

Drug Harms Assessment and Response Team (DHART)

Quarterly summary for professionals: December 2021

Summary

1.1 Opioids

Deaths of opiate users in treatment in England are higher than expected and we do not think this is predominantly due to deaths caused directly by coronavirus (COVID-19).

Methadone overdoses resulting in hospital admissions in England remained high throughout 2020. Data from the Office for National Statistics (ONS) shows a 24% increase in deaths registered in 2020 involving methadone.

A national alert was issued in August 2021 due to an increase in heroin-related overdoses and the detection of isotonitazene, a potent synthetic opioid, in some samples.

1.2 Cannabinoids

Acute harms linked to synthetic cannabinoid receptor agonists (SCRAs) have increased while use seems to have decreased.

Deaths registered where SCRAs are mentioned on the death certificate have remained at high levels for the past 3 years, more than double than in 2017, despite SCRAs being less commonly found in drug seizures.

1.3 Sedatives and dissociatives

There are continued reports of the availability of illicit drugs sold as benzodiazepines, and the harms they cause. Most illicit drugs sold as benzodiazepines do not actually contain any benzodiazepines. They are more likely to contain fake benzodiazepines or benzodiazepine analogues.

1.4 Stimulants

The number of people entering treatment for methamphetamine has increased fourfold in the last decade.

In summer 2021, synthetic cathinones were being mis-sold as other substances.

Extremely high strength MDMA tablets have been identified but are yet to be linked to harm.

Cocaine use remains at high levels and deaths involving cocaine (either powder or crack) are at a record level. The numbers of people starting treatment or being admitted to hospital for cocaine were lower in 2020 to 2021, possibly because COVID-19 restrictions meant people used less cocaine.

Ketamine availability and use has been increasing in recent years, notably in young adults.

1.5 Other substances

There have been ongoing reports of increasing use and harm associated with gabapentinoids, and infrequent reports of severe breathing problems, including some cases where the person has not also been using opioids.

1.6 General clinical advice and updates

There has been a recent spate of reports of drug 'spiking' with needles, but there is currently not enough information to confirm which, if any, drugs were used.

2. Opioids

2.1 Heroin, methadone and buprenorphine

Key clinical messages

Alcohol and some drugs depress the central nervous system, which can cause respiratory depression (slowing of a person's breathing). The drugs that do this include heroin and other opioids, benzodiazepines and gabapentinoids (including pregabalin and gabapentin). This means that using any combination of these types of drugs with or without alcohol increases the risk of overdose and death. This risk might be greater with high-potency benzodiazepines or their analogues. People who use pregabalin, gabapentin and illicit benzodiazepines often consume them alongside opioids, and research suggests they are increasingly implicated in overdose.

Drug and alcohol treatment services and pharmacies have now returned to near normal functioning following the disruption earlier in the pandemic. The availability of supervised consumption of opioid substitution treatment has also largely returned. People who need supervised consumption should now be receiving it again in line with <u>national clinical guidance</u>. Pharmacists concerned about dispensing arrangements should work with the prescriber responsible for the person's prescription.

Latest evidence

See the synthetic opioids entry below (section 2.2) for a summary of a recent national incident involving synthetic opioids.

Deaths related to heroin are at (or near) all-time highs in <u>England and Wales</u>, <u>Scotland</u> and <u>Northern Ireland</u>. The average purity of street-level heroin has been high in recent years.

The number of deaths registered in 2020 in England and Wales involving heroin or morphine are the highest on record. Heroin-related deaths make up the largest proportion of drug misuse deaths (45%) in England and have more than doubled since 2012. There were 1,264 heroin-related deaths registered in 2020. This was similar to 2019, but there was a 24% increase in deaths involving methadone, likely due to changes in dispensing during the pandemic. In Scotland, opioid-related deaths rose by 5% in 2020 to a new record of 1,339. Deaths involving methadone increased by 25% from 567 to 708.

Data from the <u>National Drug Treatment Monitoring System (NDTMS)</u> for 2020 to 2021 shows that the number of opiate users who died while they were in treatment in England was higher than the previous year. The increases in deaths are geographically widespread. It should not be assumed that COVID-19 directly accounts for this increase in

deaths, especially as some happened in months where overall COVID-19 related deaths were low.

