

September 26th 2019

Advisory Committee on Medicines Scheduling
Therapeutic Goods Administration

The NSW PIC provides a call centre service to NSW, Tasmania and the ACT on a near full-time basis and a shared after-hours service to the remainder of Australia. This results in approximately half of Australia's poisons-related calls being received by NSW PIC.

1.1 Paracetamol

Re: Proposed amendment to scheduling of Paracetamol (liquid formulations)

The NSW Poisons Information Centre (PIC) strongly supports the introduction of a limit on the amount of paracetamol that can be supplied in the liquid form in Schedule 2.

We agree that a product containing large quantities of paracetamol, particularly in liquid form, carries a potential for significant human toxicity (including delayed irreversible hepatotoxicity) if the product is accidentally ingested or deliberately misused.

Our preference would be a limit of 10g paracetamol per container of liquid preparation in Schedule 2 as this is a clearly defined toxic dose in adults. In children the toxic dose is >200mg/kg/24 hours which for a 10kg child equates to only 2g. We feel that 50g paracetamol per container of liquid preparation poses a significant risk of harm from accidental exposures, deliberate self-poisonings and repeated therapeutic errors.

A limit of 10g paracetamol per container of liquid preparation would allow the existing products to remain in Schedule 2:

24 mg/mL paracetamol in 50, 100, 200 mL pack sizes;

48 mg/mL paracetamol in 50, 100, 200 mL pack sizes;

50 mg/mL paracetamol in 60, 100, 200 mL pack sizes;

100 mg/mL paracetamol in 5 and 20 mL pack sizes;

32.5 mg/mL paracetamol + 1 mg/mL dextromethorphan in 120 and 240 mL pack sizes

Since January 2014, NSW PIC has received in excess of 6800 calls regarding accidental exposures to liquid paracetamol. More than 6220 of these exposures involved children under the age of 5 years. Of these calls 1828 patients were either in or referred to hospital and 1629 of these patients were under the age of 5 years.

In a sample period of calls (23-06-2018 to 02-09-2019) NSW PIC received 684 calls regarding accidental exposures to liquid paracetamol of which 642 calls involved children under the age of 5 years. 205 patients were either in or referred to hospital during this period due to concerns they had ingested a toxic dose of paracetamol and 196 (95.6%) of these patients were under the age of 5 years.

As illustrated by the table below, 200ml bottles of paracetamol were much more likely to be implicated in hospital referrals compared with 100ml or smaller bottles.

Paracetamol formulation	Total no. calls	In or referred to Hospital
24mg/ml <200ml bottle	36	4
24mg/ml 200ml bottle	129	34
24mg/ml unknown bottle size	78	10
48mg/ml <200ml bottle	28	14
48mg/ml 200ml bottle	124	77
48mg/ml unknown bottle size	78	19
50mg/ml <200ml bottle	16	4
50mg/ml 200ml bottle	40	17
50mg/ml unknown bottle size	23	3
100mg/ml 20ml bottle	116	13
Unknown strength	16	10

Hospital referral was due to concerns a toxic dose paracetamol may have been ingested by the child. NSW PIC has concerns that if larger volume bottles of liquid paracetamol were to become available the number of children exposed to potentially toxic doses of paracetamol following accidental exposures would increase further.

There is growing evidence from multiple sources that the rate of deliberate self-harm, including deliberate self-poisoning, is increasing amongst young people^{1,2,3} and that this behaviour is starting at a younger age. In 2018, NSW PIC received 239 calls regarding deliberate self-poisoning with paracetamol in children aged 14 years and under. In 2019 up until mid-September, NSW PIC has received 155 calls regarding deliberate self-poisoning with paracetamol in children aged 14 years and under. In almost every case these self-poisonings involved paracetamol in tablet form, however, NSW PIC has concerns that liquid paracetamol may become an increasingly popular self-harm option for younger people due to the relevant ease of ingestion of liquid formulations particularly if containers become available which contain larger amounts of paracetamol.

In the UK, reduced pack sizes of paracetamol led to a reduction in deaths resulting from paracetamol overdose⁴. NSW PIC believes it is relevant to also consider pack sizes of all forms of paracetamol freely available for public purchase. There are greatly increased risks and complexities with managing massive paracetamol exposures (>35 grams)⁵. ATOM-2 study on massive paracetamol exposures showed 14% of exposures developed hepatotoxicity and 42% of these were despite standard antidote treatment being commenced within eight hours. Nearly 40% of massive exposures to paracetamol required an increased dose of acetylcysteine antidote in the first 21 hours to reduce the risk of hepatotoxicity.

