ACMD

Advisory Council on the Misuse of Drugs

Ketamine – an updated review of use and harms: Annexes

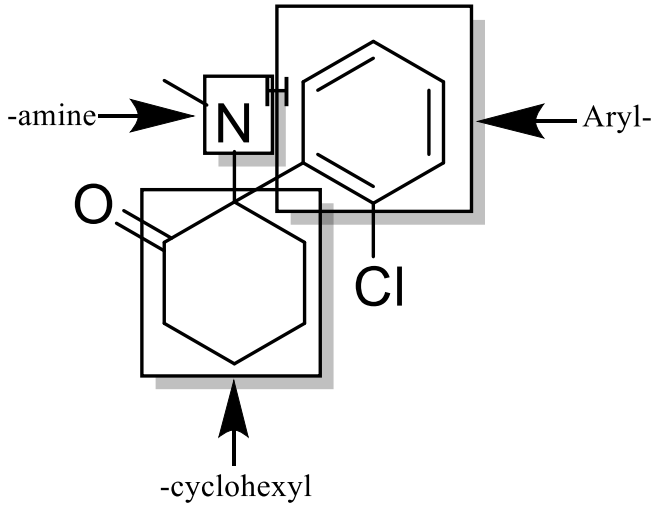
Annexes to this report are provided as a detailed evidence pack to support the information provided in it. They also provide information on abbreviations used in the report, the members of the ketamine working group and the Advisory Council on the Misuse of Drugs (ACMD) at the time of publication, the range and quality of evidence and the references. The list of annexes is shown below:

Contents

Annex 1. Chemistry

1.1 Ketamine, chemical name 2-(2-chlorophenyl)-2-(methylamino)-cyclohexanone, is an arylcyclohexylamine analogue of phencyclidine (PCP), itself a controlled drug (Class A, Schedule 2). Ketamine is characterised by 2 linked rings, one aryl and one cyclohexyl, and an amine group, as shown in Figure 1.1 below.

Figure 1.1. Chemical structure of ketamine.



1.2 Ketamine and some of its derivatives possess a chiral centre and therefore exist as two 'mirror image' enantiomers. The *S(+)*-enantiomer ('esketamine') of ketamine has higher affinity at the *N*-methyl-D-aspartate receptor (NMDAR), is metabolised more rapidly and has a shorter duration of action in comparison with the *R*(-)-enantiomer ('arketamine'). While differences in the effects of *S*(+)- and *R(-)*-ketamine are well studied, this is not the case for ketamine derivatives.

1.3 Identification of pure *S*(+)-enantiomer may indicate the theft or illegal acquisition of esketamine that was intended for medical purposes, while samples containing a racemic mixture are more commonly associated with illicit ketamine, including that diverted from medical resources.

1.4 Analogous β-keto-arylcyclohexamines have been detected, with many of the originally identified analogues now giving rise to their own derivative analogues. For example, methoxpropamine (MXPr), methoxisopropamine (MXiPr), methoxmetamine (MXM) and deoxymethoxetamine (DMXE) are all analogues of methoxetamine (MXE). Details and chemical structures of ketamine analogues are provided in Table 1.1.

1.5 Ketamine was previously considered difficult to manufacture due to the requirement for multi-stage synthesis and unusual precursors that are rarely traded. However, in 2015, the Government of China informed the Commission on Narcotic Drugs (CND) that most ketamine marketed illicitly in Asia at that time had been synthesised in clandestine laboratories that were able to manufacture the precursor 'hydroxylimine' (1-((2-chlorophenyl)-(methylamino)methyl)cyclopentanol) from a variety of other precursor chemicals (UNODC, 2022a).

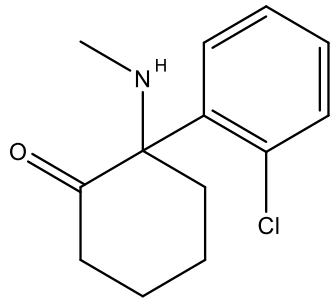
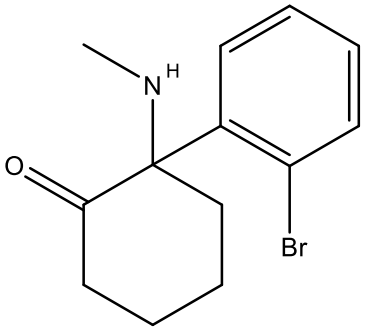
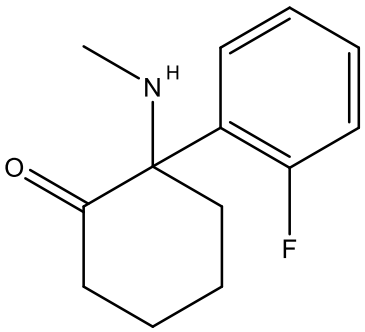
1.6 A new precursor chemical used in the synthesis of norketamine, 2-(2-chlorophenyl)-2-nitrocyclohexanone, was identified in a 2022 Taiwan seizure, demonstrating the use of a new synthesis process (Yen and others, 2022).

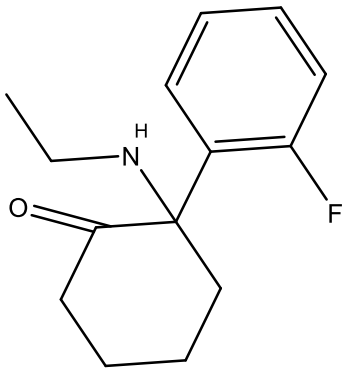
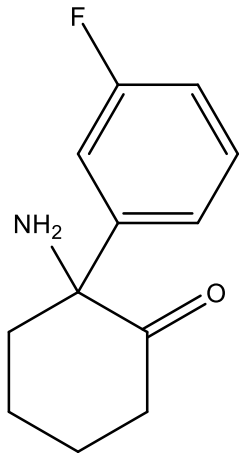
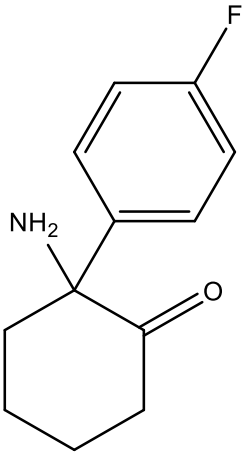
1.7 In addition, a novel synthetic route to the ketamine precursor 2-chlorophenyl cyclopentyl ketone has been identified, starting from cyclopentanone *p*-toluenesulfonylhydrazone and 2-chlorobenzaldehyde (Yen and others, 2024).

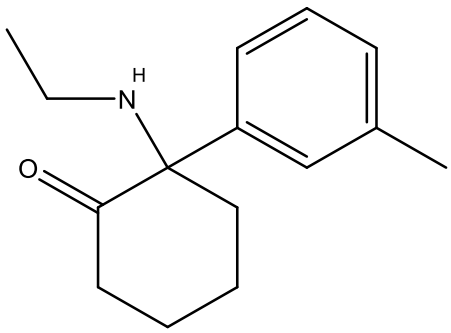
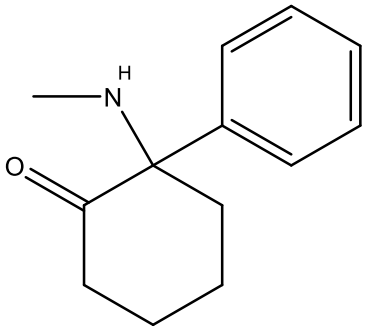
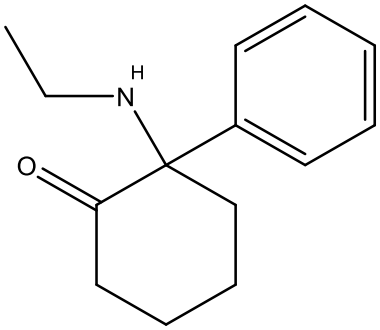
1.8 Characteristic impurities have been identified that can be identified to support chemical profiling initiatives, allowing the differentiation of illicitly manufactured ketamine (Liu and others, 2024).

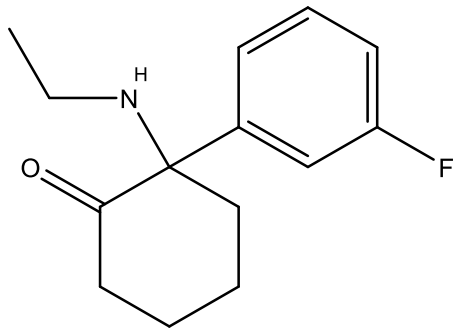
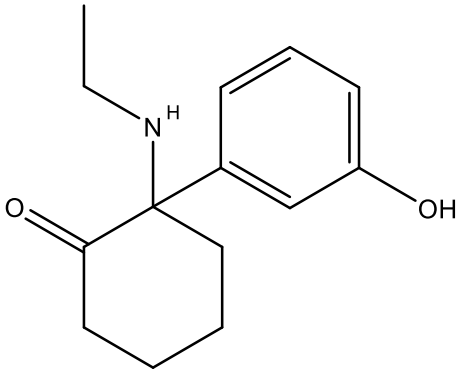
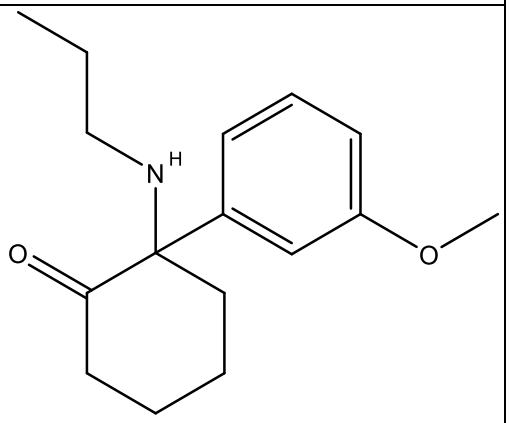
1.9 There are several Home Office type approved kits for ketamine, including the TruNarc Analyser, Alere Rapid Solids Test Kit and Itemiser 3. Unlike many other commonly encountered drugs of abuse, such as amphetamine or cocaine, there are no approved colour reagent tests for ketamine. Instead, detection relies on technologies such as Raman spectroscopy, immunoassay and ion mobility spectrometry. While the approved methods are accurate and reliable, their effectiveness in field contexts is constrained by factors such as equipment cost, training requirements and limited availability across police forces.

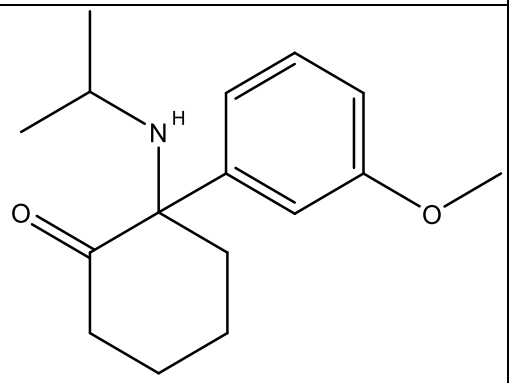
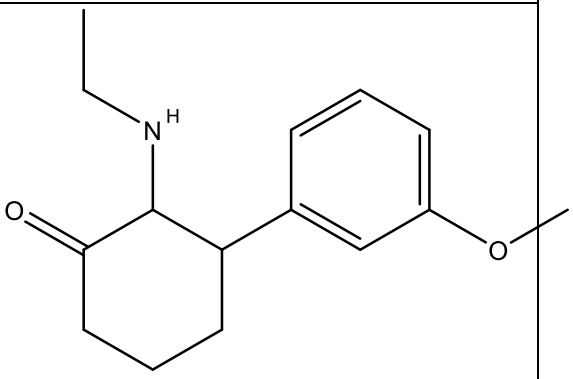
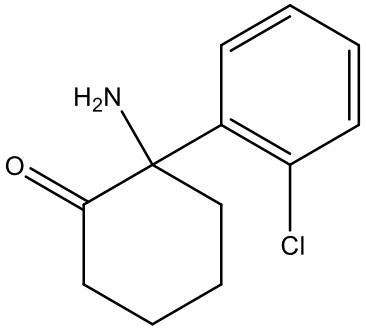
Table 1.1: The chemical structures of ketamine and other analogues.

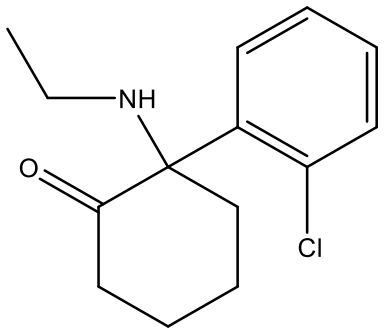
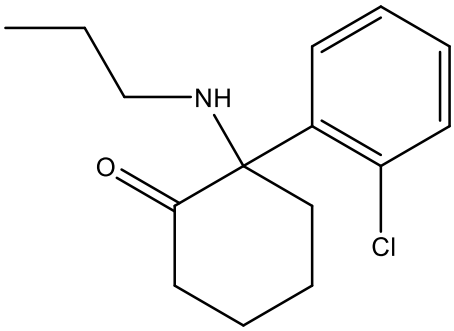
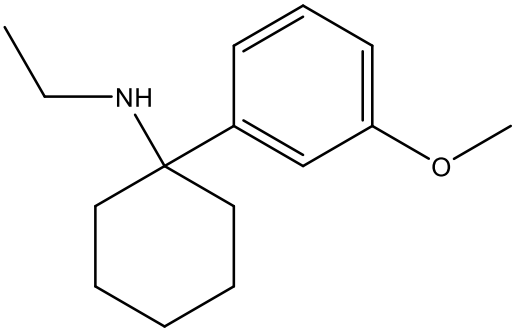
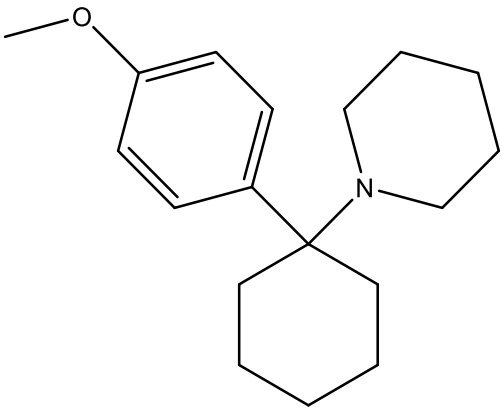
Names (including IUPAC name)	Structure
Ketamine 2-(2-chlorophenyl)-2-(methylamino)-cyclohexanone	
2-Bromo-deschloroketamine Bromoketamine 2-BrDCK 2-(2-bromophenyl)-2-(methylamino)cyclohexan-1-one 2-(2-bromophenyl)-2-(methylamino)cyclohexanone	
2-Fluorodeschloroketamine 2'-Fl-2-Oxo-PCM Fluoroketamine 2-FDCK 2-(2-fluorophenyl)-2-(methylamino)cyclohexan-1-one	

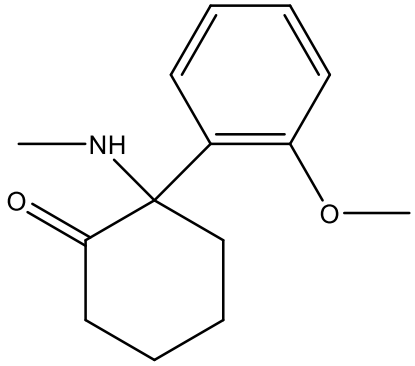
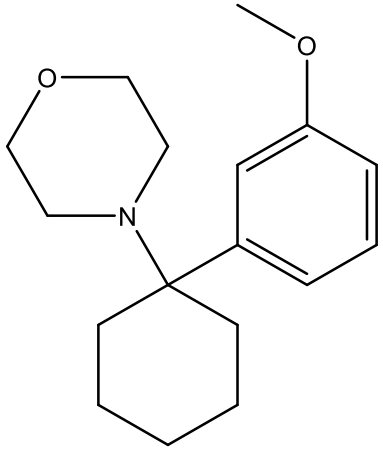
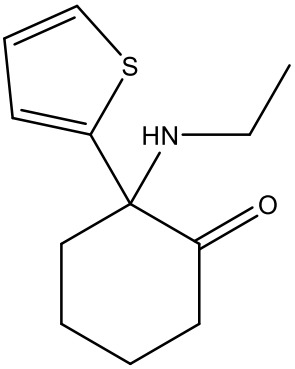
Names (including IUPAC name)	Structure
2-Fluorodeschloro-*N*-ethyl-ketamine 2-(ethylamino)-2-(2-fluorophenyl)cyclohexan-1-one 2-Fluoro-2oxo PCE 2FENDCK 2-FDCNEK CanKet	
3-Fluoro deschloroketamine 2-(3-fluorophenyl)-2-(methylamino)cyclohexan-1-one	
4-Fluoro deschloroketamine 2-(4-fluorophenyl)-2-(methylamino)cyclohexanone	

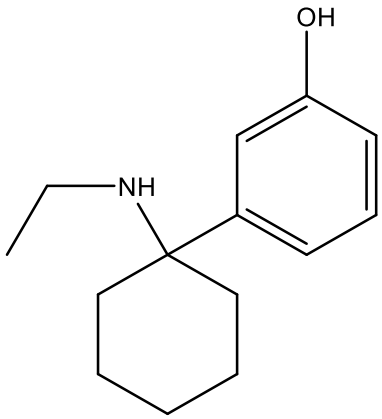
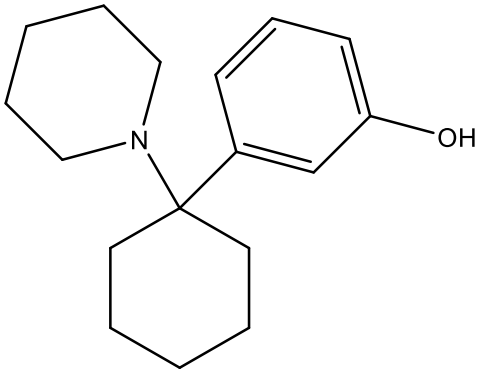
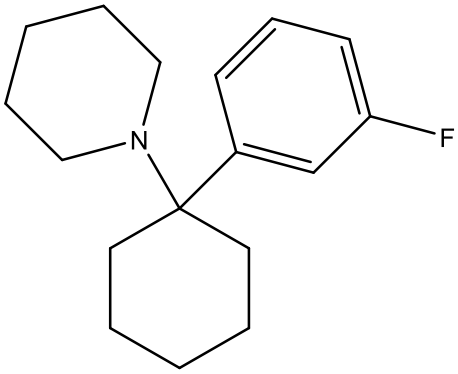
Names (including IUPAC name)	Structure
Deoxymethoxetamine 2-(ethylamino)-2-(3-methylphenyl)cyclohexan-1-one 3'-Methyl-2-oxo-PCE DMXE 3D-MXE	
Deschloroketamine 2-(methylamino)-2-phenylcyclohexan-1-one 2'-oxo-PCM O-PCM DXE DCK	
Deschloro-*N*-ethyl-ketamine 2-(ethylamino)-2-phenylcyclohexan-1-one 2'-Oxo-PCE Eticyclidone O-PCE	

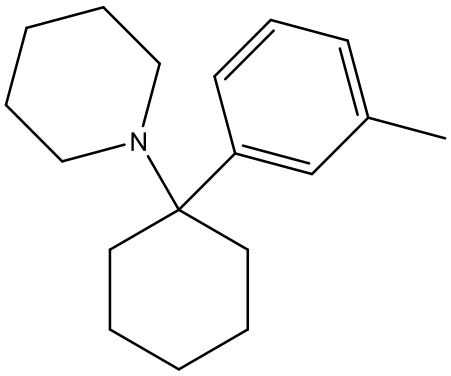
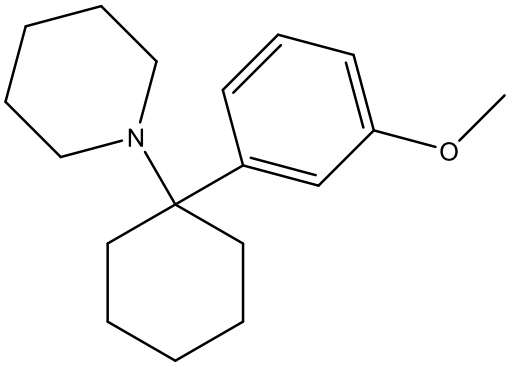
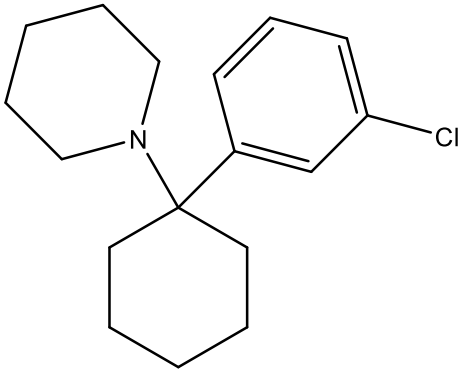
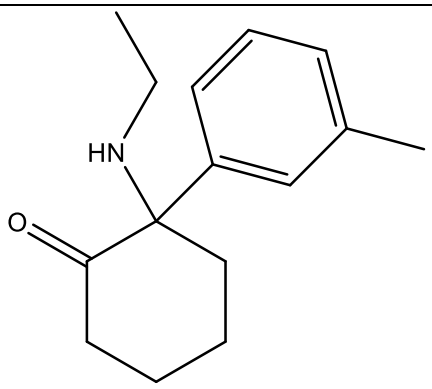
Names (including IUPAC name)	Structure
Fluorexetamine, 2-(3-fluorophenyl)-2-(ethylamino)cyclohexan-1-one FXE	
Hydroxetamine HXE 3'-hydroxy-2-oxo-PCE O-desmethylmethoxetamine 2-(ethylamino)-2-(3-hydroxyphenyl)cyclohexan-1-one	
Methoxpropamine MXPr 2-oxo-3'-methoxy-PCPr 2-(3-methoxyphenyl)-2-(propylamino)cyclohexan-1-one,	

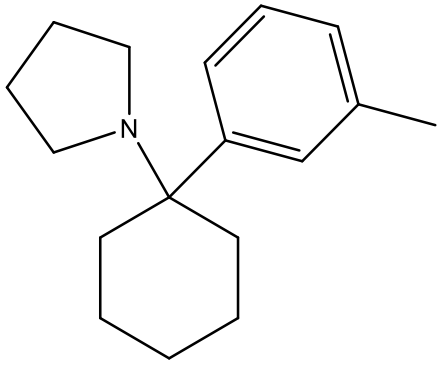
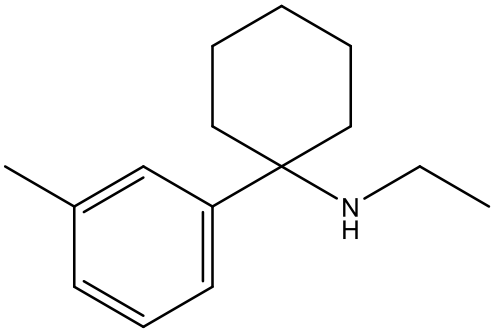
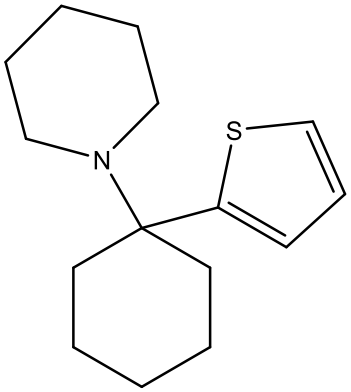
Names (including IUPAC name)	Structure
Methoxisopropamine MXiPr 2-(3-methoxyphenyl)-2-(propan-2-ylamino)cyclohexan-1-one)	
Methoxetamine 2-(ethylamino)-2-(3-methoxyphenyl)cyclohexan-1-one MXE	
Norketamine Desmethyl Ketamine 2-amino-2-(2-chlorophenyl)cyclohexan-1-one) 2-amino-2-(2-chlorophenyl)-cyclohexanone	

Names (including IUPAC name)	Structure
N-Ethylnorketamine NENK	
N-Propylnorketamine	
3-Methoxy eticyclidine 3-MeO-PCE *N*-ethyl-1-(3-methoxyphenyl)cyclohexan-1-amine	
4-Methoxy phencyclidine 4-MeO-PCP 1-[1-(4-methoxyphenyl)cyclohexyl]piperidine	

Names (including IUPAC name)	Structure
Methoxyketamine 2-MeO-ketamine 2-MeO-2-deschloroketamine 2-(2-methoxyphenyl)-2-(methylamino)cyclohexanone	
3-MeO-PCMo 4-[1-(3-methoxyphenyl)cyclohexyl]morpholine	
Tiletamine 2-(ethylamino)-2-thiophen-2-ylcyclohexan-1-one	

Names (including IUPAC name)	Structure
3-Hydroxy eticyclidine 3-HO-PCE 3-[1-(ethylamino)cyclohexyl]phenol	
3-Hydroxy phencyclidine 3-HO-PCP 3-(1-piperidin-1-ylcyclohexyl)phenol	
3-Fluoro phencyclidine 3-F-PCP	

Names (including IUPAC name)	Structure
3-Methyl phencyclidine 3-Me-PCP 1-[1-(3-methylphenyl)cyclohexyl]piperidine	
3-MeO-PCP 3-MeO-phencyclidine 1-[1-(3-methoxyphenyl)cyclohexyl]piperidine	
3-Chloro phencyclidine 3-Cl-PCP 3-chloro phencyclidine 1-[1-(3-chlorophenyl)cyclohexyl]piperidine	
Deoxymethoxetamine 3-MeO-2-oxo-PCE 2-(ethylamino)-2-(3-methoxyphenyl)cyclohexan-1-one	

Names (including IUPAC name)	Structure
3-Me-Rolicyclidine 3-Me-PCPy 1-[1-(3-methylphenyl)cyclohexyl]pyrrolidine	
3-Methyl eticyclidine 3-Me-PCE *N*-Ethyl-1-(3-methylphenyl)cyclohexanamine	
Tenocyclidine 1-((1-thiophen-2-yl)cyclohexyl)piperidine	

Annex 2. Pharmacology and toxicology

Receptor interactions

2.1 Among its many pharmacological targets, ketamine's interactions have been most extensively characterised at the excitatory NMDAR (Jevtović-Todorović and others, 1998). Like the prototypical NMDAR antagonist phencyclidine (PCP or 'angel dust'), ketamine and its analogues are non-competitive antagonists that block the NMDAR ion channel rather than the glutamate binding site (Lodge and Mercer, 2015). Although such inhibition of excitatory neurotransmission might be expected to reduce neuronal activity, ketamine paradoxically produces an 'excited' brain state reflecting its preferential binding to NMDARs at inhibitory interneurons, which causes disinhibition and a surge in upstream glutamate-mediated excitation (Zhang B and others, 2021). This hyperexcitation underlies ketamine's enduring structural and functional effects on the brain ('plasticity') which, in turn, may play a role in its long-lasting antidepressant effects (Parekh and others, 2022). However, the extent to which NMDAR antagonism is the central mechanism of ketamine's antidepressant effects (and indeed its psychotomimetic and dissociative effects) remains unclear. Some pre-clinical research suggests that NMDAR antagonism via specific NMDAR subunits underlies ketamine's antidepressant and psychotomimetic effects (Jiménez-Sánchez and others, 2014; Su and others, 2023; Tarrés-Gatius and others, 2020), but there is also evidence from animal models suggesting that the antidepressant effects of ketamine rely on its metabolism into (2*R*, 6*R*)-hydroxynorketamine, which has no measurable affinity for the NMDAR (Bonaventura and others, 2022).

2.2 The 2013 ACMD ketamine report described ketamine as having effects on other receptors and channels as well as the NMDAR. The pre-clinical data published since then has confirmed this, with other targets including dopaminergic, serotonergic, adrenergic, cholinergic, μ-opioid, and σ- receptors as well as serotonin, norepinephrine, and dopamine reuptake transporters (SERT, NET and DAT, respectively) and various ion channels (DEA, 2025; Richards and others, 2025; Savić Vujović, 2023). In general, ketamine has been characterised as a potent NMDAR antagonist (Roth and others, 2013), with reasonable affinity at the DAT. More recent data, where *R*(–)- and *S*(+)-ketamine were tested against thousands of receptor targets suggests that, apart from NMDAR, ketamine has greatest affinity for the mu opioid receptor (MOR). *S*(+)-Ketamine has greater affinity than *R*(–)-ketamine at the MOR, displacing DAMGO ((D-Ala2,*N*-Me-Phe4,Gly5-ol]-enkephalin) binding at concentrations above 1 μM. *S*(+)-Ketamine also has similar functional potency to morphine at the MOR, with a half maximal effective concentration (EC_{50}) around 500 nM (Bonaventura and others, 2022).

2.3 Of the ketamine-like drugs, perhaps methoxetamine and diphenidine have been studied the most. Methoxetamine blocks the NMDAR, but also blocks the SERT, NET and DAT, with greatest effects at SERT (Zwartsen and others, 2017), while diphenidine is a potent antagonist at NMDAR (Wallach and others, 2019) that also blocks the DAT, but with less potency than cocaine (Sahai and others, 2018).

2.4 The ketamine *S*(+)-enantiomer esketamine has approximately 4 times greater affinity for NMDAR binding site compared to the *R*(–)-enantiomer and approximately twice the analgesic potency compared with racemic ketamine (Vollenweider and others, 1997; Kalsi and others, 2011; Savić Vujović and others, 2023).

Antidepressant effects

2.5 Ketamine's antidepressant effects in humans are observed within 24 hrs of treatment with an acute low dose and sustained for up to 2 weeks. This rapid action makes it a valuable new class of treatment in psychiatry. Pre-clinical studies suggest that these effects involve remodelling of neural circuits that regulate emotional behaviour. Behavioural methods integrated with brain imaging have shown acute low-dose ketamine increases the density of the connections between neurones (synapses and spines) particularly in the prefrontal cortex (Kim and others, 2023). Using a translational rat model, specific neuropsychological effects of ketamine have been observed that are distinct from those seen with conventional antidepressants and could explain how these changes in emotional circuits lead to positive effects on mood (Stuart and others, 2015). In addition to ketamine, some of its metabolites may be important to the antidepressant effect. The hydroxynorketamines appear to have rapid antidepressant-like effects in animal studies, possibly by enhancing activity at AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptors and triggering brain growth and repair pathways involving BDNF (brain-derived neurotrophic factor) and mTOR (mammalian Target of Rapamycin) (Yang and others, 2019).

Pharmacokinetics

2.6 The pharmacokinetic values for ketamine have been reported to be minimally affected by the administered dose (Clements and Nimmo, 1981) or by age (Dinis-Oliveira, 2017), except, for example, where higher infusion rates may be required in paediatric patients to maintain steady state.