Methadone overdoses resulting in hospital admission increased substantially from April 2020 and have remained high into 2021. The data does not tell us if the people who were admitted to hospital were in drug treatment and prescribed methadone.

The number of people starting treatment for opiate problems have decreased since the beginning of the pandemic, but overall numbers in treatment have slightly increased. This suggests that people have had fewer short episodes in treatment.

The purity of street level heroin had been declining during 2020 (according to unpublished data) but has remained stable in 2021. However, the purity of imported heroin increased in April to June 2021 to the high level seen in 2019.

2.2 Synthetic opioids

Synthetic opioids found in global drug markets include tramadol, fentanyls and new psychoactive substances (NPS) including isotonitazene.

Fentanyl can either be diverted from medical sources or illicitly manufactured. Synthetic opioids can be mixed with heroin or substituted for it, resulting in people unknowingly consuming them. They may also be substituted for other opioids in counterfeit medicines.

Key clinical messages

You should consider possible synthetic opioid intoxication if people show signs and symptoms of severe opioid intoxication. If toxicology can confirm the substances involved, this will support intelligence gathering.

Clinical management of intoxication should follow existing opioid intoxication protocols. See section 7 for general clinical advice on managing poisons, including synthetic opioids. You should continue to use naloxone for all suspected opioid overdoses. You may need to give multiple doses of naloxone, or naloxone infusion, in acute settings. People might be more likely to need multiple doses if they have consumed highly potent synthetic opioids.

Research shows the <u>risk of fentanyl toxicity by absorption through the skin is low</u>. However, Public Health England (PHE) published <u>guidance for clinicians to reduce the risk of contamination from fentanyl</u>. There is no evidence for absorption of isotonitazene through the skin, but you should take the usual precautions, including wearing masks, when handling unknown substances, especially if they have become airborne.

See the heroin entry above (section 2.1) for information on concurrent use of opioids with pregabalin, gabapentin, benzodiazepines and alcohol, and the related overdose risk.

Latest evidence

In 2020, ONS dataset on deaths registered related to drug poisoning in England and Wales reported that there were 57 deaths involving fentanyl, 2 deaths involving fentanyl analogues and one involving novel opioids. These figures were similar to 2019. Oxycodone deaths were the highest on record for the third year at 102. Fentanyl deaths registered in Scotland have gone down from 25 (highest on record) in 2019 to 7 in 2020. The number of deaths attributed to synthetic opioids (including fentanyl) in the UK remains very low compared to heroin, although these may be underestimated due to inconsistent post-mortem toxicological screening.

Synthetic opioid use continues to be reported by various sources (including the <u>Identification of novel psychoactive substances (IONA) study</u>), notably isotonitazene and N-pyrrolidino etonitazene (etonitazepyne). Fentanyl is regularly reported anecdotally to be in circulation but rarely proven to be so.

In August, PHE issued a <u>national patient safety alert</u> about an increase in cases of opioid overdose that resulted in deaths in some parts of the country. Analyses from seized drugs and toxicology have linked some of these incidents to heroin laced with the potent synthetic opioid, isotonitazene. The alert was distributed widely to the NHS, local authorities and others to cascade through national and local systems.

Adulteration of opioids and other drugs with fentanyl and its analogues is common in the North American drug market, where these substances kill more people than other opioids like heroin. Confirmed presence of these substances in UK drug markets is still relatively rare, but there is a still a heightened need for vigilance.

3. Cannabinoids

3.1 Synthetic cannabinoid receptor agonists (SCRAs)

Key clinical messages

People who use SCRAs often call them 'spice' or 'mamba'. SCRAs are often sprayed onto herbal material, dried and sold to be smoked. Less often (and usually only in prisons) they are soaked into paper. SCRAs can also be vaped and there is some evidence of SCRAs in edibles. Experts advise against using illicit and unregulated vaping products or adding substances to vaping fluids.

SCRA use is most prevalent in prisons across the UK, but ONS data shows that <u>SCRA</u> use among the general population is believed to remain low. Homeless populations are still known to be using SCRAs, although prevalence is not well documented.

SCRAs are a diverse group of chemicals sold in a range of strengths. All are agonists for the CB1 receptor but some SCRAs can also work at other receptors. The chemicals sold are often changing, so harms are difficult to predict. The harms from SCRAs are often very different to those seen with herbal cannabis. SCRA toxicity can be severe, requiring management in intensive care units, and sometimes it can be fatal.

