe use of the medicine.

This is a vitamin and is substantially safe but there may be some confusion with regards to its potency with consumers perhaps not realising that it is 3 times as active as other vitamin D products on the market. Pharmacist counselling and verification would assist the consumer to reinforce this message. This is similar to the Once a Week products that are Schedule 3.

2. The use of the medicine is not expected to produce dependency at either the established therapeutic dose or at supratherapeutic doses. Where risk of misuse, abuse or illicit use is identified, the risk can be minimised through pharmacist consumer consultation.

This substance is not a drug of dependence but a vitamin. There is no risk of abuse or illicit use but it may be inadvertently overdosed and this can be addressed by Schedule 3 listing as the pharmacist would be involved in the supply.

3. The risk profile of the medicine is well defined and the risk factors for adverse effects, interactions and contraindications are known, identifiable and manageable by a pharmacist.

The risk profile of vitamin D is well defined and can be managed by a pharmacist.

4. Where the medicine is intended for recurrent or subsequent treatment of a chronic condition, pharmacist intervention is required to monitor safe use of the medicine following recommendation by a medical practitioner or other authorised prescriber. The consumer may not be able to self-monitor the safe ongoing use of the medicine. The condition does not require medical diagnosis or only requires initial medical diagnosis, and the consumer does not require close medical management.

Pharmacists can intervene to highlight that calcifediol is a direct metabolite of colecalciferol and the safe dosage for it is less than 10 microgram per day.

5. The use of the medicine at established therapeutic dosage levels may mask the symptoms or delay diagnosis of a serious condition. Pharmacist-consumer consultation is required to detect the risk of masking a serious disease or compromising medical management of a disease, and to deal with it appropriately.

As with the Once A Week vitamin D supplements the pharmacist can provide the necessary dosage advice to avoid any confusion.

[9] https://www.tga.gov.au/sites/default/files/ahmac-scheduling-policy-framework-medicines-and-chemicals.pdf

Summary

We believe that calcifediol is appropriate as a Schedule 3 substance and it does not need to be Schedule 4. The pharmacist can provide the necessary advice as they do with such products as the Once A Week vitamin D products.

4. LIDOCAINE

Proposal

This proposal would amend the Schedule 2 entry for lidocaine such that 0.6% throat sprays would be classified as “exempted from scheduling”.

Overview

We do not agree with this proposal and believe that the current scheduling for lidocaine remains appropriate given the potential dangers of this liquid preparation if available outside a pharmacy. We have concerns with the assumption that because lidocaine is available in lozenges that it is therefore as safe when available as a liquid preparation. It is very much easier to overdose with a liquid preparation that it is with a slowly dissolving oral lozenge, especially when considering access by younger children.

The risks and benefits of the use of a substance

Risks

As noted in this article[10] lidocaine is not without the potential for serious side effects.

Lidocaine is a local anesthetic drug that produces transient loss of sensory, motor, and autonomic function when the drug is injected or applied in proximity to neural tissue. It is the most common local anesthetic and used in almost all medical specialties. It also is commonly used as an antiarrhythmic agent to depress ventricular arrhythmias.

Infusions of lidocaine (and procaine) have been used to supplement general anesthetic techniques, as they are capable of reducing the minimum alveolar concentration of volatile anesthetics by up to 40% as well as providing pain relief in the peri-operative phase. It is in the class of the local amide anesthetics, which, compared to the ester-type local anesthetics, is usually well tolerated with only rare occasions of allergic reactions. Amide local anesthetics are metabolized (N-dealkylation and hydroxylation) by microsomal P-450 enzymes in the liver.

Applied either by injection, inhalation, or as a topical agent to provide anesthesia, lidocaine has a good safety margin before reaching toxic blood levels. Since it can be applied in various forms to the same patients, however, care must be taken to keep track of the total dose given to minimize its systemic toxicity. In addition, one should take into account the dose of any other local anesthetics that may have been administered to the same patient, as toxic doses appear to be additive. Lidocaine toxicity not only is determined by the total dose (usually 4.5 mg/kg) but also by the rate of absorption, which is dependent on the blood flow of that tissue. To reduce blood flow to the injection site and therefore the rate of absorption, vasoconstrictors such as epinephrine 1:200000 is frequently used and may increase the toxic dose to 7 mg/kg.

Lidocaine toxicity to muscles and peripheral or neuraxial nerves can occur locally at the site of injection. Transient neurologic symptoms (TNS) after high concentration lidocaine spinal anesthetics have been described multiple times and have led to either reducing the concentration of the dose or switching to a different agent.

