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## Short Communication

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# Medicinal products detected as novel psychoactive substances: The case of intravenous use of tropicamide.

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### Summary

Use and abuse of novel psychoactive substances (NPS) remains a public health and law enforcement challenge across Europe and bordering countries. Increasingly NPS detected on the drug market include those with legitimate use as medicines or active pharmaceutical ingredients in medicines. This Short Communication wishes to draw attention to reports on the concerning upward trend of intravenous (IV) use of eyedrops containing tropicamide by problematic opiate users. Since 2013, trends of diversion by IV route are identified as a new phenomenon in Europe. Sales in Russia and Eastern Europe in particular have increased significantly in the past five years. Key indicators of suspected misuse include online interest particularly from Russia, Ukraine and other Eastern European countries, and pharmacovigilance and clinical alerts from Turkey, Italy, France, Georgia, Russia, Tajikistan, and Kazakhstan. Tropicamide is injected as secondary to the primary opiate addiction, and reportedly occurs as self-sufficient means to get high amongst opiate injectors when primary opiates such as heroin are not available, and as poly-substitute to further enhance the opiate effect and manage heroin (and to a lesser extent methadone) withdrawals. Anecdotally, injection of tropicamide is known as the 'seven monther' in relation to the length of time it takes to kill the user. The diversion of tropicamide is high risk, concentrated within problematic drug user networks, and conducted by individuals who may not be engaging with social and medical systems. Aside from dependence and physical/psychiatric harms, the risk pertaining to this injecting phenomenon as potential contribution toward virus transmission (HIV, Hepatitis C) within injecting networks are present. The Short Communication presents extant literature on the topic, and discusses implications for drug policy and service delivery.

*Key Words:* Novel Psychoactive Substance; Tropicamide; eyedrops

Use and abuse of novel psychoactive substances (NPS) remains a public health and law enforcement challenge across Europe and bordering countries [18]. NPS notified to the EU Early Warning System (EWS) continue to rise, with the World Health Organisation reporting on a global rise of 55% in 2015. The United Nations Office on Drugs and Crime (UNODC) and the European Union (EU) define NPS as "substances of abuse, either in a pure form or a preparation, that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances, but which may pose a public health threat" [17]. Of note is that UNODC extends the concept of NPS to emerging drug trends, not necessarily new designer drugs, but also substances recently

available. The EU legal framework of Council Decision 2005/387/JHA also defines NPS as including human or veterinary medicinal products. Increasingly NPS detected on the drug market include those with legitimate use as medicines or active pharmaceutical ingredients in medicines. The European Medicines Agency (EMA) and the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) currently exchange information around abuse of medicinal products. Recent examples include those notified under the Council Decision and detected by the EU-EWS (phenibut, gabapentin, cafentanyil, pregabalin, etaqualone, zopiklone and tropicamide) [6-7].

This Short Communication wishes to draw attention to reports on a concerning upward trend of

intravenous (IV) use of eyedrops containing tropicamide by problematic opiate users. Tropicamide is a mydriatic atropenic ophthalmic drug indicated for therapeutic or diagnostic procedures to dilate the pupils [12]. It is administered for very short-term exposure periods, at starting doses of one drop (150 µg of tropicamide) and not exceeding 3 ml of the solution. Effects at higher dosages include visual hallucinations, confused states, sedation and delirium [1, 9]. Since 2013, trends of diversion by IV route are identified as a new phenomenon in Europe. Sales in Russia and Eastern Europe in particular have increased significantly in the past five years [13-14, 19]. Key indicators of suspected misuse include online interest particularly from Russia, Ukraine and other Eastern European countries [3, 11], and pharmacovigilance and clinical alerts from Turkey [5], Italy [3, 15], France [11], Georgia [2], Russia [3, 19], Tajikistan [8, 10, 20], and Kazakhstan [13-14].

Tropicamide is injected as secondary to the primary opiate addiction, and reportedly occurs as self-sufficient means to get high amongst opiate injectors when primary opiates such as heroin are not available, and as poly-substitute to further enhance the opiate effect, and to manage heroin (and to a lesser extent methadone) withdrawals [2, 4, 5, 10, 15, 19, 20]. Additional factors supporting the rapid diffusion of this new injecting phenomenon within Russia and Eastern Europe are observed by Bersani and colleagues [4] in their mini-review and centre on rapid onset of effect, ease of availability and low cost, and visibility of user interest and experiences online. Prilutskaya and Kuliev [14] also speculate that tropicamide's popularity is due to its readiness for injection, in contrast to other pharmacy sourced medicinal products such as codeine, ephedrine and desomorphine which require some level of home preparation prior to injecting (for example 'Krokodil', see [18]). Tropicamide eyedrops can easily be bought online and in pharmacies [4].

Acute intoxication characterised by hallucinations ('open eye dreams'), dizziness, hyperthermia, tremors, convulsions, suicidal ideation, psychomotor agitation, tachycardia and psychosis, diagnosis of anticholinergic syndrome and adverse chronic health problems (severe weight loss, cognitive impairment, cardiovascular toxicity, renal or liver failure, post injection purulent soft tissue complications, viral transmission and both physical and psychological dependence) are reported [3-5, 11, 13-15]. Anecdotally, injection of tropicamide is known as the 'seven monther' in relation to the length of time it takes to kill the user [3]. In the past five years, fatalities in

Russia have been reported in the media and on drug fora [3, 4, 16].

The diversion of tropicamide is high risk, concentrated within problematic drug user networks, and conducted by individuals who may not be engaging with social and medical systems [11]. Aside from dependence and physical/psychiatric harms, the risk pertaining to this injecting phenomenon as potential contribution toward virus transmission (HIV, Hepatitis C) within injecting networks are present. Given the fluctuations in opiate and diverted opioid availability in regions where tropicamide is used, this remains concerning, even though primary tropicamide abuse is not commonly reported, and it appears situated within poly substance use as 'top up' drug. Tropicamide's craving's specificity appears to get lost in addictive processes, with poly-substance abuse of tropicamide in opiate dependency going far beyond cross-tolerance mechanisms.

The rising reports in Russia and Eastern Europe, and more recently in France and Italy, of tropicamide abuse by known injecting networks of drug users therefore warrants a careful response, instigated by country and EU wide risk assessment. Gauging the public health risks within countries experiencing this injecting phenomenon is difficult, and yet are necessary to underpin further development and coverage of pharmaco and addicto-vigilance regulatory systems. National early warning systems are uniquely positioned to identify early and continued levels of abuse of this diverted medicinal product, particularly within existing problem drug user networks. Given the cross over between pharmacy and street supply of tropicamide, a multi-disciplinary approach to integrate regulation, enforcement, and surveillance of diversion and suspected abuse is imperative to monitor and respond to this type of medicinal diversion. Routine forensic detection, monitoring and surveillance of a broad reach of potential information sources both inside and outside countries experiencing this trend are therefore necessary. For countries experiencing this form of medicinal diversion, training of health, pharmacy and medical professionals in the detection of suspected abuse and appropriate clinical responses for those experiencing tropicamide related health problems and dependence are warranted [3, 5, 11, 14-15]. Research efforts can assist in the garnering of understanding tropicamide as relatively new drug situated within problem drug user populations, and can help support the development of targeted prevention and harm reduction initiatives. Within the wider EU domain, the regular surveillance of online drug

fora and trend interest in tropicamide (and other pharmaceuticals with abuse liability) should continue.

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## Conflict of interest

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## Ethics

Author confirm that the submitted study was conducted according to the WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects.

## Note

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