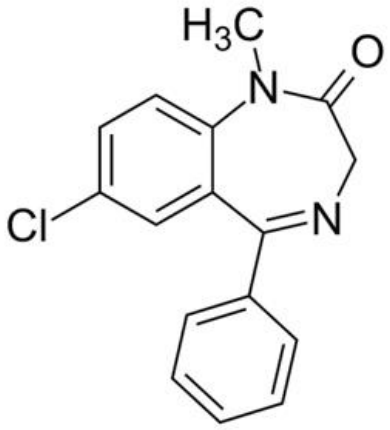
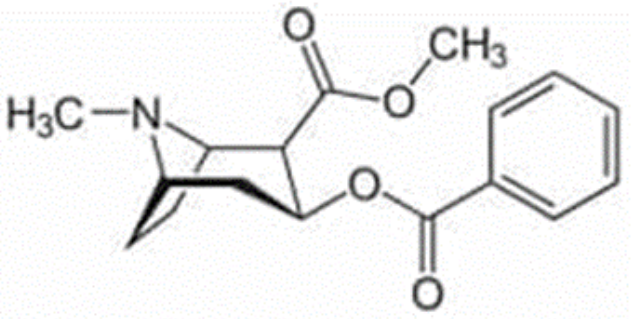
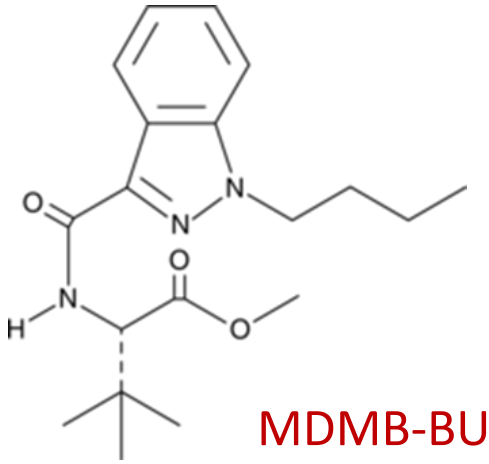
WEDINOS:
Philtre April 2023 – March 2024



Diazepam



Cocaine



MDMB-BUTINACA

Llywodraeth Cymru
Welsh Government

GIG CYMRU NHS WALES
Iechyd Cyhoeddus Cymru
Public Health Wales

CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD

GIG CYMRU NHS WALES
Bwrdd Iechyd Prifysgol Caerdydd a'r Fro
Cardiff and Vale University Health Board

Headline Figures

Total to date (Project launch 1st October 2013 to 31st March 2024):

- 43,564 samples received
- 38,884 analysed
- 641 substances identified either in isolation or combination.
- Over 300 organisations and services
  - Including: Emergency Departments, Local Health Teams, Substance Misuse Services, Housing and Homelessness, Education Centres, Training Providers, Night Time Economy (NTE) Venues, Festivals, Criminal Justice Services and Welsh Prisons
  - Samples are also provided by individuals not engaged with / accessing services

This Year (2023-2024):

- 8,466 samples received representing an increase from 7,744 in 2022/23.
  - 7,064 analysed **UP** from 6,656
- Community samples increased to 5,793 from 4,979
  - 206 substances identified **UP** from 185
  - Samples received from 96 different organisations, services and Night Time Economy (NTE) venues as well as from individuals
  - Median age of sample providers is 34 years (range 12 to 80 years)
  - As in the previous six years benzodiazepines were the most commonly identified class of psychoactive substance with 19 benzodiazepines identified
- **Cocaine** was the most commonly identified substance overall
- Most commonly identified substance in the community was **diazepam**, followed by **bromazolam**
- **Cocaine** was the most commonly identified substance in the NTE
- Criminal justice settings – the Synthetic Cannabinoid Receptor Agonist (SCRA) **MDMB-BUTINACA** was the most commonly identified substance

Wider perspective….

Global, European, England and Wales, and Welsh estimates:

October 2023 marks the **10th anniversary** of the launch of the WEDINOS programme, along with receipt, analysis and the publications of results of the first sample. This was an unknown white powder, submitted via one of the community-based drug services. Following analysis this sample that had caused the unexpected effects of nosebleeds, depression and suicidal ideation, was profiled as containing para-chloroamphetamine, amphetamine, N-ethylnorketamine and benzocaine.

Since then, WEDINOS has monitored drug trends across the UK, whilst sharing information with, and receiving information from, regional, national and international partners to ensure the continued provision of timely and pragmatic harm reduction information for people who use drugs and those working or concerned with the well-being of people who use drugs.

WEDINOS routinely feeds drug market data into a far reaching and varied collection of services, from local drug services to members of the Royal College of Emergency Medicine in Wales, through to the UK National Drug Alerts System and the Advisory Council for Misuse of Drugs; also wider to the Trans European Drugs Information project and the United Nations Office for Drugs and Crime. This is not an exclusive list, with WEDINOS providing information to a number of other organisations concerned in the welfare of people who use drugs.