Absorption

2.7 After intravenous (IV) administration, ketamine rapidly crosses into the brain as it is highly lipid soluble, with onset of psychoactive effects within 2 minutes (Savić Vujović and others, 2023). The bioavailability of ketamine (amount reaching the systemic circulation) varies significantly depending on the route of administration. Intramuscular (IM), intranasal (IN), and intrathecal routes yield bioavailabilities of approximately 93%, 45 to 50%, and 25 to 30%, respectively. Peak plasma concentrations are typically reached within 5 to 30 minutes following intramuscular administration and within 15 to 20 minutes via the IN route (Zanos and others, 2018; Rosenbaum and others, 2024). In contrast, oral administration results in substantially lower bioavailability due to extensive first-pass hepatic metabolism, with reported values ranging from 16 to 29% for racemic ketamine and approximately 10% for esketamine (Fanta and others, 2015; Pelletier and others, 2022; Zanos and others, 2018). Peak plasma levels following oral intake are typically observed at 40 to 55 minutes, with ketamine metabolites detectable in the blood as early as 10 to 17 minutes after ingestion (Pelletier and others, 2022; Peltoniemi and others, 2016).

Intravenous (IV) administration, as expected, delivers 100% bioavailability, with plasma concentrations peaking between 5 to 30 minutes (Peltoniemi and others, 2016; Clements and Nimmo, 1981). A sublingual wafer formulation has shown a median absolute bioavailability of 29%, with a time to peak concentration of approximately 45 minutes (Rolan and others, 2014). In recreational contexts, snorted or inhaled ketamine is reported to have nearly complete systemic absorption (Peltoniemi and others, 2016). Most recreational users use ketamine by snorting (see Annex 5, Misuse).

Distribution

2.8 Following administration, ketamine distributes rapidly into highly perfused tissues, including the brain and placenta. Its high lipophilicity facilitates rapid penetration into the central nervous system (CNS), contributing to its fast onset of action. Ketamine exhibits a volume of distribution of 3 to 5L/kg and becomes 10 to 50% bound to plasma proteins (Rosenbaum and others, 2024). Pre-clinical studies have shown that ketamine also accumulates significantly in adipose tissue, liver, and lungs (EMC, 2025). This rapid redistribution to inactive tissue sites limits its duration of action. Clinically, an IV bolus dose of 2.5mg/kg initiates a distribution phase lasting around 45 minutes, during which the anaesthetic effects persist for approximately 20 minutes, reflecting a distribution half-life of 10 to 15 minutes. Plasma levels measured after a 2mg/kg IV dose typically range from 1.8 to 2.0 µg/mL at 5 minutes post-injection. Similarly, IM administration of 6mg/kg yields plasma concentrations of 1.7 to 2.2µg/mL within 15 minutes in both adults and children (EMC, 2025).

Metabolism

2.9 Ketamine undergoes biotransformation predominantly in the liver. Termination of its anaesthetic action results from a combination of redistribution, primarily from the brain to less perfused tissues and hepatic metabolism. First, racemic ketamine ((*R,S*)-ketamine) undergoes *N*-demethylation to form its primary metabolite, norketamine, a reaction primarily catalysed by the CYP3A4 enzyme but with minor contributions by CYP2B6 and CYP2C9 (Andrade, 2017; EMC, 2025). Next, norketamine undergoes further changes to form either dehydronorketamine (DHNK) or several types of hydroxynorketamine. These transformations depend on where hydroxylation happens on the molecule. Lastly, DHNK can form in 2 ways: either directly from norketamine through a reaction catalysed by CYP2B6; or indirectly, by non-enzymatic dehydration of the 5-hydroxynorketamine (Zanos and others, 2018).

Elimination

2.10 After IV administration, ketamine initially distributes from the CNS into peripheral tissues. It is then cleared from the body with a typical elimination half-life of 2 to 4 hours. The primary route of excretion is renal, with the majority of the administered dose (about 91%) recovered in the urine within 5 days. However, only around 20% of this appears as unchanged ketamine or primary metabolites. Both hydroxylated derivatives of ketamine and norketamine are eliminated via the urine and, to a lesser extent, in bile. These compounds are primarily excreted as conjugated metabolites (Dinis-Oliveira, 2017).

Ketamine key metabolites

2.11 Ketamine metabolism gives rise to several key metabolites, each with distinct pharmacological and potential toxicological profiles. Norketamine is the main active *N*-demethylated metabolite of ketamine. In individuals who have been using or misusing ketamine over a long period of time, more norketamine than unchanged ketamine is found in the urine, with a mean ketamine-to-norketamine ratio of 0.743 being reported (Moore and others, 2001). It is a weaker NMDAR blocker, around 3 to 5 times less potent than ketamine itself. While it may contribute modestly to analgesic and psychotomimetic effects, it has been shown to exert greater cytotoxic effects on urothelial cells than ketamine *in vitro* (Holtman and others, 2008; Lin and others, 2022).

2.12 Among the hydroxylated metabolites, (2*R*,6*R*)- and (2*S*,6*S*)-hydroxynorketamine are the most studied. These compounds have a longer half-life and negligible NMDAR binding (Zanos and others, 2016; Yang and others, 2019). Although little is known about their direct urothelial toxicity, they are eliminated via urine and bile (conjugated and unconjugated) and have been detected in urine 1 to 3 days after a single ketamine infusion dose (Highland and others, 2021).

2.13 DHNK is another metabolite of ketamine, but it is considered a minor metabolite with very weak or unknown effects on the brain. Although it forms about 16% of the ketamine IV dose eliminated via the kidneys, its role in the drug's effects is still unclear (Zanos and others, 2018).

2.14 The pharmacokinetics of most other arylcyclohexylamine derivatives remain poorly characterised, particularly those emerging as novel psychoactive substances (NPS). However, based on structural similarities of arylcyclohexylamine analogues, many are assumed to share broad pharmacokinetic properties with ketamine (Pelletier and others, 2022).

Preclinical addictive behaviour

2.15 Animal studies have documented tolerance to ketamine, as evidenced by shorter durations of anaesthesia from the same dose or higher doses of ketamine required to reach the same level of anaesthesia (Kleczkowska and Zaremba, 2021).

2.16 Ketamine is self-administered by rodents and monkeys and also evokes drug-seeking behaviour (Chang and others, 2019; Fan and others, 2025). Its addictive liability does not appear to be as great as that of cocaine (Simmler and others, 2022). Bonaventura and others (2022) found that (*S*)-ketamine was the most active enantiomer with respect to addictive liability.

2.17 There are sex-dependent effects seen with ketamine, with female rats self-administering more ketamine than males (Wright and others, 2019; Hagarty and others, 2024; Jennings and others, 2025). Ketamine evoked greater locomotor sensitisation in female versus male rats (Schoepfer and others, 2019; Strong & Kabbaj, 2018) and greater cocaine-seeking in female versus male rats (Guo and others, 2016).

2.18 There are also age-dependent effects of ketamine with greater effect in young rodents. Repeated ketamine exposure in the early postnatal days resulted in rats that showed greater ketamine- and nicotine-seeking behaviour in adulthood (Cui and others, 2022). Similarly, early chronic ketamine treatment caused male (but not female) rats to show greater cocaine-seeking behaviour as adults. This effect was not seen in adult rats with chronic ketamine exposure (Garcia-Carachure and others, 2020).

2.19 Despite the above research, which clearly indicates that ketamine has considerable addictive liability, ketamine has been found to be a useful treatment in rodent models of cocaine, nicotine and alcohol misuse. Ketamine can reduce alcohol intake in rats (Sabino and others, 2013), while this effect was subsequently seen in female but not male rats (Bertholomey and others, 2025). Ketamine reduces cocaine-seeking behaviour in rhesus monkeys (Maltbie and others, 2019) and low-dose ketamine reduces nicotine self-administration in rats (Rezvani and others, 2018). Chronic ketamine treatment in either adolescence or adulthood evokes an enduring resilient phenotype ((Parise and others, 2013).

2.20 Of the compounds that are similar to ketamine, some have been found to have an addictive profile. Methoxetamine (Mutti and others, 2016; Botanas and others, 2015; Chiamulera and others, 2016), diphenidine (Kim and others, 2022) and deschloroketamine (Li and others, 2022; Kim and others, 2022) all show an addictive liability, although generally to a lesser extent than ketamine or PCP (Berquist and others, 2018). However, 2-FDCK, deschloroketamine, 1-phenylcyclohexan-1-amine (PCA) and diphenidine had almost an identical profile to ketamine in all pre-clinical models of drug misuse in male rats and mice (Li and others, 2022; Kim and others, 2022; Abiero and others, 2021).

Bladder toxicity

2.21 Pre-clinical studies have demonstrated that chronic exposure to ketamine results in dose-dependent and time-dependent pathological changes in the bladder, closely mirroring clinical findings in human ketamine-induced uropathy. In rodent models, chronic ketamine administration leads to significant urothelial injury and bladder inflammation within 2 weeks. Subsequently, progressive fibrosis, collagen deposition and bladder wall thickening become evident at weeks 4 to 8 onwards (Liang and others, 2015). The doses and frequency used in these pre-clinical studies are equivalent to recreational human use of ketamine of 1 g to 5 g per day. Histological analyses reveal epithelial denudation, submucosal oedema, inflammatory cell infiltration and increased expression of pro-inflammatory cytokines and oxidative stress markers (Gu and others, 2014; Liu and others, 2016; El-azab, 2020; Wang and others, 2017; Li and others, 2014; Duan and others, 2017). With continued exposure after 4 to 8 weeks, these changes progress to collagen deposition, detrusor muscular hypertrophy and reduced bladder compliance, resulting in small fibrotic bladders with decreased functional capacity, mimicking the fibrotic and contractile bladder seen in individuals following prolonged ketamine use (see Table 2.1) (Wang and others, 2017; Shen and others, 2016; Chuang and others, 2013). After 6 months daily ketamine exposure in mice, disordered autophagy in the bladder has been observed (Li and others, 2021). Urodynamic studies in animals from as early as 2 weeks old show increased urinary voiding frequency, shortened inter-contraction intervals, and

detrusor overactivity, consistent with the lower urinary tract symptoms observed in humans chronically exposed to ketamine (Liang and others, 2015; Chung and others, 2022).

2.22 Chronic exposure to ketamine and its metabolite norketamine, particularly at millimolar (mM) concentrations in urine, damages the urothelial lining of the bladder directly. These compounds can penetrate the urothelium, leading to mitochondrial dysfunction, generation of reactive oxygen species (ROS), calcium-mediated ERK1/2 stress, and ultimately apoptotic cell death (Lin and others, 2022). Such molecular insults result in epithelial denudation, ulceration and haemorrhagic cystitis, all key histopathological features of ketamine-associated bladder injury (Lin and others, 2022). In a chronic mouse model involving daily ketamine doses of 30 to 60mg/kg for 6 months, significant inflammation and autophagy dysregulation were observed. Specifically, upregulation of pro-inflammatory cytokines (IL-6, IL-1β) and autophagy markers (LC3-II, Beclin-1, P62) was associated with mast cell infiltration and collagen deposition in the bladder wall (Li and others, 2021). Over time, these changes progressed toward fibrosis, driven by epithelial-mesenchymal transition (EMT). Both ketamine and norketamine have been found to increase expression of metadherin (MTDH), which activates the P38 mitogen-activated protein kinase (MAPK) pathway, promoting EMT and leading to fibrotic bladder (Zhu and others, 2022). Progressive fibrosis shortens the ureter, produces hydronephrosis and, if unrecognised, subsequent renal impairment (Jhang and others, 2023).

2.23 Electron microscopy has revealed ultrastructural damage to the urothelium, including disrupted tight junctions (barrier dysfunction) and mitochondrial degeneration, and damage to small blood vessels and small nerve fibres in the submucosa (Chung and others, 2022), suggesting direct cytotoxic effects of ketamine. Urothelial changes reported in chronic exposure rodent studies are unlikely to result from immunologic or vascular factors, but a result of direct exposure of ketamine to the urothelium (Bureau and others, 2015). The excretion of ketamine and its main metabolite, norketamine, in urine is believed to be a primary mechanism of urothelial toxicity in recreational users due to accumulation, prolonged exposure and direct contact with bladder epithelium (Shahani and others, 2007). Ketamine applied directly to human urothelial cell lines over 48 hrs is cytotoxic, increasing urothelial cell permeability in a dose- and time-dependent manner (Shen and others, 2015) and norketamine is toxic to human urothelial cells in a concentration-dependent manner (Lin and others, 2022). Culturing of rat bladder *ex vivo* with 3 mM racemic ketamine, 3 mM *S*(+)-ketamine or 3 mM norketamine for 3 days resulted in a thinning of the epithelium and loss of mucosal cells and uroplakin III staining of umbrella cells in a concentration- and time-dependent manner (Gant and others, 2023), in line with the thinning of the epithelium observed in human ureteric organ cultures after 3 days exposure to 3 mM ketamine (Baker and others, 2016) and epithelial denudation seen within 2 weeks of chronic exposure to high doses of ketamine or norketamine.

2.24 Some pre-clinical studies have shown a partial reversal of bladder toxicity after 2 to 8 weeks cessation of chronic ketamine exposure, particularly when the damage is at an early or moderate stage, with functional improvements and partial recovery of inflammatory and epithelial changes (Rajandram and others, 2017). The extent of recovery is time- and damage-dependent; not all changes are reversible with cessation, especially if fibrotic structural changes have progressed, such as detrusor

muscle hypertrophy, collagen deposition and loss of bladder function. These findings mirror the clinical experience in individuals, validating the translational value of these pre-clinical studies in studying pathogenesis and potential therapeutic interventions (see Table 2.1).

2.25 The structurally related ketamine analogue, methoxetamine (MXE), and the structurally distinct ketamine derivatives, diphenidine (DPH) and methoxphenidine (MXP), like ketamine, are metabolised and excreted via the urinary tract, raising similar concerns regarding urological toxicity. Two pre-clinical studies have demonstrated that chronic daily exposure of a high 30 mg/kg dose of methoxetamine over 12 weeks in mice and rats causes urothelial denudation, inflammatory cell infiltration, haemorrhage, mast cell activity, detrusor muscle hypertrophy, fibrosis, reduced capacity, increased voiding frequency and detrusor overactivity (Dargan and others, 2014; Wang and others, 2017). In contrast, despite emerging consensus claims on user forums that ketamine derivatives like DPH and MXP are structurally distinct from ketamine and hence are ‘bladder safe’, no *in vivo* or *in vitro* chronic bladder histopathology or cytotoxicity peer-reviewed data currently exists clinically or pre-clinically, leaving their risk profile uncertain. Notably, research by Gant and others, (unpublished) has demonstrated that a high (3 mM) concentration of MXE, MXP or DPH causes a thinning of the epithelium and loss of mucosal cells in rat bladder organ cultures after 3 days, comparable to the effects of ketamine, demonstrating that ketamine analogues and derivatives share a class effect of direct urothelial and bladder wall toxicity when administered locally over 3 days in tissue culture. Although comparative pre-clinical systemic chronic exposure studies remain limited, current evidence suggests that ketamine derivatives pose a similar risk of direct contact urological toxicity when misused, and that their increasing recreational use may carry significant long-term bladder health implications. These ketamine derivatives and analogues are still being offered for sale as ‘research chemicals’ and are being discussed on user forums (Corkery and others, 2025).

Table 2.1: Toxicological effects of ketamine in animals and humans.

	Animal	Human (frequent, high-dose use)
Epithelial damage	✓ Thinning or loss of urothelium, reduced uroplakin expression	✓ Urothelial denudation observed via biopsy and cystoscopy in chronic users
Inflammation	✓ Neutrophil and macrophage infiltration, ↑ IL-6, TNF-α, IL-1β	✓ Cystitis with lymphoplasmacytic infiltration; ↑ urinary cytokines in some studies
Fibrosis	✓ Collagen deposition in lamina propria; ↑ TGF-β signalling	✓ Detected on biopsy; contributes to bladder wall thickening and reduced compliance
Bladder capacity	✓ ↓ Functional bladder capacity, ↑ micturition frequency in rats/mice (via cystometry)	✓ Severely reduced capacity (e.g., <100 mL) in advanced ketamine cystitis
Pain and urgency	✓ Behavioural signs of discomfort (e.g. licking, vocalisation)	✓ Severe pelvic pain, urgency, frequency; mimics interstitial cystitis
Detrusor overactivity	✓ Unstable contractions and bladder hyperreflexia in urodynamic studies	✓ Documented in urodynamic testing; detrusor overactivity common
Oxidative stress	✓ ↑ ROS, MDA; ↓ SOD, catalase in bladder tissue	**?** Limited direct evidence, but implied via histology and symptomatology
Recovery after cessation	✓ Partial reversal of epithelial damage after stopping ketamine in rodents in early stage	✓ Some recovery possible in early stages; irreversible in chronic/severe cases

Neurotoxicity

2.26 In addition to bladder toxicity, ketamine and associated compounds have toxic effects elsewhere in the body in preclinical- models. Here, we focus briefly on neurotoxicity. Prolonged exposure to moderate or high doses of ketamine contributes to cellular and metabolic changes, ultimately leading to neuronal damage and cell death (Choudhury and others 2021). The cortical parvalbumin-containing inhibitory interneurons that regulate brain network dynamics and maintain excitation-inhibition balance (Ferguson and Gao, 2018) are especially vulnerable to ketamine-induced damage (Behrens and others 2007). Loss of function of these inhibitory neurons following chronic ketamine exposure resembles the pattern of prefrontal parvalbumin interneuron dysfunction seen in numerous neuropsychiatric disorders, including schizophrenia (Lodge and others, 2009).

2.27 Aside from dose, developmental stage appears to be important, with most ketamine neurotoxicity seen in the developing brain. These pre-clinical data have been recently reviewed (Schwenk and others 2021; Choudhury and others 2021). Ketamine treatment during development may lead to NMDAR dysregulation in adulthood (Kalopita and others 2021), with consequent susceptibility to mitochondrial dysfunction. This research is relevant to chronic ketamine-related harms in humans, since many illicit users are first exposed to ketamine in their teens. Initial exposure may give rise to changes in reward circuitry that contribute to escalating misuse (Garcia-Carachure and others, 2020). Repeated exposure to moderate ketamine doses (10 to 80mg/kg) during adolescence resulted in a range of functional and structural abnormalities in brain areas involved in learning, memory, executive functioning and inhibitory control (Acevedo and Siegel, 2022). As found in mature rodents, inhibitory parvalbumin-containing interneurons are a primary target of ketamine neurotoxicity in adolescent rodents. The consequent social and cognitive impairments of this cell-specific toxicity appear to persist into adulthood (Pérez and others 2019; Zhang and others 2024) Other studies examining the consequences of chronic ketamine exposure show a failure of juvenile rodents to follow expected cognitive and social developmental trajectories (Nagy and others 2015), along with abnormalities in reward processing that increased susceptibility to addictive behaviour in adulthood (Garcia-Carachure and others, 2020).

2.28 There are relatively few studies examining sex differences; the studies that examined female rodents suggested females are more susceptible to the neurotoxic effects of ketamine (Acevedo and Siegal, 2022), possibly through sex differences in ketamine pharmacokinetics (McDougall and others, 2019).

2.29 Of the ketamine-like drugs, few have been examined for neurotoxicity. Chronic treatment of adolescent male rats with methoxetamine resulted in decreased dopamine transporter and tyrosine hydroxylase-positive fibres in the brain, specifically the medial prefrontal cortex, nucleus accumbens shell and the caudate-putamen. These neurotoxic changes were also seen in the dopamine cell body regions, the ventral tegmental area and pars compacta of the substantia nigra where decreased tyrosine hydroxylase-positive neurons were found (Costa and others 2019).

2.30 On the other hand, there is a rich literature examining the therapeutic potential of NMDAR antagonists as neuroprotective agents. While this report focuses on adverse effects of ketamine, the drug does have several potentially beneficial properties. The considerable research literature that considers the neuroprotective effects of ketamine has been reviewed recently (Rafe and others, 2024; Zhang and others 2025). In short, ketamine could be useful in stroke, epilepsy, traumatic brain injury and Parkinson's disease, while NMDAR antagonists are suggested to be useful in these conditions as well as amyotrophic lateral sclerosis (ALS), Huntington's disease and Alzheimer's disease. There are also many clinical studies examining the use of ketamine outside of anaesthesia (Pribish and others, 2020). For example, the use of *S*(+)-ketamine in reducing spreading cortical depression after subarachnoid haemorrhagic stroke (Santos and others, 2019) and ketamine and propofol combination being protective in traumatic brain injury (Maheswari and others, 2023).

Cognitive dysfunction

2.31 The acute and chronic effects of ketamine and related compounds on cognition are associated with different mechanisms. The acute effects are highly dose-dependent and the impairments in cognition are likely associated with the dissociative effects and sedation and reverse as the drug is metabolised and excreted (Young and others, 2009). There may be some post-administration amnesic effects, but these are not usually retrograde and only impact on the time when the drug was active in the body. The chronic effects of ketamine and related compounds are thought to be related to damage caused in cortical circuits following repeated exposure, which is likely related to frequency of use and dose, and with different degrees of vulnerability. In animal studies, repeated treatment with high doses of ketamine and PCP resulted in cognitive impairments that persisted beyond the treatment period and were sustained for at least several months (Dupuis and others, 2023; Sigurdsson and Duvarci, 2016).

2.32 The resulting phenotype has been used to study cognitive impairments related to schizophrenia, and there is a direct link between dysfunction in NMDAR and a form of auto-immune-induced psychosis in humans, adding clinical evidence to support the relevance of the NMDA hypofunction animal model. This suggests that repeated, high-dose use of ketamine and related compounds can lead to impairments in normal NMDAR function in cortical brain areas, with evidence suggesting changes occur in inhibitory signalling within local neural circuits (Xi and others, 2009). This will cause a complex pattern of behavioural changes, including impairments in cognitive, social and emotional processes.

Annex 3. Legal controls

International conventions

3.1 Ketamine has previously been proposed for inclusion in the 1971 Convention on Psychotropic Substances, initially in Schedule I and then later in Schedule IV. In 2015, China requested a vote during CND's annual meeting based on substantial ketamine misuse in China and elsewhere in Southeast Asia that was causing significant public health harms (UNCND, 2015). China argued that international control of ketamine was essential to counter these harms. Several medical associations and civil society groups argued that putting ketamine under international control would severely restrict legitimate medical access to a safe anaesthetic that is widely used in surgeries in low and middle-income settings and for which there is no inexpensive alternative. It was suggested that access to anaesthesia might be lost to potentially life-saving surgeries if ketamine was scheduled or would have to proceed without proper anaesthesia. It was also suggested at that time that problems being reported relating to ketamine misuse were a local Asian issue. Ultimately, China requested that the vote be cancelled. In 2016, the ECDD recommended against placing it under international control because there was insufficient information to warrant scheduling (WHO, 2016) and that "the medical benefits of ketamine far outweigh potential harm from recreational use" (IDPC, 2015), a viewpoint supported by others (Taylor and others, 2016). Consequently, ketamine is not currently placed under international control (Lohman and Barrett, 2020; UNODC, 2022) and it remains for individual countries to decide whether and how to control ketamine under their national legislation.

3.2 Since 2015, the problem of ketamine misuse has become international so that, for example, the recently released 2024 web survey data on EU drug use cites ketamine misuse as being more frequent than misuse of synthetic cannabinoid receptor agonists (SCRAs), illicit benzodiazepine and cathinones (EUDA, 2025a). It is evident the material now entering the market is not all diverted medication but is often being illicitly synthesised on a large scale, so that it has become cheap and readily available (see Section 12, 'Trafficking and Supply' and Annex 6), meaning that reconsideration of international scheduling may be justified.

3.3 Several UN member states have expressed concern about recent increases in non-medical use of ketamine and the UN Office on Drugs and Crime (UNODC) has considered several resolutions to address them. These include 'Listing Ketamine as a controlled substance' in 2006 (Resolution 49/6) and 'Responding to the threats posed by the abuse and diversion of ketamine' in 2007 (Resolution 50/3), both of which were rejected; and 'Preventing the diversion of ketamine from legal sources while ensuring its availability for medical use' in 2014 (Resolution 57/10), which was passed, encouraging member states to take steps to tackle diversion, including control under national drug legislation. In 2015, there was a further attempt to list ketamine in Schedule IV of the 1971 Convention, but a decision was postponed, awaiting further evidence from the WHO (Resolution 58/2) (UNODC, 2015).

3.4 Most recently, during the 2025 session of the UNCND, Kenya reported an increase in the misuse of ketamine and called on the WHO for further review and advice on control measures. During the same session, India highlighted that some member states may opt to control substances despite the WHO not recommending international control. The example given was India, which has controlled ketamine and tramadol as part of its commitment to “maintaining a system that caters to the healthcare needs of the world and prevents diversion of medicines”.

National controls of ketamine

United Kingdom

3.5 Ketamine was initially controlled via the MDA as Class C in January 2006, when it was placed in Schedule 4 part 1 of the MDR. It has been in Class B Schedule 2 since June 2014, following recommendations made in the previous ACMD review (ACMD, 2013). Control of drugs via the MDA also captures enantiomers, so esketamine is also controlled as Class B by the MDA and listed in Schedule 2 of the MDR.

3.6 Several other compounds with structural similarity to ketamine are controlled by name in the MDA as Class A compounds. Eticyclidine, rolicyclidine and tenocyclidine are all placed in Schedule 1 of the MDR as they have no legitimate medical use, while phencyclidine (PCP) was listed in Schedule 2 when it was controlled in 1979 as it was considered as having some potential medical applications in human or veterinary anaesthesia (ACMD, 2013). It is not, however, licensed as a medicine in the UK or elsewhere. A further related compound, tiletamine, was specifically excluded from control because there was very little evidence of misuse (ACMD, 2013).

3.7 Other analogues of ketamine are controlled via generic definitions that were added to both the MDA and the MDR to control 2 groups of arylcyclohexylamines in February 2013. These covered a range of compounds, including methoxetamine and materials related to methoxetamine or PCP. All materials covered by these controls were added to Class B of the MDA and to Schedule I of the MDR (ACMD, 2013).

3.8 The arylcyclohexyl generic was introduced in 2013 by Statutory Instrument (SI) 2013/239, following the recommendations of an ACMD report of October 2012 concerning the conversion of the Temporary Class Drug Order on methoxetamine into MDA control. This also included consideration of analogues of PCP and ketamine (ACMD, 2012). The SI placed a broad range of arylcyclohexylamine variants in Class B of the MDA. The generic text specifically excluded ketamine, which was at that time a named Class C material, although it was subsequently reclassified as Class B by SI 2014/1106, following ACMD advice in 2013 (ACMD, 2013).

3.9 The 2013 generic advice addresses 2 groups of materials with dissociative effects:

(a) those like PCP, which are based on a 1-phenylcyclohexylamine core
(b) those like ketamine which are based on a 2-amino 2-phenylcyclohexanone core, with both cores subject to a specified list of modifications.

3.10 The wording of the generic (Schedule 2, Part 2 (Class B drugs), para 1(d) of the MDA) is provided in Annex 13. This has proved robust, covering almost all of the variants reported internationally to date. One omission that should be addressed as a common bio-isostere replacement, is the incorporation of the amine nitrogen into a morpholine ring to form materials such as 3-MeO-PCMo, which has subsequently been reported by the European Union Drugs Agency (EUDA) in 2015. This material has been reported to be active (Colestock and others, 2018), is described on the internet as being "the only legal aryl cyclohexylamine" (Legal High Guru, 2015) and there are instructions on the internet on how to make it. This omission could be remedied by the addition to sub-para (i) of the generic of "4-morpholino" to the list of replacements for the amine group.

3.11 There is also a potential nomenclature anomaly within this part of subparagraph (i). This is intended to cover the amine nitrogen being integrated into a 4-, 5- or 6-membered saturated ring (larger rings are reported to decrease/eliminate potency). The nomenclature for such saturated rings containing a single nitrogen is normally:4-membered = azetidine, 5-membered = pyrrolidine and 6-membered = piperidine, hence the expected nomenclature for such groups would be 'azetidyl', 'pyrrolidyl' and 'piperidyl'. Although no such 4-membered ring compounds have been reported and the wording has not been challenged, the term 'azepyl' could usefully be corrected to 'azetidyl' if amendments to the generic are being considered.

3.12 One other substance reported by EUDA that is outside the scope of the generic is benocyclidine, which has a benzothiophene structure replacing the phenyl ring. Thiophene variants are covered by sub-para (iv) of the generic, while tenocyclidine (1-(1-(2-thenyl)cyclohexyl)piperidine) is named as a Class A material. However, although benocyclidine is reported to be a potent dopamine reuptake inhibitor, it is also reported not to have PCP-like dissociative effects. As it has not been noted as being in use as an alternative arylcyclohexylamine NPS, control via the MDA is not currently warranted and it can be left as a substance potentially captured by the Psychoactive Substances Act 2016.

Other countries

3.13 Different jurisdictions have controlled ketamine in different ways, from making it a Schedule I controlled drug through to listing it in a lower Schedule of control to facilitate its medical applications and/or by designating it as a prescription-only medicine.

3.14 In Asia, where problems of ketamine misuse have been reported for many years, control in many countries is tighter. China and Hong Kong control it as a Schedule 1 material, in Singapore it is a Class A drug, in Thailand a Category 2 psychotropic, and in Japan it is classified as a narcotic. In Taiwan, ketamine is a Schedule 4 material

and both N-boc-ketamine and *N*-boc-norketamine have also been controlled as Schedule 4 precursors.

3.15 In India, which is a major producer of ketamine for the legitimate medical market, ketamine has since 2011 been controlled as a psychotropic drug under The Narcotic Drugs and Psychotropic Substances Act 1985 (The Gazette of India, 10 February 2011, SO311(E)). Under this Act, the manufacture, possession, sale, purchase and use, and import and export of ketamine are controlled (UNODC) with penalties extending up to 20 years' imprisonment depending on the amount involved (small quantity = 10g; commercial quantity = 500g) and the nature of the offence (for example, possession, trafficking or production). In 2014, in response to an increase in non-medical use, ketamine was officially moved from Schedule H to Schedule X of India's Drugs and Cosmetics Rules 1945 under Notification GSR 724E issued by the Ministry of Health and Family Welfare. Under Schedule X, ketamine requires special licensing of pharmacies/providers, storage under lock and key, and sales recorded and prescriptions retained for at least 2 years (Goel, 2024).

3.16 In North America, ketamine is controlled as a Schedule 1 drug in Canada and as a Schedule III drug in the USA. The Schedule III status makes it less tightly regulated in the USA compared to drugs in Schedule I (for example, heroin) or Schedule II (for example, cocaine) (Kleczkowska and Zaremba, 2021).

3.17 In Australia, ketamine is classified as a Schedule 8 medicine under the Poisons Standard, that is, a medicine which has a high potential for abuse, misuse and dependence.