In addition to direct nerve toxicity, systemic toxicity affecting the brain and/or cardiac muscle can lead to sudden and dramatic changes in the patient’s vital signs.

[10] https://www.ncbi.nlm.nih.gov/books/NBK482479/

The NSW Health release a Safety Information in September 2014 regarding the risk of toxicity from topical anaesthetic products[11]. Whilst this Safety Information alert did not mention products such as lidocaine throat spray it does mention that under normal conditions systemic absorption is generally insufficient to cause major toxicity but severe lignocaine toxicity has been reported and remains a possibility particularly in susceptible people.

Benefits

There is some benefit for patients who are suffering from painful sore throats and there are a number of lozenges, sprays and gargles on the market that contain numbing agents such as lidocaine for the temporary relief of pain. We believe that medicines are not ordinary items of commerce and they should only be available from pharmacies where a consumer can consult with a pharmacist regarding their condition.

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

Lidocaine throat sprays are TGA-indicated for the *"fast relief for painful sore throats. Suitable for the symptoms of mouth and dental ulcers and discomfort associated with tonsillitis and pharyngitis. Relief of the symptoms of inflammation".*

The toxicity of a substance

There is a belief amongst consumers that if a product is available in a non-pharmacy retail outlet then the product must be safe but we believe a liquid formulation of lidocaine presents a safety hazard more so than the lozenge presentation.

Whilst a rare condition there is the possibility of methemoglobinemia where the iron in haemoglobin is stabilized in the ferric form making it unable to bind oxygen and leading to tissue hypoxia and possibility death.[12] As highlighted in the Journal of the American Osteopathic Association lidocaine is an amino-amide drug typically injected subcutaneously or applied topically for procedures such as esophagogastroduodenoscopy and fiberoptic bronchoscopy. The majority of reported cases of lidocaine-induced methemoglobinemia have been associated with upper airway or upper gastrointestinal procedures. Absorption in these cases has occurred via the mucous membranes. Methemoglobinemia secondary to lidocaine exposure is a relatively rare complication. It has been described in adult, pediatric and gynecologic patients. Whilst the Journal article no doubt refers more to injected lidocaine it does mention absorption occurring via the mucous membranes on which a throat spray would be used.

The dosage, formulation, labelling, packaging and presentation of a substance

We presume the product in question for this application is something like [redacted]. We have concerns that the formulation as a liquid would have more potential for misadventure than a box of lozenges. We do not believe that labelling, packaging and presentation would prevent misadventure especially for young children. It would be more likely to cause an overdose in a liquid form than in a lozenge formulation.

[11] https://www.health.nsw.gov.au/sabs/Documents/2014-si-003.pdf

[12] https://jaoa.org/article.aspx?articleid=2211844

The potential for abuse of a substance

There are reports abroad that there is a demand for local anaesthetics for use in cutting illegal drugs. In an article by the BBC[13] *"mild anaesthetics, found in sunburn and first-aid treatments"* are the latest substances being sought by drug dealers. Whilst lidocaine is available in lozenges one would assume that in a liquid preparation if would be easier to divert for use in nefarious activities.

Summary

We believe that the current scheduling of lidocaine remains appropriate.

[13] https://www.bbc.com/news/magazine-11177126

5. PARACETAMOL AND IBUPROFEN

Proposal

This proposal would amend the Schedule 4, Schedule 3 and Schedule 2 entries for paracetamol to allow for paracetamol+ibuprofen combination products to be supplied in pack sizes of up to 12 dosage units, without access to health professional advice.

In effect it proposes a set of controls on paracetamol/ibuprofen combinations based on pack size with:

- 12 dosage units or less as 'exempted from scheduling',
- 13 to 30 dosage units or less as 'Pharmacy Medicine' (Schedule 2),
- 31 to 50 dosage units or less as 'Pharmacist Only Medicine' (Schedule 3) and,
- larger than 50 pack sizes as 'Prescription Only Medicine' (Schedule 4).

Overview

We do not believe this proposal should be approved and the current scheduling remains appropriate.

We believe that having paracetamol and ibuprofen separately and also paracetamol+ibuprofen combination available in retail outlets where there is no access to pharmacy staff for advice can only lead to an increase in overdoses both inadvertent and intentional.

