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1 August 2022

Distributed to:

- Chief Executives
- Directors of Clinical Governance
- Director, Regulation and Compliance Unit

Action required by:

- Chief Executives
- Directors of Clinical Governance

We recommend you also inform:

Directors, Managers and Staff of:

- Drug and Alcohol services
- Mental Health services
- Emergency Departments
- Toxicology Units
- Pharmacy
- Ambulance

Expert Reference Group

Content reviewed by:

- Centre for Alcohol and Other Drugs, NSW Ministry of Health
- Standing Panel on Toxicity Risk, NSW Ministry of Health
- Emergency Care Institute Clinical Director

Clinical Excellence Commission

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Unregistered benzodiazepines and counterfeit alprazolam products in NSW

This Safety Information supersedes SN008/20.



Figure 1. Counterfeit alprazolam products reported by NSW Health clinicians. Note 'Kalma' is an Australian registered brand of alprazolam and it may be difficult to differentiate between legitimate and counterfeit products.

Background

NSW Health issued a public drug warning in July 2020 regarding counterfeit alprazolam – available [here](#).

Since this warning was issued, an increasing number of unregistered benzodiazepines and a small number of other substances have been detected in counterfeit alprazolam products. This Safety Information provides an update on these detections to February 2022, based on:

- analysis of drug composition of samples seized by NSW Police and those associated with clinical cases in NSW,
- toxicological analysis of coronial cases.

A further public drug warning has been released [here](#).

Assessment

Since 2019, there have been ongoing detections of counterfeit alprazolam products containing unregistered benzodiazepines both in police seizures and reports of patients presenting to Emergency Departments. Counterfeit alprazolam products are often poorly manufactured, with a wide variation in the drug composition. Large dose variations in the benzodiazepines detected have been found between visually similar counterfeit tablets in the same batch and have been associated with serious harm and death.¹

Counterfeit alprazolam products have been sold as the brand names “Kalma”, “Mylan”, “Xanax” (note – no longer a registered product in Australia) or “Sandoz” (see Figure 1 above). “Mylan” and “Xanax” make up most of counterfeit alprazolam products seen. It should be noted that harms related to use of flualprazolam powders have also been reported in NSW.

Only 35% of counterfeit alprazolam samples analysed contained alprazolam, and all of these were found to also contain other substances. The other substances detected were mostly unregistered illicit benzodiazepines, with a small number of samples containing other drug classes.

Ten unregistered benzodiazepines have been detected to date in NSW; etizolam, clonazolam, flualprazolam, bromazolam, flubromazolam, nimetazepam, flubromazepam, adinazolam, diclazepam, and flutoprazepam.

In a small proportion (1.8%) of samples there were other substances detected – doxepin, lidocaine, amantadine, cyproheptadine, and the stimulant N-(1, 4-dimethylpentyl)-3,4-DMA and the hallucinogen 5-methoxy-DBT.



A larger range of unregistered benzodiazepines are being detected in counterfeit alprazolam than previously reported in 2020. There is also a change in the unregistered benzodiazepines most commonly detected. In 2019, etizolam was the most commonly detected substance, however this has now shifted to other unregistered benzodiazepines, notably clonazepam and flualprazolam (see Figure 2 below). Clonazepam and flualprazolam both have a higher potency compared to alprazolam and other unregistered benzodiazepines.

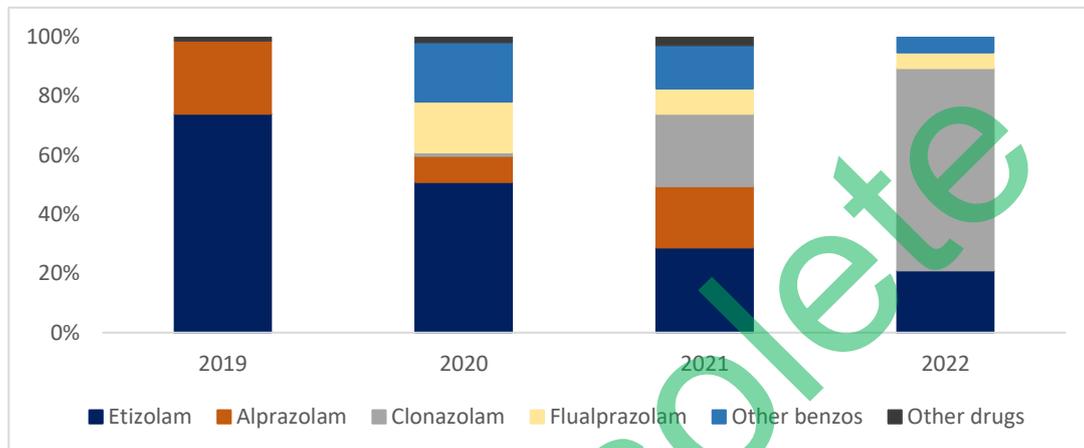


Figure 2. Proportion of substance detections in counterfeit alprazolam products from January 2019 to February 2022.

Clinical Recommendations

1. Be aware that if a patient is taking illicitly obtained alprazolam, the product most probably contains other unregistered benzodiazepines. They often contain multiple benzodiazepines and benzodiazepines with higher potency compared to registered medicines. Rarely, they may contain other drug classes with variable toxicity.
2. Take caution when interpreting urine drug screen (UDS) results if an illicit benzodiazepine is suspected. Some unregistered benzodiazepines are detected by UDS but may not be able to be identified on confirmatory testing. Misinterpretation as a false positive has been reported.² Additionally, some unregistered benzodiazepines may not be detected on initial UDS. Consult your local pathology service if results appear incongruent with suspected illicit benzodiazepine use and/or confirmatory testing is required.
3. If the patient has significant clinical signs such as central nervous system and respiratory depression, seizures, and/or ECG changes, consult your local toxicologist or the Poisons Information Centre on 13 11 26, who can advise on management and arrange specific testing as clinically indicated.

References

1. Blakey K, Thompson A, Matheson A, Griffiths A. What's in fake 'Xanax'? A dosage survey of designer benzodiazepines in counterfeit pharmaceutical tablets. *Drug Test Anal.* 2022;14(3):525-530. doi:10.1002/dta.3119, 10.1002/dta.3119
2. Puzyrenko A, Wang D, Schneider R, Wallace G, Schreiber S, Brandt K, Gunsolus IL, Urine drug screening in the era of designer benzodiazepines: Comparison of three immunoassay platforms, LC-QTOF-MS and LC-MS/MS. *J Anal Toxicol.* 2021; bkab108, <https://doi.org/10.1093/jat/bkab108>

Required actions for the Local Health Districts/Networks

1. Instruct clinicians to be alert for continued circulation of counterfeit alprazolam products and be vigilant during patient histories which report use of alprazolam or other benzodiazepines and the interpretation of urine drug screen results if illicit benzodiazepine use is suspected. Clinicians should consider referral to toxicology or the Poisons Information Centre if the patient has significant clinical signs.