Globally, the United Nations Office for Drugs and Crime (UNODC) reports that the estimated number of people who used drugs in 2021 grew to around 296 million. With almost 1 in 13 people aged 15-64 worldwide having used drugs in that year and more than 1 in 100 having a drug use disorder. There were an estimated 13.2 million people who inject drugs worldwide.

39.5 million people are estimated to be drug dependent and/or require treatment services, but only 1 in 5 people with drug use disorders received drug treatment. The majority of these individuals are people who use cannabis or opioids (1).

The Global Burden of Disease Study estimated that there were 494,000 drug-related deaths in 2019. This indicates a 17.5 per cent increase in deaths attributed to drugs between 2009 and 2019 (2) .

Of those deaths 366,000 were deaths indirectly related to drug use, e.g. liver disease due to hepatitis, HIV and self-harm associated with drug use.

Deaths attributed to drug use disorders (128,000) accounted for 26 per cent, of which opioid use disorders contributed to 69 per cent, or 88,000 deaths (3).

In the **United Kingdom**, the 2023 Crime Survey for England and Wales, reported that approximately 3.1 million people, or 9.5 per cent of adults aged 16 to 59, had taken a drug in the last year. The prevalence was higher amongst young people with 17.6 per cent of 16 to 24 year olds reporting taking a drug in the last year. However, this represents a fall in young people reporting any drug use, this is largely attributed to a fall in cannabis use.

1) World Drug Report 2021 (United Nations publication, Sales No. E.21.XI.8), https://www.unodc.org/res/wdr2021/field/WDR21_Booklet_2.pdf [accessed 2nd May 2023]
2) Institute for Health Metrics and Evaluation, "Global Burden of Disease Study 2019 Data Resources: GBD Results Tools"
3) World Drug Report 2021 (United Nations publication, Sales No. E.21.XI.8), https://www.unodc.org/res/wdr2021/field/WDR21_Booklet_2.pdf [accessed 2nd May 2023]

Wider perspective....continued...

Cannabis remains the most commonly used substance in the UK, having been reported as such since records began in 1995. There was no change in the prevalence of cocaine use, year ending March 2022, compared to the year ending March 2020 (pre-pandemic figures). However, there was a fall in MDMA use, alongside an increase in individuals reporting using hallucinogens (4).

A picture from Wales

The following section utilises data from the Public Health Wales report: Data mining Wales: The annual profile for substance misuse 2022-23

Provisional headline figures for problem drug use estimates in Wales,** including populations not in contact with any services, suggest that the total number of problem drug users in 2020-21 was 51,110 (95% confidence interval (CI) 38,100 – 68,340) (5).

There were 17,246 assessments (15,215 unique individuals) within substance misuse services in Wales in 2022-23, representing a decrease of 2.2 per cent compared to the previous year (17,644 assessments). Of the individuals assessed:

- 7,532 (48.5 per cent) were primary problematic alcohol clients
- 6,883 (44.3 per cent) were primary problematic drug clients
- 1,123 (7.2 per cent) did not have a substance recorded (5)

Amongst assessments for problematic drug use, opioids were cited as the most prevalent primary substance with 3,505 assessments (50.9 per cent). Of these, 2,784 assessments cited heroin as the primary substance. Cannabis was the next most frequently reported substance with 1,650 assessments (23.9 per cent). The number of assessments with cocaine, including crack cocaine, as the primary substance increased to 1,621 in 2022-23. This is an increase of 6.4 per cent and represents 23.5 per cent of all referrals to substance misuse services in 2022-23 (5).

In Wales, overall, the number of hospital admissions for poisonings with named illicit drugs has decreased over the past four years to 4,342 in 2022-23. There has been a 27.6 per cent decrease in illicit drug admissions since 2018-19. Opioids accounted for the highest number of individuals admitted to hospital for illicit drugs, followed by cannabinoids.(5), ***

In 2022, 318 deaths due to drug poisoning were registered in Wales, a decrease of 1.2 per cent from the previous calendar year. Of all drug-poisoning deaths, 205 (64.5 per cent) were identified as a drug misuse death, remaining high with only a slight decrease from the previous year (5).

Cannabis remains the most commonly used substance in the UK, having been reported as such since records began in 1995. There was no change in the prevalence of cocaine use, year ending March 2022, compared to the year ending March 2020 (pre-pandemic figures). However, there was a fall in MDMA use, alongside an increase in individuals reporting using hallucinogens (6).

4) Drug misuse in England and Wales: year ending March 2023; Office for National Statistics; 14th December 2023; https://www.ons.gov.uk/peoplepopulationandcommunity/crimeandjustice/articles/drugmisuseinenglandandwales/yearendingmarch2023 {accessed 31st May 2024}

* This should be regarded as a minimum estimate due to reporting biases.

** In this context problem drug use (PDU) is defined by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) as "injecting drug use or long duration or regular use of opioids, cocaine and/or amphetamines [including amphetamine type substances]".

