

Health risks associated with Mephedrone

Other than clinical data on acute mephedrone toxicity, and limited reports on fatalities, the studies available on mephedrone are few, largely preliminary and focused on user self-reports. To date no epidemiological data on prevalence has been published. The majority of studies originate from the United Kingdom and evidence from other Member States is scarce. The most detailed studies have been undertaken through surveys of UK clubbers, although some information can be found on mephedrone use and potential risks regarding other subpopulations.

Individual health risks

The assessment of individual health risks includes consideration of mephedrone's acute and chronic toxicity, its dependence potential, and similarities and differences to other reference stimulants.

Systematic data are not routinely collected in Europe on acute toxicity related to mephedrone or closely comparable recreational drugs. Therefore, information on these effects of mephedrone is limited to user reports and clinical data on individuals presenting with acute mephedrone toxicity to specialist hospitals with a focus on recreational drug toxicity. The reported short-term effects of mephedrone use have much in common with those of other stimulants. Some self-reports from users favourably compare mephedrone's effects, saying the high can be both better and longer lasting than cocaine.

The **main routes of administration** for mephedrone are reported as snorting (nasal insufflation) and swallowing (oral ingestion), sometimes after dissolving with water. As mephedrone is primarily available in powder form, injecting use is reported but appears to be rare.

Adverse effects reported by users include sweating, headaches, tachycardia, palpitations, nausea, chest pain, bruxism (teeth grinding), agitation/aggression and paranoia. In addition, nasal insufflation of mephedrone is reported to be associated with significant nasal irritation and pain which has led to some users switching to oral use of mephedrone. Users report increased sexual arousal but there is insufficient information to detect whether this is associated with high risk sexual behaviour.

Some detailed information on the patterns of acute mephedrone toxicity is available from clinical case series from poisons information services and specialist hospitals in the United Kingdom and Sweden, including one series of analytically confirmed acute mephedrone toxicity from the United Kingdom. In this data, patients typically present with sympathomimetic features (dilated pupils, agitation, tachycardia, hypertension); severe clinical features such as chest pain, significant hypertension, arrhythmias and seizures have been reported in a small number of cases to date. Similar to other stimulant drugs, it is likely that the risk of toxicity is related to the dose of mephedrone used; however there is insufficient information available from toxicity reports to determine a 'dose threshold' and/or whether particular routes of use are more likely to be associated with toxicity. It is possible that certain rare, but clinically significant, severe effects are associated with mephedrone use. However, as experience of the toxicological profile of the drug is currently limited to a few hundred cases it is difficult to be sure.

Data from individuals presenting with acute mephedrone toxicity suggest that the majority of individuals have used at least one other substance together with mephedrone. However there are analytically confirmed cases of lone mephedrone toxicity. This is similar to individuals presenting with acute toxicity related to other stimulant drugs.

There are two reported **fatalities** in which mephedrone appears to be the sole cause of death (one in Sweden and one in the United Kingdom). In addition to these cases, there are at least another 37 deaths in the United Kingdom and Ireland in which mephedrone has been detected in post-mortem blood and/or urine toxicology screening. In some of these cases it is likely that other drugs and/or other medical conditions or trauma may have contributed to or been responsible for death. The inquests into the deaths are pending for the majority of these cases therefore it is not possible at this time to determine the contribution of mephedrone.

Strong craving for the substance is reported by some users' self-reports, sometimes rated higher than that experienced with other stimulant drugs. This is cited as a main reason for using more mephedrone than intended, and for using for longer periods than planned. Withdrawal symptoms do not appear to be significant for most users with the primary symptoms of nasal congestion and fatigue most probably related to route of use and lack of sleep secondary to staying up late. However the other reported findings, in heavier users, would be consistent with a stimulant withdrawal syndrome. There is some evidence that the drug has a high abuse liability with over 30 % of the UK telephone survey sample reporting three or more DSM criteria of dependence and being classified as dependent. Tolerance, loss of control, a strong urge to use and using despite problems predominate. In addition, there are reports from the United Kingdom of mephedrone dependence being reported to drug treatment services that suggest psychological rather than physical dependency similar to other stimulant drugs.

No studies have been published investigating the potential for chronic mephedrone toxicity associated with mephedrone use, including reproductive toxicity, genotoxicity and carcinogenic potential.

