



# Drug Harms Assessment and Response Team

## Quarterly summary for professionals: August 2020

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### 2. Coronavirus update

The Drug Harms Assessment and Response Team (DHART) is monitoring the impact of coronavirus (COVID-19) on drug markets and drug harm through a range of indicators. It is also collecting intelligence via various networks. Early indications suggest that:

- overall national drug supply seems to have been fairly resilient
- at a local level, there have been reported fluctuations in price, purity and availability
- there have been reports of increased use of and harm linked to benzodiazepines and pregabalin

- there may have been fewer presentations to emergency departments with acute drug toxicity
- there is not currently evidence suggesting widespread substitution of heroin with fentanyl

You should be aware that:

1. Opioid substitute treatment (OST) practice has changed, supported by **Public Health England (PHE) guidance**, in response to the risk of COVID-19 transmission. As a result, there has been less use of supervised consumption which increases the risk of medicines being diverted or not used as prescribed.
2. Use of drugs such as opioids, benzodiazepines, gabapentinoids and alcohol can exacerbate breathing impairment from COVID-19.

Public Health Scotland has issued **harm reduction advice and information about drug use during COVID-19**.

## 3. Stimulants

### 3.1 MDMA/ecstasy

#### Key clinical messages

MDMA remains widely available. 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/ecstasy such as n-ethyl-pentylone, a synthetic cathinone.

#### Latest evidence

Harm associated with MDMA use has been increasing among younger people. **Deaths registered involving MDMA in England and Wales** increased from 56 in 2017 to 92 in 2018. The increase in deaths was primarily seen in the under 30s. Of those presenting to drug treatment in England, Wales and Scotland in 2018, one-quarter were aged under 15, with three-quarters aged under 20.

### 3.2 Synthetic cathinones

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

#### Key clinical messages

**Use of synthetic cathinones** among the general population has decreased over the past decade.

Clinical management should follow existing stimulant protocols.

#### Latest evidence

The number of seizures of synthetic cathinones in England and Wales may have stabilised having previously fallen since 2018.

There were 16 deaths registered involving synthetic cathinones in England and Wales in 2018.

In January 2019, 3 people were hospitalised in Bury, Greater Manchester, after taking 'UPS' pills that contained high levels of alpha-PVP. Symptoms lasted 20 hours, including agitation and psychosis. The availability of these pills appears to have been localised and contained.

### 3.3 Cocaine (including crack cocaine)

#### Key clinical messages

Prevalence of cocaine use (including crack) appears to be increasing across the UK.

There is increasing evidence that co-ingestion of cocaine and sildenafil (including Viagra) increases the risk of cardiac harms. You should consider asking cocaine users about sildenafil use, especially if there is pre-existing cardiovascular disease including a history of **aortic dissection**.

#### Latest evidence

Deaths involving cocaine (powder or crack) registered in **England and Wales**, **Scotland** and **Northern Ireland** in 2018 all reached the highest levels on record.

Cocaine (powder and crack) purity and availability have been rising for several years and are currently high by historical standards. As well as more crack being taken by heroin users, there are signs of **newer crack users** who are not using heroin.

The problem drug using population in Glasgow is increasingly injecting powder cocaine, and this was linked to a rise in **HIV transmission**.

## 4. Sedatives and dissociatives

### 4.1 Benzodiazepines

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

There is increased availability and use of illicitly manufactured 'street' benzodiazepines and their analogues, including alprazolam, etizolam, flualprazolam and temazepam. These substances are often sold as diazepam (Valium) or alprazolam (Xanax).

Newer street benzodiazepines may not be detected in regular drug screens. The strength and toxicity of new benzodiazepines and their analogues can be unpredictable and often more potent than diazepam.

Benzodiazepine use is particularly **prevalent** in Scotland and Northern Ireland. Street benzodiazepines, particularly etizolam, are often used by people who use opioids such as heroin in **Scotland**.

In England, Xanax appears to be mainly used by young people, often with alcohol, and sometimes with other illicit drugs. However, etizolam is increasingly being identified in England and Wales, and may be sold as Xanax.