3.18 In Germany, ketamine, as a prescription-only medication, is controlled under the Medicinal Products Act 1961 (Arzneimittelgesetz – AMG). It is recognised as a medically essential anaesthetic and therapeutic agent. Ketamine is not controlled in Germany under the Narcotic Drugs Act 1971 (Betäubungsmittelgesetz – BtMG) but is covered by the generic control on arylcyclohexylamines in the Neue-psychoaktive-Stoffe-Gesetz – (NpSG, 'New Psychoactive Substances Act'). Under the Medicinal Products Act 1961, unauthorised manufacture, sale or distribution of ketamine is illegal and punishable by fines and/or imprisonment up to 3 years increasing to 10 years if the offence endangers public health or involves significant financial gain (Section 95 of the AMG). However, personal possession without a prescription is not an offence.

3.19 In Belgium, ketamine is classified as a controlled substance and a prescription-only medication. Thus, ketamine is illegal if it is not prescribed, and possession and supply offences are punishable under the 1921 Act. Ketamine was brought into the 1921 Act through the Royal Decree of 2017 due to concerns about rising non-medical use across the country and increasing mentions of ketamine in treatment episodes (Antoine and others, 2022). Under the 1921 Act, ketamine is included in Schedule I (the highest control) and possession without a prescription or medical purpose is punishable by up to 5 years in prison and/or fines (Federale Overheidsdienst Justitie, 1921). Supply and production offences are punishable by between 5 and 20 years in prison and/or a fine up to 500,000 Euros depending on the scale and whether there are aggravating circumstances.

3.20 Under the Dutch Medicines Act 1964, ketamine is legal for medical and veterinary use with appropriate licences and prescriptions. Under Article 40, it is prohibited without proper authorisation to manufacture, import or export, trade or supply medicinal products, including ketamine. Violations of this article can lead to criminal prosecution and penalties, including fines and conditional sentences for possession for personal use and heavier penalties including imprisonment (up to 6 years for serious offences) for supply and trafficking offences.

3.21 Other examples include Norway, where it is a Class A drug, and Italy, where it is a Schedule 1 material. In Switzerland, it is controlled as a Table b material, in Spain and Sweden it is a Schedule 4 material, and in France it is listed as a Schedule IV stupefiant.

3.22 This inconsistent pattern of national controls combined with a significant legitimate pharmaceutical trade, facilitates the diversion of ketamine to the illicit market (EUDA, 2024).

Annex 4. Legitimate use

Use in humans

Anaesthesia

4.1 Ketamine remains a unique and valuable agent in modern clinical anaesthesia/pain management practice due to its dissociative anaesthesia, analgesic and antidepressant properties (Kurdi and others, 2014). It has been used since the 1970s for its dose-dependent anaesthetic, sedative and analgesic effects, and it features in the WHO list of essential medicines (WHO, 2025). The (*S*)-enantiomer esketamine, given via the intravenous (IV) or intramuscular (IM) routes, is also licensed for anaesthesia and analgesia in acute settings.

4.2 Ketamine produces a 'dissociative' anaesthetic state that has been described as functional and electrophysiological dissociation between the thalamo-neocortical and limbic systems (Miyasaka and others, 1968). It decreases central sensitisation (wind up) in acute and chronic pain via its non-competitive channel blockade of NMDAR (Zhang Y and others, 2021). Thus, ketamine is now increasingly being used as an adjunct analgesic in acute and chronic pain conditions (Richards and others, 2025).

4.3 Ketamine is a useful drug for prehospital and field anaesthesia (Paix and others, 2005; Buckland and others, 2018), pain management (McArthur and others, 2025; Vanolli, 2020), rapid sequence intubation (anaesthesia), and sedation and anaesthesia for extrication and field amputations (Porter, 2010; Baker and others, 2025).

4.4 In paediatric anaesthesia and intensive care (Groth and others, 2024), ketamine is used extensively for procedural analgosedation, such as dressing changes in burns patients (Deniau and others, 2022), premedication (Stoelting and Hillier, 2006) as an adjunct to regional anaesthesia (Mossetti and others, 2012) and post-anaesthesia shivering (Norouzi and others, 2011).

4.5 In adult anaesthesia practice, IV ketamine retains a place as an IV induction agent for haemodynamically unstable patients in trauma (Kim and others, 2023), critically ill septic patients (Jabre and others, 2009) and children with congenital heart disease (right to left shunt) (Goyal and others, 2013), due to its sympathomimetic effects. Ketamine also has bronchodilator effects, making it valuable for induction of anaesthesia in patients with severe bronchial asthma as well as for treating refractory severe acute asthma in intensive care settings.

4.6 Perioperative ketamine reduces post-operative analgesia use and pain (Brinck and others, 2018). IV ketamine infusions are offered for refractory complex pain patients in hospital (usually post-surgery). The doses used in anaesthesia range from 0.5 to 1.5mg/kg IV for induction and 4 to 10mg/kg for sedation (Van Amsterdam and Van Den Brink, 2022).

4.7 Emergence reactions or emergence phenomena are psychomotor symptoms experienced by some when waking from ketamine anaesthesia. Further information is provided about these in Section 8, ‘Health harms’.

4.8 In chronic pain, ketamine is used as an adjunct analgesic as it reduces opioid tolerance and hyperalgesia and improves the efficacy of co-administered opioids. Emerging indications in chronic pain include complex regional pain syndrome (Niesters and others, 2014), refractory neuropathic pain and refractory headaches (Lauritsen and others, 2016; Guimarães Pereira and others, 2022; Schwenk and others, 2018; Swanson and others, 2024). Currently, however, the National Institute for Health and Care Excellence (NICE) has concluded that ketamine should not be initiated for chronic primary pain due to a lack of supporting evidence and concerns about potential harms (NICE, 2021).

Psychiatry

4.9 Considerable evidence exists for the efficacy of ketamine or esketamine in depression (Popova and others, 2019; Bahji and others, 2022; d’Andrea and others, 2025; Li and others, 2025; Molero and others, 2025). Low-dose ketamine has a rapid antidepressant effect lasting, on average, 10 days. People suffering from depression who have not responded to conventional monoaminergic antidepressants such as selective serotonin reuptake inhibitors can feel abruptly better. However, as with all antidepressants, it needs to be taken repeatedly for the benefit to be maintained.

4.10 While Medicines and Healthcare products Regulatory Agency (MHRA) and NICE rules substantially constrain use of ketamine for treatment-resistant depression (TRD) (NICE, 2022a), this may change. For example, IV ketamine is now approved for reimbursement in Norway, with the pharmacoeconomic case strongest when the comparison was with electroconvulsive therapy (ECT) (Ohm and others, 2024; NPMA 2025).

Self-treatment

4.11 The knowledge that ketamine has an antidepressant effect is very widespread. The fact that self-treatment is linked with addiction is less well known. Dose escalation due to tolerance can occasionally occur when ketamine is prescribed medically, especially if the interval between doses reduces below weekly (Bonnet, 2015). However, it is much more common during unsupervised self-treatment.

4.12 In the largest UK sample of people with self-identified ketamine use disorder (274), 53% cited self-medication as the primary initial motivation for use, and 50% cited it as the primary use for continuation. Ketamine cravings were reported on abstinence by 71%, including low mood (62%), anxiety (59%) and irritability (45%) (Harding and others, 2025).

4.13 Analysis of data from the 2020 Global Drug Survey (Smith and others, 2025) explored the experience of 1,314 individuals who reported using ketamine to address emotional worries/concerns or psychiatric disorders. The majority considered self-treatment was successful. Many (68%) had self-treated with other psychedelics in the last 12 months. Individuals who were self-treating used ketamine more frequently

and at higher doses than recreational users. At the age of maximum use (30 years), self-treaters reported using 20 to 30g of ketamine a year. For comparison, the maximum annual intravenous dose of ketamine used in a UK ketamine clinic is currently about 2.5g (Oxford Clinic, unpublished).

Esketamine

4.14 Esketamine nasal spray is licensed in the UK and elsewhere for clinic-based use in TRD alongside an oral antidepressant. The MHRA mandates that the manufacturer runs a formal Risk Management Strategy, which includes routine data collection about side effects. Licensed doses are of 28, 56 and 84mg, initially twice-weekly. Although some patients receiving maintenance esketamine are dosed on a 4-weekly, or longer, basis, the most common interval between doses is every 7 days.

4.15 Esketamine is not recommended for NHS use by National Institute for Clinical Excellence (NICE, 2022b) and is therefore not used in the NHS in England, Wales and Northern Ireland. Esketamine is accepted for NHS use in Scotland (SMC, 2020) but, in the absence of mandatory funding, is very rarely used.

4.16 In the US but not UK, esketamine also has a licence for depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behaviour, in conjunction with an oral antidepressant, and as a monotherapy for TRD.

4.17 In randomised controlled trials (RCTs), esketamine has a small beneficial effect on mood for patients with TRD, which persists with repeated dosing (standardised mean difference 0.21) (Fountoulakis and others, 2025). Esketamine nasal spray does not have an effect on suicidal ideation or behaviour (Li, 2025).

4.18 Real-world, open-label studies (100 to 200) of esketamine nasal spray in France and Australia (Samalin and others, 2024; Hopwood and others, 2024) have found significant improvements in work and occupational function, as well as quality of life. For example, of the 83% who were taking sick leave, 24% were back at work within 3 months (Samalin and others, 2024).

4.19 A long-term, open-label extension (3,777 patient-years) study (‘SUSTAIN-3’) provides high-quality, prospective evidence detailing adverse effects in a highly selected clinical trial population (Zaki and others, 2025). Of the 1,148 participants, 6.4% discontinued due to adverse events, and up to 4.4% had depression-related serious adverse events. The effect of esketamine treatment on rates of suicide is difficult to evaluate because of confounding by indication (people at higher risk of suicide are more likely to be prescribed esketamine). Across the studies sponsored by Janssen, there have been 3 suicides in 979 patients treated with esketamine and none in 795 treated with a placebo. There was no increase in suicidal ideation with esketamine nasal spray compared with a placebo across the 5 placebo RCTs (Fountoulakis and others, 2025).

4.20 The most active antidepressants occasionally cause a switch from depression to mania. In the SUSTAIN 3 study, 3 of the 1,148 cases switched. A real-world study in Italy reported higher rates of 2% for unipolar and 5.6% for bipolar disorder (d'Andrea and others, 2025).

4.21 Side effects reported at any point during follow-up in SUSTAIN 3 included headache (36.9%), dizziness (33.9%), nausea (33.6%), dissociation (25.5%), nasopharyngitis (23.8%), somnolence (23.1%), abnormal taste (20.2%) and back pain (20%). No treatment-related ulcerative or interstitial cystitis occurred; urinary tract infections occurred in 16% and dysuria in 3%. Dissociation reduced with repeated use, with no reduction in benefit.

Racemic ketamine in psychiatry

4.22 Racemic ketamine can be given via a variety of routes. The large majority of research is on IV ketamine given at 0.5mg/kg body weight over 40 minutes. Intramuscular and subcutaneous routes are also established. Oral or sublingual prescribing for at-home use is common in American clinical practice. The range of doses of off-label racemic ketamine used in the real world for TRD is 0.5 to 1.5mg/kg (40 to 150mg) IV and 150 to 750mg orally. There is no 'standard' interval for maintenance IV or IM ketamine. Oral and subcutaneous ketamine are typically given at weekly intervals. The frequency is constrained by practical and cost considerations and the need to avoid tolerance.

4.23 Racemic IV ketamine is as effective as ECT for TRD, especially in those under 50 years. Notably, ketamine does not cause the enduring cognitive impairment reported by some people who receive ECT (Ekstrand and others, 2024; Anand and others, 2023). Racemic ketamine acutely reduces suicidal ideation (Li, 2025), particularly in bipolar disorder (Abbar, 2022).

4.24 Racemic IV ketamine is superior to licensed doses of esketamine nasal spray in head-to-head trials, but this may be due to differential dosing. A definitive 5-year head-to-head comparison began in 2025, with the evaluation report expected in 2030 (Yale University, 2025).

4.25 There have been multiple replications in moderately sized RCTs, mostly Chinese, of prophylactic and treatment benefit in peripartum depression, including in the context of caesarean section (Hung and others, 2024).

4.26 While the large majority of trials assessing ketamine have been for depression, more preliminary evidence, based on short-term treatment, exists of short-term benefit for all affective disorders including post-traumatic stress disorder (PTSD), obsessive-compulsive disorder, social anxiety, anorexia nervosa, and for use in substance use disorders, including the management of opioid use disorder and opioid withdrawal (Zanos and others, 2018; Almeida and others, 2024; Shen and others, 2025). A UK phase 3 study of ketamine for severe alcohol use disorder (MORE-KARE) will likely report in 2027-8.

4.27 The risks associated with long-term medical use of ketamine for depression, particularly those arising because of tolerance, are incompletely known. Misuse can be driven by dissociation and tolerance, both of which are related to dose and frequency of ketamine and esketamine administration. Prior or current history of substance use disorder likely increases this risk. Both the Spravato® (esketamine nasal spray) data sheet and guidelines on racemic ketamine caution use in this population.

4.28 There are no long-term prospective data on the potential of hospital or at-home administration of prescribed ketamine to induce ketamine use disorder (KUD), but this is likely to be rare.

4.29 The largest available review of ketamine maintenance treatment (Smith-Apeldoorn, 2022) found that cognitive impairment and addiction (1 each of 1,495 cases treated with maintenance ketamine) are reported but seem very uncommon based upon the currently available data.

4.30 A single small study (Chubbs and others, 2022) reported the experience of 33 patients receiving intranasal or sublingual ketamine. Ketamine was 'liked' by 17 patients (52%). No patients reported more than one substance use disorder criterion. Of the criteria endorsed, 6 of the 33 patients reported "needing more ketamine over time to get the dissociative effects you want"; 3 reported "cravings and urges to use ketamine"; 1 reported "wanting to cut down or stop using ketamine but being unable to do so" (for reasons other than worsening depression), and 1 reported "not managing what you should at work, home, or school because of ketamine use". A desire to use ketamine in doses greater than prescribed was reported by 6 out of 23 and 3 out of 30 reported actually using it in doses higher than prescribed, one of whom had prior ketamine addiction.

4.31 Ketamine-related interstitial cystitis is known to be related to dose and frequency of ingestion and the related ability of the urothelium to recover. A prospective study of 295 TRD patients treated with IV and oral ketamine for 324 person-years in a UK clinic found no clinically significant problem with urological symptoms (Oxford Clinic – unpublished). The single reported case of cystitis following ketamine treatment involved a very high dose of oral ketamine (240mg, 4 times a week) (Chang and others, 2024).

4.32 The Summary of Product Characteristics for racemic ketamine for injection states "Ketamine is not indicated nor recommended for long-term use". Racemic ketamine does not have an MHRA licence for psychiatric use. Unlike in Norway, it cannot therefore be considered for a UK NICE Technology Appraisal.

4.33 In the UK, oral ketamine can be prescribed and supplied for use at home through 'Specials' pharmacies. These typically reformulate IV ketamine into a liquid suitable for oral ingestion or a lozenge suitable for sublingual use. Sustained over-prescribing of ketamine for at-home administration is effectively prevented by strong retrospective auditability of prescriptions, both NHS and private. Pharmacies must return original private controlled drugs (CD) prescriptions on a monthly basis and CD Accountable Officers and Local Information Networks have oversight. In-clinic use of

ketamine is subject to procurement visibility, CD register versus stock reconciliation and the requirement by regulators for Standard Operating Procedures (NICE, 2016).

4.34 The Royal College of Psychiatrists (2025) “recommends the use of ketamine in specialist settings with appropriate oversight and long-term monitoring arrangements in place.” This monitoring should be “via centralised systems including dose, indication, therapeutic response and adverse effects. These systems should also be capable of gathering information on any adverse consequences arising from self-medication. Such multidrug monitoring systems are not without precedent, as is the case with controlled drug prescription surveillance or clozapine monitoring, for example.” The Royal College of Psychiatrists is pursuing a proposal for short-term (14 administrations) of IV racemic ketamine as an alternative to ECT. However, the Medicines Repurposing Committee, to which the proposal was sent, was wound up following the announcement of the abolition of NHS England.

4.35 New formulations (Oral, IV and subcutaneous) of racemic ketamine are being developed by about 10 companies seeking formal licensure for psychiatric indications. Of these, those that have advanced to phase 3 include oral (Douglas Pharmaceuticals), intranasal (Seelos) and IV preparations (NRx pharmaceuticals). Based on detailed understanding of ketamine’s action, pharmaceutical companies are researching alternative compounds that lack ketamine’s dissociative side effects.

4.36 In the UK, ‘off-label’ ketamine is used in a handful of NHS psychiatric hospitals (Oxford, Middlesbrough, Maudsley, Birmingham) and a small number (about 8) of private clinics. The Oxford Clinic has treated over 400 patients, of whom 40 have been treated continuously for over 5 years. Patients are treated either via the NHS or privately. The median interval between dosing is shorter in the NHS patients (3 weekly) than private patients (4 weekly), likely reflecting a combination of factors: geographical proximity and ease of access, severity of illness, fewer social and financial resources, and expectations.

4.37 In the USA, ketamine has become a routine offering at many private psychiatric clinics and also at specialist ketamine clinics. There are some 500 to 1,500 infusion sites depending on definition (DEA/IQVIA 2024). Longer term, repeated, off-label use for psychiatric illness, particularly TRD, is the norm. As well as for TRD, the majority of clinics offer ketamine to patients who are treatment naïve or have subclinical depression (Pacilio, 2025). Over 80% offer maintenance ketamine and over 40% prescribe ketamine for at-home use. Fewer than 30% of clinics are run by psychiatrists and over 25% are run by non-physician prescribers.

4.38 A model of telehealth administration of oral ketamine, with no in-person review, facilitated by changes in legislation during COVID-19, has resulted in businesses which provide ketamine treatment at scale in the US. There are no legal barriers to this occurring in the UK. Three large real-world studies of telehealth administration may give pointers to patterns of use and adverse effects if at-home ketamine use becomes widespread (Swanson and others, 2024; Hassan and others, 2022; Mathai and others, 2024). In summary, they show marked variability in doses used, a reassuring safety profile, but substantial missing data and little focus on misuse. They are considered here in a little more detail.

4.39 Swanson and others (2024) describe the treatment of 431 patients at the Wondermed clinic (sic), including many with generalised anxiety and social anxiety, with sublingual ketamine lozenges. Of 1,028 patients, 597 (58%) did not return complete data and were excluded. Patients were initially given a month's worth of medication that could be renewed. Most patients received the standard dose of 150 to 200 mg lozenge once-weekly, but the dose could vary from 50 to 400 mg and be given up to twice-weekly based on clinician discretion. Of the overall sample, 8% received a third month of treatment on a twice-weekly basis. For 18% of the sample, their third month of treatment was at weekly or twice-weekly doses of 300 mg or more. Overall, 92% received less than a 6-month duration of prescriptions. Patients were also given daily exercises (journaling, meditation, 'breath work' and therapy-based cognitive challenges). All side effects were resolved without reported medical assistance and did not persist for longer than 24 hours. No late-onset side effects were reported. There were no reports of misuse, development of addiction or diversion. No serious adverse events (including suicidal ideation, suicides or attempted suicides, or self-harm behaviours) were observed. One of the 431 patients reported worsening anxiety/depression, which resolved within 24 hours.

4.40 Hassan and others (2022) described 1,101 patients treated during COVID-19 (Nue Life - My Ketamine Home). A dose of 300 mg for sublingual administration was determined by providers with experiential training in ketamine therapy. After an initial single lozenge was taken and data reported, 2 further lozenges were mailed (300 or 450 mg), a process that was repeated with 3 lozenges for a total maximum of 6 treatments. Dosing was twice a week. A total of 4,404 patients were assessed, 1,101 were enrolled and 669 had at least 3 doses, of whom 210 had 6 doses. Side effects that were rated as 'severe' were reported as follows: anxiety (1%), blurred vision (3%), dizziness (4%), loss of balance (3%) and nausea (3%). Mild or moderate pain with urination was reported by 2%. The extent of missing data was not reported.

4.41 Mathai and others (2024) (Mindbloom) reported the experience of 11,441 patients receiving at-home sublingual ketamine in 'a supportive digital environment' with 'structured clinical, psychosocial and peer support'. Patients were asked to hold the tablets under the tongue or between the cheek and gums, without swallowing for 7 minutes, after which they were instructed to spit out all saliva. Two lozenges were supplied twice for a course of 4 once-weekly treatments. A flexible-dosing strategy was used, targeting a mild-to-moderate level of dissociation. Dosing was "300 mg to 600 mg to approximate 5 mg/kg body weight" but averaged 590 mg (7.3 mg/kg). Patients who did not respond received a second course with a mean dose of 758 mg. Data on adverse events were not returned by 34% after 2 treatments and 56% after 4 treatments. Five patients required admission for suicidal ideation, suicidal behaviour, severe depression or psychosis. Discontinuation due to adverse effects occurred in 46 (0.4%) of whom 12 (0.1%) had intense dissociation or other psychological overwhelming experiences, 8 had anxiety/agitation, 2 had mania/hypomania, and the remainder experienced vomiting, syncope and headache. The most common adverse effects, all reported with a frequency of less than 1%, were memory impairment (0.6 to 1.1%), suicidal ideation (0.6 to 0.7%), abdominal pain (0.4 to 0.6%), dysuria (0.2 to 0.5%), hypertension (0.1 to 0.4%), chest discomfort (0 to 0.4%), headache (0 to 0.4%), dyspnoea (0.2 to 0.4%) and cravings (0.2 to 0.4%).

Other uses

4.42 Further indications for ketamine have been suggested as appropriate for further research, including neuroprotection in conditions such as stroke, brain injury, cardiac arrest, epilepsy, asthma, Alzheimer's disease or Parkinson's disease (Hudetz and Pagel, 2010; Jat and Chawla 2012; Shen and others, 2025). Potential use as an anti-inflammatory/immune modulator (for example, in septic shock or for tumour inhibition) may also be the subject of research in the future. It is also sometimes used off-label in intensive care units for patients with refractory bronchospasm in acute severe asthma or peri-operative anaphylaxis or as part of certain sedation protocols (Amer and others, 2021).

4.43 Doses recommended for licensed indications are summarised in Table 4.1. Ketamine doses reported for unlicensed indications include 136 to 150 mg daily orally, 0.1 to 0.25 mg/kg or 7 to 480 mg IV for chronic pain and 150 mg daily for TRD. It should be noted that these doses are much lower than those involved in heavy illicit ketamine use, where mean doses of 7,300 mg per day (usually snorted) over a mean of 6 years have been reported (Van Amsterdam and Van Den Brink, 2022).

Table 4.1: Licensed indications and adult doses for human medicinal use of ketamine and esketamine in the UK

Ketamine	Esketamine*
Induction and maintenance of anaesthesia for short procedures (IV: 1.0 to 4.5 mg/kg; IM 6.5 to 13 mg/kg) Diagnostic manoeuvres and procedures not involving intense pain (initially 4 mg/kg) Induction and maintenance of anaesthesia for long procedures (initially 0.5 to 2.0 mg/kg, maintenance 10 to 45 mcg/kg/minute)	Induction and maintenance of anaesthesia (IV: 0.5 to 1 mg/kg, then 0.25 to 0.5 mg/kg every 10 to 15 minutes; IM: 2 to 4 mg/kg, then maintenance 1 to 2 mg/kg every 10 to 15 minutes; continuous infusion 0.5 to 3 mg/kg/h) Analgesic supplementation of regional and local anaesthesia (IV infusion: 0.125 to 0.25 mg/kg/hour) Analgesia in emergency medicine (IV: 0.125 to 0.25 mg/kg; IM 0.25 to 0.5 mg/kg) MDD** (intranasal: 56 mg on day 1, then 56 to 84 mg initially twice-weekly (weeks 1 to 4) then every 1 to 2 weeks (weeks 5 to 8) thereafter once-weekly)

*Specialist use only.
**Lower doses are recommended for Japanese patients.

All maintenance doses should be adjusted according to response.

Source: BNF (2025)

Use in animals

4.44 In the UK, 8 veterinary medicinal products containing ketamine are currently authorised, the first in July 1997. All are injectable solutions, and across these 8 products there is authorisation for use in a wide range of animals, including companion animals (cats, dogs, rabbits, guinea pigs, hamsters), livestock (cattle, goats, sheep, pigs), equines (horses, donkeys) and laboratory animals (for example, mice, rats).

4.45 Ketamine is a widely used anaesthetic agent in veterinary practice, valued for its effectiveness and versatility (Kohtala, 2021). It can be used in various ways depending on the species and the procedure. It can be administered by a multitude of routes, including intravenous (IV), intramuscular (IM), subcutaneous (SC), extradural and oral (BSAVA, 2023; Gurney, 2024).

4.46 A systematic review of 14 studies involving 203 dogs and 102 cats determined that, despite the widespread use of ketamine, effective analgesic doses and corresponding plasma concentrations in veterinary species remain poorly defined, leading to reliance on human data for dosing guidance. Plasma concentrations above 200 ng/ml have been associated with changes in nociceptive thresholds, indicating effective analgesia. However, when dosing regimens are extrapolated to veterinary species, plasma concentrations often fall below expected levels. This highlights a significant gap in species-specific pharmacokinetic data (Wickstead, 2025).

4.47 Ketamine is commonly used to induce anaesthesia, either prior to maintenance with inhalant agents, or as the sole agent for restraint, or for minor surgical procedures where muscle relaxation is not essential. Due to its tendency to cause muscle rigidity, it is rarely used alone. Instead, it is typically combined with other agents such as alpha 2 agonists or benzodiazepines to achieve smoother induction and recovery (VMD, 2025a). Protective reflexes (laryngeal, palpebral, corneal) are typically retained, and ketamine has a wide safety margin, allowing for approximate dosing based on estimated body weight. Therefore, it is often the drug of choice for captive wildlife, free-ranging wildlife and is the preferred drug for big cats and wild ruminants (Vesal, 2007).

4.48 Ketamine produces a dissociative state, where the animal appears detached from its surroundings, accompanied by analgesia and sensory loss. It provides profound analgesia, particularly for visceral and somatic pain. As an NMDAR antagonist, ketamine can help reverse central sensitisation, which is a heightened pain response often seen after trauma or surgery (Maddison, 2008). This makes it a valuable adjunctive agent for perioperative analgesia. Ketamine is frequently used in soft tissue, orthopaedic and neurological procedures. Growing awareness of multimodal anaesthesia and analgesia has contributed to increased ketamine use in the veterinary field.

4.49 Ketamine is also being used more in the management of chronic pain in dogs as part of a multimodal analgesia plan, at a sub-anaesthetic dose of 0.5 mg/kg injected subcutaneously every 3 to 4 weeks. This produces minimal adverse effects in animals (Gurney, 2024). This chronic, intermittent use of ketamine in dogs is at a significantly lower dose than that of the average participant out of 274 individuals who self-identified with KUD from November 2023 to April 2024 from the UK, US, Canada, Europe and Australia (2 g of ketamine daily) (Harding, 2025). Therefore, the chance of adverse events in animals is significantly lower.

4.50 The livestock sector faces growing challenges, including climate change, emerging diseases, resource competition, rising global demand for animal source foods, genetic diversity for resilience, adaptability and sustainable production. In livestock production (sheep, pigs, cervids and cows), ketamine plays a key role in assisted reproductive technologies such as embryo transfer, artificial insemination and laparoscopic ovum pick-up. These improve productivity, reduce costs, and are vital tools in addressing the growing global demand for food (Paris-Oller, 2021; Baldassarre, 2021; Duarte, 2023). Artificial insemination and multiple ovulation and embryo transfer programmes help propagate genetically superior animals (Souza-Fabjan, 2023).

4.51 Ketamine also supports wildlife and zoological conservation efforts by enabling safe anaesthesia during procedures such as oocyte and embryo collection, artificial insemination and cryopreservation (De Oliveira Silva, 2023). These procedures are essential for gene banking and preservation of genetic diversity in livestock and endangered species alike. Furthermore, the Food and Agriculture Organisation (FAO) highlights the importance of ex situ conservation, and ketamine facilitates the application of these technologies in the field. Thus, ketamine supports the safe and humane application of advanced reproductive technologies that underpin genetic conservation efforts (Boes, 2023).

4.52 Under the Veterinary Medicines Regulations (VMR), veterinary surgeons in the UK are permitted to exercise their individual clinical judgement to use authorised medicines outside the terms of their marketing authorisation when no suitable veterinary medicinal product is available. This is known as ‘cascade use’ and with regards to ketamine, it is also prescribed for use in ferrets, birds, reptiles, camelids, wildlife and zoo animals, fish and amphibians, for induction and maintenance of anaesthesia, or to facilitate handling and reduce stress (BSAVA, 2023; Archer, 2025; VetPartners 2024). Cascade use ensures that animals do not suffer unnecessarily due to the lack of a specifically authorised product.

4.53 Ketamine is also used in euthanasia protocols to induce sedation, reduce distress and facilitate handling and restraint prior to administration of euthanasia solutions in companion animals, wildlife, equids, laboratory animals, captive marine mammals, amphibians, reptiles and fish. Ketamine helps to create a more humane environment for euthanasia, especially during owner-attended euthanasia (AVMA, 2020).

4.54 In summary, ketamine is an essential tool in modern veterinary anaesthesia and analgesia and is used widely in the veterinary field. It has a wide margin of safety and is used in a wide variety of species. It is essential for all sectors of the veterinary industry.

Regulatory requirements in the UK

4.55 According to the Misuse of Drugs Regulations (2001), Ketamine and esketamine are Schedule 2 CDs and are subject to the strict storage, prescription, dispensing, destruction and record-keeping requirements that apply to all CDs in this Schedule (VMD, 2025b). They must be stored in a locked cabinet compliant with Safe Custody Regulations. All intake and use must be recorded in a CD register, and destruction must be witnessed by an authorised person.

Human use

4.56 CD local intelligence networks (LINS) are established by lead controlled drugs accountable officers (CDAOs) within their respective geographical areas to facilitate the sharing of concerns and best practices related to CDs. The aim is to improve the safe and effective management of CDs within the healthcare system and with enforcement agencies. CD LINs facilitate the sharing of information about potential risks, incidents and best practices related to CDs. CD LINs cover all aspects of CD management, including prescribing, dispensing, administration and storage, and

should monitor trends in prescribing locally and highlight cases of potential diversion from health and care settings into the illicit market.

4.57 There is no national template for ketamine use, although the Royal College of Psychiatrists has recommended that, for use in psychiatry, a psychiatry-led (or co-led) multidisciplinary team should be involved in its administration, which should be in highly specialised settings by registered and competent clinical professionals with suitable knowledge of the psychopharmacology of the relevant medications (RCPsych, 2025).

Veterinary use

4.58 As a prescription-only veterinary medicine, ketamine can only be prescribed and administered by a veterinary surgeon or administered under the direct supervision of a veterinary surgeon (for example, by a veterinary nurse or a trained wildlife professional using a dart gun).

4.59 Veterinary practices are typically inspected every 4 years by the Veterinary Medicines Directorate (VMD) and weekly internal audits of Schedule 2 drugs are required as part of Royal College of Veterinary Surgeons (RCVS) Core Standards according to 'The RCVS Controlled Drugs Guidance – A to Z' (RCVS, 2026).

