Public Health England

Protecting and improving the nation's health

Drug Harms Assessment and Response Team (DHART)

Quarterly summary for professionals: May 2021

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1. Opioids

1.1 Heroin

You should continue to treat overdose from heroin and other opioids with naloxone.

Alcohol and some drugs depress the central nervous system, which affects 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 may 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.

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

Latest evidence

Provisional data from the National Drug Treatment Monitoring System (NDTMS) for April 2020 to February 2021 suggests deaths of opiate users in treatment in England are higher than expected. The increases in deaths are geographically widespread. It should not be assumed that COVID-19 directly accounts for this increase in deaths, especially as it happened in months where overall COVID-19 related deaths were low.

Methadone overdoses resulting in hospital admission increased substantially between April and September 2020 (more up-to-date data is not yet available). This may be relevant, but it is not known if the people who were admitted to hospital were in drug treatment and prescribed methadone. Drug treatment services are encouraged to ensure treatment provided is personalised and in line with national clinical guidance as far as current circumstances allow. This personalised care should include supervised consumption of opioid substitution treatment according to the outcome of regular assessments, including of risk.

The number of deaths registered in 2019 in England and Wales involving heroin or morphine stayed the same as the previous year and are the second highest on record.

1.2 Synthetic opioids

Synthetic opioids detected in global drug markets include fentanyls and opioid new psychoactive substances (NPS) including AH-7921 and MT-45.

Key clinical messages

Synthetic pharmaceutical and illicit opioid use continues to be reported. Fentanyl is regularly reported anecdotally to be in circulation but rarely proven to be so. Fentanyl 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.

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. You may need to give multiple doses of naloxone, or naloxone infusion, in acute settings. These may be more likely to be needed if the patient has consumed highly potent synthetic opioids.

Analysis shows the risk of fentanyl toxicity via dermal absorption is low. However, Public Health England (PHE) has published guidance for clinicians to reduce the risk of contamination from fentanyl.

See the heroin entry above (1.1) for information on concurrent use of opioids with pregabalin, gabapentin, benzodiazepines and alcohol, and the related overdose risk.

Latest evidence

In 2019 there were 59 deaths registered in England and Wales involving fentanyl, 1 death involving fentanyl analogues and 1 involving novel opioids. All of these figures represented decreases from 2018. Fentanyl deaths registered in Scotland in 2019 were the highest on record (25). The number of deaths attributed to synthetic opioids (including fentanyl) in the UK remains very low compared to heroin, although may be underestimated due to inconsistent post-mortem toxicological screening.

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 continued vigilance.

2. Synthetic cannabinoid receptor agonists (SCRAs)

People who use SCRAs often call them ‘spice’ or ‘mamba’.

Key clinical messages

SCRA use is most prevalent in prisons across the UK. In comparison, SCRA 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; some SCRAs may 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 may be fatal.

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

Latest evidence

There is evidence that acute harms associated with SCRAs have continued to increase. Longer-term trends, including deaths, suggest that acute harms have increased while chronic issues (measured through treatment demand) and use (drug seizures) may have decreased.

MDMB-4en-PINACA is increasingly dominant, though 4F-MDMB-BINACA and 5F-MDMB-PICA remain common. These compounds were the most seized SCRAs in drug seizures analysed in England and Wales in the first 3 quarters of 2020. There are claims that these substances are more potent than, and have different effects to, other SCRAs.

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.

Since July 2020, there have been reports that edible cannabis products are in circulation and in use primarily by young people but increasingly also by adults in drug treatment. These products have been linked to hospitalisations. They are variously reported to contain tetrahydrocannabinol (THC), cannabidiol (CBD) or, more recently and concerningly, SCRAs.

In 2019, SCRAs were mentioned on the death certificate in 56 deaths registered in England and Wales, a similar number to 2018 (60) and more than double the number registered in 2017 (25). This is despite signs of decreased use of these substances compared to previous years. There were 4 deaths in Scotland involving cannabis and cannabinoids including one involving SCRAs in 2019.

3. Sedatives and dissociatives

3.1 Benzodiazepines

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

There is increased availability and use of illicitly manufactured ‘street’ benzodiazepines and their analogues, including alprazolam, etizolam, flualprazolam, flubromazolam and temazepam. These substances are often sold as diazepam or alprazolam. Illicit benzodiazepines are often used by people who use opioids but also by some young people who do not use opioids.

Newer illicit 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. Etizolam, but also flualprazolam and flubromazolam, is increasingly being identified in England and Wales, and may be sold as Xanax.

Latest evidence

Reports of benzodiazepine availability and related harm in England have been increasing in recent years, notably in the north-east, north-west and south-west. Health data in England suggests increasing numbers of people are experiencing acute and chronic harm linked to benzodiazepine use.

In July 2020 PHE issued a national alert about illicit drugs sold as benzodiazepines. It contained advice on the availability of and harm from these drugs, particularly when used with alcohol and drugs that have a respiratory depressant effect (including gabapentinoids and opioids). This alert was based on toxicology results of illicit tablets sold as diazepam, temazepam and alprazolam linked to hospitalisations and deaths, as well as from police drug seizures. Tablets known as or marked with ‘DAN 5620’ (on one side) and ‘10’ (on the other), ‘T-20’, ‘TEM 20’, ‘Bensedin’ and ‘MSJ’ may contain dangerously potent benzodiazepines such as flubromazolam, flualprazolam, etizolam, clonazolam or phenazepam. The tablets causing concern currently are often blue or green but come in various colours. There has also been a re-emergence of red ‘Xanax’ bars or pills, and green ‘Xanax’ sometimes with ‘S 90 3’ markings.