Latest evidence

There is some unpublished evidence that acute harms associated with cannabinoids (including SCRAs) remained high throughout 2020. We do not know if this harm is being caused by SCRAs or increased potency of natural cannabis. Longer-term trends, including deaths, suggest that acute harms have remained high through 2020 while use (measured through numbers in treatment and drug seizures) may have decreased.

While MDMB-4en-PINACA remains the most detected SCRA in seizures in England and Wales (unpublished data), seizures containing this compound decreased in the first half of 2021. ADB-BUTINACA seizures have seen a steep increase and this compound is now found in similar numbers to MDMB-4en-PINACA. While 4F-MDMB-BINACA and 5F-MDMB-PICA were the most seized SCRAs in most of 2020, seizures of these compounds have reduced significantly.

5F-MDMB-PICA and 4F-MDMB-BINACA are now subject to international control under the United Nations Convention on Psychotropic Substances 1971. The European Monitoring Centre on Drugs and Drug Addiction (EMCDDA) is intensively monitoring MDMB-4en-PINACA (since July 2020) and 4F-MDMB-BICA (since September 2020). In March 2021, the European Commission proposed the control of these compounds, and enforcement by the European Parliament was planned for May 2021 but no action has been taken so far. China, the main producer of SCRAs globally, has introduced a generic control for SCRAs as of July 2021, which is likely to affect the market.

ONS has reported that in 2020, SCRAs were mentioned on the death certificate in 53 deaths registered in England and Wales. This is a similar number to 2019 and 2018 (56 and 60) and more than double the number registered in 2017 (25). These deaths have happened despite signs of decreased prevalence of SCRA use in recent years. National Records of Scotland statistics on drug-related deaths reported that there were 4 deaths involving cannabis and cannabinoids in 2020.

3.2 Cannabis

Key clinical messages

Increases over recent years in the potency (tetrahydrocannabinol (THC) content) of cannabis combined with possible reductions in cannabidiol (CBD) content mean that

people who use cannabis are more likely to experience severe symptoms of cannabinoid intoxication.

Latest evidence

<u>Cannabis</u> is the most commonly used illicit drug in the UK. The prevalence of cannabis use in England and Wales has been increasing since 2015 to 2016, from 6.7% adults aged 16 to 59 having used cannabis in the last year to 7.8% in 2019 to 2020. Last year prevalence among 16 to 24-year olds increased to 18.7% from 15.7% in 2015 to 2016.

Cannabis remains the most common non-opiate drug that people seek treatment for (excluding alcohol). In 2020 to 2021, 1 in 5 people who started drug and alcohol treatment reported cannabis as their primary drug. See section 3.1 for the latest evidence on acute harm linked to cannabinoids.

Hospital admissions for cannabinoids in England have also been increasing.

There is evidence from Europe that herbal cannabis and cannabis resin have increased in potency over the last decade. In recent years, new cannabis products, such as vaping products and edibles, have gained popularity both in legal cannabis markets abroad and the illicit market here. Edibles often come in the form of sweets and are branded similarly to regular sweets. Over the last 18 months, edible cannabis products have reportedly been in circulation and in use, mainly by young people. These products have been linked to 35 hospitalisations, most of which were for precautionary assessment, and patients were released shortly after being admitted. It's likely that young people who are not used to cannabis are taking too much and getting ill. These edibles are variously reported to contain THC, CBD or (more recently and concerningly) SCRAs, which could further increase harm.

4. Sedatives and dissociatives

4.1 Benzodiazepines

Benzodiazepines and their analogues include diazepam (Valium), alprazolam (Xanax), etizolam, diclazepam, flualprazolam and flubromazolam.

Key clinical messages

Illicit benzodiazepines are often used by people who also use opioids, but also by some young people who do not use opioids. <u>Using benzodiazepines and opioids together is particularly common in Scotland</u>.

A 2020 <u>national alert about illicit drugs sold as benzodiazepines</u> provides information and advice on the appropriate actions to take, including information to share with people who use drugs or are at risk of taking these drugs. It outlines the harm associated with benzodiazepines and their analogues, particularly when used with alcohol and other drugs that can slow a person's breathing (including gabapentinoids and opioids). If you are in contact with people who use drugs, you should be aware of the high risk of overdose for someone using potent illicit benzodiazepines and their analogues. This is so you can raise awareness of the risks associated with these drugs, recognise possible symptoms of overdose and respond appropriately.