Reports suggest mephedrone may be used as an alternative to illicit stimulants. The reasons given for using mephedrone include: value for money, product purity and consistency as well as the poor availability or low quality of other stimulants (cocaine, ecstasy/MDMA). Some users noted a preference for mephedrone over other stimulant drugs with data from the UK clubbers rating mephedrone above ecstasy and cocaine for strength and pleasurable high. Mephedrone users in the UK telephone survey reported on the considerable impact mephedrone had on their consumption of cocaine and ecstasy, with approximately two thirds of the sample reporting that they now took less MDMA, and a third reporting that they now consumed less cocaine. Just under half of the group reported they would choose mephedrone over cocaine and only a quarter said that they would take mephedrone over ecstasy.

The physical effects reported by mephedrone users are typical of other stimulants and may be particularly similar to MDMA. However, mephedrone's relatively short duration of action, leading to repeat dosing, is more analogous to cocaine.

In summary, from the data sources available, it appears that the effect profile and clinical presentations of mephedrone intoxications share some features seen with MDMA and some features seen with cocaine. Additionally, there are very limited reports of fatalities directly related to mephedrone. Some users have reported negative effects and in some cases these have required medical attention. Similar to other stimulant drugs, the extent to which users experience problems requires further investigation. Data also suggest that mephedrone has a potential to cause dependency. However, more in-depth studies would be required to explore in detail the dependence potential of this drug.

Public health risks

The public health risks associated with mephedrone may be categorised in terms of the extent, frequency and patterns of use; availability and quality of the drug; information availability and levels of knowledge amongst users; and negative health consequences.

Evidence of use of mephedrone and toxicity associated with its use has been increasing, particularly in 2009 and 2010. In the absence of representative studies, prevalence rates are difficult to estimate. Non-representative studies provide self-reports that place lifetime use of mephedrone at around 40 % amongst UK clubbers responding to an Internet survey (33 % last month use), 20 % amongst Scottish students and 40 % amongst Northern Irish school children attending focus groups. In other countries, levels of use are largely undocumented. Data from the French TREND system describe its use as restricted to a small, primarily Parisian milieu.

Qualitative reports note the use of the drug in other countries but give no indication of prevalence even within high-risk subpopulations.

Mephedrone users are reported to be predominantly male and aged between their late teens and late twenties, although both younger and older users are identified in UK studies. Some surveys suggest individuals use mephedrone alone while other surveys suggest that users combine mephedrone with other drugs including alcohol, cannabis and often cocaine, and ecstasy. The evidence suggests mephedrone has some appeal for a range of recreational stimulant users — with respondents from UK studies also using cocaine/ecstasy/amphetamine, and the Dutch respondents also using ecstasy. There is limited data available on where mephedrone is used, although it is likely that it is used in the same environments as other stimulant drugs, typically clubs/discos, bars/pubs, outdoor music festivals and home environments.

Mephedrone consumption has been identified in a range of sub-populations. In addition to 'psychonauts' (7), mephedrone use has been identified in the clubbing and party scene, amongst school and university students (United Kingdom) and gay men (France). There is some evidence to suggest rapid spread of mephedrone use, particularly in the United Kingdom and in Ireland, but also among clubbers in Slovenia. Use reported in France is described as rather localised and limited, whilst in the Netherlands, the available data are confined to a group of primary ecstasy users. Although much of the evidence is linked to use amongst clubbers, the UK studies also include unemployed users and students from Scotland and Northern Ireland. In addition, there are reports of spread of mephedrone use amongst opiate users in Ireland.

In terms of frequency of use, reports suggest recreational, weekend/monthly use is a common pattern for those who try, and choose to continue to use, mephedrone. As such mephedrone is used in a similar way to ecstasy or cocaine in party and nightlife settings. Around 15 % of UK Internet survey respondents reported using mephedrone at least weekly. A small number of users appear to progress to daily use. Mephedrone is reported as being used primarily in combination with alcohol, cannabis and other stimulants. These combinations of substances makes it more difficult to identify mephedrone-specific effects. Relatively high concurrent

consumption of ketamine was reported by UK clubbers. There are anecdotal reports of opiates injecting users switching to mephedrone when opiates are not available.

Some concerns have been raised about young people experimenting with the practice of snorting the drug, a **route of administration** commonly associated to cocaine. However, a significant proportion of those using mephedrone by nasal insufflation report nasal irritation and pain, leading to a change to the oral route.