4.60 Increased inspections of veterinary premises since 2009 have led to greater compliance with the VMR 2013. Ketamine is considered a highly valuable and tightly regulated drug in veterinary medicine. VMD's enforcement team is involved with the surveillance of wholesalers and the distribution of CDs, ensuring compliance with the VMR to protect public health, animal welfare and the environment. The misuse of ketamine within the veterinary sector is regarded as very low.

Other legitimate uses

4.61 Other than use in research and in standards for laboratory analysis, the ACMD is not aware of other legitimate uses for ketamine or ketamine analogues. While the MHRA is aware of several clinical trials involving ketamine or esketamine, no trials involving the related compounds phencyclidine, methoxetamine, 4-MeO-PCP, 3-MeO-PCP or 3-MeO-PCE were reported.

Annex 5. Misuse

5.1 Recreational use of ketamine was first recognised in California in 1971, a few years after it was first patented for human medicinal use in 1966 (Schep and others, 2023). In Europe and the UK, ketamine misuse was first recorded in the 1990s, with initial users often those with access to pharmaceutical products (for example, anaesthetists, veterinary surgeons). Ketamine subsequently becomes popular as a 'club drug', associated in particular with electronic music dance culture (Kleczkowska and Zaremba, 2021; Corkery and others, 2021). According to respondents to our online survey, ketamine is one of the three primary substances associated with clubbing and electronic dance music scenes, alongside methylenedioxymeth-amphetamine (MDMA or 'ecstasy') and cocaine powder. It is also used post-clubbing to relax at after-parties and to aid sleep following stimulant use.

5.2 Illicit ketamine is typically found in crystal form or crushed into a powder. It is commonly known as 'ket', 'K' or 'shard'. Ketamine powder or crystals are usually snorted, with many users taking short lines or 'bumps' (ACMD, 2025c). This results in a 'high' within 5 to 10 minutes and effects lasting between 45 and 75 minutes (Wolff and Winstock, 2006; Barrios and others, 2024). Ketamine may also be mixed in drinks, smoked, used to make tablets or capsules, rolled into paper for swallowing ('bombing') or applied rectally ('boofing'). Ketamine can also be supplied as a liquid, which can be injected, sprayed nasally, applied on smoking materials, or consumed in drinks. Ketamine has also been detected in e-cigarettes ('vapes') (ACMD, 2025c). Onset of action is more rapid after intravenous (in seconds) or intramuscular (1 to 5 minutes) use but delayed after oral ingestion (15 to 20 minutes), although effects persist for longer (1 to 2 hours) (Kleczkowska and Zaremba, 2021). Use of ketamine by injection is reported to be more common in older injecting opioid users (ACMD, 2025c).

5.3 A typical average dose of ketamine is reported to be 100 mg (EUDA, 2024; DEA, 2025). Stakeholders report dosing of 25 to 100 mg per use (ACMD, 2025c). The dose used recreationally to obtain euphoria and dissociation is usually at least 250 mg or more; these are much higher doses than those used for treating depression (0.1 to 0.75 mg/kg IV, that is 7 to 52.5 mg for a 70 kg adult). Volumetric dosing is reported to be emerging as a method of harm reduction. People with problematic ketamine may take 2 to 4 g ketamine per day. While most people who use ketamine in the UK use it infrequently in socially constrained settings such as festivals, around 5 to 8% of users develop problematic use, with such use more common in those with a history of traumatic life events and/or having been in care (ACMD, 2025c).

5.4 Ketamine may be used by itself, but it is also commonly consumed with other illicit substances including MDMA, amphetamine, methamphetamine, cocaine, nitrous oxide and alcohol (DEA, 2025; Ralphs and others, 2024; ACMD, 2025c). In younger people, ketamine use with cannabis is also common (Ralphs and others, 2024). Stakeholders report co-use of drugs to balance or deepen sedation or to intensify euphoria or hallucinations, as well as to help with 'come down'. Use with cocaine is popular in party settings to enhance stimulant effects and to counteract the negative psychological effects of excessive cocaine use such as paranoia, edginess and anxiety, while cannabis may be co-used to augment relaxation, dissociative effects

and/or pain relief or reduce nausea. (ACMD, 2025c). Of 2,071 patients presenting to the 57 emergency departments participating in the European Drug Emergencies Network (Euro-DEN) Plus network across Europe and reporting ketamine use, 70% reported use with at least one other substance including MDMA (19%), amphetamine (14%), cannabis (13%) or gamma hydroxybutyrate (12%). Co-use of ethanol was reported by 55% (Naylor and others, 2025).

5.5 Mixtures of ketamine with cocaine, such as in a 1 to 1 ratio, may be encountered and are sometimes referred to as 'CK'. Mixtures sold as 'pink cocaine', 'tucibi' (after the stimulant 2C-B) or 'tuci' often contain ketamine with stimulant drugs, especially MDMA and/or caffeine (UNODC, 2022; Europol, 2024; EUDA, 2024). These may be marketed in Europe with similar branding to that used where they emerged originally in South America. 'Tussi' or 'pink cocaine' first came to attention in the UK in 2020.

5.6 In a study of ketamine purity in the Greater Manchester area, project MANDRAKE (Manchester Drug Analysis and Knowledge Exchange) tested 16 samples finding an average purity of 57% (range 14% to 100%), with 7 of the 17 samples demonstrating greater than 90% purity. Some ketamine preparations may contain monosodium glutamate, which (like ketamine) can form crystalline shards. These are regarded by users as a sign of good quality (Ralphs and others, 2024). Ketamine samples containing xylazine have also been reported (Ralphs and others, 2024). Other adulterants that have been reported by stakeholders include fentanyl, xylazine and nitazene opioids (ACMD, 2025c).

Desired effects

5.7 The effects of ketamine sought by users include altered senses, a feeling of wellbeing, increased energy and creativity, relaxation or stress release, euphoria, empathy, auditory and visual hallucinations, enhanced colour vision, a feeling of timelessness and dissociation from reality, out-of-body experiences and, in some cases, enhancement of the effects of other drugs. It has been described as a 'chill out' drug, useful for 'switching off' and also as an aid for sleep (Ralphs and others, 2024).

5.8 Those with lived or living experience who responded to our call for evidence reported desired effects as warmth, confidence, relaxation, feelings of euphoria, detachment from stress, escapism and relief from anxiety, depression or physical pain. They also reported use for chemsex, weight loss and exercise endurance. Use was encouraged in some cases by peer pressure and perceived safety of ketamine compared to other drugs. They also reported that use often began in adolescence and was normalised in some youth settings. Of 11 people identifying as users of ketamine who responded to ACMD's Call for Evidence, motivations for use of ketamine included: help with mental health conditions (6); escapism, to cope or to 'forget about things' (5); to experience euphoria, dream-like hallucinations or to have fun (3); pain relief (1); and to treat symptoms of dependency(1) (ACMD, 2025c).

5.9 In an Australian study conducted in 2003, 100 people who used ketamine underwent semi-structured interviews. In this study, the most commonly reported 'best things about ketamine use' were altered senses (78%), out-of-body experience (52%), euphoric rush (50%), the group experience (49%), to bring on the effects of other

drugs (42%), escaping reality (38%), feeling of wellbeing (26%), being able to dance all night (23%), creativity (20%) and stress release (4%) (Dillon and others, 2003).

5.10 Ketamine is one of several substances used for ‘microdosing’, where doses of the substance smaller than those required to produce a psychoactive effect are taken. It is believed by those involved to improve general wellbeing and, in some cases, to address underlying physical and mental health disorders (GDS, 2021; Syed and others, 2024).

User profiles

5.11 Ketamine use in the UK and internationally commonly involves teenagers and young adults in particular (Kleczkowska and Zaremba, 2021; DEA, 2025). In the Crime Survey for England and Wales (CSEW), those reporting use were more often male and in the 20 to 24 age range. The popularity of ketamine use among university students is well documented (Foster and others, 2023). In a survey conducted between November and December 2024 by Students Organising for Sustainability UK (SOSUK, 2025), 23% of respondents reported use of ketamine, with the only substances reported more often being cannabis (69%) and powder cocaine (26%). The University of Western England conducted a survey of 11,000 students attending various UK universities in 2017; the proportion reporting previous ketamine use ranged from 17% (Warwick) to 53% (Manchester) (Nash, 2017). Use by children is also well documented (see UK prevalence in Section 10 for more details), with the age of initiation typically from 14 years upwards (Ralphs and others, 2024). Use of ketamine in clubs or at festivals is common. Other groups that may use ketamine include ‘psychonauts’ and men who have sex with men (GBMSM) in the context of chemsex parties. Ketamine may also be used to alleviate boredom, for example amongst prisoners, and this may also account for increased popularity during the COVID-19 pandemic (Ralphs and others, 2024; Kleczkowska and Zaremba, 2021) The Global Drug Survey, using data from respondents predominantly from Germany, England and Denmark, compared characteristics between self-reported users of ketamine (in the last year) with non-users. In multivariate analysis, people who used ketamine were younger, more likely to report ‘gay’ sexual orientation, more likely to be studying and more likely to report no prior mental health diagnoses (Barrios and others, 2025).

5.12 There is evidence of significant transformation of ketamine use in the UK, with increasing use by vulnerable populations and to manage psychological distress. This includes use by people with neurodiversity (including attention-deficit/hyperactivity disorder (ADHD)), homelessness and/or social deprivation (ACMD, 2025c).

5.13 In one US study, 58% of those legitimately prescribed ketamine therapy agreed that they either accidentally or purposefully used more than the recommended dose (APN, 2023). Stakeholders have also reported use by athletes for performance enhancement or pain control (ACMD, 2025c).

5.14 Ketamine may therefore be used in private settings or in public areas such as clubs and schools where it may be considered a fun communal experience (Kleczkowska and Zaremba, 2021; Ralphs and others, 2024).

5.15 There is increasing evidence of ketamine use becoming more frequent and habitual, driven by rapid development of tolerance to the drug and leading to accelerated health harms including dependency, as well as the social and financial consequences of high-volume use (Muetzelfeldt, 2008; Ralphs and others, 2024).

5.16 Harding and others (2025) reported findings from 274 people (45% female) with current or previous problematic ketamine use. Most were using ketamine currently (69%) and not seeking treatment (60%), with 93% using ketamine by insufflation. A small number (4) sourced ketamine via prescription. For those not seeking and seeking treatment respectively, mean ages were 27 (range 18 to 59) and 28 (range 18 to 67) with first use reported at 18.9 years (12 to 50) and 19.6 years (15 to 45). Ketamine was used on average 5.44 and 5 days out of every 7, and the mean reported daily dose was 2.67 g (0.25 to 10 g) and 1.68 g (0.01 to 20 g).

5.17 The Bexley Ketamine Project was a retrospective case series of 100 people who used ketamine (mean age 26 years, 70% males). The mean age of onset of use was 19 years and a mean ketamine daily dose of 2.74 g. In the cohort, 38% used ketamine only, 66% had evidence of mental health problems and 45% evidence of ketamine uropathy. The latter was more common in daily users (66%) compared to infrequent users (3 days or fewer per week). Mental health problems included depression (59%), anxiety (51%), self-harm (37%), a history of psychological trauma (32%), ADHD (12%) and Emotionally Unstable Personality Disorder (EUPD, 10%). People with mental health issues were significantly younger than those without, earlier engagement with structured treatment among individuals with mental health conditions.

Motivations for use

5.18 Perceived advantages of ketamine include:

- **Low cost**. Ketamine is generally cheaper than cocaine, typically costing £20 to £40 per gram. It may also be cheaper than alcohol for a night out. The price per gram is lower for larger amounts, sometimes as low as £10 per gram, and users may pool their money to buy ketamine in larger amounts as this is more cost effective (but may also encourage use of higher doses) (Ralphs and others, 2024; ACMD, 2025c). Respondents to our call for evidence cited prices varying from £5 to £10 per bag or £10 to £40 per gram, with regional variations (ACMD, 2025c). Furthermore, ketamine may initially be gifted to vulnerable populations, such as the homeless, as a ‘loss leader’ towards future sales or for subsequent exploitation (ACMD, 2025c).

- **Accessibility**. Ketamine appears easy to obtain from either local dealers, the internet, the dark web or mobile phone apps such as Instagram, Snapchat or Tik Tok. Encrypted messaging apps such as Telegram or Signal are also used. Access can also be obtained from fly-posted QR codes that link to suppliers. Products may then be delivered by post or dropped off by couriers. Peer to peer (friends, acquaintances, family) sales are also common, including in schools, and on-campus marketing is common in universities. Of note, ketamine purchased online is sometimes perceived to be of better quality. Dealers selling ketamine are also commonly involved in selling MDMA and cocaine (Ralphs and others, 2024;

ACMD, 2025c). The 11 people identifying as using ketamine who responded to our call for evidence had all sourced ketamine from street-level dealers; use of social media, including encrypted apps or the dark web, were less commonly employed by this group (ACMD, 2025c).

- **High-quality product**. Users may perceive that ketamine is safer, more reliable and less prone to adulteration due to its legitimate use as a medicine and because it is believed that ketamine sold illicitly is diverted from product originally manufactured to high-quality standards for medicinal and veterinary use (ACMD, 2025c).

- **Improved social acceptability.** Ketamine may be perceived as more sociably acceptable compared to some other drugs such as cocaine (Ralphs and others, 2024). This may be amplified by the use of ketamine by celebrities, and peer pressure may also encourage use (ACMD, 2025c).

- **Favourable pattern of effects**. The powerful psychoactive effects of ketamine at sub-anaesthetic doses are popular with users. Other perceived advantages are its short duration of effects (usually less than 3 hours) and the lack of after-effects ('comedown'), as might be experienced after use of alcohol, cannabis or cocaine. This allows people who use ketamine to function normally at school, college or work the day after use. Some users also specifically seek the dissociative effects of the drug, causing distortions of sight and sound and detachment from the environment ('falling into the K-hole') (Ralphs and others, 2024; Kleczkowska and Zaremba, 2021; ACMD, 2025c).

- **Perceived mental health benefits**. Illicit ketamine may be used as self-medication for mental health problems, especially anxiety and depression, to relieve boredom and loneliness and, in some cases, as a temporary escape from traumatic memories associated with adverse childhood experiences (Ralphs and others, 2024). Those with lived or living experience also reported use for anxiety, loneliness and trauma. Related to this, mental health issues are common in those in ketamine treatment. The growth of private clinics offering ketamine to treat depression and other psychiatric conditions, alongside upbeat media coverage, risks normalising unsupervised or self-directed use (Guerrini, 2025). It should be noted, however, that adverse effects of ketamine on mental health are also reported (see Section 8, 'Health harms').

- **Low risk of detection**. Some users believe that ketamine is not tested in drug screens; even if it is, it will not be found a few hours after use because of rapid metabolism (ACMD, 2025c).

Annex 6. Trafficking and supply

6.1 Ketamine continues to dominate synthetic NPS seizures globally (UNODC, 2025a) and the number of seizures reported within Europe has increased year on year since 2015 (EUDA, 2024). Ketamine used illicitly in the UK and other European countries is likely to come from one of three possible sources:

(1) Diverted bulk pharmaceutical-grade ketamine

This is ketamine manufactured legitimately in bulk and originally intended for use by the pharmaceutical industry but subsequently diverted for illicit use. This appears to be the major source of ketamine in Europe.

The drug is imported to EU Member States such as the Netherlands, Germany or Belgium, where there is less regulation, and subsequently trafficked illegally into other countries, including the UK.

(2) Diverted medicinal product

This is legitimately manufactured medicinal ketamine in final form, which has been diverted into the illicit market, for example after being stolen from medical or veterinary premises.

In the UK, thefts from veterinary premises occasionally occur, but this is unlikely to be a significant source for the criminal market because of the strict storage and disposal requirements associated with a Schedule 2 drug and the regulations of the VMD (ACMD, 2025c).

Data provided by the MHRA demonstrates very little evidence of diversion from legitimate human medical stocks in the UK. They are aware of 9 vials of ketamine stolen in transit in January 2020, as reported to the Home Office and the police by the company involved. There is also a single case from 2021 where a wholesaler identified a theft of ketamine after opening a box and finding an air cushion had been substituted. This was reported by the police to the MHRA, but the quantity stolen was not stated.

(3) Illicit manufacture of ketamine from precursor materials

There is evidence of illicit ketamine production in parts of Southeast Asia. For example, clandestine industrial-scale laboratories, processing centres and storage warehouses for ketamine have been identified in Cambodia, exploiting a relatively weak rule of law and utilising existing cross-border routes also used for heroin supply (UNODC, 2022a; 2025b). As an indication of the scale of production, countries in Southeast Asia seized over 27 tonnes of ketamine in 2022, a 167% increase on seizures during the previous year. Many of these arise from the Golden Triangle area between Myanmar and Thailand and from the Mekong region (INCB, 2024).

There appears to be very limited illicit production of ketamine within Europe, although at least 4 ketamine production sites were dismantled in the Netherlands

and Belgium between 2017 and 2021. These facilities were used to produce ketamine crystals by evaporation of ketamine from commercial medicinal ketamine solutions (EUDA, 2024). In addition, ketamine hydroxylimine, which is an important ketamine precursor, was seized from 2 productions sites in the Netherlands in 2019 and 2020, one seizure involving 50 kg of the precursor (EUDA, 2024). European authorities have recently seized increasing amounts of chemical precursors and detected clandestine laboratories for several synthetic drugs, including ketamine, suggesting a shift in production to meet demand on the continent (EMCDDA, 2022).

Domestic manufacture of ketamine in the UK is thought to be unusual, due to issues of competency and capability, and an inability to meet the substantial UK demand (ACMD, 2025c).

6.2 Overall, most ketamine seized in Europe is believed to originate from India, and to a lesser extent Pakistan and China. Cambodia is also reportedly an emerging country of production (EUDA, 2024; EUDA, 2025; UNODC 2022; 2025a; 2025b). Shell companies may be used to import ketamine via pharmaceutical companies in Europe (EUDA, 2024). It is also reported that insolvent pharmaceutical companies may be purchased so that existing licences can be misused (Bundeskrimilalamt, 2024). Information from Indian authorities indicates that over 82 tons of ketamine was shipped from India to Germany in 2023. This amount, which includes legal imports for legitimate pharmaceutical use, far exceeds these legitimate requirements for that country (EUDA, 2024; Bundeskrimilalamt, 2024).

6.3 The Netherlands, Germany and the UK are the countries from which most ketamine is shipped worldwide (Bundeskrimilalamt, 2024). In 2024, a seizure of 2 tons of ketamine was made in the Netherlands and 1 ton in Germany (Bundeskrimilalamt, 2024). Single ketamine shipments may exceed the annual legitimate pharmaceutical requirement for ketamine several fold. For example, Belgian police estimate that about 28 tonnes of ketamine was diverted between 2019 and 2021. One method used to avoid detection is substituting ketamine with sugar or salt. The quantities and the professionalism involved suggest the involvement of organised crime groups (OCG) (EUDA, 2024; Bundeskrimilalamt, 2024). As with other drugs, such as fentanyls, use of encrypted phones, such as the encrypted messaging network Sky ECC (now shut down), has been used commonly by those trafficking ketamine.

6.4 According to a 2023 report by the International Narcotics Control Board (INCB) as reported by the Bundeskrimilalamt in Germany, the UK is the country of origin for the highest number of ketamine shipments, totalling 594 in 2023 and involving 652 kg ketamine, although Germany shipped a larger amount than the UK (282 shipments, total 724 kg) (Bundeskrimilalamt, 2024).

6.5 The number of ketamine seizures within the EU increased steeply between 2015 and 2022, indicating substantial and rising ongoing demand (EUDA, 2024). In 2022, there were almost 3,500 seizures reported to the EU Early Warning System involving a total of 2.79 tonnes of ketamine. In the Netherlands, there was a doubling in adult use of ketamine between 2018 and 2023, with a quarter of those visiting nightclubs or festivals reporting use and 3% reporting weekly use (Marongiu and others, 2025).

6.6 Between 2021 and 2024, ketamine seizures in England and Wales increased significantly, highlighting rising concerns over diversion and illicit use. According to the Home Office's Seizures of Drugs in England and Wales reports, seizures peaked in March 2022 with 1,837 kg confiscated, an 884% increase from the previous year, driven largely by Border Force interceptions (1,664 kg) (Home Office, 2022). In March 2023, seizures declined by 22% to approximately 1,430 kg but remained historically high, with police seizures notably rising to 500 kg (a 189% increase) (Home Office, 2023). By March 2024, total seizures fell further to 855 kg, including 86 kg seized by police (down 83%) and 769 kg by Border Force (down 18%) (Home Office, 2024), indicating a potential shift in trafficking patterns or enforcement dynamics. It should be noted that these data may underestimate the situation because ketamine may not be identified in seizures due to the cost of testing, and suspect drugs may not feature in crime statistics in the absence of user admission (ACMD, 2025c).

6.7 For comparison, data submitted voluntarily to the Home Office Drugs and Firearms Licensing (DFLU) by companies, reflecting legitimate activity up to the point of wholesale supply, showed just over 800 kg ketamine was consumed in 2024, with 30 kg recorded as destroyed and end-of-year stocks totalling 268 kg. There was a marked increase in ketamine consumed comparing 2024 (for which data may be provisional or incomplete) with the 3 earlier years (Table 6.1). No legitimate domestic manufacture has been recorded.

Table 6.1: Summary of voluntary submissions to the Home Office DFLU by companies using ketamine legitimately.

Year	Quantity consumed (kg)	Quantity destroyed (kg)	End-of-year stocks (kg)
2024	803.74*	30.10	268.12
2023	154.21	9.94	208.04
2022	185.56	6.27	175.07
2021	208.32	3.00	207.26

*2024 data may be provisional or incomplete.

6.8 Substantial profits are available to those importing and selling ketamine. Cost per kilogram to suppliers was estimated at €0.24 (powder/sugar/needles) or €0.39 (chunks/lumps) per gram, but product was sold to users at an average street price of €21.8 per gram, a 56 to 91-fold profit. Similarly, it was reported that ketamine purchased for €250 in India sold for €30,000 in Belgium (Bundeskrimilalamt, 2024). In the UK, it is reported that the wholesale price of ketamine has dropped in recent years, from £7,000 to £8,000, to £2,500 to £3,000 per kilogram. Nevertheless, the street value of ketamine has largely stayed the same, often being sold between £10

and £40 per gram, increasing the profit margins for sales. Ketamine remains significantly cheaper than cocaine, which is typically sold at £80 to £100 per gram.

6.9 The National Crime Agency (NCA) deems that the threat from drugs to the UK is on the increase (NCA, 2025). OCGs are working to increase importation to meet demand, such as the increasing use of ketamine. The amount of laundered money in the UK is increasing due in part to increased profits made from drug supply. Reports from the NCA and regional forces are that ketamine is often trafficked by the same OCGs that traffic cocaine, heroin and firearms. Modes of importation include multi-kilo consignments concealed in vehicles entering the UK via roll-on roll-off ferries and other general maritime routes. Ketamine is also imported via parcel post (ACMD, 2025c). Ketamine is often sold by dealers, whether in person or via internet-facilitated markets, alongside other Class A and Class B drugs, such as cocaine, MDMA and cannabis. There is no evidence to suggest that ketamine usage is a substantial driver of particular criminality, although the supply of drugs on the street (directly to 'end users') is closely associated with street violence.

6.10 Within the UK, ketamine may be distributed via county lines networks and smuggled into prisons during visits, using drones or by 'throw overs'.

Annex 7. International trends in misuse

7.1 There is evidence of substantial and recently increasing international illicit trade involving ketamine. Countries in East and Southeast Asia seized over 27.4 tons of ketamine in 2022, an increase of 167% compared with the previous year and a figure that surpasses the number of seizures in the last 6 years combined (INCB, 2024). These originated in locations in the Golden Triangle border region of the Lao People's Democratic Republic, Myanmar and Thailand but also Cambodia, Malaysia and Vietnam. They are sold online and at entertainment venues. Products marketed as 'happy water' and 'K-powdered milk' have recently emerged on the illicit market. These contain various psychoactive substances but commonly ketamine. K-powdered milk was associated with 13 deaths in Thailand in 2021 and samples from these cases contained ketamine, diazepam and caffeine in varying combinations and concentrations (UNODC, 2022; 2025b).

7.2 There has been declining use of ketamine in China, as evidenced by wastewater analysis and number of registered users. Conversely, the number of those using ketamine has been increasing in Hong Kong, especially in those aged under 21 years (UNODC, 2022).

7.3 In Latin America, products have been sold as 'pink cocaine', 'tuci' or 'tucibi' (the name derived from the stimulant 2C-B, but containing instead ketamine in combination with MDMA, methamphetamine, cocaine, opioids and/or other NPS). Pink powders containing ketamine (referred to as tuci, 'tusi', pink cocaine or 2C-B) have also recently been reported in Europe (including the UK) and North America (UNODC, 2022b).

7.4 In the US, ketamine seizures increased sharply from 55 in 2017 (total 58 kg) to 247 (total 703 kg) in 2022 (Palamar and others, 2023). Accompanying this, self-reported ketamine use in the last year by those aged 12 to 34 increased sharply between 2017 and the end of 2019 (Palamar and others, 2021). Similarly, data from the 2015 to 2022 National Survey on Drug Use and Health, focusing on adults in the US, demonstrated an increased prevalence of past year use from 0.11% in 2015 to 0.28% in 2022, with the greater increases amongst those who reported depression compared to those who did not (Yang and others, 2025). Accompanying this increase in use, US poisons control centres have documented increasing numbers of reported ketamine exposures between 2019 (205 cases) and 2023 (414 cases) (Palamar and others, 2025). As well as misuse, these include enquiries related to therapeutic (including off label) ketamine use, which has increased substantially, especially for the treatment of depression (IQVIA, 2024). The percentage of overdose deaths with ketamine detected in toxicology samples increased from 0.3% (47 deaths) in July 2019 to 0.5% (107 deaths) in June 2023. Approximately 82% of these deaths involving ketamine also involved other substances, including illegally manufactured fentanyls, methamphetamine or cocaine (Vivolo-Kantor and others, 2024).

7.5 In Australia, the use of ketamine increased from 0.4% in 2016 to 0.9% in 2019 and more than doubled amongst young people in their 20s. There was also an increase in ketamine detected in wastewater since between 2020 and 2023 (Brassets Group, 2024).

7.6 The European Web Survey on Drugs 2024 surveyed adults in the EU and reported that 14% of respondents reported use of ketamine in the last year (EUDA, 2025b). A sharp increase in ketamine seizures has been reported to EUDA since 2015, increasing from 0.87 tonnes in 2021 to 2.8 tonnes in 2022. Ketamine was submitted for testing to drug checking services in 11 cities in 4 EU countries in the first half of 2023, with an average purity of 83%. Most ketamine originated from India, but some may also have arisen from Pakistan and China. Ketamine accounted for 9% of the quantity of NPS substances seized in the EU in 2022. The number of clients who reported receiving treatment for problems related to ketamine use remains low, but has risen from around 240 cases reported in 2018 to 600 in 2022 (Europol, 2024).

7.7 Ketamine was included in wastewater analysis in Europe for the first time in 2022. Of the 42 cities for which there was ketamine data for 2023 and 2024, amounts increased in 14, reduced in 15 and were similar in the remainder. Highest mass loads were detected in cities in Belgium, the Netherlands, Hungary and Norway (EUDA, 2025a).

7.8 The European Drug Emergencies Plus (Euro-DEN Plus) network collects data on all acute adult recreational drug toxicity presentations to 57 participating emergency departments located in multiple European countries. The data demonstrate an increase in the proportions of ketamine to other drug presentations from 2% in 2013 to 2014 to 4.1% in 2023. The median age of those presentations involving ketamine was younger (26 years) than that of the overall Euro-DEN Plus population (33 years), but the sex proportions were similar, with 75% of those reporting ketamine use being male. There were no ketamine presentations in 33 of the Euro-DEN Plus centres, including those in Germany, Italy, Israel, Lithuania, Palestine or Turkey. In contrast, 45% of all ketamine presentations originated from the 3 centres in the UK, which are located in London, Glasgow and York (Naylor and others, 2025).

7.9 In a recent study involving data collected between 2021 and 2024, all 6 participating European poisons control centres reported the highest rates of ketamine exposures during 2024. The centres in the UK and the Netherlands reported the highest rates (Hondebrink and others, 2025).

Annex 8. Health harms

8.1 Ketamine is relatively safe when used as an anaesthetic by well-trained staff in a highly controlled environment. It has a high therapeutic index, meaning that the doses needed to produce serious harms are much higher than those needed to achieve anaesthesia. As a result, an accidental overdose of 10 times the intended dose is only likely to produce more prolonged anaesthesia. Emergence phenomena may occur as anaesthesia wears off, and these can range from mild disorientation and euphoria to frank delirium, with an incidence of 5% to 30% and more common in women. Other adverse effects reported after anaesthetic use include tachycardia and hypertension, abnormal liver function tests, small increases in intraocular pressure, hypersalivation and bronchorrhoea (Richards and others, 2025).

8.2 After ketamine misuse, clinical effects are likely to reflect the dose and route of administration used. The presence of tolerance from previous regular use will increase the doses required to produce acute effects. Clinical features may also be modified by other substances taken at the same time, including adulterants.

Short-term (acute) effects

8.3 Early features include inebriation, euphoria, a sense of wellbeing, calmness and relaxation, increased empathy and enhanced smell, taste and vision. Hallucinations, agitation, dizziness, loss of co-ordination, nystagmus, tinnitus, miosis or mydriasis, slurred speech, blank staring, tremulousness with hyperreflexia, increased muscle tone, clonic movements, paraesthesia, analgesia (especially of the face and extremities) and muscle weakness may develop. Users may develop a feeling of detachment from surroundings and reduced reflexes. At higher doses, dissociation may occur, with an impairment of responses to external stimuli, out-of-body experiences, de-realisation and de-personalisation and a profound sense of complete detachment from reality, sometimes described as a near-death experience. This is commonly known by recreational users as “going down the K-hole”.

8.4 After high doses, reductions in conscious level occur and may be accompanied by agitation, psychosis and mild stimulant features. Toxicity may also involve respiratory depression and prolonged sedation. Cardiovascular features include hypertension and sinus tachycardia. Vasospasm can cause severe systemic hypertension and cerebral haemorrhage. Electrocardiographic changes, including QT prolongation, have been reported.

8.5 Severe features include catatonic-like posturing, sometimes progressing to myoclonic movements, dystonic reactions, convulsions and coma. Autonomic dysfunction, rhabdomyolysis, acute kidney injury, acute lung injury and hyperthermia have all been reported in rare cases (Weiner and others, 2000; Ng and others, 2010; Kalsi and others, 2011; Kleczkowska and Zaremba, 2021; Schep and others, 2023).

8.6 Acute psychotic emergence reactions can occur during the recovery phase from ketamine use. These include agitation, delirium, dream-like state, hallucinations, vivid disturbances and dysphoria (Schep and others, 2023).