If you are in contact with people who use drugs, you should be alert to the increased possibility of overdose from illicit benzodiazepines. This is so you can raise awareness, recognise possible symptoms of overdose and respond appropriately. The national 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 64% (814) of the 1,264 drug-related deaths registered in Scotland in 2019, more than in any year on record. Etizolam was involved in 752 of these cases, most of which also involved opioids. The number of deaths registered in England and Wales involving benzodiazepines decreased slightly from 420 in 2018 to 399 in 2019. Deaths involving benzodiazepine analogues increased from 9 to 26 in the same period.

Most illicit benzodiazepines no longer contain the substances they are sold as. For example, of the samples from across the UK submitted to the Welsh Emerging Drugs and Identification of Novel Substances (WEDINOS) project between October to December 2020 that were purchased as alprazolam, only 40% contained alprazolam. Fifty-one percent contained other benzodiazepines or their analogues (notably 30% flubromazolam and 11% flualprazolam). Flualprazolam and flubromazolam are being increasingly identified in the UK market and are reported to have a higher potency than alprazolam.

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

3.2 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, dysuria and haematuria.

Latest evidence

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

3.3 Nitrous oxide (N2O)

Key clinical messages

Heavy and repeated use of N2O has been associated with severe peripheral neuropathy and rarely sub-acute combined degeneration of the spinal cord.

Latest evidence

Some reports link heavy use of N20 (up to 75 cannisters per day) to peripheral neuropathy.

4. Stimulants

4.1 Cocaine (including crack cocaine)

Key clinical messages

Prevalence of cocaine use (including crack) appears to be increasing across the UK. The latest European Drug Report from the EMCDDA shows that England and Wales had the highest prevalence of cocaine use in Europe in 2019.

Latest evidence

Deaths involving cocaine (powder or crack) registered in England and Wales, Scotland and Northern Ireland in 2019 all reached the highest levels on record. Data from England and Wales shows that this trend has continued. There were 708 deaths registered in 2019 mentioning cocaine on the death certificate, an increase from 637 deaths registered in 2018.

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 latest data from the Unlinked Anonymous Monitoring survey shows that the number of current injectors reporting crack injection remains high in England and

Wales. In 2019, 59% of current injectors 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 a rise in HIV transmission. In 2019, the proportion of people presenting to drug treatment reporting primary use of powder cocaine was higher in Scotland than in England or Wales for the first time.

4.2 MDMA and ecstasy

Key clinical messages

MDMA availability and use reportedly fell during periods of COVID-19 restrictions but it is anticipated that availability and use will increase this summer as restrictions ease. 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

Harm associated with MDMA use has been increasing among younger people in recent years. Deaths registered in England and Wales involving MDMA increased from 56 in 2017 to 92 in 2018. This increase in deaths was primarily seen in the under 30s. In 2019, the number of deaths registered involving MDMA decreased to 78.

Of those presenting to drug treatment in England, Wales and Scotland in 2019 who reported MDMA as their primary problem drug, 16% were aged under 15, with 69% aged under 20 (unpublished data analysis submitted by the National Drug Evidence Centre to the UK Focal Point on Drugs).

4.3 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 drug seizures of synthetic cathinones in England and Wales has fallen since 2018.

There were 14 in drug-related deaths registered in England and Wales in 2019 involving synthetic cathinones.

5. Other substances

5.1 Gabapentinoids

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

Key clinical messages

Evidence shows prescriptions for pregabalin and gabapentin are increasing. Gabapentinoids are licensed for treating 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.

Pregabalin has been associated with infrequent reports of severe respiratory depression, including some cases without concomitant 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

Registered deaths in England and Wales involving gabapentinoids have been increasing. Between 2017 and 2019, the number of deaths involving pregabalin went from 136 to 187 to 244, and for gabapentin from 60 to 93 to 89. The number of deaths in Scotland involving gabapentin and pregabalin rose from 144 to 195 and from 121 to 280 respectively over the same period. There were 77 deaths registered in Northern Ireland involving pregabalin in 2019, an increase from 9 in 2016.

5.2 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 you are dealing with people 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. You should refer all patients with symptoms of toxicity 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 March 2021, there have been 142 separate episodes of systemic DNP exposure discussed with the NPIS. Of these, 26 (19%) are known to have died. During 2020, the NPIS recorded 8 cases of DNP toxicity and 2 deaths, both decreased compared to 2019 (14 cases, of which 4 were fatal) and 2018 (20 cases, of which 6 were fatal).

6. General clinical advice and updates

The chemical makeup of 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 common SCRAs, effects and treatment.

PHE has published evidence-based recommendations to protect first responders from exposure to fentanyl.

7. Recent statistics and other data sources

Drug misuse: findings from the latest Crime Survey for England and Wales.

Substance misuse treatment for adults: statistics 2019 to 2020.

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

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).

The latest Office for National Statistics report Deaths related to drug poisoning in England and Wales.

The latest National Records of Scotland Drug-related deaths in Scotland report and data.

The EMC DDA's European Drug Report 2020.

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.

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