Mephedrone is **available for purchase** on the Internet, from head shops and from established street-level dealers. Where information on purchase of mephedrone is available, it appears most common to buy the drug from a dealer or from friends. Some users reported buying from the Internet, and this tended to be higher quality mephedrone, but for some users the risk of Internet data security was a deterrent. Internet suppliers will ship mephedrone to EU countries often marketed as 'plant food', 'bath salt' or 'research chemical', presumably to circumvent control measures. Very rarely mephedrone is sold explicitly as a 'legal high'. EMCDDA Internet monitoring shows that the number of websites selling mephedrone increased from December 2009 to March 2010. But subsequent to the April 2010 classification of mephedrone in the United Kingdom, there was a rapid and considerable decrease in the number of sites found to be operating. Prior to UK control, many suppliers appeared to be based in the United Kingdom, or targeting the UK market.

Most sites do not have restrictions on the countries that they will ship mephedrone to, but advise buyers to check the legal status in their countries. Internet sites selling mephedrone typically differ from those selling other 'legal highs' as they are mephedrone/cathinone specific. There is generally information available on the supposed purity of the product supplied but rarely information on the potential for unwanted effects associated with its use, although most sites state that it is not for human consumption. Many sites supply mephedrone in bulk (kilogram) quantities in addition to single user doses. However, they typically provide minimal information on the dose of mephedrone. Any information that is provided is very general and often cryptic in nature; for example mephedrone sold as 'plant food' may contain advice on 'number of doses for an average-sized plant'. It is likely that users will interpret this information as the number of doses to be taken by an adult. The UK control seems to have prompted the appearance of at least two new substances and products marketed on the Internet as 'legal highs'. There is also some evidence to suggest that where mephedrone has been controlled, the drug continues to be available on the illicit market.

In general, the **quality and purity** of mephedrone available to users is reported as high, and the analysis of seized and purchased mephedrone confirms this. However, some samples of

mephedrone have been found to contain pharmaceutical agents (e.g. benzocaine, lidocaine, caffeine and paracetamol), other synthetic cathinones (e.g. butylone, methylone, ethylcathinone, fluoromethcathinone, methylenedioxypropylone/MDPV) and/or other recreational drugs (e.g. MDMA, mCPP, ketamine).

There is anecdotal evidence that extensive media coverage of mephedrone has led to increased general population and user awareness of the drug and, in particular, to the fact that it is legally available over the Internet for delivery to Europe. Some users have stated that they first bought and used mephedrone after reading reports about it in the popular press. The media is also cited as a primary source of (often inaccurate) information about the drug. Typically, there appears to be a low level of knowledge amongst some groups of users of the chemical content of products and chemical make-up of mephedrone. However, the Internet has also been a source of information for those interested in drugs. Specialist websites/user forums indicate that users are aware that mephedrone is effective in producing the desired effects and may compare favourably to other stimulants.

Misunderstanding and misinformation about mephedrone may also be an important issue both with respect to the use and to the supply of the drug. It should be noted that there are a number of other synthetic cathinones that are used recreationally — these include methedrone, methylone and MDPV. Some of these, along with other non-cathinone drugs such as methadone, have similar sounding names to mephedrone which may cause confusion amongst users, healthcare professionals, law enforcement agencies and the media. As cathinone derivatives are also sold under generic brand names, with no labelling of the active constituent chemicals, both users and sellers may be unaware of what particular substance is being consumed. This problem may be amplified by the fact that products can contain mixtures of cathinones and other drugs. It is likely that this is more of an issue with products purchased mostly from street dealers rather than from the Internet. Feedback from pill/powder-testing (Netherlands, France) report that some users were unaware that the substance they had purchased was mephedrone before test results were provided. This suggests that mephedrone has also been used unknowingly by those buying ecstasy tablets on the illicit market. Finally, the marketing of mephedrone may itself cause further confusion, as illustrated by a report of school pupils being uncertain as to whether all regular plant food also contained the drug.

Mephedrone has been detected on post-mortem analysis in four road traffic accident related deaths in the United Kingdom; however inquests into these deaths are awaited and so it is not possible to determine the role that mephedrone played. There is no data available from other European countries or from law enforcement agencies to suggest that mephedrone use has been implicated in road traffic accidents or other trauma. This may, at least in part, be due to the fact that, at this time, mephedrone is not widely tested for by forensic laboratories.

(7) There is no agreed definition of the term 'psychonaut' but here it is used to broadly describe individuals who seek to explore their mind by intentionally inducing altered states of consciousness, in particular, by experimenting with psychoactive substances.