Newer illicit 'street' benzodiazepines and benzodiazepine analogues (see below) may not be detected in regular drug screens.

Latest evidence

There is increased availability and use of illicitly manufactured 'street' benzodiazepines and their analogues. The strength and toxicity of new benzodiazepines and their analogues can be unpredictable and often more potent than diazepam. The long-acting nature of some benzodiazepines and their analogues also contributes to the risk of overdose. Benzodiazepine seizures rose throughout 2020 and reached their highest level between July and September 2021. The most seized substances are:

- etizolam
- flubromazolam (which has markedly increased since the start of 2020)
- diazepam
- alprazolam

Street benzodiazepine tablets known as or marked with 'DAN 5620' (on one side) and '10' (on the other), and 'MSJ' are widely available.

Drug treatment and hospital data in England suggests increasing numbers of people who use benzodiazepines and their analogues are experiencing acute and chronic harm and entering drug treatment. The number of <u>deaths registered in England and Wales</u> involving benzodiazepines increased by 20% from 399 in 2019 to 476 in 2020, a record high. Deaths involving benzodiazepine analogues increased from 26 to 62 in the same period, making 2020 the second year in a row with a record high. Most (73%) drug-related deaths in Scotland in 2020 involved benzodiazepines, predominantly with opioids. Street benzodiazepines were involved in 66% (879) of the 1,334 <u>drug-related deaths registered in Scotland</u> in 2020. Etizolam was involved in 806 of these cases, most of which also involved opioids.

Most illicit benzodiazepines do not contain the substances they are sold as. These substances are often sold as diazepam or alprazolam. For example, of the samples from across the UK submitted to the WEDINOS) project from April to June 2021 that were bought as alprazolam, only 42% contained alprazolam. Forty-nine percent contained other benzodiazepines or their analogues (notably flualprazolam and flubromazolam).

Etizolam and flualprazolam became subject to international control in November 2020 under the UN Convention on Psychotropic Substances 1971.

4.2 Ketamine

Key clinical messages

Ketamine use has increased over recent years. You should ask patients reporting ketamine use about urological symptoms of 'ketamine bladder', including:

- polyuria (excessive urine production)
- dysuria (painful urination)
- haematuria (presence of blood in urine)

Similarly, urologists should be aware that ketamine can cause urological symptoms. They should routinely ask about a patient's history of drug use if they have urological problems and are in a group with higher prevalence of ketamine use (for example, young adults, club goers, and people involved in chemsex). See section 4.13.3.1 of NEPTUNE's clinical guidance for more information on ketamine-induced damage to the urinary tract.

Latest evidence

There have been recent increases in:

- police seizures of ketamine
- numbers of people starting treatment reporting ketamine use
- the <u>prevalence of ketamine use</u> among 16 to 24 year olds

5. Stimulants

5.1 Cocaine (including crack cocaine)

Key clinical messages

The number of people using cocaine has continued to increase, as has the number of cocaine-related deaths. Cocaine use causes a range of acute and chronic harm, so it's important to consider cardiotoxicity (muscle damage to the heart) in acute presentations. Using alcohol and cocaine together increases the risk of overdose and makes a new chemical in the body called cocaethylene, which is cardiotoxic and hepatotoxic (toxic to the liver).

Latest evidence

In 2019, England and Wales had the <u>highest prevalence of cocaine use in Europe</u>. Cocaine (powder and crack) use, purity and availability have been rising in the last decade across the UK. After a decrease in 2020 in England and Wales, cocaine (powder and crack) purity increased in 2021 to a level similar to 2019. For crack alone, purity has been on a downward trend over the last 3 years.

In contrast to previous years, there has been a fall in the number of adults entering treatment for crack cocaine in 2020 to 2021. This includes people who are using crack with opiates, which is the group with most crack users. This, alongside the fall in purity, suggests crack is less available.

In recent years, there are signs of new crack users who are not using heroin as well. A similar number of people started treatment in 2020 to 2021 as the previous year who said they were only using crack. In 2019, the proportion of people starting drug treatment who were mainly using powder cocaine was higher in Scotland than in England or Wales for the first time.