Restricting the amount of paracetamol that can be supplied in Schedule 2 to a maximum 10g paracetamol per container of liquid would help to reduce the likelihood of massive paracetamol poisonings from both accidental paediatric exposures and single impulsive purchases, while having minimal impact on access to affordable OTC liquid paracetamol.

1. Perera, J., Wand, T., Bein, K.J., Chalkley, D., Ivers, R., Steinbeck, K.S., et al. Presentations to NSW emergency departments with self-harm, suicidal ideation or intentional poisoning, 2010-2014. *Med. J. Aust.* 2018; 208(8):348-53.
2. Hiscock, H., Neely, R.J., Lei, S., Freed, G. Paediatric mental and physical health presentations to emergency departments, Victoria, 2008-15. *Med. J. Aust.* 2018; 208(8) 343-8.
3. Cairns, R., Buckley, N.A. Increased self-poisoning in young Australians: Why? 2Ks? In: 15th International APAMT Scientific Conference. Singapore; 2016.
4. Hawton, K., Bergen, H., Simkin, S., Dodd, S., Pocock, P., Bernal, W., Gunnell, D., Kapur, N. (2013) long term effect of reduced pack sizes of paracetamol on poisoning deaths and liver transplant activity in England and Wales: Interrupted time series analyses. *British Medical Journal*, 346(7895), 1-9. <http://doi.org/10.1136/bmj.f403>

5. Angela L. Chiew, Geoffrey K. Isbister, Katharine A. Kirby, Colin B. Page, Betty S.H. Chan & Nicholas A. Buckley (2017) Massive paracetamol overdose: an observational study of the effect of activated charcoal and increased acetylcysteine dose (ATOM-2), Clinical Toxicology, 55:10,1055-1065, DOI: [10.1080/15563650.2017.1334915](https://doi.org/10.1080/15563650.2017.1334915)

1.3 Calcifediol monohydrate

NSW PIC supports the Schedule 4 - new entry [CALCIFEDIOL MONOHYDRATE for human internal therapeutic use except in preparations containing 10 micrograms or less of calcifediol monohydrate per recommended daily dose.](#)

The table below shows the total number of calls received by NSW PIC regarding exposures to Vitamin D supplements. Since 2015 more than two thirds of all calls were in regards to therapeutic dosing errors.

Year / Type of calls	Therapeutic errors (% total calls)	Other: accidental paediatric, deliberate self-poisoning, etc	Total number of calls
2014	159 (63%)	93	252
2015	232 (70%)	98	330
2016	282 (74%)	99	381
2017	301 (72%)	119	420
2018	334 (68%)	154	488
2019	288 (74%)	99	387

NSW PIC supports the proposed scheduling given that the TGA has identified that the potency of calcifediol appears to be approximately three times greater than colecalciferol. The safe daily dosage recommended by the TGA after evaluation is <10 micrograms/day in comparison to the Vitamin D scheduling limit of <25 micrograms/day. We support the Schedule 4 entry of calcifediol monohydrate except in preparations containing 10mcg or less per recommended daily dose to reduce confusion among consumers and to minimise the risk of further therapeutic dosing errors occurring.

1.4 Lidocaine

NSW PIC does not support the proposed amendment to Schedule 2

LIDOCAINE in preparations for topical use other than eye drops:

containing 10 per cent or less of total local anaesthetic substances, except:

ii) in aqueous sprays for oromucosal use containing 0.6 per cent or less of total local anaesthetic substances

Whilst there may be legitimate reasons for people to prefer the use of a low-dose spray in preference to a lozenge in relieving the pain of a sore throat we feel that the potential risks outweigh these benefits.

Ingestions of >6mg/kg lidocaine can cause toxicity in children. Symptoms can include drowsiness, dizziness, tremors, paraesthesia, hypotension, bradycardia and respiratory depression. Ingestions >10mg/kg can cause seizures.

A 0.6% solution lidocaine contains 600mg/100ml or 6mg/ml. Ingestion of just 10ml of this solution by a 10kg child would put them at risk of toxicity. Whilst lidocaine throat lozenges are currently available at higher doses without access to health professional advice NSW PIC has concerns that a liquid spray solution may be ingested in an amount capable of causing toxicity, particularly if in non-sealed containers or larger volumes. We do not believe these products should be exempt from scheduling.