#### **Latest evidence**

Reports of benzodiazepine-related harm in England appear to have been increasing in recent years notably in the North East and North West.

PHE issued a **national alert** in July 2020 containing advice on the availability and harm from illicit drugs sold as benzodiazepines, particularly when used with alcohol and drugs which have a respiratory depressant effect (including gabapentinoids and opioids).

There is significant evidence from toxicology results of illicit tablets being sold as diazepam, temazepam and alprazolam linked to recent hospitalisations and deaths, and from police seizures, that some illicit drugs sold as benzodiazepines are causing harm. This includes tablets known as or marked with 'DAN 5620' (on one side) and '10' (on the other), 'T-20', 'TEM 20', 'Bensedin' and 'MSJ' which may contain dangerously potent benzodiazepines or their analogues such as flubromazolam, flualprazolam and etizolam. Most of the tablets causing concern are blue (but they come in various colours) and these may stain people's mouths.

If you are in contact with people who use drugs, you should be alert to the increased possibility of overdose from illicit drugs sold as benzodiazepines, so you can raise awareness, be able to recognise possible symptoms of overdose and respond appropriately. The alert provides information and advises on the appropriate actions to take, including information to share with people who use drugs or are at risk of taking these drugs.

Street benzodiazepines were involved in 675 of the 1,187 drug-related deaths registered in Scotland in 2018. Etizolam was involved in 548 of these cases, most of which also involved opioids.

Flualprazolam is increasingly being identified in the UK market and is reported to have a higher potency than alprazolam. Only 20% of samples purchased as alprazolam submitted to the **Welsh Emerging Drugs and Identification of Novel Substances (WEDINOS)** project so far in April to June 2020 contained alprazolam, with 25% containing flualprazolam. Also, 60% of supposed diazepam samples contained diazepam.

Etizolam, diazepam and alprazolam were the most commonly identified benzodiazepines in seizures data from January to March 2020 in England and Wales.

Etizolam and flualprazolam will become subject to **international control** under the United Nations (UN) Convention on Psychotropic Substances 1971 in November 2020.

## 4.2 Ketamine

### Key clinical messages

Ketamine use appears to be increasing. You should ask patients reporting ketamine use about urological symptoms of 'ketamine bladder', including polyuria, dysuria and haematuria.

### Latest evidence

There have been recent increases in ketamine-related **police seizures**, **presentations to treatment**, and prevalence of **use in the last year** among those aged 16 to 24.

## 4.3 Nitrous oxide (N<sub>2</sub>O)

### Key clinical messages

Heavy and repeated use of N<sub>2</sub>O has been associated with severe peripheral neuropathy and rarely sub-acute combined degeneration of the spinal cord.

### Latest evidence

**Reports** link heavy use (up to 75 cannisters per day) to peripheral neuropathy.

## 5. Opioids

### 5.1 Synthetic opioids

Synthetic opioids detected in global drug markets include fentanyls, U-type opioids, AH-7921 and MT-45.

### Key clinical messages

Synthetic pharmaceutical and illicit opioid use continues to be reported. The most common is fentanyl which can either be diverted from medical sources or illicitly manufactured. Some synthetic opioids (such as carfentanil) are highly potent, although they are rarely seen in the UK at present.

Synthetic opioids may be mixed with, or substituted for, heroin resulting in users unknowingly consuming them. They may also be substituted for other opioids in **counterfeit medicines**.

The number of deaths attributed to synthetic opioids (including fentanyl) in the UK remains very low compared to heroin, although this may be underestimated due to inconsistent post-mortem toxicological screening.

You should consider possible synthetic opioid intoxication if patients present with signs and symptoms of severe opioid intoxication. Toxicology to confirm the substance(s) involved will support intelligence gathering.

**Clinical management** of intoxication should follow existing opioid intoxication protocols.

You should continue to use **naloxone** for all suspected opioid overdoses. Multiple doses of naloxone, or naloxone infusion, may be needed in acute settings. These may be more likely to be needed if highly potent synthetic opioids have been used.

Risk of fentanyl toxicity via dermal absorption is **low**. However, PHE has published **guidance** for clinicians to reduce the risk of contamination.