8.7 Ketamine is sometimes used with other drugs or alcohol, which may increase the risk of adverse effects; for example, co-use with sedatives is likely to increase the risk of coma and respiratory depression.

Management of acute toxicity

8.8 Management of acute toxicity is primarily supportive and directed at the clinical features present. There is no specific antidote. In some cases, agitation or delirium may be severe enough to require administration of benzodiazepines or haloperidol. Should seizures occur and be prolonged or persistent, treatment with anticonvulsant medicines, especially benzodiazepines, is necessary.

Severe and fatal effects

8.9 Ketamine is sometimes detected in cases of drug-related deaths. Of 182 deaths in the UK where ketamine was implicated between 1997 and 2020, only 14 were attributed to sole ketamine exposure, and a further 7 were attributed to ketamine plus ethanol. Three-quarters of the deaths were classified as accidental poisonings. Ketamine-induced adverse effects such as poor judgement and reduced motor co-ordination were identified as contributing factors in several fatalities (Corkery and others, 2021). Similarly, in a large international systematic review of deaths related to use of ketamine or ketamine analogues, only 6.5% were considered to have been caused by ketamine or an analogue directly, with another substance of misuse the cause of death in a third of cases; in the remainder there were diverse causes of death including suicide, drowning and trauma (Chaves and others, 2023). Co-use of other substances is also commonly demonstrated in those who become critically ill after ketamine use. In one series involving 233 patients, their admission to critical care was only required in cases who had also used other substances (Ng and others, 2010).

8.10 A retrospective review of all recorded cases where self-administered ketamine contributed to deaths in Australia between 2000 and 2019 identified 68 cases (mean age 35 years, range 16 to 63, 76% male). Death was attributed to toxicity in 82% of cases (59% accidental, 23% deliberate), suicide (by violent means, 9%) and traumatic accident (9%). In 6 cases, ketamine had been prescribed. Other substances were detected in 95% of cases including opioids (59%), hypnosedatives (58%), psychostimulants (50%), alcohol (27%), Δ-9-tetrahydrocannabinol (18%), antidepressants (29%) and antipsychotics (9%) (Darke and others, 2021).

Long-term (chronic) effects

Ketamine-induced uropathy

8.11 Lower urinary tract symptoms (LUTS) and upper urinary tract damage may occur in people who are long-term recreational users of ketamine. It has been reported after therapeutic (prescribed) use, but this appears uncommon (Schifano and others, 2020; Feifel and others, 2020; Ng and others, 2021; Chang and others, 2024; Chiappini and others, 2025). Although commonly referred to as ‘ketamine bladder’ or ‘ketamine cystitis’, the preferred terminology is ‘ketamine-induced uropathy’ as the whole of the urinary tract can be affected. Reported symptoms include increased

daytime urinary frequency (passing urine more often than normal in the daytime), nocturia (waking from sleep to pass urine), urinary urgency (sudden desire to pass urine which cannot be deferred), urinary incontinence (involuntary leakage of urine), dysuria (burning feeling on passing urine), haematuria (blood in the urine) and bladder pain (Chan and others, 2022; Belal and others, 2024). Pain can promote further ketamine use. Symptoms are dose and duration dependent, but with an apparent initial lag phase between initiation of recreational use and the development of LUTS (Belal and others, 2024). It is reported that 27% of regular users report at least one urological symptom (dysuria, frequency, incontinence, haematuria or retention), with the prevalence of symptoms related to the frequency of use and the doses of ketamine involved (Winstock and others, 2012). It is thought that the metabolites of ketamine excreted by the kidneys into the urine are directly toxic to the lining of the urinary tract (urothelium) (Shahani and others, 2007). Further detail on potential mechanisms is provided in Section 2 ‘Pharmacology and toxicology’.

8.12 Three stages are described that affect the bladder (Wu and others, 2016). Stage 1 refers to inflammatory stimulation, and stages 2 and 3 to initial and subsequently severe fibrosis. There may be some improvement in LUTS if exposure is discontinued in the initial phases (Shahani and others, 2007; Chu and others, 2008; Kidger and others, 2016; Castellani and others, 2020; Anderson and others, 2022). However, with time, the bladder becomes of smaller capacity, thickened and inflamed, and the lining becomes ulcerated. Cystoscopy reveals cystitis, while histopathology reveals urothelial ulceration with eosinophilic infiltration (Shahani and others, 2007). In severe cases, these changes can further progress, and the bladder becomes poorly compliant (inelastic and generating high pressure) with subsequent hydronephrosis, renal impairment and ultimately end-stage renal failure. The ureters can also develop strictures (narrowings) that further compromise kidney function.

8.13 The key to bladder management is, first and foremost, ketamine cessation. There is a need for a multidisciplinary approach alongside addiction services, pain management and psychology/psychiatric services. Hepatobiliary input may also be needed if liver function tests are abnormal or there is other evidence of hepatobiliary dysfunction. Symptoms are often managed initially with oral analgesics, anticholinergic drugs or beta 3 agonists to help with pain and LUTS. Subsequently, bladder instillations (glycoasminoglycan layer replacement) or botulinum toxin-A bladder injections can be considered. In selected cases, more complex reconstructive surgery may be required. This might involve enlargement of the bladder or creating a new bladder with using bowel tissue (enterocystoplasty/neobladder) or urinary diversion using an ileal conduit or continent diversion, with the goals of lowering bladder pressure, preventing renal damage or stabilising renal deterioration as well as improving quality of life. It is critical that ketamine cessation is confirmed for at least 6 to 12 months before considering reconstructive surgery. Early outcomes have been promising, but longer-term follow-up is lacking and it is clear that with ongoing ketamine use upper tract strictures may develop, leading to failure of the procedure (Vizgan and others, 2023). Long-term follow-up, permanent cessation of ketamine use, patient engagement and attendance at review clinics are critical for ongoing long-term success in reconstructed patients.

8.14 Evidence from a designated ketamine clinic suggested the average age at presentation was 26, three-quarters were male, mental health issues such as depression and anxiety were present in 31%, and that a significant proportion of patients were poorly compliant with hospital visits and follow-up (Sturgess and others, 2023). Late presentation was common (ACMD, 2025c).

8.15 It has previously been suggested that ketamine-induced uropathy affects only a few recreational users who take high doses (Taylor and others, 2016). Urologists in the UK, however, have seen a significant increase in ketamine-related uropathy in their clinics and as a result the British Association of Urological Surgeons developed a consensus document to help guide assessment and treatment in this area (Belal and others, 2024).

Chronic abdominal pain

8.16 Chronic abdominal pain ('K-cramps'), commonly felt in the epigastrium and often associated with vomiting, is also reported with chronic ketamine use. This affects a quarter to a third of people who use ketamine and is more common in women and those using larger amounts (Poon and others, 2010; ACMD, 2013; Schep and others, 2023). It remains unclear whether these result from direct gastrointestinal toxicity or the effects of ketamine on the liver and biliary tree described below (Schep and others, 2023).

8.17 In a cross-sectional study of 611 patients who originally presented to hospital with symptoms of ketamine-induced uropathy, there were 168 (27.5%) who also reported upper GI symptoms including epigastric pain (25.4%), recurrent vomiting (7.9%), anaemia (5.9%) and gastrointestinal bleeding (3.3%). Risk factors associated with GI symptoms were older age, active ketamine misuse (especially by inhalation) and longer duration of ketamine misuse. In most patients, uropathy symptoms had preceded GI symptoms by a mean of over 4 years (Liu and others, 2017). Abdominal symptoms typically resolve when ketamine use is discontinued (Poon and others, 2010).

8.18 Stakeholders also report constipation, rectal prolapse and blood in the stools associated with ketamine use (ACMD, 2025c).

Liver and biliary tract abnormalities

8.19 Transiently abnormal liver function tests with a hepatocellular pattern may occur after acute ketamine use, including anaesthesia, but no cases of chronic hepatitis or liver failure have been reported in this context to date (Keta-Cov Research Group, 2021; Thakkar and Wu, 2025). A few cases of abnormal liver function, biliary dilatation, cholangitis, periductal fibrosis and/or cirrhosis have been reported after longer-term medical use of ketamine (Cotter and others, 2021).

8.20 There is increasing evidence that chronic ketamine exposure may be associated with severe hepatobiliary injury, entailing biliary dilatation, bile duct injury and liver fibrosis (Schep and others, 2023; Thakkar and Wu, 2025). Liver injury has been reported in 9.8% of people who misuse ketamine regularly (Wong and others, 2014), but may also occur in those receiving longer term or repeated medically-supervised ketamine

treatment (Thakkar and Wu, 2025). The common bile duct (CBD) may be dilated to up to 14 mm diameter, and this may be associated with cholestasis. Segmental strictures of the intrahepatic ducts and inflammation and fibrosis of the portal tracts have also been described. Deaths from progressive sclerosing cholangitis, decompensated cirrhosis, biliary sepsis and portal hypertension have been reported (Ng and others, 2009; Wong and others, 2009; Lo and others, 2011; Schep and others, 2023; Teymouri and others, 2024).

8.21 Chun and others (2025) reviewed 8 patients (6 men, 3 women) with long-term ketamine use, abnormal liver function tests and histological or radiological evidence of cholangiopathy. Ketamine was prescribed for pain control in one case and used recreationally in the other 7, with the overall median duration of use being 12 years (range 3 to 24 years). Six people also had ketamine-induced uropathy or urinary symptoms. Common cholangiographic abnormalities were diffuse irregular narrowing of the intrahepatic bile ducts (5) and mild dilatation of the extrahepatic bile ducts with a smooth contour (5). Liver biopsies showed features of chronic cholangiopathy with mild or absent portal and lobular inflammation. Periductal concentric fibrosis or fibrous duct obliteration was observed in 4 cases, mimicking primary sclerosing cholangitis, but unlike that condition, there were no associations with inflammatory bowel disease. Features were improved in the 3 cases that discontinued ketamine, with liver function tests normalising in one.

8.22 In one study, liver biopsies were performed on 7 patients with abnormal liver function tests. All demonstrated some degree of active biliary injury, as evidenced by biliary epithelial disarray, lymphocytic cholangitis and ductular reactions resembling sclerosing cholangitis. Fibrosis was observed in 3 patients, portal in one case and peri-portal with bridging fibrosis in the other 2 (Wong and others, 2014).

8.23 An imaging survey used either abdominal computerised tomography or magnetic resonance cholangiopancreatography scans to evaluate 26 patients with ketamine misuse and deranged liver function tests and/or abdominal pain. Of these, 18 (69%) had fusiform dilatation of the CBD without evidence of intrinsic or extrinsic obstruction and with non-dilated intrahepatic ducts. The degree of CBD dilation correlated with the duration of ketamine misuse and, in 5 patients, the dilatation improved to some extent after ketamine discontinuation (Yu and others, 2014).

8.24 A systematic review of the literature identified 17 cases (11 male, mean age 26, range 18 to 38 years) with documented ketamine misuse with reported cholangiopathy or biliary tract disease, 15 of whom had presented with abdominal pain. Abnormal liver function tests were demonstrated in 14 of 16 patients with results available. Those affected had a duration of ketamine misuse ranging from 2 months to 15 years. CBD dilatation was recorded in 12 patients (Teymouri and others, 2024).

8.25 The most important aspect of management of hepatobiliary abnormalities is discontinuation of ketamine. Early cholangiographic abnormalities may then resolve, but more prolonged use results in irreversible liver fibrosis and even decompensated cirrhosis (Thakkar and Wu, 2025). Management of cholangiopathy may require pain management and, where necessary, biliary stenting to alleviate obstructions (Schep and others, 2023). In the 17 patients described above, 9 received endoscopic

retrograde cholangiopancreatography (ERCP) with biliary drainage procedures (for example, sphincterotomy, sphincteroplasty, papillotomy, stenting of the bile duct or other forms of biliary drainage). Other treatments used included antispasmodic drugs, analgesia and drug rehabilitation programmes and all patients were reported to have improved prior to discharge from hospital (Teymouri and others, 2024).

Neuropsychiatric effects

8.26 Legitimate medical use of ketamine typically involves intermittent and/or low-dose exposures. In the case of esketamine for TRD, extended infrequent exposures (once a week or once every other week) are not associated with cognitive impairments, even after 3 years of intermittent treatment (Morrison and others, 2024). This section, therefore, only deals with chronic, frequent and relatively high-dose ketamine effects, which are relevant to problematic illicit use (for example, KUD). High doses or sustained exposures lead to a disruption of the homeostatic regulation of extracellular glutamate levels, which, in turn, cause NMDAR hyperactivation, calcium overload and consequent neuronal death ('excitotoxicity'). These aetiological mechanisms are also relevant to several neurological disorders, including epilepsy, ALS, Parkinson's, Alzheimer's and Huntington's diseases (Lewerenz and Maher, 2015).

8.27 Although the acute effects of ketamine on cognition, psychiatric symptoms and brain functioning have been extensively studied in carefully controlled experiments in healthy human participants (Zhornitsky and others, 2022), the effects of repeated and prolonged exposure to high doses of ketamine cannot be ethically studied in healthy volunteers or clinical groups. Instead, observational and quasi-experimental studies of 'naturalistic' exposures to harmful levels of ketamine have been performed in illicit users, who consume amounts of ketamine (more than 1g/day) far exceeding those used clinically (except for anaesthesia) over prolonged periods (months to years).

Structural and functional changes in the brains of chronic illicit ketamine users

8.28 Abnormalities in brain structure and function have been repeatedly observed in people after long-term illicit ketamine use, alongside changes in neuropsychological functioning and mental health symptoms (Li and others, 2025; Morgan and Curran, 2006; Strous and others, 2022; Van Amsterdam and Van Den Brink, 2022).

8.29 Structural neuroimaging studies have shown reductions in grey matter volume, loss of white matter integrity (Strous and others, 2022) and cortical thinning in chronic users relative to drug-free controls (for example, Tang and others, 2024; Zhong and others, 2021). Key brain areas affected include the prefrontal cortex, hippocampus, and retrosplenial cortex, which are critical for inhibitory control, reasoning, judgement, and learning and memory. Several studies suggest that the extent of observed structural brain changes in chronic users is associated with cumulative exposure or severity of ketamine dependence (Chesters and others, 2022; Strous and others, 2022; Tang and others, 2024; Zhong and others, 2021), although the reported correlations were generally weak.

8.30 Differences in brain function between chronic ketamine users and non-users have also been reported (Strous and others, 2022). By and large, these studies showed lower levels of resting-state connectivity between brain regions (for example, thalamic nuclei and cortical regions) (Liao and others, 2016). However, enhanced connectivity has also been observed and attributed to compensatory processes activated by cognitive deficits in chronic users (Zhong and others, 2024). In addition, cognitive task-related brain (hippocampal) activity was lower in chronic ketamine users than polydrug-using controls during a memory task (Morgan and others, 2014).

Neuropsychological deficits in chronic illicit ketamine users

8.31 Complaints about cognitive impairments are common among those who use ketamine frequently (Muetzelfeldt and others, 2008). Studies using standardised neuropsychological instruments corroborate the subjective experience of frequent illicit ketamine users by consistently demonstrating impairment relative to healthy, drug-free controls. Observed impairments include difficulties in executive functioning, short- and long-term (verbal and visual) memory, working memory and attention (Morgan and Curran, 2006; Van Amsterdam and Van Den Brink, 2022). Amongst illicit drugs, an apparently unique feature of ketamine is its capacity to cause impairments in semantic memory, which parallel the word-finding difficulties seen in schizophrenia (Morgan and others, 2004; Morgan and Curran, 2006).

8.32 Although some studies of chronic ketamine use and cognition have implied a dose-response relationship between the degree of ketamine exposure and the severity of impairment, such as correlations between duration, frequency, dose/session and cognitive performance (Van Amsterdam and Van Den Brink, 2022), these relationships were unlikely to be statistically reliable. On the other hand, a well-designed case-control study with carefully matched control conditions showed that chronic and frequent illicit ketamine users (average around 75 g per month) were substantially impaired on visuospatial recognition memory, working memory, contextual (‘source’) memory and aspects of executive functioning (planning) compared to infrequent users (average 5 g per month), who in turn were not impaired relative to non-drug-using controls (Morgan and others, 2010). This study also showed that some cognitive functions were preserved in chronic illicit users (for example, short and long-term verbal memory, verbal fluency). Overall, these findings suggest that cognitive harms are likely linked to cumulative dose, that impairments are circumscribed rather than generalised, and that infrequent use may not lead to cognitive harms.

8.33 One published study longitudinally assessed potential restoration of cognitive functioning after a period of abstinence (Tang and others, 2019). This showed significant recovery of cognitive functioning across virtually all assessed domains of memory and executive functioning after 3 months of abstinence. A small-scale study in previously frequent, chronic ketamine users who had substantially reduced their ketamine use (by around 90%) but were not abstinent at 3 years follow-up, showed a substantial recovery on some tests of executive functioning and memory, including semantic memory. However, the extent to which these improvements represented a return to premorbid levels of performance is unknown. Moreover, some impairments (for example, memory for events or ‘episodic memory’) persisted after 3 years of

follow-up, despite the substantial reduction in ketamine use (Morgan and others, 2004).

Psychiatric symptoms associated with chronic illicit ketamine use

8.34 Acute sub-anaesthetic doses of ketamine produce a reversible schizophrenia-like state comprising positive and negative symptoms in healthy individuals (Beck and others, 2020). This observation was the original basis for the 'ketamine model of schizophrenia' (Frohlich and Van Horn, 2014). Other researchers have proposed that chronic ketamine use is a more valid model of schizophrenia than acute administration models (Jentsch and Roth, 1999). Indeed, studies of chronic illicit ketamine use tend to report elevated scores on self-reported measures of schizophrenia-like symptoms (Chesters and others, 2022; Morgan and others, 2014; Stone and others, 2014). Although milder than 'endogenous' (non-drug-induced) schizophrenia, the profile of positive and negative symptoms (for example, delusional beliefs and blunted affect, respectively) in chronic users more closely resembled endogenous schizophrenia than the temporary psychosis syndrome produced by acute ketamine (Xu and others, 2015).

8.35 Chronic ketamine use is also associated with mild-to-moderate baseline depressive symptoms (Morgan and others, 2008; Tang and others, 2019; Liang and others, 2013; Zhang C and others, 2020). Of note, however, a substantial proportion of illicit users specify 'self-medication' (53%) as a motivation for initiating ketamine use (Harding and others, 2025). Frequent users were slightly (though significantly) more depressed than infrequent users and polydrug-using controls, who reported minimal depressive symptoms (Morgan and others, 2009). Abstinence was associated with mood improvement, such that chronic, frequent illicit ketamine-using participants went from being mildly depressed (on average) to minimally depressed (on average) after 3 months of abstinence (Tang and others, 2019).

8.36 Stakeholders have reported that ketamine use can be a barrier to access to mental health support, or conditions may be placed on accessing support, such as stopping use before therapy can begin. This is especially harmful for those using ketamine to cope with trauma, anxiety, or depression (ACMD, 2025c).

Caveats

8.37 A significant interpretational challenge in assessing neuropsychiatric harms of illicit ketamine is that ketamine users often use other harmful substances simultaneously, making it difficult to parse the specific contribution of ketamine use to structural, functional and behavioural abnormalities. In recent systematic reviews examining long-term illicit ketamine use-related harms, only a small proportion of studies attempted to control for this confound by recruiting non-ketamine-using polydrug controls (Strous and others, 2022; Van Amsterdam and Van Den Brink, 2022). Other limitations of published research include insufficient reporting of key metrics (for example, use of other substances, acute and cumulative doses of ketamine, presence of psychiatric disorders), small sample sizes, insufficient washout periods to allow chronic versus sub-acute effects to be distinguished and uncertainty about the contribution of withdrawal symptoms to observed impairments/symptoms (for example, withdrawal-related dysphoria contributing to elevated depression).

8.38 It is not yet clear whether structural differences between chronic illicit ketamine users and control volunteers (mostly drug-free individuals) reflect a pre-existing vulnerability or a consequence of escalating ketamine use. A stronger causal link between chronic recreational ketamine use and these neuroanatomical changes cannot be made in the absence of longitudinal studies with appropriate control conditions.

Other health effects

8.39 Other health harms mentioned by stakeholders responding to our call for evidence included, in some cases, very low body mass index, suicidality, amenorrhoea, infertility, sexual dysfunction, tooth decay and nasal septal damage from snorting ketamine.

8.40 Diagnosis of ketamine-induced health harms depends on obtaining an adequate history of ketamine use. Drug screens are of limited value for assessing toxicity associated with any drug, and in any event those in common use do not detect ketamine (Marongiu and others, 2025).

Prevalence of symptoms

8.41 In one series of 22 ketamine users who were interviewed, 5 reported being hospitalised due to their ketamine use (Ralphs and others, 2024).

8.42 In a study involving 274 patients with current or previous problematic ketamine use, physical effects included bladder symptoms (60%), nasal issues (60%), K-cramps (56%) and headaches (17%). Other symptoms (kidney issues, gall bladder issues, body aches, pancreas issues, liver issues, heart palpitations, erectile dysfunction, blood in urine, constipation, or brain fog) were reported by 12%, while 13% reported no symptoms. Most (56%) did not seek treatment for their physical symptoms; 26% went to A&E and 25% consulted their general practitioner. A minority of those seeking treatment (36%) were happy with the healthcare they received. They reported healthcare professionals being unaware of the addictive properties of ketamine, using Google to access information, and sometimes providing no adequate treatment for severe symptoms such as pain. This often leads users to feel defeated, hopeless and helpless (Harding and others, 2025).

Dependency, treatment and recovery

8.43 Animal (see Section 4, ‘Pharmacology and toxicology’) and human studies have demonstrated the potential for ketamine users to develop tolerance and psychological dependence (Sassano-Higgins and others, 2016; Schep and others, 2023). Increasing doses of ketamine are needed to achieve the same level of anaesthesia with repeated use, while recreational users need to use increasing doses to achieve their desired effects (Muetzelfeldt, 2008; Kleczkowska and Zaremba, 2021) or may combine ketamine with other substances such as alcohol or ketamine to enhance effects (ACMD, 2025c).

8.44 Regular medicinal use of ketamine is unlikely to produce dependency because of the low doses involved, and previous authors have suggested a lack of a physiological withdrawal syndrome (Jansen and Darracot-Cankovic, 2001). There is increasing

recognition, however, that physical dependency can develop in regular high-dose users (Ralphs and others, 2024; Van Amsterdam and Van Den Brink 2022). The addictive potential of ketamine is indicated by the greater and dose-related attentional bias to ketamine in heavy users compared with controls (Morgan and others, 2008).

8.45 Withdrawal symptoms typically occur in heavy users within 24 hours of discontinuation of use and generally last about 3 days, although can last up to 2 weeks. They include cravings, depression, dysphoria, shaking, sweating, palpitations, tiredness, low appetite, low mood, chills, autonomic arousal, lacrimation, restlessness, anxiety, nightmares, paranoia, delusions and hallucinations (Lerner and Klein, 2019). The evidence available to guide management of ketamine withdrawal is limited and of low quality, but haloperidol or reducing doses of benzodiazepines with or without other drugs such as propranolol, olanzapine or clonidine have been used (Roberts and others, 2024; Ilves and others, 2025). Pharmacological approaches advocated for prevention of relapse or treatment of cravings have included naltrexone, palperidone and/or bupropion, but no high-quality studies have addressed this issue and evidence for benefit is anecdotal (Roberts and others, 2024).

8.46 In a survey of 1,285 people who used ketamine, 218 (17%) met Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria for dependence, with this strongly associated with the amount of ketamine used per session and frequency of ketamine use sessions (Winstock and others, 2012).

8.47 The rapid onset of dependence to ketamine may take users by surprise. In a study of 187 inpatients hospitalised for KUD, the average time from initiation of ketamine to requiring treatment was 3.1 years (Fan and others, 2016).

8.48 Ongoing ketamine use may also be stimulated by the need for the drug to control pain associated with long-term complications of use, such as ketamine-induced uropathy. Relapse after detoxification is common due to the urge to manage ongoing physical pain through further ketamine use (Ilves and others, 2025; ACMD, 2025c).

8.49 Management of KUD involves psychosocial interventions focusing on supporting behaviour change to achieve abstinence or a reduction in use to a less harmful level. Interventions to address co-occurring psychological, social or physical problems are also required. Detailed description of psychosocial interventions in the management of drug use disorders is beyond the scope of this report, but can be found elsewhere (Dept of Health, 2017). Unlike opioids, for example, there are no specific drug treatments for those dependent on ketamine. The evidence available to guide the drug treatment of KUD is generally limited and of low quality.

8.50 Within inpatient settings, pharmacological treatment protocols for ketamine are based on individual and shared clinical experience from inpatient detoxification units across the UK. The key principles for treatment options offered to people undergoing inpatient detoxification for ketamine are:

- low-dose benzodiazepine regimes to manage intoxication and withdrawal symptoms; short-acting benzodiazepines can be considered where liver metabolism and/or renal clearance is compromised

- medication to manage anxiety, sleep disturbance and symptomatic relief for pain

- psychosocial support alongside the pharmacological treatment, followed up with resident rehabilitation

8.51 There are case reports advocating use of various drugs to help prevent cravings and for relapse prevention, including naltrexone, lamotrigine and paliperidone palmitate plus bupropion, but these require further evaluation (Roberts and others, 2024).

Awareness of adverse effects among users and health professionals

8.52 Stakeholders report limited awareness of the adverse health effects of ketamine use, especially amongst initial or low-level users. Those initiating ketamine, especially younger users, commonly underestimate their personal risk, believing they will not be affected. They sometimes believe that ketamine is safer than other drugs because of its low cost and lack of hangover effects. They may be influenced by social media messaging spreading harm reduction advice that in some cases is inaccurate. Many are not aware of gastrointestinal or hepatobiliary effects (ACMD, 2025c).

8.53 Long-standing habitual users have greater awareness but may already be experiencing chronic adverse health effects. Users may also be surprised by the addictive nature of ketamine and the rapidly developing tolerance that may occur. Sensationalist media reports of bladder damage have led to mistrust of messaging, with some users considering these ‘scare tactics’ to discourage use. There is also poor understanding of the support options available for those experiencing adverse effects (ACMD, 2025c).

8.54 In some cases, users overestimate what treatment can offer in terms of correcting urological symptoms, believing that bladders can be stretched or repaired when damage is already irreversible.

8.55 Those with lived and living experience consistently report that frontline health professionals display a lack of knowledge about ketamine and its adverse health effects. Symptoms may be misdiagnosed, such as abdominal pain as menstrual pain or haematuria as urinary tract infection. The history of ketamine use may not be sought, so that recognition of the underlying cause and appropriate referral for specialist treatment is delayed. Medicines prescribed for pain (for example, paracetamol) are often reported to be inadequate (ACMD, 2025c).

Barriers to treatment

8.56 Access to treatment for the health harms of ketamine often appears delayed, and shame and/or stigma may prevent users from presenting to health services and/or disclosing ketamine use. Late presentation is common and affected patients may not attend appointments due to a chaotic lifestyle or their urinary symptoms. The frequency of urinary symptoms amongst those who use ketamine within their social

circle may also ‘normalise’ these features and discourage help-seeking (Gill and others, 2016). A substantial proportion of ketamine users want to continue to use ketamine (Harding and others, 2025).

8.57 Barrios and others (2025) used data from the 2018 Global Drug Survey to explore correlates of ketamine use. They found that a high proportion of respondents, including those who used ketamine in the past year (95%), and those with probable ketamine dependence (87%), were reluctant to seek emergency medical treatment. Harding and others (2025) surveyed 274 individuals with self-identified KUD and found that fear of judgement or stigma was one of the most common barriers preventing people from seeking treatment (42%). Another important barrier for seeking treatment was the desire to continue using ketamine (ACMD, 2025c).

8.58 Gill and others (2018) examined the experience of ketamine bladder syndrome amongst people using ketamine regularly and found that feelings of embarrassment and self-loathing were common and compounded by fears of stigmatisation. When they did eventually seek help, they were not routinely asked about ketamine use, and they did not volunteer this information because they were too embarrassed to do so.

8.59 Fear of cystectomy may also prevent affected users from seeking health advice or attending appointments. Users also perceive that healthcare professionals may not be aware of the addictive potential of ketamine or its physical health effects (Gill and others, 2018; Ralphs and others, 2024). There are also often long waiting lists for specialist clinics, such as urology or pain management. As discussed above, ketamine use may be a barrier to accessing mental health services.

Ketamine use in pregnancy and lactation

8.60 After administration to the mother, ketamine is known to pass through the placenta into the foetus. It also appears in the breast milk if administered to those who are lactating. This is of concern because the developing brain may be particularly susceptible to the neurotoxic effects of ketamine (Zhao and others, 2016). Animal studies have demonstrated altered behaviour, reduced discriminative learning ability (without loss of performance), impaired spatial learning and memory, and anxiety-like behaviour after in-utero ketamine exposure. These effects, however, were inconsistent (Cheung and others, 2019).

8.61 Some neonates have developed respiratory depression and low Apgar scores after use of ketamine during delivery, but administration during surgery for abdominal delivery or vaginal delivery is not contraindicated and ketamine is widely used in obstetric anaesthesia (Tang and others, 2017; EMC, 2025). In the context of recreational ketamine use, there is a single case report of a baby with intrauterine growth retardation, severe hypotonia, and poor reflex responses after in-utero ketamine exposure due to maternal recreational use. These features improved over several weeks (Su and others, 2010). There is no information available on the risk of structural foetal abnormalities after therapeutic or recreational ketamine exposure in pregnancy (Pacilio and others, 2025).

Annex 9. Social harms

9.1 While ketamine has long been used for medical and therapeutic uses, its non-medical use has been linked to a range of social harms at both individual and societal levels. The evidence base is broadly consistent in showing that the social harms are associated with heavy, prolonged and dependent use of ketamine rather than light, occasional and recreational use.

Interpersonal impacts

9.2 Non-medical ketamine use has been found to negatively affect interpersonal relationships in several ways. Ketamine induces dissociative effects that vary depending on the dose (Anderson and others, 2022). At lower doses, ketamine can distort time and space. At higher doses, it can lead to altered states of consciousness and feelings of intense detachment, which can result in a decrease in sociability (Morgan and Curran, 2012) and social withdrawal (Fan and others, 2016). As with most other drugs, the financial burden of frequent ketamine use may also contribute to increasing debt, isolation and emotional distress, which can strain relationships. Loss of housing may also occur. Domestic violence and child safeguarding issues may be associated with ketamine use, although the evidence base for ketamine specifically is limited. Stakeholders report effects of ketamine use on relationships with friends and family, sometimes requiring the involvement of social services. In extreme cases, families may accumulate debt by paying for private detoxification (ACMD, 2025c).