There were fewer powder cocaine users starting treatment in 2020 to 2021 in England than the previous year. This indicates less availability and fewer opportunities to use the drug socially (which can lead to problematic use requiring treatment).

In 2020, <u>deaths involving cocaine</u> (<u>powder or crack</u>) <u>registered in England and Wales</u> and <u>deaths involving cocaine in Scotland</u>, as well as <u>deaths involving cocaine in Northern</u> <u>Ireland</u> in 2019, all reached the highest levels on record. There were 777 deaths registered in England and Wales in 2020 mentioning cocaine on the death certificate, an increase from 708 deaths registered in 2019.

The latest data from the <u>Unlinked Anonymous Monitoring survey</u> shows that the number of people currently injecting crack remains high in England and Wales. In 2019, 59% of people currently injecting drugs in England and 47% in Wales reported injecting crack in the last 4 weeks. The problem drug using population in Glasgow is increasingly injecting powder cocaine, and this has been linked to <u>a rise in HIV transmission</u>.

5.2 MDMA and ecstasy

Key clinical messages

Reported short-term harm can include psychiatric (anxiety, confusion and psychosis) and physical (liver, kidney and heart problems) symptoms. Other substances are sometimes sold as MDMA or ecstasy such as n-ethyl-pentylone, a synthetic cathinone.

Latest evidence

While MDMA availability and use reportedly fell during periods of COVID-19 restrictions, it was anecdotally reported that availability and use increased in summer 2021 with the easing of restrictions. Between July and September, synthetic cathinones and caffeine were being mis-sold as MDMA. In November, extremely high strength MDMA tablets were identified in the North West but are yet to be linked to harm.

Harm associated with MDMA has been increasing among younger people in recent years. Deaths registered in England and Wales involving MDMA increased between 2017 and 2018, from 56 to 92. This increase in deaths was primarily seen in people aged under 30. The number of deaths registered involving MDMA has remained steady since 2019, with 82 registered in 2020.

Sixteen per cent of people starting drug treatment in England, Wales and Scotland in 2019 who reported MDMA as their primary problem drug were aged under 15, and 69% were under 20 (unpublished data analysis submitted by the National Drug Evidence Centre to the UK Focal Point on Drugs).

5.3 Methamphetamine

Key clinical messages

Clinical management should follow existing stimulant protocols.

Latest evidence

The European Drug Report 2021 has some evidence that <u>European labs are increasingly producing methamphetamine</u>.

There are anecdotal reports that methamphetamine is increasingly available and being used in England. The number of people starting treatment for methamphetamine use has increased by 8% since 2019 to 2020, and almost fourfold in the last decade, from 131 in 2011 to 2012 to 505 in 2020 to 2021.

Healthcare professionals are increasingly <u>concerned about patients' amphetamine use</u>. There may have been a small increase in the number people attending A&E with amphetamine poisoning, but the numbers are very small and the change from last year is not statistically significant.

5.4 Synthetic cathinones

Synthetic cathinones include mephedrone, alpha-PVP, n-ethyl-pentylone and MDPHP.

Key clinical messages

Clinical management should follow existing stimulant protocols.

Latest evidence

<u>Use of synthetic cathinones</u> among the general population has decreased over the past decade. While seizures of synthetic cathinones in England and Wales had been increasing since the middle of 2020, current numbers are low compared to 2018.

There were 6 <u>drug-related deaths registered in England and Wales</u> in 2020 involving synthetic cathinones, a decrease from 14 in 2019. However, lab and back-of-house pill testing (samples confiscated by police or event security and those put into amnesty bins) from festivals in the North West and East Midlands in July to September found caffeine, and synthetic cathinones (such as eutylone, N-ethylhexylone, 3-methylmethcathinone (3-MMC), metaphedrone), and 4-chloromethcathinone (4-CMC, clephedrone)) being widely mis-sold as MDMA.

6. Other substances

6.1 Gabapentinoids

Gabapentinoids include gabapentin (Neurontin) and pregabalin (Lyrica).

Key clinical messages

Gabapentinoids are licensed for treating epilepsy, neuropathic pain and, in the case of pregabalin, generalised anxiety disorder.

Gabapentinoids are sometimes misused to <u>increase the effects of opioids</u>. They can lower opioid tolerance and induce respiratory depression at high doses. Opioids are often present in deaths involving gabapentinoids.