See the [heroin](#) entry below for information on concurrent use of opioids with pregabalin, gabapentin and benzodiazepines, and the related overdose risk.

#### Latest evidence

In [England and Wales](#) there were 75 deaths registered involving fentanyl, 31 deaths involving fentanyl analogues and 2 novel opioids in 2017. In 2018, 74 deaths registered involved fentanyl, 31 involved fentanyl analogues and 11 involved novel opioids.

The number of deaths involving synthetic opioids has been rising since 2013 and may be under-reported due to difficulties with detection. Twelve fentanyl deaths were registered in [Scotland](#) in 2018. Fentanyls are involved in relatively few deaths compared with heroin due to low prevalence.

Adulteration of opioids and other drugs with fentanyl and its analogues is an established and common practice among suppliers in North American drug markets where these substances kill more drug users than other opioids like heroin. This is not currently the case in the UK but there is a clear need for vigilance.

## 5.2 Heroin

You should continue to treat overdose from heroin and other opioids with naloxone. Pregabalin, gabapentin and benzodiazepines are widely consumed by drug users alongside opioids, and are [increasingly](#) implicated in overdose.

Deaths related to heroin are at an all-time high in [England and Wales](#), [Scotland](#) and [Northern Ireland](#). The average purity of street-level heroin has been high in recent years.

## 6. Synthetic cannabinoid receptor agonists (SCRAs)

People who use SCRAs will often call them 'spice' or 'mamba'.

### Key clinical messages

SCRA use is most prevalent in prisons across the UK. Use among the **general population** is now low. Homeless populations are still known to be using SCRA, although prevalence is less well documented.

SCRAs are a diverse group of chemicals sold in a range of strengths. All are agonists for the CB1 receptor; some SCRAs may also work at other receptors. The chemicals sold are frequently 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 may be fatal.

SCRAs can be vaped. Experts **advise** against using illicit and unregulated vaping products or adding substances to vaping fluids.

### Latest evidence

Increased ambulance callouts in an area of the North West in early June 2020 were linked to a new SCRA or more potent blend of SCRAs. Subsequent testing of samples from this incident, a further incident in late July and samples seized in the city centre have found MDMB-4en-PINACA, 5F-MDMB-PICA and a mix of SCRAs. A hospital in the West Midlands also confirmed that it has been increasingly identifying MDMB-4en-PINACA in toxicology.

In 2018, SCRAs contributed to 60 deaths registered in **England and Wales**, more than double the 24 deaths in 2017. This is despite signs of decreased use of these substances compared to previous years. There were 2 deaths involving SCRAs in **Scotland** in the same year.

5F-MDMB-PICA and 4F-MDMB-BINACA increased in circulation in 2019. There are claims that they are stronger than and have different effects to other SCRAs. Although there were few detections of it prior to late 2019, MDMB-4en-PINACA is now also common and causing concern. New SCRAs are still entering the market, although there have been fewer new detections of these substances across **Europe** than seen previously.

5F-MDMB-PICA and 4F-MDMB-BINACA are now subject to international control under the UN Convention on Psychotropic Substances 1971.

Vitamin E acetate, an additive in some unregulated vaping products, has been strongly linked to cases of e-cigarette or vaping product use associated lung injury (EVALI) that has caused hospitalisations and deaths **in the US**. While the US

outbreak appeared to relate mainly to products containing THC, the risk of other unregulated vaping products causing EVALI cannot be discounted.

## 7. Other substances

### 7.1 Gabapentinoids

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

#### Key clinical messages

Prescriptions for pregabalin and gabapentin, together called **gabapentinoids**, are increasing. Gabapentinoids are licensed for the treatment of epilepsy, neuropathic pain and, in the case of pregabalin, generalised anxiety disorder.

Gabapentinoids may be misused to **increase the effects of opioids**. They can lower opioid tolerance and induce respiratory depression at high doses. Opioids are often present in deaths involving gabapentinoids.

#### Latest evidence

Registered deaths in **England and Wales** involving gabapentinoids have been increasing. Between 2017 and 2018, deaths increased for gabapentin from 60 to 93 and for pregabalin from 136 to 187.