We would remind the Committee that an application for paracetamol + ibuprofen was considered at its 16th meeting in November 2015[14] and the following were some of the points were raised opposing the downscheduling:

- The use of paracetamol in combination with ibuprofen is not considered to be first-line therapy for the treatment of mild to moderate pain.
- A responsible quality use of medicines approach is to retain paracetamol–ibuprofen combinations in Schedule 3. This will facilitate a consistent environment where pharmacists can consider the most appropriate over-the-counter analgesic medicine (including consideration of paracetamol–ibuprofen combination products) and provide tailored advice for consumers.
- Concerns regarding safety, particularly with respect to gastrointestinal bleeding and perhaps renal adverse effects.
- Pharmacists can recommend a paracetamol/ibuprofen combination product to consumers who request Schedule 3 CCA for pain relief. Rather than advertise to consumers, it is considered that paracetamol-ibuprofen combination analgesics products should be better promoted to pharmacists. Approving this scheduling proposal circumvents these concerns.
- Buying multiple small packs would not flag the need for pharmacist intervention.
- The proposed scheduling change would too easily result in inconsistencies and potential for abuse that is more than adequately catered for in the current scheduling.
- No new data is available in the published literature to revert the prior decision. The reasons for the prior rejections in relation to paracetamol/ibuprofen combination analgesics remain relevant and should be given due consideration in any decisions relating to the current application.

[14] https://www.tga.gov.au/scheduling-decision-final/scheduling-delegates-final-decisions-paracetamol-ibuprofen-may-2016

We believe that these concerns should be considered when discussing this application to further downschedule combination paracetamol + ibuprofen products so that they become available in non-pharmacy retail outlets where there is no access to professional advice.

The risks and benefits of the use of a substance

Risks

We note the recent article in The Medical Journal of Australia[15] *"Paracetamol poisoning-related hospital admissions and deaths in Australia 2004-2017"* that stated amongst other things that:

> The NHMD included 95 668 admissions with paracetamol poisoning diagnoses (2007–08 to 2016–17); the annual number of cases increased by 44.3% during the study period (3.8% per year; 95% CI, 3.2–4.6%).
>
> Toxic liver disease was documented for 1816 of these patients; the annual number increased by 108% during the study period (7.7% per year; 95% CI, 6.0–9.5%).
>
> The NSWPIC database included 22 997 reports of intentional overdose with paracetamol (2004–2017); the annual number increased by 77.0% during the study period (3.3% per year; 95% CI, 2.5–4.2%).
>
> The median number of tablets taken increased from 15 (IQR, 10–24) in 2004 to 20 (IQR, 10–35) in 2017.
>
> Modified release paracetamol ingestion report numbers increased 38% between 2004 and 2017 (95% CI, 30–47%).
>
> 126 in-hospital deaths were recorded in the NHMD, and 205 deaths (in-hospital and out of hospital) in the NCIS, with no temporal trends.

The article concluded that the frequency of paracetamol overdose-related hospital admissions has increased in Australia since 2004, and the rise is associated with greater numbers of liver injury diagnoses.

To have yet another product that contains paracetamol in combination with ibuprofen would only lead to an increase in misadventure. Consumers are already confused with the active ingredients and it's not unusual for consumers to be inadvertently be taking a product for their headache containing paracetamol, another product for their head cold (which also contains paracetamol) and yet another product they believe contains ibuprofen (but also includes paracetamol).

Benefits

There are presumably benefits to the use of a combination product but it must be remembered that the indications for these preparations for the short term treatment of mild pain and the risks in having these available in general retail will outweigh the benefits of easy accessibility.

Consumers can already buy paracetamol and ibuprofen in general retail and one or the other should be sufficient to treat a mild condition for sufficient days until the condition resolves or they can consult with a medical practitioner or pharmacist if the condition persists.

[15] https://www.mja.com.au/journal/2019/211/5/paracetamol-poisoning-related-hospital-admissions-and-deaths-australia-2004-2017?utm_source=carousel&utm_medium=web&utm_campaign=homepage

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

[redacted] tablets are indicated for temporary relief of pain associated with: headache, migraine headache, tension headache, sinus pain, toothache, dental procedures, backache, sore throat, arthritis, tennis elbow, period pain, muscular pain, rheumatic pain, aches and pains associated with colds and flu. Reduces fever.

[redacted] is indicated for the temporary relief of acute (short-term) pain and/or inflammation associated with headache, migraine headache, tension headache, sinus pain, toothache, dental procedures, backache, muscular aches and pains, period pain, sore throat, tennis elbow, rheumatic pain and arthritis, and the aches and pains associated with colds and flu.

These products are used for the temporary relief of short term pain and we do not believe that there is a pressing clinical need for the combination products to be made available in a retail outlet where there is no opportunity for consultation with a healthcare professional.

The toxicity of a substance

The combination is available in two different formulations which have different dosing regimens. This could and will lead to confusion amongst consumers which will lead to inadvertent over dosing.