Pregabalin has been associated with <u>infrequent reports of severe respiratory</u> <u>depression</u>, including some cases without associated opioid use. Patients might be at higher risk of experiencing these events if they:

- have compromised respiratory function
- have respiratory or neurological disease
- have renal impairment
- are using accompanying central nervous system depressants
- are older than 65 years

You might need to adjust doses or dosing regimens for these patients.

Latest evidence

Evidence shows <u>prescriptions for pregabalin and gabapentin are increasing</u>. <u>Deaths involving gabapentinoids have been increasing</u>. Between 2017 and 2020, the number of deaths registered involving:

- pregabalin in England and Wales rose by 153%, from 136 to 34
- gabapentin in England and Wales rose by 97%, from 60 to 118
- pregabalin<u>in Scotland</u>rose by 176%, from 121 to 334
- gabapentin in Scotland rose by 50%, from 144 to 216

There were 77 <u>deaths registered in Northern Ireland</u> involving pregabalin in 2019, a 755% increase from 9 in 2016.

6.2 Nitrous oxide (N2O)

Key clinical messages

Heavy and repeated use of N2O has been associated with severe peripheral neuropathy (damage to the nerves located outside the brain and spinal cord) and sub-acute combined degeneration of the spinal cord (although this is rare).

Latest evidence

Some <u>reports link heavy use of N2O (up to 75 cannisters per day) to peripheral</u> <u>neuropathy</u>. Healthcare professionals are <u>increasingly searching for information about</u> nitrous oxide.

7. General clinical advice and updates

Since October 2021, there has been a spate of reports of drug 'spiking' with needles in England, mainly in areas of the East Midlands and North West. To date, few cases are confirmed to have involved needles. Also, there is not enough evidence of any drugs involved in these incidents or the motives behind them. The Office for Health Improvement and Disparities has issued advice on how people can protect themselves from spiking if they feel unsafe.

The chemical makeup of NPS varies widely so you should treat acute presentations based on their symptoms.

Poly-substance use is common and can influence clinical presentation. The actual substances taken are often not known, so treatment should be guided by the observed effects, for example sedative, dissociative, stimulant or hallucinogenic. The National Poisons Information Service's (NPIS) TOXBASE, an online clinical toxicology database (registration required), has a symptom search function. This is useful if you do not know which drug was taken (for example, you can search 'Drug of Abuse – unknown'). Always ask if the person has used other drugs and alcohol. Healthcare professionals can also get advice on the managing intoxication with unknown substances via the 24-hour NPIS telephone service (0344 892 0111).

<u>Project NEPTUNE</u> provides free e-learning modules and guidance on the clinical management of acute and chronic harms of club drugs and NPS.

<u>Drug misuse and dependence: UK guidelines on clinical management</u> contains some information on the clinical management of people seeking treatment for NPS use.

PHE published guidance on NPS use for substance misuse commissioners and an NPS toolkit for prison staff.

Manchester Health and Care Commissioning has produced a <u>Spice information sheet</u>, which provides information on common SCRAs, their effects and treatment.

8. Recent statistics and other data sources

<u>Drug misuse: findings from the latest Crime Survey for England and Wales (2020).</u>

Substance misuse treatment for adults: statistics 2020 to 2021.

Smoking, drinking and drug use among young people in England 2018.

Scottish Schools Adolescent Lifestyle and Substance Use Survey 2018.

<u>Unlinked Anonymous Monitoring (UAM) Survey of HIV and viral hepatitis among people who inject drugs (PWID)</u> 2021 report.

The latest ONS report on Deaths related to drug poisoning in England and Wales (2020).

The latest National Records of Scotland <u>Drug-related deaths in Scotland report and data</u> (2020).

The latest Northern Ireland Statistics and Research Agency <u>drug-related deaths in Northern Ireland data (2019)</u>.

The EMCDDA European Drug Report 2020.

Advisory Council on the Misuse of Drugs 2020 reports <u>Misuse of fentanyl and fentanyl analogues</u> and <u>Novel benzodiazepines</u>: a review of the evidence of use and harms of novel benzodiazepines.

UK Focal Point on Drugs report and data on the <u>national prevalence, impact, prevention</u> and treatment of drug use.

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