

# **Ketamine**

## **Expert peer review on critical review report (2)**

**35<sup>th</sup> Expert Committee on Drug Dependence, Hammamet, Tunisia  
June 4-8, 2012**



## 1. Comments based on the review report

### a. Evidence on dependence and abuse potential

Ketamine has been misused as a hallucinogen for almost 30 years with effects similar to those of phencyclidine, but with a much shorter duration. Pre-clinical studies have shown its self-administration and drug discrimination properties, propensity to produce tolerance and observable withdrawals.

Human studies have assessed its subjective effects in recreational users as well as in experimental studies. Ketamine affects perception of body, time, surroundings and reality, producing a 'psychedelic' state of mind that resembles schizophrenic psychosis. It causes a dose related high and a biphasic effect on anxiety. The dissociative experience may discourage some experimental users from continued use. Tolerance to the effects of ketamine develops. Some users take ketamine in a compulsive bingeing pattern. There is insufficient evidence to show that ketamine causes an abstinence syndrome in humans.

### b. Consequences to individual and society because of misuse

Ketamine acutely affects cognitive performance, including attention, working memory and semantic memory. Frequent ketamine users exhibit profound impairments in memory which may be reversible on stopping use of drug. The main effects of recreational use are neuro-behavioural that pose a risk for injury and accidents. Cystitis, bladder dysfunction and secondary renal damage (in severe case) have been reported.

The studies on fatality usually report poly-substance use. Deaths occurred in much higher doses than usual recreational doses.

### c. Magnitude of the problem in countries (misuse, illicit production, smuggling etc)

#### *Misuse*

Ketamine was earlier used as a club drug in specific populations only or in certain groups such as gay men taking more sexual risks. Based on the WHO questionnaire for Review of Psychoactive Substances for the 35th ECDD, 16 of the 64 countries now reported harmful ketamine use. In Australia, 1.1% of the general population had used ketamine at least once in their lifetime. In Denmark, it is presumed that < 2 % of the youth had used ketamine. In Thailand, the prevalence was estimated to be 0.1% among 12-65 year olds. Ketamine use is reported among school students in USA through Monitoring the Future Surveys.

In the African countries that were visited (Ethiopia, Nigeria, Tanzania and Benin) to assess the impact of ketamine availability on Anglophone African medical practice (as a part of the ketamine critical review being prepared for the 35th ECDD), no cases of ketamine misuse were reported by the health care practitioners interviewed.

*Illicit production/smuggling/diversion*

A total of 19 countries reported tracking illicit activities involving ketamine (clandestine manufacturing/ smuggling/diversion). The biggest reported seizures have been from China and USA.

**d. Need of the substance for medical (including veterinary) practice**

Sixty countries have authorized ketamine as a medical or veterinary product mostly for anesthesia and in some countries also for analgesia and other indications. Ketamine as anesthesia is widely used in the developing world for elective and emergency surgery due to its safety in settings with paucity of highly skilled manpower, equipment and lack of resources for expensive alternatives. It was used in 10% to 90% of the cases in various hospitals in Africa visited for the 35<sup>th</sup> ECDD report. In some hospitals, nurses provide anesthesia as specialist doctors were not available.

The safety of ketamine is attributed to the property that it does not depress the cardio-respiratory system unlike other anaesthetic agents and that it preserves the laryngeal and the pharyngeal reflexes. It has a unique role in obstetrics and in children thus reducing morbidity and mortality as tracheal intubation in the obstetric patient is usually difficult and requires expertise.

In developed nations, ketamine is reserved for use in specific cases such as haemorrhagic shock and hemodynamic instability, as a bronchodilator in intractable asthmatic patients and in the emergency department for sedation of children.

Ketamine is widely used in veterinary practice and is considered an essential anaesthetic for veterinary use because it is the only injectable anaesthetic that is safe and well tested in the full range of species.

**e. Need of the substance for other purposes (e.g. industrial)**

Not applicable

**f. Measures taken by countries to curb misuse**

In 2009, 48 countries as compared to 34 countries in 2008 reported placing ketamine on the list of controlled substances under national legislation. It may be argued that de facto over the years a situation of international control has emerged due to CND resolutions and the INCB pressure on Member States.