Crime

9.3 While there is limited evidence of an association between ketamine use and violent behaviour (Morgan and Curran, 2012), some research has highlighted its emerging use as a tool to facilitate rape and sexual assault (DEA, 2017; Dermitzaki and Nystazaki, 2021; Lahane and Kaur, 2022; GMP, 2025). Drink-spiking and drug-facilitated sexual assaults were also reported by stakeholders (ACMD, 2025c). Of note, kits are available for testing drinks potentially spiked with ketamine, although limited information of their reliability is available (Germain and others, 2023).

9.4 Drugs in general are a major driver of violence across the nation (Home Office, 2020) and ketamine is likely to be important in this regard because of the high profits associated with sales, the involvement of organised crime groups and its supply on the street directly to users, which may be associated with violence. The dissociative effect of ketamine can potentially place the user in a position where they are vulnerable to robbery, assault and/or rape (see above). Few studies, however, have investigated the links between ketamine use and other forms of criminal behaviour. A US study found that fewer than 5% of drug-related offences among ketamine-injecting youths were directly related to ketamine use (Sanders and others, 2009). Notably, burglaries associated with ketamine were more likely to involve veterinary clinics rather than residential homes, and offending following ketamine use was rare, possibly due to ketamine's sedative effects hindering capacity (and possibly its relatively low cost). Although acquisitive crime is less associated with ketamine than some other drugs, stakeholders did report shoplifting and petty crime linked to

dependency. Young people may also be entrapped by debt bondage or otherwise groomed into county lines activities (ACMD, 2025c).

9.5 Substantial social harms result from convictions for drug-related offences, including loss of housing and employment, reduction in life prospects and restriction on foreign travel.

Driving and public safety

9.6 The impact of ketamine on psychomotor performance also heightens the risk of road traffic accidents. Concurrent use of ketamine with substances such as alcohol further exacerbates the risks, with potentially fatal outcomes (Kobayashi and others, 2022).

9.7 Ketamine has been frequently identified in cases of drug-impaired driving in Asia (Arango and others, 2021). In Hong Kong, ketamine was present in 71% of drug-driving cases from 2010 to 2011 and 68% from 2012 to 2015. In Australia, its prevalence among drivers tested between 2009 and 2010 was 1.5% (Arango and others, 2021). One US study found that people who use ketamine were significantly more likely to report driving under the influence and engaging in property offences compared to non-users (Oser and others, 2008). This study also found that ketamine use was associated with high-risk sexual behaviours, a pattern reported in many other empirical studies (see below). In a UK study, ketamine was detected in 14 out of 376 drug-driver cases, with concentrations ranging from 170 to 850 ng/mL. Analysis by Transport Research Laboratories (TRL) for the Department for Transport (Hammond and others, 2017) identified 144 road traffic collision deaths in which ketamine was detected between 2014 and 2018. In 29 cases, the concentration was above the legal limit of 20 ug/L (20 ng/ml) of blood, which is a zero-tolerance detection limit, constituting 1% of all fatalities for which drug data was available. Other drugs that impair performance, including alcohol, may also be present in some cases.

9.8 Those affected by dissociative and hallucinogenic effects may also be at increased risk of falls, jumping from heights or fights. Stakeholders report that it is increasingly common to encounter intoxicated users in public spaces (ACMD, 2025c).

Sexual health risks

9.9 Ketamine is commonly used in the context of ‘chemsex’ to enhance sexual performance, arousal and experience, most commonly but not exclusively among MSM (Sansone and others, 2022). The main problem with this is that chemsex is associated with a greater number of partners and also with unprotected intercourse, which increases the risk of spreading blood-borne viruses and sexually transmitted diseases (Hibbert and others, 2021). There is also the risk of unplanned pregnancies among those engaging in unprotected sex, but the extent to which this happens among people who use ketamine is unclear. A small study of young people injecting ketamine in the US reported an association with a range of high-risk injection practices such as group injection with shared paraphernalia (Lankenau and Clatts, 2002). A recent systematic review identified a link between ketamine use and sexual dysfunction among both men and women (Pominville and others, 2023). Ketamine

use was also a marker for engaging in high-risk behaviour for contracting HIV among offenders entering US prisons (Oser and others, 2008).

System costs

9.10 Management of ketamine-induced uropathy, ketamine dependence and other long-term complications of ketamine use may require a variety of costly procedures involving lifelong care, placing a significant burden on the healthcare system (Morgan and Curran, 2012; Zheng and others, 2025). With increasing numbers seeking treatment, the cost to already overstretched treatment services is likely to rise. There are also costs to the criminal justice system from prosecution of ketamine-related offences.

Employment and education impacts

9.11 Frequent ketamine use is associated with impairments in working memory, episodic memory, and executive functioning (Perlowski and others, 2024). Several studies have linked non-medical ketamine use to poorer academic outcomes and employment issues (Marongiu and others, 2025). In one interview study, a fifth of recreational users reported employment-related problems due to ketamine use, including reduced clarity affecting their performance and lower productivity (Dillon and others, 2003). Another study found that more frequent users spent significantly fewer years in education than either less frequent or non-users (Morgan and others, 2010). Stakeholders report significant impact of ketamine use on both attendance and performance in educational settings, with some users stopping attendance completely. Loss of employment may also occur with consequent effects on family finances and housing (ACMD, 2025c). Bladder-related symptoms caused by long-term ketamine use can further challenge the maintenance of employment (ACMD, 2025c).

Environmental impacts

9.12 Ketamine cannot be removed by conventional wastewater treatment plants and has been detected in riverbanks and oceans (Li and others, 2017; Thapa, 2021). These residues are harmful to aquatic life, with studies highlighting their high ecotoxic potential and the need for ongoing environmental monitoring (Li and others, 2017).

Stigma

9.13 People with harms from the use of ketamine may feel stigma and shame from use of an illegal substance, because they perceive others consider these self-inflicted. Stigma is exacerbated by the types of harms from ketamine, such as urinary incontinence or the need for a stoma. Stigma may delay help-seeking and exacerbate underlying mental health problems (Harding and others, 2025).

Annex 10. UK Prevalence

10.1 The ACMD has examined published data on prevalence of harms associated with ketamine and its analogues in the UK. The ACMD also wrote to a range of stakeholders in April 2025, including public health authorities, forensic service providers and academic researchers. Quantitative information was requested about ketamine and analogues recently identified in submitted sample analysis, drug seizures by law enforcement or Border Force, samples from those attending emergency departments with drug toxicity and forensic analysis of drug-related deaths.

Prevalence surveys

10.2 The CSEW is an annual study asking members of the public living in households in England and Wales about their experiences of crime over the previous 12 months. Those aged 16 to 59 are also asked questions on drug use; data are provided for this group as a whole and for the subgroup aged 16 to 24 and reported by financial year, although no data are available for years ending March 2021 or 2022 (ONS, 2024).

10.3 Data on ketamine use have been requested since the year ending March 2007. Responses show an increase in the prevalence of ketamine use in both the 16 to 59 and 16 to 24 age ranges between the years ending March 2016 and 2023. This applies to ever use or use in the last year or last month (Table 10.1). There have since been reductions in last year and last month use, especially in the 16 to 24 age group. In the most recent CSEW estimates for the year ending March 2025, there were there were 1,369,000 people in England and Wales aged 16 to 59 who had ever used ketamine, with 264,000 using in the previous year and 95,000 in the last month. Of these 385,000, 120,000 and 47,000 respectively were aged 16 to 24. To put these data into perspective, the CSEW estimates that there were 3,350,000 people in England and Wales aged 16 to 59 who had ever used MDMA, with 392,000 using in the previous year and 91,000 in the last month. For those aged 16 to 24, the figures were 373,000, 116,000 and 30,000 respectively. Recent ketamine use (in the last month or year) is now more common for ketamine than for ecstasy in the younger age group. Annual trends in use for ketamine, ecstasy and cocaine (all types) are provided the main report (Section 10, Figure 1).

10.4 The peak age group for reported last year ketamine use in the UK is 20 to 24 (2.9%), although there is considerable use in people aged 16 to 19 (0.9%). People of mixed or multiple race ethnicity (1.9%) or who self-identify as gay/lesbian (1.5%) or bisexual (5.6%) are more likely to report last year ketamine use than the general population aged 16 to 59 (0.8%) (ONS, 2025).

10.5 A potential drawback of the CSEW is that drug use may be underestimated because those surveyed may be reluctant to disclose their use of illegal drugs. The Adult Psychiatric Morbidity Survey (APMS) collects information about mental health, including drug use, from a random sample of adults aged 16 to 100 by face-to-face interviews that take place in their homes, which is likely to be a more reliable method of data collection. In the year ending March 2024 APMS survey, ketamine use in the

last year was reported by 4.3% of those aged 16 to 24, a higher figure than that obtained the same year by the CSEW, which was 2.9% (NHS England, 2025).

Table 10.1: Percentages of people aged 16 to 59 and 16 to 24 reporting use of ketamine ever, in the last year or in the last month

Years ending 31 March	16 to 59 years			16 to 24 years		
	Ever	Last year	Last month	Ever	Last year	Last month
2007	1.3	0.3	0.1	2.3	0.8	0.4
2008	1.3	0.4	0.2	2.2	0.9	0.3
2009	1.7	0.5	0.2	3.5	1.9	0.8
2010	2.0	0.5	0.2	3.8	1.7	0.9
2011	2.2	0.6	0.3	4.3	2.0	0.9
2012	2.5	0.6	0.2	3.9	1.7	0.5
2013	2.2	0.4	n/a	3.3	0.8	n/a
2014	2.7	0.6	n/a	4.7	1.8	n/a
2015	2.6	0.5	0.1	4.0	1.6	0.2
2016	2.4	0.3	0.1	3.7	1.0	0.3
2017	2.3	0.4	0.2	3.4	1.3	0.5
2018	2.8	0.8	0.3	4.7	3.1	1.3
2019	3.1	0.8	0.3	5.6	2.9	1.4
2020	3.0	0.8	0.3	5.6	3.2	0.9
2023	3.7	0.9	0.4	6.6	3.8	1.6
2024	3.8	0.8	0.4	6.5	2.9	1.3
2025	4.1	0.8	0.3	6.5	2.0	0.8

Source: CSEW (ONS, 2025d)

10.6 NHS Digital provides information on reported drug use from their periodic surveys of school pupils in school years 7 to 11 in England and Wales. This involves children and young people who are mostly aged 11 to 15 (NHS England, 2024a). In the most recent survey (2023), 1.1%, 0.9% and 0.3% of these school pupils reported ketamine use ever, in the last year or in the last month respectively. The numbers involved are relatively small, making analysis of trends unreliable, but there have been increases in ever use and last year use in recent years (see Table 10.2). Data on other ketamine analogues are not available.

10.7 The GM-Trends survey of 400 young people in Greater Manchester reported that 1 in 6 had used ketamine in the past year, while 64% of those in treatment for ketamine use were under the age of 18 (ACMD, 2025c).

Table 10.2: Reported ketamine use by school pupils (school years 7 to 11) in England and Wales (% respondents).)

	Ever use	Last year use	Last month use
2011	0.6	0.5	0.2
2012	0.5	0.5	0.3
2013	0.5	0.4	0.2
2014	0.4	0.4	0.2
2016	0.6	0.5	0.2
2018	1.2	1.0	0.6
2021	0.8	0.6	0.1
2023	1.1	0.9	0.3

Source: NHS England (2024b)

10.8 The Scottish Schools Adolescent Lifestyle and Substance Use Survey (SALSUS) was last conducted in 2018 and showed that the proportion of 15-year-olds who had been offered ketamine had increased from 5% in 2015 to 10% in 2018 (SALSUS, 2018).

10.9 The Young Persons' Behaviour and Attitudes Survey is a school-based survey conducted among 11- to 16-year-olds in Northern Ireland. In the 2022 survey, 0.5% of 3,684 respondents reported ever using ketamine, which is a similar percentage to those using ecstasy. Only cannabis, synthetic cannabinoids, solvents, cocaine and nitrous oxide were reported to have been used by a higher proportion. Ever use of ketamine had been reported by 0.4% in the previous survey conducted in 2019 (DoH (NI), 2023).

10.10 These data are consistent with the observations of healthcare professionals completing a survey, where two-thirds noted increased ketamine use in populations that they work with and especially involving young people. Ketamine was often the main substance of concern. Consistent with this, there have been increasing numbers of those under 18 years seeking treatment. Furthermore, in a survey conducted in Greater Manchester in 2023 to 2024, there was an increase in numbers reporting ketamine use (16% of 400) compared to 6% in the previous year, with 41% of users also reporting increased use (Ralphs and others, 2024).

10.11 These findings are also consistent with the increasing referrals reported to specialist paediatric urology services in Cheshire and Merseyside for those under 16 years of age with ketamine-induced uropathy, which may be linked with the low cost of ketamine locally (Isba and others, 2025).

Submitted sample analysis

10.12 Information was provided by the Public Health Wales Substance Misuse Programme from the Welsh Emerging Drugs and Identification of Novel Substances Project (WEDINOS), which analyses samples of drugs submitted anonymously by users from across the UK (Table 10.3). Between 1 January 2015 and 31 March 2025, 1,170 samples were submitted to WEDINOS as ketamine, methoxetamine, 2-fluorodeschloroketamine, *N*-ethylnorketamine, deoxymethoxetamine or deschloroketamine. Where reported (1,146), 81% of sample providers were male and their median overall age was 29 (range 14 to 67 years).

Table 10.3: Country of origin for WEDINOS samples submitted as ketamine or a ketamine analogue per year.

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
England	**16**	**9**	**10**	**26**	**44**	**50**	**133**	**143**	**198**	**219**	**38**
Northern Ireland		**1**	**1**					**2**	**1**	**1**	
Scotland				**1**	**2**	**5**	**4**	**7**	**17**	**17**	**8**
Wales		**8**		**9**	**8**	**15**	**18**	**21**	**32**	**60**	**16**
No postcode provided					**1**	**25**	**1**		**2**	**1**	

10.13 A further 1,581 samples were profiled upon analysis to contain ketamine or ketamine analogues, but the purchase intent is unknown for 1,233 samples submitted via nighttime economy venue amnesty bins, from prisons within Wales (as unattributable finds) or as unknown substances (Table 10.4). The content of these samples usually matched the purchase intent (Table 10.5). A minority of ketamine samples contained an adulterant (Table 10.6).

Table 10.4: Number of samples submitted to WEDINOS by year as ketamine or a ketamine analogue

	201	201	201	201	201	202	202	202	202	202	202
Ketamine	10	14	8	36	51	91	156	173	247	294	62
Methoxetamine	4	4	1	0	4	2	0	0	1	0	0
2-FDCK	0	0	2	0	0	2	0	0	2	2	0
N-Ethylnorketamine	2	0	0	0	0	0	0	0	0	0	0
Deoxymethoxetamine	0	0	0	0	0	0	0	0	0	1	0
Deschloroketamine	0	0	0	0	0	0	0	0	0	1	0
TOTAL*	**1,489**	**1,393**	**1,425**	**2,021**	**3,957**	**3,156**	**6,093**	**6,321**	**7,271**	**8,193**	**1,640**

*Total number of samples analysed by WEDINOS per year

Table 10.5: The percentage of samples per year (by substance) that matched the purchase intent.

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Ketamine	50	50	75	83	90	75	87	91	86	87	97
Methoxetamine	50	75	100		100	50			100		
2-FDCK						100				50	
N-Ethylnorketamine	0										
Deoxymethoxetamine										100	
Deschloroketamine										100	

Table 10.6: Percentage of ketamine samples containing an adulterant.

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Ketamine	10			6	2	11	7	3	7	31	

10.14 There were 348 samples profiled as containing ketamine where the purchase intent was declared. The 10 most common of these purchase intents is shown in Table 10.7, with MDMA, cocaine, pink cocaine and amphetamine the most common.

Table 10.7: Ten most common purchase intents for samples profiled to contain ketamine.

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
MDMA			1	3	1	5	9	10	16	19	3
Cocaine				4	1	8	10	7	9	14	7
Pink Cocaine					1		1	4	14	15	1
Amphetamine				2	1	4	3	1	7	5	3
Diazepam					2	2	2	4	2	10	2
2C-B					3	2	3	6	3	4	
Alprazolam				1	2	5		5	5	2	1
Mephedrone		7			4		1	3	4	2	
LSD				1	1	2	2		3	1	
Heroin										9	

10.15 Over the period of data collection, 1,142 samples were submitted as ketamine. Of these, 62 were profiled as containing ketamine and at least one other substance (Table 10.8).

10.16 Samples submitted as ketamine were most commonly in the form of powders or crystalline materials (Table 10.9).

Table 10.8: Substances profiled alongside ketamine (where ketamine was the purchase intent) and the number of occasions per year they were identified in combination.

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
2C-B										1	
2-MMC										1	
3-MMC									1		
4-CMC										1	
4F-3-methyl-α-PVP										1	
5F-ADB										1	
Amphetamine								1			
Benzocaine	1						1	1	4	1	
Caffeine							1			1	
Chlorpheniramine				1							
Cocaine	1			1		1	2		7	7	
Levamisole						7	6	1		1	
Lidocaine								1			
MDMA				1		1		2	1	1	
MDMB-4en-PINACA										1	
Mephedrone									2	2	
N-ethylpentedrone										1	
Paracetamol							1		1	1	
Phenmetrazine										1	
Promethazine									1		
Quetiapine										1	

Table 10.9: Form of samples submitted to WEDINOS as ketamine by year.

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Capsule					1	1				3	
Crystalline	6	4		12	26	45	81	92	115	152	32
Granules				5		6	8	20	33	24	8
Liquid						2				4	
NA		1		1		7	2	3	1	3	2
Plant Matter						1	1				
Powder	4	9	8	17	24	29	64	55	97	105	19
Solid				1				3	1	1	
Tablet										2	1

10.17 As part of WEDINOS data collection, providers are asked to detail their method of consumption when a portion of the sample has been consumed. This information is available for 524 (46%) samples submitted as ketamine, with 493 of these (94%) reporting snorting or sniffing their ketamine.

10.18 Of 173 samples submitted to WEDINOS from Scotland between December 2024 and February 2025, 12 (7%) tested positive for ketamine, as reported by Public Health Scotland (PHS) Rapid Action Drug Alerts and Response (RADAR).

Seized sample analysis

10.19 The annual number of seizures of ketamine by police forces has increased consistently between the years ending March 2014 (when ketamine was upgraded to a Class B drug) and 2024. The seizures by Border Force UK have also followed a similar trending with both reached highs in year ending March 2024 (Table 10.10). In that year, police forces and Border Force carried out the highest number of ketamine seizures (2,252) since data collection began in the year ending March 2007, a 51% increase on the 1,487 seizures made in the previous year (Home Office, 2025a).

Table 10.10: Number and weights of ketamine seizures made in England and Wales by police forces and Border Force UK.

	Police forces		Border Force	
Year ending 31 March	Number	Weight (kg)	Number	Weight (kg)
2013	1,315	23	181	222
2014	1,502	31	130	334
2015	392	2	164	106
2016	481	10	108	299
2017	504	55	68	198
2018	654	132	73	114
2019	865	23	97	133
2020	1,080	31	185	37
2021	971	33	538	154
2022	995	173	341	1,664
2023	1,337	500	150	934
2024	2,046	86	206	796

10.20 Eurofins, a provider of comprehensive forensic analysis service to police forces, legal and criminal justice organisations throughout the UK, reported increasing numbers of ketamine detections since 2015 and especially since 2019. Over this period, it has also provided data on ketamine analogues detected over this period, recording a few detections involving 7 compounds for which data were available over the period 2020 to 2025 (Table 10.11).

Table 10.11: Number of separate instances a sample has been analysed and ketamine, ketamine hydrochloride or an analogue has been identified by Eurofins

Year	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025*
Ketamine	429	585	601	621	556	869	820	1,110	1,020	1,827	1,332
2-FDCK	n/a	n/a	n/a	n/a	n/a	20	9	1	3		1
2-F2oxo-PCE	n/a	n/a	n/a	n/a	n/a					3	2
DCNEK	n/a	n/a	n/a	n/a	n/a						2
3-MeO-PCP	n/a	n/a	n/a	n/a	n/a			1	2	2	
Methoxetamine	n/a	n/a	n/a	n/a	n/a			2			2
3-HO-PCE	n/a	n/a	n/a	n/a	n/a			1			
DCK	n/a	n/a	n/a	n/a	n/a	1	1				

*part-year to June 2025

Key: 2FDCK = 2-Fluorodeschloroketamine, 2F2oxo-PCE = 2-Fluoro-2-oxo-PCE, DCNEK = Deschloro-*N*-ethyl-ketamine, 3-MeO-PCP = 3-Methoxy-phencyclidine, 3-HO-PCE = 3-hydroxy-PCE, DCK = Deschloro-ketamine

10.21 The Emerging Drugs and Technologies Programme (EDAT) provided seizure data generated through collection plans under the now-discontinued Forensic Early Warning System project. The data are from samples seized both at the UK border and within UK prisons. The data detail the primary substance detected, any other substances detected, and where available physical information such as colour and form.

10.22 There were 79 seizures containing ketamine or an analogue reported by EDAT from UK Border Force for the period 2019 to 2024 (Table 10.12), with the highest numbers for ketamine in 2020. Analogues were detected in small numbers of seizures. Eight of the 66 ketamine samples also contained another active substance; these were dextromethorphan (2), MDMA (3), cocaine (2) and 2C-B (1).

10.23 The data from HM Prison and Probation Service (HMPPS) involved 25 seizures made between 2017 and 2022, 24 containing ketamine and 2 containing fluorodeschloroketamine (one seizure contained both). Other substances were detected in 9 samples and included synthetic cannabinoid receptor agonists (AMB-CHMICA, 5F-MDMB-PINACA, AMB-FUBINACA in 4 samples of green herbal material also containing ketamine, 5F-MDMB-PICA in one sample impregnated on paper with cocaine and ketamine and 2 samples containing benzocaine. All samples containing ketamine only were in the form of powders.

Table 10.12: Ketamine and ketamine analogue detections by year on ketamine and ketamine analogue seizures by UK Border Force and within UK prisons, as reported by EDAT

Primary component	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
UK Border Force								
Ketamine	n/a	n/a	2	25	15	12	4	8
N-Ethyldeschloroketamine	n/a	n/a	0	0	0	1	1	0
Deschloroketamine	n/a	n/a	0	0	1	1	0	0
Fluorodeschloroketamine	n/a	n/a	0	0	0	3	3	0
Deoxymethoxetamine	n/a	n/a	0	0	0	2	0	0
Methoxpropamine	n/a	n/a	0	0	0	1	0	0
HMPPS								
Ketamine	4	1	1	7	8	3	n/a	n/a
Fluorodeschloroketamine	0	0	0	2	0	0	n/a	n/a

10.24 TICTAC Communications Ltd has provided results of analysis of samples from amnesty bins and seized drugs at a total of 30 events over the years to July 2017 to 2025. Analysis is performed using gas chromatography-mass spectroscopy (GC-MS) and Fourier Transfer Infrared (FT-IR) spectrometry. Over this period, increases were seen in the average number of seizures, bags seized and amount of ketamine crystals (99%) or powder (1%) involved (Table 10.13). During 2024 and 2025, there were sharp increases in samples containing other drugs in pink powder (tusi or pink cocaine). This was mostly ketamine in combination with other drugs, especially MDMA and caffeine, but also occasionally 2C-B, cocaine or benzocaine. Ketamine is also sometimes detected in tablets sold as 'ecstasy', with at least 61 such seizures identified between 1995 and 2024. Of these, 7 contained ketamine alone, with most recently MDMA, cathinones and caffeine the most common other drugs detected in addition to ketamine. During 2025, branded packages of tusi have been encountered for the first time.

Table 10.13: Average numbers of seizures, bags and ketamine weights from seizures or amnesty bin submissions as analysed by TICTAC Communications Ltd

	Average per event		
Year	**Seizures (n)**	**Bags (n)**	**Amount (g)**
2017	122	205	154
2018	161	252	189
2019	233	453	340
2021	259	355	266
2022	176	357	268
2023	227	334	250
2024	232	378	283

10.25 The Scottish Prisons Non-Judicial Drug Monitoring Project is a collaboration between the Scottish Prison Service and the Leverhulme Research Centre for Forensic Science at the University of Dundee. Data are obtained from the analysis of non-judicial drug seizures from Scottish Prisons using gas chromatography-mass spectrometry (GC-MS). Over the period May 2018 to May 2025, there were 16 samples reported to contain ketamine, 1 in 2019, 1 in 2021, 5 in 2022, 7 in 2023 and 2 in 2024. Of these, 7 contained ketamine alone and 9 contained at least one other substance including cocaine (4), phenacetin (2), ADB-BUTINACA (2), nicotine (2). oxymetholone (1) and 2-FDCK (1). All samples were powders, except for 2 where ketamine was detected in clothing and 2 in e-cigarettes (in both cases with ADB-BUTINACA and nicotine).

10.26 The MANDRAKE project performs forensic/chemical analysis of seized samples using a variety of presumptive (FT-IR, IonScanner) and confirmatory (nuclear magnetic resonance (NMR) and GC-MS) tests. The samples undergo qualitative and quantitative analysis (in triplicate, by GC-MS), using certified reference standards to confirm the purity of the seized samples. The analysed samples were obtained from across Greater Manchester by Greater Manchester Police from the following sources: police seizures (property stores); nighttime economy sources, including bars, nightclubs, and festivals; prison/custodial institutions; and healthcare/drug treatment/coronial sources.

10.27 Results for the period April 2019 to April 2025 are shown in Table 10.14. The number of samples containing ketamine increased substantially between 2020 and 2023, with a subsequent reduction in 2024 and 2025. Most contained ketamine alone with a range in purity. Other active substances were detected in a minority of samples, including cocaine, MDMA, 2C-B, levamisole, caffeine and benzocaine. Additionally, 5 samples collected during 2024 contained xylazine.

Table 10.14: Project MANDRAKE data: numbers of samples containing ketamine or an analogue as the primary component, with or without adulterants, April 2019 to April 2025

Adulterant(s)	2019*	2020	2021	2022	2023	2024	2025*	Purity (w/w, primary component)
None	20	88	124	282	335	104	69	2.4 to 99.9%
2C-B + MDMA	0	0	0	0	0	0	1	21.0%
Benzocaine	0	0	0	0	1	0	0	18.4%
Caffeine	0	0	0	0	1	0	0	14.2%
Caffeine + paracetamol	0	0	0	0	0	0	1	5.9%
Cocaine	0	0	2	4	5	0	0	18.2 to 82.3%
Levamisole	0	0	0	2	0	0	0	52.3 to 78.6%
MDMA	0	0	1	0	1	4	0	27.4 to 57.1%
MDMA + Caffeine	0	0	0	0	1	0	0	39.4%
Xylazine	0	0	0	0	0	5	0	12.2 to 78.7%

*Part-year

10.28 Police Scotland's Statement of Opinion (STOP Unit) reported an increase in the recovery and identification of ketamine within the illicit drugs market during the start of 2025.

Wastewater sampling

10.29 The Home Office Wastewater Analysis Programme (WWAP) has taken samples from wastewater treatment plants (WWTPs) across England and Scotland since 2011, and these are used to calculate the quantity consumed of several key illicit drug types, including ketamine. Results are available from phase 2 of the programme (November

2023 to September 2024), involving wastewater sampling in England at 16 WWTPs, which cover 18% of the population. These data indicate that ketamine consumption increased by 85% comparing the first quarter of 2024 with the equivalent quarter in 2023, from a mean (95% confidence intervals) of 545 (128) to 1,008 (305) mg/1,000 people/day (Home Office, 2025b).

10.30 This increase could result from an increased number of users and/or in the amount used by each user. There will also be a small contribution from legitimately prescribed ketamine or esketamine, and this could increase in the future if ketamine and esketamine prescribing becomes more widespread. The latter cannot currently be differentiated from ketamine as the analysis does not involve chiral separation.

Drug treatment service data

10.31 The National Drug Treatment Monitoring system (NDTMS) is a database run by OHID that collects data on those in treatment in England (OHID, 2024). The data demonstrate an increase in the prevalence of reported ketamine use in recent years for all those in treatment and for new treatment entries (Table 10.15). The number of ketamine users starting treatment in the year ending March 2025 (5,365) was more than 12 times higher than it was in the year ending March 2015 (426) (OHID, 2025). Increases also apply to young people in treatment, where the prevalence is higher (OHID, 2024). It should be noted, however, that ketamine use disorders remain inadequately defined by currently used classifications, with neither ICD-11 or DSM-5 including ketamine-specific criteria for dependence, withdrawal or clinically relevant harm (Guerrini, 2025). Ketamine involvement may be underestimated as, like other drugs, it would not be captured if not listed as 1st, 2nd or 3rd drug in polysubstance users.

10.32 In Greater Manchester, 64% of people who use ketamine and were in treatment were under the age of 18 years, with 42% aged 13 to 16 years (ACMD, 2025c).

10.33 In Wales, the total number of assessments and treatments involving ketamine either as a primary drug or where there is any mention of ketamine have increased several fold over the last decade (Table 10.16). Between April 2022 and March 2025, 81 individuals accessing Needle Syringe Programme (NSP) services in Wales reported ketamine use within the previous 3-year period. Of these, 49 reported injecting (in the context of a needle/syringe exchange). There were 28 people who reported using once a day, 20 who reported using once/twice a month and 12 who reported using ketamine more than once a day.

10.34 PHS reported that there were 150 detections of ketamine in 11,854 urine samples collected by NHS Greater Glasgow and Clyde (NHSGGC) between 1 December 2023 (when testing started) and 31 December 2024. These samples were collected from people receiving drug treatment from NHSGGC and tested using mass spectrometry in their toxicology lab. It should also be noted that the UK clinical guidance does not recommend testing where a person has already disclosed details of drug use. These results are, therefore, not representative of drug use among the wider population of people with problem drug use, or among those receiving specialist drug treatment.