The dangers of paracetamol have been made clear in the recent Medical Journal of Australia article[16] on paracetamol poisoning and given the concerns with paracetamol we do not believe that it is appropriate to downschedule a product that contains paracetamol AND ibuprofen. A recent article in the Townsville Bulletin (see attachment) highlights the dangers of this product already which can only be magnified if it is made more widely available.

The dosage, formulation, labelling, packaging and presentation of a substance

The dosage of the two products available in Australia are:

[redacted]

Adults and children over 12 years. The usual dosage is one to two tablets taken every six hours, as required, up to a maximum of eight tablets in 24 hours.
[redacted] is not recommended for children under 12 years.

[redacted]

Adults under 65 and children from 12 years. 1 tablet every 8 hours as necessary (maximum 3 tablets in 24 hours). Keep to the recommended dose.

[redacted] should not be used for more than 3 days at a time (or not more than 2 days at a time for adolescents aged 12 to 17 years).

Not recommended for children under 12 years of age.
Not recommended for adults 65 years and over.

[16] https://www.mja.com.au/journal/2019/211/5/paracetamol-poisoning-related-hospital-admissions-and-deaths-australia-2004-2017?utm_source=carousel&utm_medium=web&utm_campaign=homepage

There are two formulations of paracetamol and ibuprofen which explains the differences in dosing and this will no doubt cause confusion amongst consumers. Whilst the applications states that it will prominently highlight the difference is dosing of their particular product it is well know that consumers don't always read the instructions and often don't know or look to see what the active ingredient is. It is highly likely that consumers will end up taking a paracetamol and/or an ibuprofen in addition to a [redacted] and/or [redacted] not realising that they are doubling up on the active ingredients.

The potential for abuse of a substance

There is little potential for intentional abuse as paracetamol+ibuprofen are not substances subject to addiction like opioids. However there is potential for inadvertent misuse due to the combination product and that fact that there are two different formulations which have different dosing regimens.

There is an assumption amongst consumers that if a product is available in a general retail outlet then it is safe and can be taken in combination with any other over-the-counter product. However, this may lead to inadvertent overdose if someone is not aware that they are taking paracetamol in a combination product.

Any other matters necessary to protect public health

Given the recent reports of misadventure with combination products containing paracetamol and ibuprofen now is not the time to relax the scheduling of this particular combination product.

We would refer the Committee to the recent article in The Medical Journal of Australia *"Paracetamol poisoning-related hospital admissions and deaths in Australia, 2004-20187"*[17], in addition to a number of main stream media articles on this issue.

[17] https://www.mja.com.au/journal/2019/211/5/paracetamol-poisoning-related-hospital-admissions-and-deaths-australia-2004-2017

12 Sep 2019
Townsville Bulletin, Townsville

Author: Tess Ikonomou • Section: General News • Article type : News Item
Classification : Regional • Audience : 16,484 • Page: 9 • Printed Size: 244.00cm²
Region: QLD • Market: Australia • ASR: AUD 1,481 • Words: 320 • Item ID: 1170936944

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Common pain pills behind hospital rush

TESS IKONOMOU

MORE than 100 people have landed themselves in the Townsville Hospital's emergency department this year after overdosing on over-the-counter medicine including paracetamol and ibuprofen.

According to data from Queensland Health, 116 people had to present to the emergency department up to June this year because they took too much medicine.

There have been 451 presentations for poisoning by drugs, including medicine, anaesthetics and illicit substances.

Last year there were 782 presentations for overall poisoning, with 203 resulting from over-the-counter treatments.

That jumped from 733 overall ED presentations in 2017, and was a slight decrease from 205 paracetamol and ibuprofen poisonings.

Townsville Hospital emergency department director Dr Luke Lawton said people needed to read instructions about administration carefully, as over-the-counter medication in large quantities could be "very dangerous".

"Generally speaking, if the instructed prescribed medication is not working, then there may need to be a different class of drug ... which requires medical assessment from the GP," Dr Lawton said.

"It's also very important to take in existing medication to check in with their pharmacists if any medication may interact with what they have been prescribed ... some of those side-effects can be serious."

Dr Lawton said the ED wanted to see as few patients as possible who had become ill through medication "misadventures".

"We want the community to be taking care of themselves," he said.

Taking more than the recommended dosage of ibuprofen or paracetamol can poison the body, causing dizziness, drowsiness, nausea, vomiting and diarrhoea.

The Queensland Poisons Information Centre receives about 10 calls a day about medication errors.

Manager Carol Wylie said people could protect themselves against overdosing by reading labels carefully, checking medicine strength and the maximum number of tablets per day.

"People who are sick or injured and in pain might also become groggy, confused, anxious and forgetful," she said.

"They may also be susceptible to making mistakes, especially when it comes to taking medicine."