

10 May 2018
Advisory Committee on Medicines Scheduling
Therapeutic Goods Administration

Consultation: Invitation for public comment - ACMS meeting, June 2018

- *Amending the Appendix A entry for lubricants to clarify use for 'preparations that provide a lubricating action between machinery parts'; and*
- *Including a group entry for volatile alkyl nitrites in Schedule 4.*

We support tighter and more inclusive scheduling of volatile alkyl nitrites but advocate for a more restrictive schedule than Schedule 4 due to concerns over misuse and toxicity. At minimum we would recommend alkyl nitrites being Appendix D, but preferably Schedule 9 or Schedule 10 (rather than Schedule 4 or Schedule 8 since these substances do not have an established therapeutic value). In addition amending Appendix A to clarify exemptions from scheduling is supported.

Lack of established therapeutic value:

Amyl nitrite has been used as a first aid measure to induce methaemoglobinaemia after cyanide exposure. However, current recommendations include sodium thiosulphate plus hydroxocobalamin, or sodium nitrite plus sodium thiosulfate [1]. Thus volatile nitrites have been superseded for this indication. Volatile nitrites were also historically used for angina, however have been replaced by nitrates. Thus, there is minimal therapeutic role for alkyl nitrites so we do not believe they need the widespread availability of Schedule 4. Alternatively, they could be made Schedule 4 for cyanide antidote kits under the Special Access Scheme, and Schedule 9 or 10 otherwise.

Toxicity and abuse potential:

In addition to this lack of therapeutic utility, alkyl nitrites have a potential for misuse, abuse and illicit use. Poisons centre experience indicates that alkyl nitrites are often used as party drugs. Harm can result as an adverse effect of inhalational use, or when accidentally swallowed or splashed in the eye. In addition, we have evidence of home use of alkyl nitrites for their euphoric properties and as sex aids. We have managed several cases of co-use with phosphodiesterase type 5 (PDE-5) inhibitors (e.g. sildenafil), posing a risk of severe hypotension.

In addition to potential harms from misuse, use of volatile nitrites poses risks to the community (these sweet-smelling liquids are a child safety hazard). To avoid detection by authorities, alkyl nitrites are often labelled and sold as leather cleaner, video head cleaner, incense or room-odorising products. This can result in misidentification and impair the risk assessment. Toxicity of alkyl nitrites is primary due to vasodilatory actions. This includes tachycardia, hypotension, headache, flushing, dizziness, nausea, and syncope [2]. In addition, methaemoglobinaemia is a relatively uncommon but potentially life threatening consequence of alkyl nitrite exposure [3]. Any ingestion (even an accidental sip) can cause severe toxicity and warrants hospital assessment. Local splash contact with alkyl nitrites can result in mucosal, dermal and corneal injury. In addition, long term inhalation of alkyl nitrites has been associated with retinal damage and vision loss [4].

The poisons centre experience: evidence of increasing misuse and harms

Over an eleven-year period, 2004-2014 Australian PICs received 273 calls about alkyl nitrite exposures (note data was only available from May 2005 onwards from Victorian PIC and Jan 2009 for Queensland PIC). This includes 86 inhalational exposures, 169 ingestions, 18 dermal exposures and 36 ocular exposures (note that one case can have several routes). Over 96% of these calls (263) were regarding adults, with 10 calls (3.7%) regarding accidental paediatric exposures. There appears to be an increasing trend with time, with a 56% increase in exposures from 2009 (first year with nationwide capture) to 2014. In addition, a recent audit of NSW PIC (handles approximately half of national call volume) calls shows 30 unique calls in 2017, 28 in 2016, 27 in 2015.

Australian PICs do not routinely conduct follow up calls and thus we lack complete outcome data. However, we have evidence of toxicity at the time of the call to PIC. This is particularly evident for cases of ingestion, where the vast majority (159 cases, 94.1%) had features of toxicity present. In addition, 83% (30 cases) of ocular exposures were symptomatic at the time of call. 198 cases (72.5%) required hospitalisation (the call either originated from hospital or the patient was referred to hospital for management). Over 60% of hospital calls were referred to a clinical toxicology consultant, indicating high perceived risk or severity.

41 patients (15%, 39 ingestions and 2 inhalational exposures) had methaemoglobinaemia at the time of call; 14 patients required treatment with the antidote, methylene blue.

References:

- [1] Therapeutic Guidelines, Toxicology and Wilderness, Therapeutic Guidelines Ltd (eTG March 2018 edition)
- [2] Romanelli, F. et al., 2004. Poppers: Epidemiology and Clinical Management of Inhaled Nitrite Abuse. *Pharmacotherapy*, 24(1), pp.69–78.
- [3] Hunter, L. et al., 2011. Methaemoglobinaemia associated with the use of cocaine and volatile nitrites as recreational drugs: A review. *British Journal of Clinical Pharmacology*, 72(1), pp.18–26.
- [4] Audo, I. et al., 2011. Foveal damage in habitual poppers users. *Archives of Ophthalmology*, 129(6), pp.703–708.

Yours sincerely,



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