Table 10.15: Drug treatment for ketamine in adults and young people; new treatment entries and all in treatment, for ketamine Data from the NDTMS

	Years ending 31 March											
	2013-14	**2014-15**	**2015-16**	**2016**-17	**2017-18**	**2018-19**	**2019-20**	**2020-21**	**2021-22**	**2022-23**	**2023-24**	**2024-25**
All in treatment	1,632	1,030	863	1,073	1,136	1,388	1,660	2,070	2,334	3,041	4,838	7,366
% of total	*0.54%*	*0.35%*	*0.30%*	*0.38%*	*0.42%*	*0.52%*	*0.61%*	*0.75%*	*0.81%*	*1.05%*	*1.56%*	*2.23%*
New treatment entries	1,043	426	550	686	752	960	1,140	1,444	1,551	2,211	3,609	5,365
% of total	*0.71%*	*0.30%*	*0.40%*	*0.52%*	*0.59%*	*0.73%*	*0.86%*	*1.11%*	*1.16%*	*1.61%*	*2.27%*	*3.31%*
Young people (<18) in treatment	434	243	128	211	327	440	549	526	512	719	1,201	1,465
% of total	*2.01%*	*1.29%*	*0.73%*	*1.25%*	*2.06%*	*2.98%*	*3.84%*	*4.78%*	*4.52%*	*5.79%*	*8.37%*	*9.04%*
Young people (<18) - new treatment entries	297	99	98	160	249	338	388	333	335	560	917	1,054
% of total	*2.15%*	*0.76%*	*0.81%*	*1.37%*	*2.27%*	*3.27%*	*3.88%*	*4.79%*	*4.12%*	*6.27%*	*8.81%*	*8.91%%*

Table 10.16: Annual numbers of assessments and treatments for ketamine (both primary substance and any mention) for the years ending March 2015 to March 2025 taken from the Welsh National Database for Substance Misuse

Years ending 31 March	Primary substance ketamine		Any mention of ketamine		Total no of assessments	Total assessments (illicit drugs)	Total treatments	Total treatments (illicit drugs)
	No of assessments	No of treatments	No of assessments	No of treatments				
2015	21	17	56	48	23,312	10,409	18,891	8,649
2016	17	15	35	32	19,813	8,771	17,676	7,714
2017	22	19	59	52	19,274	9,242	17,270	8,355
2018	38	37	92	89	19,355	9,705	17,222	8,638
2019	46	43	124	116	19,969	9,970	17,732	8,905
2020	51	39	166	144	19,769	10,095	17,369	9,027
2021	87	77	181	156	18,675	9,275	16,022	8,053
2022	96	81	189	153	17,999	8,615	15,019	73,669
2023	170	151	274	234	17,562	7,825	15,743	6,626
2024	250	228	392	347	16,536	7,179	15,307	6,574
2025	333	302	486	439	16,574	7,627	15,105	6,900

Emergency department and poisons centre data

10.35 The National Poisons Information Service (NPIS) is commissioned by the UK Health Security Agency to provide information and clinical advice to UK health professionals managing patients who may have been exposed to potentially toxic substances, including drugs of misuse. In most cases, information is provided via an internet database available to registered healthcare professionals called TOXBASE®, but a 24/7 telephone enquiry line is available with consultant support for more complex cases or when TOXBASE® cannot be accessed. The number of accesses to TOXBASE® and NPIS telephone enquiries reflects (but does not measure directly) the frequency of contacts between health professionals and patients presenting following suspected exposures to different substances. Note that analytical confirmation of suspected exposures is rarely available.

10.36 There were 435 telephone enquiries involving 413 separate patients with reported recreational ketamine misuse for the calendar years 2014 to 2024, with annual numbers increasing from 14 in 2014 to 91 in 2024. This increase was particularly marked after 2020, and male patients predominated (269, 65.1%). The median patient age was 23 (IQR 19 to 28, range 12 to 64). Ketamine misuse was reported alone in 40%, with alcohol in 8% and with other substances of misuse in 52%, most frequently cocaine (18%), MDMA, (16%), cannabis, benzodiazepines (each 10%), nitrous oxide, amphetamines or pregabalin (each 2.4%). Duration of exposure was acute (less than 1 day, 71%), sub-acute (1 to 31 days, 6.1%), chronic (more than 1 month, 18%) and unknown (5.1%). Features frequently reported were reduced consciousness (19%), abdominal pain (15%), tachycardia (14%), agitation (9.4%), vomiting (8.7%) and coma (8.5%). Bladder or renal complications were documented in 35 (8.5%) patients, commonly involving renal impairment or acute kidney injury (2.9%), dysuria (7.9%), polyuria (1.0%), haematuria (1.0%), urinary incontinence (0.7%), urinary retention (0.5%) and ‘ketamine bladder’ (0.5%). Deranged liver function tests were documented in 4.1% patients. Seven deaths (4 female and 3 male) were reported, with 5 involving polysubstance use.

10.37 Annual numbers of accesses by health professionals to information about ketamine provided by the online poisons information database TOXBASE® (online or app version) has increased substantially from 2,111 in 2014 to 9,262 in 2024. While not all of these accesses may be made in the context of managing a person who has been exposed to ketamine, they are likely to reflect healthcare professionals coming into contact with those reporting exposure increasingly often.

10.38 The Identification of Novel Psychoactive Substances (IONA) study collected clinical data and analysed biological samples (blood and/or urine) from consenting patients attending 39 participating UK emergency departments with suspected toxicity due to substance use between March 2015 and March 2023. Over the 8 years of the study, samples from 1,815 patients were analysed and samples from 259 of these contained ketamine or a major metabolite. In 12 cases this could have arisen from ketamine administered by medical staff. The number of patients recruited differs from year to year, so this needs to be accounted for by dividing detection numbers by the number of patients to produce a detection rate. Detection rates have increased substantially between 2017 and 2023, with ketamine present in samples from about one-fifth of patients since 2020 (Table 10.17).

Table 10.17: Numbers and percentages of patients attending emergency departments with ketamine detected in at least one sample (data from the IONA study)

	2015[1]	2016	2017	2018	2019	2020	2021	2022	2023[2]
Ketamine detected*	4	9	8	20	23	40	50	69	24
% total	7	5	4	12	10	21	19	17	21
Total cases	56	179	225	170	221	193	262	396	113

[1] Partial year from March 2015; [2] Partial year to March 2023.

*12 Patients with therapeutic ketamine recorded as administered by medical staff have been excluded.

10.39 RADAR in Scotland reported ketamine use along with alcohol, benzodiazepines, heroin, powder and crack cocaine, synthetic cannabinoids, cannabis, synthetic opioids, 'lean' (codeine +/- promethazine), 2C-B, tuci or pink cocaine. Many reports concern a perceived increase in the prevalence of ketamine use, particularly among young people. There have been a few reports of ketamine use in prisons. Reports to RADAR describe ketamine use alongside powder cocaine called 'Calvin Klein', 'CK' or 'party-mix'. People report that ketamine takes the edge off the intensity of cocaine, and a pleasant effect is given through combining both. Crack cocaine and ketamine mixed for injecting has also been reported, called 'crunch'. Ketamine use among young people has been reported from multiple areas in Scotland, with concerns around perceived increasing prevalence. Multiple reports concerned young people taking ketamine and cocaine together, possibly as an alternative to taking ecstasy.

10.40 Adverse effects reported include non-fatal and fatal overdoses commonly in the context of polysubstance use, feeling sick and light-headed, collapse requiring ambulance call out, mouth ulcers and heart palpitations (after use of 'rhino ket'), amnesia and seizures. Concern about increasing urological issues seen in young people said to have taken ketamine has been raised by medical professionals. Adverse mental health effects have also been reported.

Involvement in drug-related deaths

10.41 Several datasets are available that record drug-related deaths. Data are collected separately in different devolved administrations, and the precise definitions of what constitutes a drug-related death may differ. Data on deaths in the same country may be available from more than one source and there may be overlap between cases included. It is not possible to remove this overlap as the data are fully anonymised. The possibility that ketamine detected in post-mortem samples arises from therapeutic ketamine administered prior to death cannot always be excluded.

England and Wales

10.42 The Office for National Statistics (ONS) has published the annual numbers of drug-related poisonings in England and Wales where ketamine is mentioned on the death

certificate for the years 2014 to 2023 in England and Wales. This also provided information on deaths by sex, age and region. There were 244 deaths where ketamine was mentioned, including 197 in males and 47 in females (Table 10.18). The age group most commonly affected was 25 to 29 years for both males and females, but deaths were also recorded for those aged as young as 15 to 19 (10 males, 5 females), and as old as 65 to 69 years (1 male). The number of deaths increased from 18 in 2014 to 53 in 2023 (Table 10.18) (ONS, 2025b). There has since been a further increase to 60 deaths in 2024 (ONS, 2025c). To put these data into perspective, the annual number of deaths registered in 2024 were 1,279 for cocaine and 78 for MDMA (ONS, 2025c).

10.43 A limitation in ONS analyses is that deaths due to specific substances cannot be identified where ambiguous causes of death are used (for example, multidrug toxicity, polydrug use). The ONS figures are therefore likely an underestimate of the true number of deaths associated with ketamine use.

10.44 ONS data on drug-related deaths in Wales have been provided separately. In none of the 20 deaths occurring between 2008 and 2023 in which ketamine was detected in toxicology samples was its sole use identified as the cause of death.

Scotland

10.45 PHS is provided with post-mortem toxicology testing data for deaths occurring in the west, east and parts of the north of Scotland by Forensic Medicine and Science at the University of Glasgow (for data up to 2022) and by the Scottish Police Authority Forensic Services (SPAFS). These data show increasing numbers of fatal cases where ketamine was detected since 2019 (Table 10.18).

10.46 The SPAFS provides a service that covers approximately 85 to 90% of Scottish casework and has also provided data on 514 deceased cases where ketamine was detected in at least 1 biological sample, with cocaine or its metabolite benzoylecgonine also present in 116 cases. Annual numbers of deaths involving ketamine have increased consistently from 3 in 2016 to 33 in 2024. It should be noted that this data set includes infants and the very elderly in whom ketamine is more likely to have arisen as a result of therapeutic use. Of the 514 fatalities where ketamine was detected (median age 44, range 1 to 99 years) there were 53 where no other substance of potential misuse was also present.

10.47 The National Records of Scotland (NRS) provided information about registered drug misuse deaths and drug poisoning deaths involving ketamine. Data on substances involved in the death are provided by forensic pathologists. Information on the drugs involved in the death are separated into those which were implicated in, or potentially contributed to, the cause of death and those which were present but were not considered to have had any direct contribution to the death. There were 91 such deaths (73 males, 18 females) registered between 2013 and 2023 (Table 10.18). Other substances were implicated in the cause of death in all but 2 cases and these included cocaine (40), benzodiazepines or related substances (40 cases, methadone (23 cases), pregabalin (22), heroin or morphine (26), codeine dihydrocodeine and/or co-codamol (17), alcohol (12), MDMA (8), amphetamine (8), gabapentin (7) and alcohol (3).

10.48 The EU-MADNESS project provided the number of drug poisoning deaths registered by the NRS where ketamine was listed by the pathologist as being implicated in death (alone or in combination) for the calendar years 2013 to 2024 (Table 10.18). Registrations for 2024 are provisional and subject to revision, probably upwards, so should be regarded as a minimum. As with the other data sets for deaths in Scotland, those involving ketamine increased substantially between 2013 and 2024.

10.49 From May to August 2024, a local group investigated deaths in Scotland where ketamine was suspected to have been involved. Key features of those experiencing harm included young people with diagnosed or non-diagnosed mental health conditions and regular use of ketamine while not in the company of other people.

Northern Ireland

10.50 The Northern Ireland Statistics and Research Agency (NISRA) provided details of deaths registered in Northern Ireland for the period 2013 to 2023 where ketamine was mentioned on the death certificate. Annual numbers of deaths are shown in Table 10.18, with the highest number occurring in 2023.

The National Programme on Substance Use Mortality

10.51 The National Programme on Substance Use Mortality (NPSUM) receives reports from approximately 90% of coroners in England, Wales and Northern Ireland on deaths related to drug use (KCL, 2025). It receives the full toxicology findings for these cases so is able to identify from the list of detected drugs which were involved in deaths (where ambiguous causes were cited by the coroner) and which drugs were deemed as incidental post-mortem findings. An advantage of NPSUM data is that it is possible to examine the other substances used in ketamine-related deaths, contextual details and demographic trends.

10.52 Since ketamine was classified as a Class B drug in 2014, the annual number of ketamine-related deaths has increased more than 10-fold from 15 in 2014 to a projected 197 in 2024. However, the proportion of deaths where the detected illicit ketamine was implicated in causing death declined over this period from 60% in 2014 to 43% in 2024, with detections deemed incidental findings concomitantly increasing (Figure 10.1), while polydrug use increased and the demographic profile of decedents shifted towards greater deprivation and dependence-related contexts (Pullen and others, 2025).

Table 10.18: Numbers of fatal cases involving ketamine in England and Wales (ONS data, NPSUM), Scotland (PHS, NRS, EU-MADNESS) and Northern Ireland

Source	Type of data	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
ONS	Drug poisoning deaths involving ketamine registered in England and Wales.[1]	N/A	18	7	12	14	26	21	27	33	33	53	N/A
NPSUM	Drug-related deaths reports made by coroners across most parts of England, Wales and Northern Ireland, but not Scotland	20	11	9	10	23	27	31	33	42	20	55	9
PHS	Ketamine detections in post-mortem toxicology testing[2]	0	0	0	0	0	0	51	44	39	62	106	112
SPA	All deceased where ketamine detected in at least one biological sample	14	32	24	25	33	36	50	45	38	50	81	86
SPA	All deceased where ketamine and cocaine/BZE were detected in at least one biological sample	0	0	0	3	5	4	9	10	10	14	28	53
EU-MADNESS	Number of drug poisoning deaths registered by the NRS where ketamine was listed by the pathologist as being implicated in death (alone or in combination).	0	1	1	1	2	5	8	8	11	9	17	23
NRS	Number of drug misuse deaths where substance was implicated in, or potentially contributed to, the cause of death (Scotland)	0	1	1	1	2	5	7	7	8	10	16	N/A
NISRA	Deaths recorded in Northern Ireland at time of registration. It is not clear if the main drug is only recorded if the drug is featured on death certificate,	1	1	1	0	0	2	1	2	1	1	5	N/A

[1] Deaths are recorded by year of registration rather than year of death. For example, many of the deaths registered in 2023 will have occurred in years *prior to 2023.*

[2]Data are for the whole of Scotland for 2022 and 2023. Prior to that, data for the far north and north-east of Scotland were not reported. This may contribute to the increase in numbers observed after 2022.

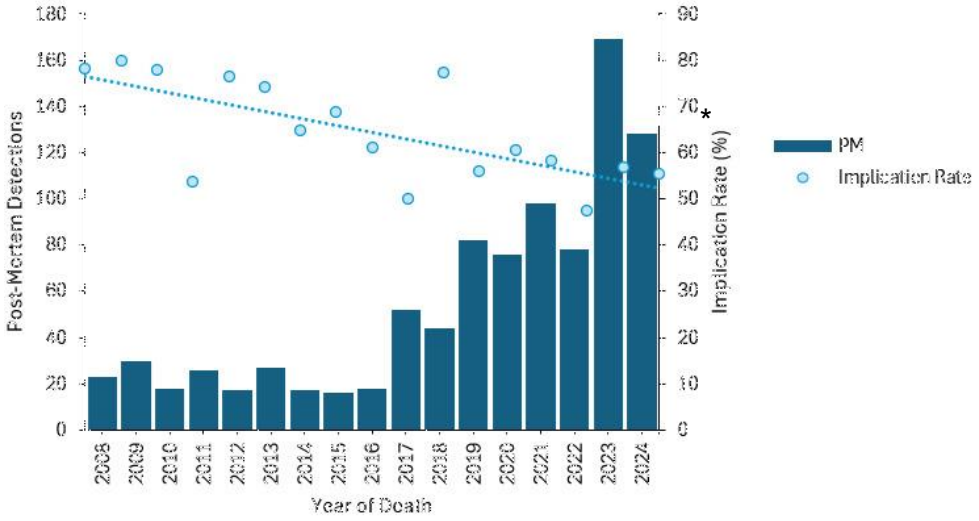
NRS data https://www.nrscotland.gov.uk/media/ei3fioso/drug-related-deaths-sub1-23.xlsx https://www.nrscotland.gov.uk/media/y1bpb5qw/drug-related-deaths-sub2-23.xlsx

10.53 The number of co-administered substances increased over time with a median of 3 substances detected at post-mortem for the period 1999 to 2005, rising to 6 substances between 2015 and 2024. The most commonly co-implicated substances were stimulants (in 46% of cases), especially cocaine (in 31% of cases), opioids (in 39% of cases) and heroin and/or morphine (in 22% of cases). Note that it is not always possible to distinguish between heroin and morphine at post-mortem as heroin is rapidly metabolised to morphine.

10.54 Death was deemed accidental in most cases (89%) with small proportions determined as suicides (10%; note: in line with the ONS definition, deaths concluded as open in those aged 15 and above are deemed suicides by NPSUM) or natural (1%). In deaths concluded as accidental and where the context in which the ketamine used was stated, the proportion of deaths which occurred in a recreational use context has declined over time, while those that occurred in a dependent use context increased (Table 10.19).

10.55 The NRS has reported the number of deaths where ketamine was an incidental finding at post-mortem and the number of deaths where it was deemed causative since 2008 (NRS, 2025). When combining NPSUM and NRS data to provide a UK picture, it is clear that deaths where ketamine was detected at post-mortem have increased; however, the proportion of deaths where ketamine was implicated in causing death has declined (Figure 10.1) (Pullen and others, 2025).

Figure 10.1. Annual numbers of deaths in which ketamine was detected at post-mortem and the proportion where ketamine was implicated in causing death.



*2024 data are incomplete: NRS data are only available for 2008 to 2023 at time of writing, and NPSUM data valid with cases received as of 1 March 2025, so further deaths are anticipated to be reported from 2024 following coronial inquest conclusion.

Table 10.19: Context of ketamine use associated with accidental death (data from NPSUM)

5-year range	Recreational use	Dependent use
2008 to 2012	56%	44%
2013 to 2017	39%	61%
2018 to 2022	15%	85%

10.56 Since the publication of previous NPSUM research examining ketamine deaths up to 2019 (Corkery and others, 2021), the median age at which people died has increased significantly (1999 to 2019: 32±10 years, 2020 to 2024: 34±11 years), although this still remains well below the NPSUM average age at death (41±13 years). Decedents who were white (97% of cases), male (84% of cases) and living with others (57% of cases) continued to predominate illicit ketamine deaths; however, the proportion of decedents in employment at the time of their death significantly decreased recently (1999 to 2019: 54%; 2020 to 2024: 42%; X^2 $p<0.05$) trending towards the NPSUM average (31%), while the proportion living in the most deprived areas of the countries increased (quintile 1 1999 to 2019: 26%; 2020 to 2024: 34%) also trending towards the NPSUM average (48%). A significantly greater proportion of decedents in 2020 to 2024 were known drug users (1999 to 2019, 79%; 2020 to 2024, 91%; X^2 $p<0.05$).

10.57 Taken together, while deaths following ketamine use have continued to increase, the context in which these deaths have occurred has changed. Polydrug use, particularly with Class A substances, in a dependent setting is increasingly common, with those dying often socially deprived, unemployed individuals who have an established drug dependence.

10.58 There have been several deaths worldwide involving the ketamine analogue 3-MeO-PCP, including one reported from the UK. (Copeland and others, 2022).

Summary of the mortality data

10.59 Overall, the data indicate that the annual incidence of deaths involving ketamine has increased across the UK in recent years and since it was controlled as a Class B compound in 2014. Deaths linked exclusively with ketamine, however, are uncommon, and other drugs or co-morbidities (for example, sepsis or liver damage) are commonly involved in those where ketamine is detected.

10.60 Data from NPSUM in particular show increasing numbers of deaths recently in the context of dependent (as opposed to recreational) use, with increased involvement of other substances and a higher proportion of those affected living in areas of social deprivation.

Annex 11. Education and harm reduction

Education and training

11.1 Education and training activities target groups of people who may use ketamine, or may consider using it, and those who may offer specialist and non-specialist support. The aim of these approaches is to provide information about ketamine, including in the context of other behaviours (for example, consent, mental health), skills development (such as professional skills, health literacy and self-efficacy), and support pathways (for example, sources of help; referral pathways). Education and training activities should also target parents and carers to increase their awareness of ketamine's effects and related risks, to promote open and non-judgemental communication with young people, and improve knowledge of available support services. Education and training often form part of prevention and harm reduction approaches (see below). Although young people aged 11 to 18 are typically thought to be the primary targets of drug education activities, ketamine use and harms occurs over a wide age range (see Section 10, ‘Prevalence of use and harms’) drug education and prevention activities are therefore relevant for both younger and older age groups.

11.2 ACMD is unaware of any evaluated drug prevention programmes that have reported positive outcomes on ketamine use, reflecting a lack of research on the topic, rather than ineffective programmes. The ACMD report on a whole-system approach to drug prevention (ACMD, 2025) describes the importance of both whole of school and whole of community approaches to prevention, which recognise the complex and multifaceted ways in which these shape the health and wellbeing of populations. This includes drug education as part of wider activities to improve multiple aspects of health and wellbeing. We are aware that some schools and other education providers have developed and deliver ketamine-specific content as part of drug education, especially where this has been identified as a specific issue for the school or local area. We were unable to assess how materials were developed or the quality of provision. Statutory school-based drug education should be delivered in accordance with the updated Relationships, Sex and Health Education (RSHE) guidance published by the Department for Education (DfE, 2025) or equivalent curricula in the devolved administrations.

11.3 Some universities have also introduced ketamine-specific information and harm reduction campaigns in response to concerns relating to ketamine use in the student body. These include activities performed by the University of the West of England (see below) and guidance made available by Newcastle University (NUSU, 2025). While we describe some of these approaches to illustrate the range of activities currently being delivered, these remain to be evaluated and so we are unable at present to recommend any particular approach.

Case study – Education for university students

In response to increasing student concerns about ketamine, an education campaign was launched by the University of the West of England (UWE) in 2025. UWE already has a partnership with a local drugs service (Bristol Drugs Project), which provides on-campus support. A data-gathering exercise was undertaken by canvassing students in person to identify the information and advice that they considered to be most useful, and a leaflet was produced based on this feedback. As a pilot, copies were printed and distributed at on-demand drug awareness workshops and in 5 student accommodation awareness workshops. UWE reports high demand for the materials from students. Ketamine education endorsed by Avon and Somerset Police is also delivered to students who are caught using ketamine as a diversionary alternative to a police referral.

A further harm reduction and signposting campaign will be launched in the 2025 to 2026 academic year, in addition to continuing availability of the ketamine leaflets, with posters on cubicle doors of public toilets on campus. This will include a QR code for those who want to find out more, which links to information and advice on the UWE website. There will also be a 1-hour ketamine workshop provided at the start of term to complement the campaign, open to all students and staff.

11.4 The government has recently launched a scheme to alert young people in particular to the dangers of using certain drugs, including ketamine. This includes online films, clips from influencers and fact sheets, and targets those aged 16 to 24 and social media users (DHSC, 2025).

11.5 The first point of contact between someone with concerns or problems with ketamine might not be a specialist professional or service. This might be a family member, educator, or other trusted figure. Resources and guidance for these groups should raise awareness of ketamine, and provide basic information about drug effects, risks and sources of support. Regardless of the drug of concern, materials and support for non-specialists should include advice on how to initiate conversations, active listening, and how to provide support without judgement (ACMD, 2025a). Conversations about drugs might also be in the context of risk-taking and safety more generally, and signposting to more specialised support. Information available through the Talk to Frank, DAN 24/7 and Know the Score websites are a useful starting point, although some local areas have now begun to produce their own materials about ketamine.

11.6 Training needs have also been highlighted for healthcare professionals that may encounter individuals experiencing bladder-related issues or unexplained abdominal pain, including general practitioners, nurses, emergency medical staff, urologists and community pharmacists. Stakeholders have reported a lack of knowledge among NHS staff about ketamine and its harms, especially within primary care, leading to poor history, multiple misdiagnoses and inappropriate referrals (ACMD, 2025c). Gill and others (2018) also note that if treatment is sought, a poor understanding of drug-related issues from medical professionals can result in misdiagnosis and recurrent patient dismissal. This was reinforced in the lived experience of people who use

ketamine (Ralphs and others, 2024), with a clear message from those experiencing harm that improved training was needed (Harding and others, 2025), including an understanding that the specific needs of ketamine patients may result in missed appointments and cases consequently being closed. Practitioners in primary care and mental health services should also be aware of the possibility of ketamine use in patients presenting with depression (Abdulrahim and Bowden-Jones, 2015; Morgan and others, 2010) or memory loss (Barrios and others, 2024), with ketamine both being a possible cause and also a substance that can be used to self-medicate for pre-existing mental ill health or past trauma (Ralphs and others, 2024).

11.7 Since the publication of the 2013 ACMD ketamine review, changes in regulations mean that community pharmacists across the UK are now authorised to prescribe antibiotics for uncomplicated urinary tract infections (in 2017 in Scotland, 2023 in Northern Ireland and 2024 in England and Wales), increasing their need for training to recognise and manage patients with ketamine use disorders, including related harms such as bladder toxicity as well as support with withdrawal symptoms.

Harm reduction

11.8 Limited research has been undertaken on effective harm reduction responses to ketamine use. However, available evidence, and evidence on drugs harm reduction more generally, can underpin responses.

11.9 Although the scale and burden of ketamine-related harms have increased, harm reduction recommendations included in ACMD's 2013 ketamine report remain relevant. These stated that effective ketamine harm reduction and harm prevention strategies should aim to delay age of initiation, reduce frequency and dose per episode, prevent escalation to injection, and encourage cessation where appropriate. A key component of ketamine harm reduction education is raising awareness of the potential long-term physical harms associated with heavy and frequent ketamine use, in particular the early signs of bladder and urinary tract damage (pain, frequent urination or incontinence). Self-treatment and coping strategies to reduce pain, such as prolonged bathing while intoxicated or use of opioid analgesics, may increase risk of harm. Providing information on where to get appropriate support at early signs of harm is critical.

11.10 Harm reduction education should also extend to primary care providers and frontline professionals, who should be trained to identify signs of ketamine use and offer non-judgemental, evidence-based advice tailored to the individual's needs, particularly for higher-risk groups such as young people, and GBMSM.

11.11 Since 2013, a few studies and reports have examined ketamine harm reduction strategies, and their relation to risk behaviour and harm (for example, Vidal Giné and others, 2016; Pavarin and others, 2024). These have identified several harm reduction strategies associated with lower risk and harm.

11.12 Strategies that may reduce ketamine harm include spacing out use sessions, pre-setting a dose limit prior to a use episode, having a sober person present during sessions, and ensuring adequate hydration. In one survey-based study (Vidal Giné and others, 2016), adoption of ketamine frequency and dose reduction strategies

was significantly associated with lower mood, cognitive and behavioural problems; reduced psychological dependence; fewer adverse impacts on relationships, work or studies; and a lower need for acute emergency medical care or treatment. Importantly, avoiding mixing ketamine with other drugs was associated with significantly lower rates of self-reported bladder-related problems (such as cystitis), abdominal pain and other negative physical health outcomes. However, other research has suggested that only complete cessation of ketamine use was associated with reduced abdominal pain (Hong and others, 2018).

11.13 Recently published guidance from the UK treatment provider Change Grow Live (CGL) summarises key harm reduction practices to help mitigate risks associated with ketamine use (McVeigh and Welch, 2025) and ACMD supports this advice. The report recommends that people using ketamine should be encouraged to start with small test doses and pre-measured amounts (for example, in milligrams) to avoid estimating doses and inadvertently over-consuming while intoxicated. This is also supported by the earlier NEPTUNE NPS and club drug guidance (Abdulrahim and Bowden-Jones, 2015). People should be encouraged not to use ketamine alone, and to space out both individual doses and the frequency of use episodes, ideally limiting sessions to at least every 4 weeks, to prevent rapid tolerance and dependence (also see GDS, 2025). Finely chopping ketamine powder may improve nasal absorption and reduce nasal damage, and rinsing the nasal cavity after use is advised. However, the benefits of spitting out the ‘drip’ (mixture of mucous and ketamine powder that might be lodged at the back of the throat) to prevent gastrointestinal issues (K-cramps) remains largely anecdotal.

11.14 Injection of ketamine is relatively uncommon, but in keeping with NICE guidance on needle and syringe programmes (NSPs) (NICE, 2014), those doing this are advised to dissolve the drug in sterile water (for ketamine powder), and access sterile injecting equipment through NSPs to reduce the risk of blood-borne virus infections. New sterile equipment should be used for each use episode. To prevent infection, injecting equipment (including equipment used for drug preparation for injection) should not be shared. People choosing to inject ketamine should be encouraged to get tested for blood-borne viruses such as Hepatitis C and HIV. NSP services can also provide naloxone and naloxone training.

11.15 Considering the role of concomitant polysubstance use in ketamine-related deaths (Corkery and others, 2021), people using ketamine should be advised to avoid combining it with other drugs, particularly depressants such as alcohol, opioids or benzodiazepines, as these significantly increase the risk of overdose.

11.16 Although the average frequency of drug use across the population of people is infrequent (monthly or less) (ONS 2024), individual use episodes can still be associated with harm. As ketamine causes cognitive and psychomotor impairment, harm (including harms to others) has resulted from falls, violence perpetration and victimisation, and road traffic accidents. Acute ketamine intoxication may impair decision making, and the ability to consent to sexual activity. Deaths associated with ketamine use have been associated with external factors such as drowning (including in the bath), hypothermia, road traffic collisions, and falls from heights. Harm reduction advice should therefore extend to environments and settings of use, and co-occurring behaviours.

11.17 As with the purchase of all drugs from the illicit market, harms may arise through mis-selling of ketamine, inconsistent purity and/or accidental/deliberate adulteration of products (Europol, 2024). As described in Section 5 ‘Misuse’, street-submitted ketamine samples analysed by MANDRAKE in Greater Manchester indicate mean purity of 57% (range 14 to 99%). Currently (as of January 2026), there is no consistent evidence of systematic mis-selling or contamination of ketamine in the UK. Since the beginning of 2025, WEDINOS has reported that drugs purchased as cocaine, MDMA, amphetamine, 2-CB, 2-Fluorodeschloroketamine, 2-Methylmethcathinone, Xanax, clonazepam, diazepam and cannabis have been found to contain ketamine. Conversely, all samples purchased as ketamine have been found to contain ketamine upon analysis without the presence of other drugs of concern. However, one ketamine sample analysed by MANDRAKE in Manchester contained xylazine (analysed in June 2024), and in November 2024, the Victoria Department of Health identified protonitazene mis-sold as ketamine in Melbourne, Australia.

11.18 There is currently very limited public access to formal drug checking services in the UK, and the utility and effectiveness of ketamine reagent kits and testing strips is currently unknown. People who are considering using ketamine should be advised that it is not possible to identify drug content simply through inspection of dosage form, and that similar looking products may contain different drugs or purities. However, caution is warranted if the colour, smell, taste or consistency of a drug preparation is different to what has been encountered before. With the emergence of potent novel synthetic opioids in the UK illicit drugs market (ACMD, 2022), people using drugs or likely to encounter drug use should be advised about the availability and administration of naloxone, and how to respond to a drug overdose.

Annex 12. Consideration of reclassification of ketamine

12.1 While there is a large body of work that has examined the effectiveness of punishment of drug offences, including increasing or repealing punishments (Babor and others, 2018), it is beyond the scope of this report to review this here. Instead, we summarise key considerations from the literature in relation to the potential effects of reclassification on demand, supply and the harms of ketamine.