There have been multiple cases overseas where infants & children have been harmed after consuming lidocaine products. Since January 2018 NSW PIC has received 47 calls regarding accidental paediatric exposures in children under 5yrs of age to lidocaine containing products and

9 of these children were referred to hospital or in hospital due to concerns they had ingested a toxic dose lidocaine. NSW PIC therefore does not support the exemption of lidocaine from scheduling in aqueous sprays for oromucosal use containing 0.6 per cent or less of total local anaesthetic substances.

1.5 paracetamol and ibuprofen

Re: Proposed amendments to scheduling of Paracetamol & Ibuprofen combination products

The NSW Poisons Information Centre (PIC) strongly disagrees with the proposed scheduling changes to combination paracetamol & ibuprofen preparations. The risks associated with poisoning from these products due to therapeutic errors, inappropriate usage, accidental paediatric exposures and particularly deliberate self-poisonings, far outweighs the few benefits associated with changes to existing schedules.

We believe that the Schedule 4 entry for paracetamol should remain: "when combined with ibuprofen in a primary pack containing no more than 30 dosage units" rather than the proposed change to 50 dosage units. We believe the Schedule 3 entry for paracetamol should remain "when combined with ibuprofen in a primary pack containing 30 dosage units or less except when included in Schedule 2."

We believe the schedule 2 entry should remain: "when combined with ibuprofen in preparations for oral use when labelled with a recommended daily dose of 1200mg or less of ibuprofen in divided doses in a primary pack containing no more than 12 dosage units per pack". We do not support the increase to 30 dosage units or the amendment "[except in preparations for oral use when labelled with a recommended daily dose of 1200 mg or less of ibuprofen in divided doses in a primary pack containing no more than 12 dosage units per pack](#)".

The table below shows that since the introduction of combined paracetamol-ibuprofen products the number of calls received at NSW PIC regarding these products has substantially increased each year. 2019 is also currently showing a proportional increase in call numbers compared to 2018. The number of calls received in 2019 up until 15th September involving these products taken in a deliberate self-poisoning already exceeds the total number of deliberate self-poisoning calls received in 2018.

Year / Call Type	Therapeutic Errors	Adverse Reactions	Deliberate self-poisonings	Accidental / other exposures	Total
2014	1	0	3	1	5
2015	10	2	12	7	31
2016	31	6	28	10	75
2017	102	6	35	12	155
2018	166	12	45	26	249
2019 (till 15/9)	134	6	50	25	215
	444	32	173	81	730

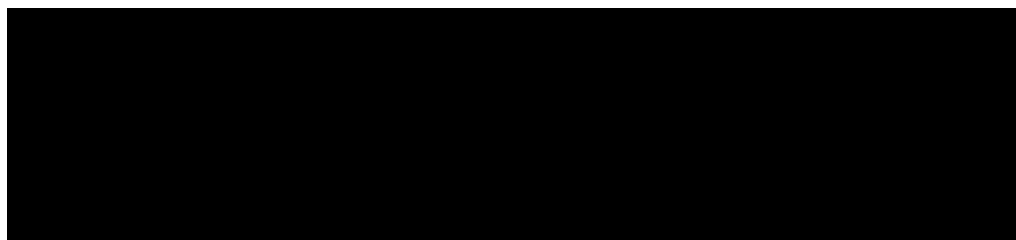
Research recently presented at the Toxicology and Poisons Network Australasia (TAPNA) 2018 annual scientific conference¹ shows paracetamol overdose in Australia is increasing, in both frequency and size (number of tablets). Calls to NSW PIC regarding intentional paracetamol overdose increased by 80%, 2004 to 2017. The median number of tablets ingested in each overdose has increased from 15 to 20 tablets in that period. Increasing the pack size of paracetamol - ibuprofen combination products which are available without either a prescription or

consultation with a pharmacist, further increases the likelihood of overdose of a larger number of tablets. Ingestions of larger amounts of tablets are much more likely to result in significant harm including the risk of delayed and irreversible liver toxicity and kidney damage.

The increasing number of calls regarding therapeutic errors also indicates ongoing confusion amongst the general public about the correct dosing of these products. Increasing the pack size available as an S2 medication and allowing pack sizes up to 12 to be unscheduled will further increase the likelihood of incorrect dosage. The availability of larger pack sizes may also mean therapeutic errors will continue for longer before the patient discusses their medication use with a health professional such as a pharmacist or doctor.

1. Cairns, R., & Buckley N.A. (2018) Flavour of the decade: increasing frequency and size of paracetamol overdose reported to Australia's Largest Poisons information Centre. In; Toxicology and Poisons Network Australasia 2018 Scientific Meeting, Sydney, 2018.

Regards



NSW Poisons Information Centre