**g. Impact if this substance if scheduled**

Based on the WHO questionnaire, eight of the 64 countries (Bhutan, Greece, Netherlands, republic of Korea, Tuvalu and others) reported that if ketamine is placed under more strict international control, its availability for medical use will be affected. Responses reflected an effect on availability due to stringent import regulation, impact on the

distribution, effect on allocated quantity or acceptability in medical/veterinary practice. Doctors from the four African countries where hospitals were visited for the ketamine critical review reported that international control would result in a public health crisis due to the rigours of procurement. The Head of Anaesthesia from a hospital in Africa said “Anaesthesia without ketamine in this part of the world is unthinkable, especially for the haemodynamically unstable patient, and in trauma etc”. This is largely because of lack of adequate number of specialised anaesthesia doctors in Africa. Several Member States (Sweden, Denmark, Germany, Portugal) also indicated that ketamine is indispensable for its indications in veterinary medicine.

## **2. Additional information to the critical review report**

### *Misuse*

Ketamine use is common in Hong Kong, Taiwan, UK, Australia and in the USA. While the use of ketamine was initially confined to certain subcultures, it has recently become more mainstream in certain countries (Morgan and Curran, 2011). Among substance abusers seeking treatment in Hong Kong, ketamine is a major drug of abuse (Tang et al, 2011). Of the 395 injured drivers reporting to a trauma centre in Hong Kong (Wong et al, 2010), it was the most commonly detected abusive substance and was particularly high in young drivers in contrast to another study where ketamine was found in only a small proportion of the drivers in China who tested positive for drugs (Zhuo et al, 2010). In the national survey data (2004-2006) in Taiwan (Chen et al, 2009), ketamine was the second commonly used illegal drug among middle and high school students and was often used with other drugs. Recent data from Monitoring the Future Study (2011) from US reports the annual prevalence in school students as 0.8%, 1.2% and 1.7% for 8th, 10th and 12th grade.

National Drug Strategy Household Survey in Australia (2004) reported that although lifetime use of ketamine occurred in 1% Australians, recent use was reported in 0.3% (Degenhardt and Den, 2008). Those who reported ever using these drugs described a pattern of occasional use and the large majority were abstinent in the past year. Similarly, use in last one year was reported in 1.7% although ever use occurred in 4% of the young people in UK (Morgan and Curran, 2011).

Records of ketamine abusers in emergency services in Hong Kong showed that they presented with acutely transient central nervous system depression, abdominal pain, or lower urinary tract symptoms (Ng et al, 2010) suggesting a lack of severe acute physical health consequences. In a study on consequences of chronic ketamine self-administration at one year (Morgan et al, 2010), heavy use was found to be harmful to both cognitive function and psychological wellbeing (delusional and depressive symptoms).

Morgan and Curran (2011) have used the 'rational scale' developed by Nutt and colleagues as a framework for assessing the harms associated with ketamine use in terms of the 'physical harms', 'dependence-related harms' and 'social harms'. They have commented that there is concern that some individuals develop dependence to ketamine, although the incidence of this is currently hard to gauge. Many daily users report having tried but failed to stop using ketamine. Cravings seem to be a key problem in frequent users.

#### *Illicit production/smuggling/diversion*

The INCB report (2012) mentions that 99% of all ketamine seizures worldwide in 2009 took place in Asia. Ketamine is illicitly manufactured in China, although India is also an important source of ketamine seized in the region. INCB report (2012) also mentions that ketamine has been classified as a schedule I drug in Hong Kong since 2000. Hydroxylamine hydrochloride, a precursor used in the manufacture of ketamine has been placed under national control in China in 2009. In 2011, ketamine has been added to the list of psychotropic substances controlled under the Narcotic Drugs and Psychotropic Substances Act in India. In the United Kingdom, ketamine was classified as a Class C substance in 2006 and in the United States as a schedule III drug (Morgan and Curran, 2011).

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### **3. Other comments or opinions**

The report should specifically examine the published articles in last 5 years on ketamine and the INCB reports of last five years. Certain information need to be modified e.g. the report mentions that ketamine is difficult to manufacture illicitly but clandestine manufacture of ketamine is now reported in China.

### **4. Expert reviewer's recommendation on scheduling with rationale**

Ketamine is being used as an important anaesthetic agent especially in some developing countries such as in Africa due to its safety, ease of use in absence of adequate number of specialists and equipment. Strict procedures required for procurement following international control is likely to create a public health crisis in these countries.

Many of the countries facing problem due to abuse or illicit trade, manufacture or diversion of ketamine have already taken control measures based on the suggestion by the INCB. It may be advisable for other countries to review their national situation and come up with control measures based on reports of abuse/diversion/illicit trafficking and need for therapeutic use rather than international control.