12.2 While the text of the Misuse of Drugs Act 1971 (MDA) does not specifically explain the purpose of the classification system, it is commonly understood that drugs are classified based on their potential for harm to individuals and/or society (House of Commons, 2006; Home Office, 2025c). Classification determines the maximum penalties available to courts for offences under Section 4 of the MDA, with offences involving drugs in Class A having the most serious legal consequences (Duddy and Downs, 2024).

12.3 The ACMD Standard Operating Procedure (2024) specifies options for control of substances following a harms assessment. Where a recommendation for classification is given, placement into Class A, B, or C is not based on thresholds of absolute harm, but on relative harm to individuals and/or wider society. Recommendations for Class A are typically for those substances that have the greatest risk of harm to individuals and/or wider society; Class B for substances that have a lower associated risk of harm to individuals and/or wider society than substances in Class A; and Class C for those substances that have the lowest associated risk of harm to individuals and/or wider society than substances classified under Class A or Class B.

12.4 As no harm thresholds exist to determine classification, recommendations can be made based on structural or pharmacological similarities to substances that have already been controlled, or because the harms of substances under review are considered comparable to other drugs in the class. This can also include potential harm, where there is currently no evidence of significant use. Due to historical classification decisions, drugs within the same classification band may not always be comparable in harms or may not have been subject to a review of harms.

12.5 Although other considerations will come into play, for substances such as ketamine that are already classified, reclassification is likely to reflect a judgement that the threat the drug poses has changed, either due to changes in levels of use (either within the UK or internationally), health and social harms associated with its use, or both (House of Commons, 2006).

12.6 Reclassification may be recommended by ACMD if an (updated) assessment suggests that a substance's harms are comparable to other substances in that class. Reclassification therefore does not necessarily have to be justified on the basis that it will reduce harm. The final decision on legislative change is for the government to make and this may consider a wider range of factors beyond ACMD's remit (ACMD, 2024).

12.7 With respect to the current Ministerial Commission, the objective of reclassification upwards (for example, from Class B to A) would be to (potentially) reduce harm by curbing both demand and supply. To understand if and how reclassification might achieve this goal, it is useful to identify putative mechanisms linking legal change with harm. It should be noted that while there is a body of informative research that has examined mechanisms after reduction or elimination of legal penalties (for example, decriminalisation of possession offences (Stevens and others, 2022)), no similar body of work has examined the mechanisms of increasing sanctions/ punishments.

12.8 Reclassification to Class A would increase the penalties available to courts for supply or possession with intent to supply offences. Guidance from the Sentencing Council specifies that the starting point for conviction for a 'significant role' in a Class B Category 3 supply offence (for ketamine, this would be more than 5 g but less than 150 g, an amount typically associated with 'street-level' supply), is a one-year custodial sentence, which is often suspended in practice (Sentencing Council, 2021). For a Category 4 supply offence (more than 5 g, typically associated with 'personal' supply), the starting point is a high-level community order.

12.9 These sentences would increase significantly for Class A drugs within the same category (assuming sentencing guidance on the weight of products within each category did not change with reclassification). For a Category 3 offence, the starting point increases to 4.5 years, and for a Category 4 offence, 3.5 years.

12.10 Similarly, starting points for custodial sentences for higher weight supply of Class A drugs (Category 2 offences begin at more than 1 kg ketamine) are much higher than for Class B. For example, custodial sentences after conviction for supply of ketamine amounts of 1 to 5 kg begin at 4 years for a Class B drug, but would be 8 years if it were a Class A drug.

12.11 The increased legal and financial risks associated with supplying a Class A drug may therefore deter people from commencing supply offences. It may lead to an increase in resources for law enforcement that might result in more targeted operations, enhanced surveillance, and greater international cooperation, further increasing risk to suppliers. These actions could help disrupt supply chains and reduce the availability of ketamine. However, there is currently little evidence to support deterrent effects of arrest and drug seizures on drug crime and associated harms (Eggins and others, 2020; Home Office, 2025a). Disruption of local Class A drug markets tends to be short-lived, with markets rebounding back. This is partly due to the large profits generated, and because 'risk premiums' are factored into their operation (Black, 2020; Salinas, 2023). We also note the overall robustness of global drug markets, and the continued availability and affordability of drugs despite recent major geopolitical and pandemic events, and (inter)national law enforcement activity (Europol, 2024; Home Office, 2025a; UNODC, 2024; 2025).

12.12 Sentences available for simple possession offences are not determined by drug weight (Sentencing Council, 2021). The starting point for a Class B drug possession offence is a Band B fine (75 to 125% of relevant weekly income), with the maximum sentence available being 26 weeks custody. For Class A possession offences, this

increases to a starting point of a Class C fine (125 to 175% of relevant weekly income), with a maximum sentence available of 51 weeks custody.

12.13 Regarding demand, stricter penalties such as longer prison sentences and larger fines may have a deterrent effect that discourages individuals from using ketamine. However, this relies on knowledge of the specific penalties, and perceptions of the certainty and severity of punishment (Kleiman, 2009). We are unaware of recent UK studies on public awareness of the penalties associated with drug offences or perceptions of certainty of punishment if an offence has been committed.

12.14 For context, there were 137,262 drug possession offences (all classes) recorded by police in 2024 to 2025 in England and Wales (ONS, 2025), and 22,649 conviction outcomes were recorded in calendar year 2024 (Ministry of Justice, 2025). Of these outcomes, 9,287 were for Class A drugs (most frequently cocaine), 12,927 for Class B drugs (most frequently cannabis), and 435 for Class C drugs. No data were available for possession offences recorded for repeat offenders. This suggests that only a small proportion of the estimated 2.7 million people in England and Wales (aged 16 to 59) who reported using a controlled drug in the year ending March 2024, will come to the attention of the police, which may influence perceptions of the certainty of punishment.

12.15 As there is currently no field test for ketamine powders, and it has a similar appearance to many other Class A drug powders, the likelihood of arrest for possession offences would be largely unchanged if ketamine was reclassified. Upon discovery of the drug, police would decide whether to arrest depending on other factors, including whether the person had previous convictions or there were other offences present. One reason that people found in possession of Class A drugs such as heroin or cocaine are more likely to be arrested, is because of their offending history, rather than field identification of the drug. Hence, reclassification may not increase the certainty of punishment (or in this example, arrest).

12.16 Regarding severity of punishment, of the 8,936 sentences for Class A drug possession offences recorded in England and Wales in 2024, 5.4% resulted in custody, with a mean sentence length of 4.2 months and a mean fine of £164 (Ministry of Justice, 2025). Custody rates ranged from 3.5% for MDMA possession to 7.7% for heroin possession. For non-cannabis Class B drugs, the custody rate was 4.3%. Mean fines ranged from £115 for possession of heroin to £212 for MDMA, and £114 for non-cannabis Class B drugs.

12.17 The impact of a drug possession conviction on an individual can be significant, irrespective of classification. Early contact with the criminal justice system, including first arrest, may deter some people or provide opportunities for intervention. For others, however, even minor contact can increase the risk of re-offending, and have negative effects on health and future prospects, including education, employment and travel (Bretteville-Jensen and others, 2017; Sandøy and others, 2022). Criminal justice contact can erode important social relationships (for example, family, educational organisations) that are themselves protective against future drug harms, and can lead to further marginalisation, especially of more vulnerable young people (Moskalewicz and others, 2021).

12.18 There has been increased use of non-custodial and out-of-court disposals across many police force areas in response to drug possession offences, including for Class A drugs (Duddy and Downs, 2024). This includes the use of cautions (including conditional cautions), community resolutions, deferred prosecutions, and taking no further action where a diversionary activity is offered as an alternative. Drug possession offences are the largest contributing offence group for out-of-court disposals, accounting for around a third of the total (Ministry of Justice, 2025). This means that detection of a Class A possession offence may not necessarily lead to a more severe punishment compared to a Class B substance. However, the lack of national guidance, and the non-statutory status of disposals means that the availability and application of these alternatives is not consistent across the UK and can be offered at the discretion of attending officers.

12.19 In YouGov polling conducted with the public in Great Britain in 2022, most respondents (79%) who had never taken drugs reported this was because they were not interested in taking them (YouGov, 2022). Among the other most frequently reported reasons for non-use, 38% reported that they were afraid of drug effects, 33% because drugs were illegal, 21% that they thought use was morally wrong, and 12% were afraid of getting caught by the police. No data were presented on potential deterrent effects on future use in those reporting previous drug use. Although not asking about reclassification, an earlier poll (YouGov, 2021), suggested that 60% of British respondents thought that making a drug illegal was ‘ineffective in preventing people from taking it’ (24% Effective; 16% Don't know).

12.20 Reclassification upward may trigger public health messaging and increased media attention (as was seen when gamma hydroxybutyrate (GHB) was reclassified to Class B in 2022). This may help to raise awareness of the risks associated with ketamine use. This could help to encourage those currently using ketamine to stop or to seek support, and/or deter other people from starting use. However, there is nothing currently preventing such messaging from taking place, and submissions to our call for evidence suggest that relevant action is already taking place at a local level.

12.21 On the relationship between risk perceptions and drug use, cross-sectional and longitudinal studies have found bi-directional relationships, albeit weak, between lower-risk perceptions and greater experience with substances (for example, Grevenstein and others, 2014; Salloum and others, 2018; Wang and others, 2025). In contrast, there is a lack of research examining the relationship between legal classification of drugs and risk/harm perceptions, with the only UK studies on the topic finding no correlation (Morgan and others, 2010; 2013). Increased public recognition of ketamine as a Class A substance may affect its social acceptability ('send a message'), potentially aligning it with other Class A drugs such as heroin and crack cocaine that are subject to more social disapproval (Scottish Government, 2016), rather than with more accepted Class B drugs such as cannabis (Savonen and others, 2023). This shift in perception may help to reduce its appeal, particularly among younger people. However, researchers have cautioned that social disapproval, however well-intentioned, may lead to stigmatisation of people who use such drugs, which can have significant negative impacts on help-seeking, and care outcomes (Lancaster and others, 2017; Morris and others, 2024). We also note that the CSEW reports that last year prevalence (2023 to 2024) in 16 to 24-year-olds of

the Class A drugs ecstasy (2.2%), powder cocaine (3.8%), and 'magic mushrooms' (2.3%) are comparable to ketamine (2.9%), suggesting a complex relationship between classification, social acceptability and population prevalence.

12.22 Overall, there has been little robust research, and none from the UK, on the relationship between changes in legal sanctions (such as reclassification) and drug use prevalence and harms. Previous studies have primarily examined cannabis use in North America, Australia and the EU, and the removal of punitive sanctions (for example, decriminalisation, legal regulation) rather than changes in the severity of sanctions. These studies have reported mixed findings, leading to the conclusion that changes in sanctions do not have a direct impact upon prevalence of use (Hall and others, 2023; Hughes and others, 2018; Home Office, 2014; Babor and others, 2018). Trends in drug use and related harms are driven by a complex set of factors, which may include (changes in) legal status, but isolating these effects is challenging (ACMD, 2018; Nawi and others, 2021). If increasing legal sanctions did deter the onset or escalation of use, then preventative effects, particularly of heavier and more harmful use, may take many years to manifest (Babor and others, 2018).

12.23 In its 2025 advice on reclassification of synthetic cathinones, ACMD recommended that despite increased evidence of harm, pyrrolidino-cathinones (including drugs colloquially known as 'monkey dust') should remain Class B. The justification for this was ACMD's view that the “disadvantages of reclassification outweighed any possible advantages” (ACMD, 2025b). Disadvantages included concerns about increasing the stigma and social exclusion of people who used these drugs, and that harms were best addressed through public health interventions rather than the criminal justice system.

12.24 The size of the market of the synthetic cathinones under review, and the population affected by its harms, was estimated to be small and localised to North Staffordshire and its environs (ACMD, 2025b). The people primarily affected by harm were characterised as having multiple and complex needs, including serious mental health conditions and homelessness. Hence, ACMD was concerned that reclassification might increase barriers to support. As discussed above, it was acknowledged that the more severe sentences available for possession and supply offences for Class A compared with Class B drugs may not have sufficient additional deterrent effect on criminal enterprise. It was also acknowledged that reclassification to Class A would have provided greater sentencing powers for courts, which might increase the deterrent effects for (potential) offenders. However, with respect to suggestions that higher classification under the MDA 1971 would increase the priority for action by police and Border Force, it was clarified that drug class was only one component of threat prioritisation using the Management of Risk in Law Enforcement (MoRILE) tool, and that other considerations such as the scale of harm were also important. It was the view of ACMD that reclassification “…would not necessarily increase the priority for action by police forces, especially in places where use of reclassified compounds was not common” (ACMD, 2025b).

12.25 In contrast to synthetic cathinones, use of ketamine is of national (and international) concern, the market is larger, and both the general population and higher-risk groups are affected by its harms. Reclassification may therefore trigger increased law enforcement activity due to the larger scale of the threat. However, as with the

synthetic cathinones, concerns remain about increased stigmatisation of people experiencing ketamine harms. Considering its use across the general population, not all people using ketamine would be considered vulnerable or at higher risk of harm, but evidence submitted by stakeholders for this review suggests that people experiencing harm also frequently report other vulnerabilities including mental ill health, neurodiversity, childhood trauma and family disruption, educational non-attendance and exclusion, and criminal exploitation. As with the synthetic cathinones, it is therefore vital that if ketamine is reclassified, it does not increase barriers to support through fear of criminalisation and stigma.

12.26 In its 2013 report on ketamine, ACMD advised that ketamine should be reclassified to a Class B (Schedule 2) substance. The report also made recommendations designed to improve understanding of ketamine use in the UK and to reduce harms. These included research on the incidence of bladder damage, and long-term psychological and psychiatric impacts. Service and practice recommendations included guidance and training for healthcare practitioners on early identification of harms; harm reduction advice for people using ketamine (see Section 11, 'Education, training and harm reduction'); and the development of services for people with ketamine use disorders or urological problems. All recommendations were accepted by the government in its formal response to ACMD's advice (Home Office, 2014). However, it is unclear whether these were subsequently enacted.

12.27 In conclusion, it is possible that reclassifying ketamine as a Class A drug may reduce harm via a reduction in demand and supply through the mechanisms outlined above. However, there is currently a lack of evidence to support this. It is our view that regardless of classification decisions, comprehensive public health strategies, including education, prevention, mental health support, treatment and harm reduction services, remain the most effective means to address the harms of ketamine use to individuals and society.

Annex 13: Current and proposed generic text

Current generic text (Schedule 2, Part 2 (Class B drugs), para 1(d) of the MDA)

"1-Phenylcyclohexylamine or any compound (not being ketamine, tiletamine or a compound for the time being specified in paragraph 1(a) of Part 1 of this Schedule) structurally derived from 1-phenylcyclohexylamine or 2-amino-2-phenylcyclohexanone by modification in any of the following ways, that is to say,

(i) by substitution at the nitrogen atom to any extent by alkyl, alkenyl or hydroxyalkyl groups, or replacement of the amino group with a 1-piperidyl, 1-pyrrolidyl or 1-azepyl group, whether or not the nitrogen containing ring is further substituted by one or more alkyl groups;

(ii) by substitution in the phenyl ring to any extent by amino, alkyl, hydroxy (see Note below), alkoxy or halide substituents, whether or not further substituted in the phenyl ring to any extent;

(iii) by substitution in the cyclohexyl or cyclohexanone ring by one or more alkyl substituents;

(iv) by replacement of the phenyl ring with a thienyl ring."

(Note: Para 2A then invokes the 'esters and ethers' clause for any such compounds containing an hydroxy group)

Proposed revised generic text (subject to consultation, change shown in bold underlined)

"1-Phenyl, cyclohexylamine or any compound (not being ketamine, tiletamine or a compound for the time being specified in paragraph 1(a) of Part 1 of this Schedule) structurally derived from 1-phenylcyclohexylamine or 2-amino-2-phenylcyclohexanone by modification in any of the following ways, that is to say,

(i) by substitution at the nitrogen atom to any extent by alkyl, alkenyl or hydroxyalkyl groups, or replacement of the amino group with a 1-piperidyl, 1-pyrrolidyl, ***1-azetidyl or 4-morpholino group****, whether or not the nitrogen containing ring is further substituted by one or more alkyl groups;*

(ii) by substitution in the phenyl ring to any extent by amino, alkyl, hydroxy (see Note below), alkoxy or halide substituents, whether or not further substituted in the phenyl ring to any extent;

(iii) by substitution in the cyclohexyl or cyclohexanone ring by one or more alkyl substituents;

(iv) by replacement of the phenyl ring with a thienyl ring.

Annex 14: List of abbreviations used in this report

ACMD	Advisory Council on the Misuse of Drugs
ADHD	Attention-deficit/hyperactivity disorder
BDNF	Brain-derived neurotrophic factor
BSAVA	British Small Animal Veterinary Association
CBD	Common bile duct
CD	Controlled drugs
CDAO	Controlled Drugs Accountable Officers
CGL	Change, grow, live
CND	Commission on Narcotic Drugs
CSEW	Crime Survey for England and Wales
DAMGO	(D-Ala2,*N*-Me-Phe4,Gly5-ol)-enkephalin
DAT	Dopamine transporter
DEA	Drug Enforcement Administration
DFLU	Drugs and Firearms Licensing Unit
DHNK	Dehydronorketamine
DHSC	Department of Health and Social Care
DPH	Diphenhydramine
DSM	Diagnostic and Statistical Manual of Mental Disorders
ECDD	Expert Committee on Drug Dependence
ECT	Electroconvulsive therapy
EMC	Electronic Medicines Compendium
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
EMT	Epithelial-mesenchymal transition
ESRC	Economic and Social Research Council
EUDA	European Union Drugs Agency
EU-MADNESS	EUropean-wide, Monitoring, Analysis and Knowledge Dissemination on Novel/Emerging pSychoactiveS
Euro-DEN	European Drug Emergencies network
FDCK	Fluorodeschloroketamine
GBMSM	Gay, bisexual and other men who have sex with men
GHB	Gamma hydroxybutyrate
GMC	General Medical Council
GPhC	General Pharmaceutical Council
HMPPS	HM Prison and Probation Service
IONA	Identification of Novel Psychoactive Substances
IUPAC	International Union of Pure and Applied Chemistry
IM	Intramuscular
IV	Intravenously
KUD	Ketamine use disorder

LIN	Local intelligence network
LUTS	Lower urinary tract symptoms
MANDRAKE	Manchester Drug Analysis and Knowledge Exchange
MDA	Misuse of Drugs Act 1971
MDD	Major depressive disorder
MDMA	Methylenedioxymethamphetamine
MDR	Misuse of Drugs Regulations 2001
MHRA	Medicines and Healthcare products Regulatory Agency
MOR	Mu opioid receptor
mTOR	Mammalian Target of Rapamycin
MXE	Methoxetamine
MXP	Methoxphenidine
NACPO	National Association of Chief Police Officers
NCA	National Crime Agency
NDTMS	National Drug Treatment Monitoring System
NET	Norepinephrine transporter
NMDAR	*N*-methyl-D-aspartate receptor
NHSGGC	NHS Greater Glasgow and Clyde
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NISRA	Northern Ireland Statistics and Research Agency
NMC	Nursing and Midwifery Council
NMDAR	*N*-methyl-D-aspartic acid receptor
NPIS	National Poisons Information Service
NPS	Novel Psychoactive Substances
NPSUM	National Programme on Substance Use Mortality
NRS	National Records of Scotland
OCG	Organised crime groups
OHID	Office for Health Improvement and Disparities
ONS	Office for National Statistics
PCA	1-Phenylcyclohexan-1-amine
PCP	Phencyclidine
PHS	Public Health Scotland
PSA	Psychoactive Substances Act 2016
PTSD	Post-traumatic stress disorder
QR code	Quick response code
RADAR	Rapid Action Drug Alerts and Response
RCT	Randomised controlled trial
RCVS	Royal College of Veterinary Surgeons
RSHE	Relationships, Sex and Health Education
SALSUS	Scottish Schools Adolescent Lifestyle and Substance Use Survey
SERT	Serotonin transporter

SMC	Scottish Medicines Consortium
SPA	Scottish Police Authority
SPAFS	Scottish Police Authority Forensic Services
TRD	Treatment-resistant depression
UKRI	UK Research and Innovation
UN	United Nations
UNCND	United Nations Commission on Narcotic Drugs
UNODC	United Nations Office on Drugs and Crime
US	United States
VMR	Veterinary Medicines Regulations
WEDINOS	Welsh Emerging Drug and Identification of Novel Substances
WHO	World Health Organization
WWAP	Wastewater Analysis Programme
WWTP	Wastewater treatment plants

Annex 15: Chair and members of ACMD Ketamine Working Group

Chair of Working Group	
Professor Simon Thomas	Emeritus Professor of Clinical Pharmacology and Therapeutics, Newcastle University
Members of Working Group	
Dr Caroline Copeland	Senior Lecturer in Pharmacology and Toxicology, King's College London. Director, National Programme on Substance Use Mortality
Professor Colin Davidson	Professor of Neuropharmacology, University of Central Lancashire
Mohammed Fessal	Chief Pharmacist, Change Grow Live
Professor Amira Guirguis	Professor of Pharmacy, MPharm Programme Director and Deputy Pro Vice Chancellor at Swansea University Chief Scientist at the Royal Pharmaceutical Society
Jason Harwin	Director and co-founder of E-T-E Solutions Limited
Professor Katy Holloway	Professor of Criminology, University of South Wales
Professor Sunjeev Kamboj	Professor of translational clinical psychology at University College London and an honorary consultant clinical psychologist in the North London Foundation NHS Trust
Professor Roger Knaggs	Professor in Pain Management and Clinical Pharmacy Practice, University of Nottingham
Dr Lorna Nisbet	Principal Investigator for Forensic Toxicology at the Leverhulme Research Centre for Forensic Science, University of Dundee
Jon Privett	Detective Sergeant and Expert Witness in Drug Trafficking, Metropolitan Police Service

Fiona Spargo-Mabbs	Director and Founder, Daniel Spargo-Mabbs Foundation; Chair, Drug Education Forum
Dr Richard Stevenson	Emergency Medicine Consultant, Glasgow Royal Infirmary
Professor Harry Sumnall	Professor in Substance Use, Liverpool John Moores University (LJMU)
Professor David Wood	Professor of Clinical Toxicology and Consultant Physician, Guy's and St Thomas' NHS Foundation Trust, King's Health Partners and King's College London
****Professor Paul Dargan**	Professor of Clinical Toxicology at King's College London and consultant physician and clinical toxicologist at Guy's and St Thomas' NHS Foundation Trust
****Professor Emma Robinson**	Professor of Psychopharmacology, University of Bristol
****Dr Arun Sahai**	Consultant Urological Surgeon in Functional Urology at Guy's and St Thomas' Hospital
****Dr Devjit Srivastava**	Consultant in Anaesthesia and Pain Medicine, Raigmore Hospital, Inverness, NHS Highland
****Dr Heilin-Anne Leonard-Pugh**	Veterinary Surgeon and Veterinary Efficacy Assessor at the Veterinary Medicines Directorate
****Dr Lisa Lione**	Associate Professor in Translational Pharmacology, University of Hertfordshire
****Dr Rupert McShane**	Associate Professor at University of Oxford and Consultant Psychiatrist in Treatment-Resistant Depression
****Dr Kirstin May**	Associate Specialist in Anaesthesia, Council member at the Royal College of Anaesthetists

**denotes co-opted member of the Working Group

Annex 16: ACMD Novel Psychoactive Substances (NPS) Committee Membership

(At time of publication)

Chair of NPS Committee	
Professor Simon Thomas	ACMD NPS Committee Chair, Emeritus Professor of Clinical Pharmacology and Therapeutics, Newcastle University
Members of the NPS Committee	
Mr Paul Bunt**	Director of Casterton Event Solutions Ltd, former Drug Strategy Manager for Avon and Somerset Constabulary
Mr Peter Cain**	Drugs Scientific Advisor, Eurofins Forensic Services
Dr Caroline Copeland	Senior Lecturer in Pharmacology and Toxicology at King's College London, and the Director of the National Programme on Substance Abuse Deaths
Dr John Corkery**	Associate Professor in Research (Psychoactive Substances' Epidemiology, Toxicology and Mortality), University of Hertfordshire; mortality. Epidemiological lead for EU-MADNESS project
Professor Colin Davidson	Professor of Neuropharmacology, University of Central Lancashire
Professor Amira Guirguis	Professor of Pharmacy, MPharm Programme Director and Deputy Pro Vice Chancellor at Swansea University Chief Scientist at the Royal Pharmaceutical Society
Dr Hilary Hamnett	Associate Professor in Forensic Science, University of Lincoln
Professor Graeme Henderson	Professor of Pharmacology at the University of Bristol
Dr Simon Hill**	Consultant Clinical Toxicologist, National Poisons Information Service, Newcastle Unit
Professor Stephen Husbands	Professor of Medicinal Chemistry, University of Bath
Professor Roger Knaggs	Professor in Clinical Pharmacy Practice at the University of Nottingham

Professor Fiona Measham**	Professor and Chair in Criminology at the University of Liverpool; co-founder and co-director of The Loop
Dr Lorna Nisbet	Senior Lecturer at the Leverhulme Research Centre for Forensic Science, University of Dundee
Dr Richard Stevenson***	Emergency Medicine Consultant, Glasgow Royal Infirmary
Mr Ric Treble**	Retired Laboratory of the Government Chemist (LGC) Expert
Professor David Wood	Professor of Clinical Toxicology and Consultant Physician, Guy's and St Thomas' NHS Foundation Trust, King's Health Partners and King's College London

**Denotes co-opted member of ACMD Novel Psychoactive Substances Committee.

***Member of ACMD Novel Psychoactive Substances Committee until end December 2025.

Annex 17: ACMD Chair and Membership at the time of publication

Chair of the ACMD	
Professor David Wood	Professor of Clinical Toxicology and Consultant Physician, Guy's and St Thomas' NHS Foundation Trust, King's Health Partners and King's College London
ACMD Council Members	
Professor Judith Aldridge	Professor of Criminology at the University of Manchester
Professor Anne Campbell	Professor of Substance Use and Mental Health, and Co-Director of the Drug and Alcohol Research Network at Queen's University Belfast
Dr Caroline Copeland	Senior Lecturer in Pharmacology and Toxicology, King's College London and the Director of the National Programme on Substance Abuse Deaths
Professor Colin Davidson	Professor of Neuropharmacology, University of Central Lancashire
Professor Karen Ersche	Professor of Addiction Neuroscience at the Department of Psychiatry at the University of Cambridge
Mr Mohammed Fessal	Chief Pharmacist, Change Grow Live
Professor Amira Guirguis	Professor of Pharmacy, MPharm Programme Director and Deputy Pro Vice Chancellor at Swansea University Chief Scientist at the Royal Pharmaceutical Society
Dr Hilary Hamnett	Associate Professor in Forensic Science at the University of Lincoln
Mr Jason Harwin	Director and co-founder of E-T-E Solutions Limited
Professor Graeme Henderson	Professor of Pharmacology at the University of Bristol

Professor Katy Holloway	Professor of Criminology, University of South Wales
Professor Stephen Husbands	Professor of Medicinal Chemistry, University of Bath
Professor Sunjeev Kamboj	Professor of Translational Clinical Psychology at the Research Department of Clinical, Educational and Health Psychology at University College London
Professor Roger Knaggs	Associate Professor in Clinical Pharmacy Practice at the University of Nottingham
Mrs Sapna Lewis	Senior Lawyer, Welsh Government Legal Services Department
Dr Lorna Nisbet	Senior Lecturer at the Leverhulme Research Centre for Forensic Science, University of Dundee
Detective Sergeant Jon Privett	Expert witness in drug trafficking with the Metropolitan Police
Mrs Fiona Spargo-Mabbs	Director and Founder, Daniel Sargo-Mabbs Foundation. Chair, Drug Education Forum
Professor Harry Sumnall	Professor in Substance Use, Liverpool John Moores University (LJMU)
Professor Simon Thomas	Emeritus Professor of Clinical Pharmacology and Therapeutics, Newcastle University

Annex 18: Range and quality of evidence

18.1 This report draws on evidence from peer-reviewed literature (UK and international publications) and government reports and considered international approaches when drafting its recommendations. Evidence gathered was considered in line with ACMD's standard operating procedure for quality of evidence (ACMD, 2020b).

18.2 ACMD issued a public call for evidence to gather qualitative insight from stakeholders, including individuals and organisations with a range of lived and professional experience. The data gathered from received submissions is presented within the report alongside information from peer-reviewed research (ACMD, 2025c).

18.3 The call for evidence invited responses to a detailed questionnaire covering multiple domains, including patterns of ketamine use, associated health and social harms, access to support, and the impact of legal classification. Submissions were welcomed from a broad spectrum of participants, including healthcare professionals, service providers, researchers, advocacy groups, and individuals with lived or living experience. ACMD received over 200 survey responses and more than 30 written submissions. These included responses from more than 70 people reporting lived or living experience of ketamine use, either personal use (11) or use by a family member or friend (61). This evidence has been used to inform ACMD's assessment of ketamine-related harms.

18.4 ACMD also took oral evidence from the following people with particular expertise and/or experience of ketamine:

- Irene Guerrini, Consultant Psychiatrist and Clinical Lead for Bexley Addictions – South, London & Maudsley NHS Trust
- Celia Morgan, Professor of Psychopharmacology, University of Exeter
- Robert Ralphs, Professor of Criminology and Social Policy, Manchester Metropolitan University
- Alex Frost, vicar of St Matthew's Church, Burnley
- Rebecca Harding, Clinical Psychopharmacology Unit, University College London

18.5 To further evidence the identification and prevalence in the UK of ketamine (and its analogues) misuse and harms, ACMD's Secretariat wrote to stakeholders requesting available data. Responses were received from the following:

Drug seizure and submitted sample data:

- UK Border Force (UKBF)
- Drug Team at Public Health Scotland (PHS) (RADAR)
- Emerging Drugs and Technologies Programme (EDAT)

- Manchester Drug Analysis and Knowledge Exchange (MANDRAKE)
- Scottish Police Authority (SPA)
- Leverhulme Research Centre for Forensic Science (LRCFS)
- Eurofins
- Welsh Emerging Drugs and Identification of Novel Substances (WEDINOS)
- TICTAC

Mortality and post-mortem forensic analysis data:

- Office for National Statistics (ONS)
- Office for Health Improvement and Disparities (OHID)
- National Programme on Substance Use Mortality (NPSUM)
- Public Health Scotland (PHS)
- Scottish Police Authority Forensic Services (SPA)
- EU-MADNESS Project
- National Records of Scotland (NRS)
- Northern Ireland Statistics and Research Agency (NISRA)

Drug poisoning data:

- Office for National Statistics (ONS) – England and Wales
- National Records of Scotland (NRS)
- Northern Ireland Statistics and Research Agency (NISRA)

Drug treatment data:

- National Drug Treatment Monitoring System (NDTMS)
- Public Health Wales (PHW)

The ACMD also sought information on medicinal use of ketamine and its analogues from the Medicines and Healthcare products Regulatory Agency (MHRA).

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