In **Scotland**, gabapentin- and pregabalin-related deaths rose from 142 to 194 and from 120 to 211 respectively over the same period.

There were 54 deaths involving pregabalin in **Northern Ireland** registered in 2018, an increase from 9 in 2016.

There are reports of increasing use and harm associated with gabapentinoids particularly pregabalin.

### 7.2 2,4-Dinitrophenol (DNP)

#### Key clinical messages

DNP is a toxic chemical which has fat-burning properties and is sometimes used by body builders or by others seeking weight reduction. DNP interferes with cellular metabolism and prevents energy being stored as fat; instead the energy is released as heat. These effects are toxic to the cells of organs such as muscle, kidney and brain. Toxic effects are more common with higher doses.

There is a myth that if DNP is used in small amounts, users will be safe. Although toxicity is common after overdose, severe and even fatal adverse effects have

occurred when the drug has been taken in the doses recommended on websites or by suppliers.

If DNP toxicity is suggested, urgent referral to hospital is indicated. If you are dealing with individuals suspected of consuming DNP, you should seek advice on clinical management from the National Poisons Information Service (NPIS) by referring to [TOXBASE](#). You can ring the NPIS on 0344 892 0111.

You should also inform patients of the dangers and tell them to stop use immediately. All patients with features suggesting toxicity should be referred to hospital immediately for assessment and observation, and all symptomatic cases should be discussed with the NPIS by phone.

#### Latest evidence

From 2007 until the end of July 2020, there have been 137 separate episodes of systemic DNP exposure discussed with the NPIS. Of these, 25 (18%) are known to have died. During 2019, the NPIS recorded 14 cases of DNP toxicity and 4 deaths, both slight decreases from 2018 (20 cases, of which 6 were fatal).

## 8. General clinical advice and updates

The chemical makeup of new psychoactive substances (NPS) varies widely so you should treat acute presentations based on the symptoms at clinical presentation.

NPIS's [TOXBASE](#) has a symptom search function, which is useful if you do not know which drug was taken. Always ask about the use of other drugs and alcohol.

Poly-substance use is common and may influence clinical presentation. If the actual substance taken is not known, consider treating according to broad psychoactive effect (for example sedatives and dissociatives, stimulants, hallucinogens or cannabinoids).

[Project NEPTUNE](#) provides guidance on the clinical management of acute and chronic harms of club drugs and NPS and free e-learning modules.

[Drug misuse and dependence: UK guidelines on clinical management](#) contains some information on the clinical management of people seeking treatment for NPS use.

PHE has published guidance on NPS use for [substance misuse commissioners](#) and [prison staff](#).

Manchester Health and Care Commissioning has produced a [Spice information sheet](#), which provides information on its chemical make-up, effects and treatment.

PHE has published evidence-based [recommendations to protect first responders from exposure to fentanyl](#).

## 9. Recent statistics and other data sources

The [Crime Survey for England and Wales 2018 to 2019](#) examines the extent and trends in illicit drug use among a sample of 16 to 59 year old residents in households in England and Wales.

Annual statistics on alcohol and drug misuse treatment from PHE's National Drug Treatment Monitoring System, includes reports on:

- adults
- young people
- prisons and secure settings

[Smoking, drinking and drug use among young people in England in 2018](#).

[Scottish Schools Adolescent Lifestyle and Substance Use Survey 2018](#).

[Unlinked Anonymous Monitoring \(UAM\) Survey of HIV and viral hepatitis among people who inject drugs \(PWID\) in 2018](#).

The Office for National Statistics report on [Deaths related to drug poisoning in England and Wales: 2018 registrations](#).

The National Records of Scotland report on [Drug-related deaths in Scotland in 2018](#).

The European Monitoring Centre for Drugs and Drug Addiction's [European Drug Report 2019](#).

In 2020, the Advisory Council on the Misuse of Drugs published [Misuse of fentanyl and fentanyl analogues and Novel benzodiazepines: a review of the evidence of use and harms of novel benzodiazepines](#).