*** It is important to note that no distinction is possible in hospital admission data for differentiation between cannabinoid products: cannabis resin, stronger strains of herbal cannabis 'skunk;' or newer forms of synthetic cannabinoid receptor agonists (SCRAs), sometimes referred to as 'Spice'

5) Data mining Wales: The annual profile for substance misuse 2022-23; Public Health Wales; 11th April 2024; https://publichealthwales.nhs.wales/news/latest-data-on-substance-misuse-in-wales-published/ {accessed 31st May 2024}

6) Drug misuse in England and Wales: year ending March 2023; Office for National Statistics; 14th December 2023; https://www.ons.gov.uk/peoplepopulationandcommunity/crimeandjustice/articles/drugmisuseinenglandandwales/yearendingmarch2023 {accessed 31st May 2024}

WEDINOS

Samples Submitted

In total WEDINOS received and analysed 7,064 samples from 96 services and settings across the UK, as well as from individuals. These samples can be separated into three broad categories:

- Community
- Night Time Economy (NTE)
- Criminal Justice Settings

Samples submitted from the NTE and Criminal Justice Settings are submitted from amnesty bins or are non-attributable finds and therefore are not accompanied by any information relating to purchase intent, effects or demographics.

Key findings

Most commonly identified substances – All samples

Within the 7,064 samples analysed by WEDINOS, 206 substances were profiled either in isolation or combination.

The most commonly identified chemical group of psychoactive substances for the sixth year were benzodiazepines, with 19 benzodiazepines identified (20 were identified in 2021/22).However, seven of these substances were identified on ten or less occasions.

Diazepam was the second most commonly identified substance and the most commonly identified benzodiazepine with 819 identifications (up from 593), despite it being reported on 1,408 occasions as the purchase intent. Bromazolam was the second most commonly identified benzodiazepine, a substance that is 98 per cent of the time profiled as a substitute within the illicit benzodiazepine market, having been identified on 715 occasions, but only being listed as a purchase intent 13 times.

Bromazolam is more potent than Diazepam. This is a potential risk for individuals using benzodiazepines as dosage and potency varies greatly.

Cocaine was the most commonly identified psychoactive substance identified by WEDINOS. This is heavily influenced by the number of samples from the Night Time Economy, accounting for almost 50 per cent of cocaine identifications

The most recently published Crime Survey for England and Wales on Drug Misuse in England and Wales stated that there was no change in last year's use of cocaine among adults aged 16 to 59 or young people aged 16 to 24 from year ending March 2020 (pre-pandemic) (6).

However, Public Health Wales has reported the number of assessments with cocaine, including crack cocaine, as the primary substance by drug services in Wales has increased from 1,523 in 2018-19 to 1,621 in 2022- 23. This is an increase of 6.4 per cent and represents 23.5 per cent of all drug referrals in 2022-23 (7).

7) Drug misuse in England and Wales: year ending March 2023; Office for National Statistics; 14th December 2023; https://www.ons.gov.uk/peoplepopulationandcommunity/crimeandjustice/articles/drugmisuseinenglandandwales/yearendingmarch2023 {accessed 31st May 2024}

8) Data mining Wales: The annual profile for substance misuse 2022-23; Public Health Wales; 11th April 2024; https://publichealthwales.nhs.wales/news/latest-data-on-substance-misuse-in-wales-published/ {accessed 31st May 2024}

WEDINOS

Consistent with previous years, caffeine was the most popular bulking/cutting agent identified, as well as being found in combination with other substances, primarily other stimulants, such as amphetamine, MDMA and cocaine. Several samples of powders and tablets were found to contain caffeine in isolation, in particular amongst samples submitted as MDMA

2023/2024	2022/2023
Cocaine	Cocaine
Diazepam	MDMA
MDMA	Bromazolam
Bromazolam	Diazepam
Ketamine	Ketamine
Caffeine	Caffeine
Paracetamol	Tetrahydrocannabinol
Tetrahydrocannabinol	Alprazolam
Alprazolam	Paracetamol
Heroin	Nicotine

Table 1: Most commonly identified psychoactive substance WEDINOS samples.

.

WEDINOS

Community settings

As previously mentioned, WEDINOS receives samples from a wide variety of community settings. WEDINOS works closely with the six Welsh prisons, reporting separately on finds that have no evidentiary value. In the next section we focus on samples from community settings.

5,793 samples were submitted from community settings including education, health (incl. Emergency Departments), mental health, housing and homelessness, substance misuse services and individuals.

Of these 5,793 samples, demographic information was available for 96 per cent (n=5,544).

Where demographic data was available 80 per cent of the samples were submitted by males and 20 per cent by females. This is similar to the sex split amongst sample providers in 2022-23 (79 per cent male and 21 per cent female).

The median age for all mind altering / psychoactive sample providers (Wales and wider UK) was 34 years, range 12 to 80 years, in comparison to 33 years and 12 to 80 years in 2022-2023.

- Females - median age was 33 years (34 years in 2022-2023) (range: 12-80 years)
- Males - median age was 34 years (33 years in 2022-2023) (range: 13-77 years)

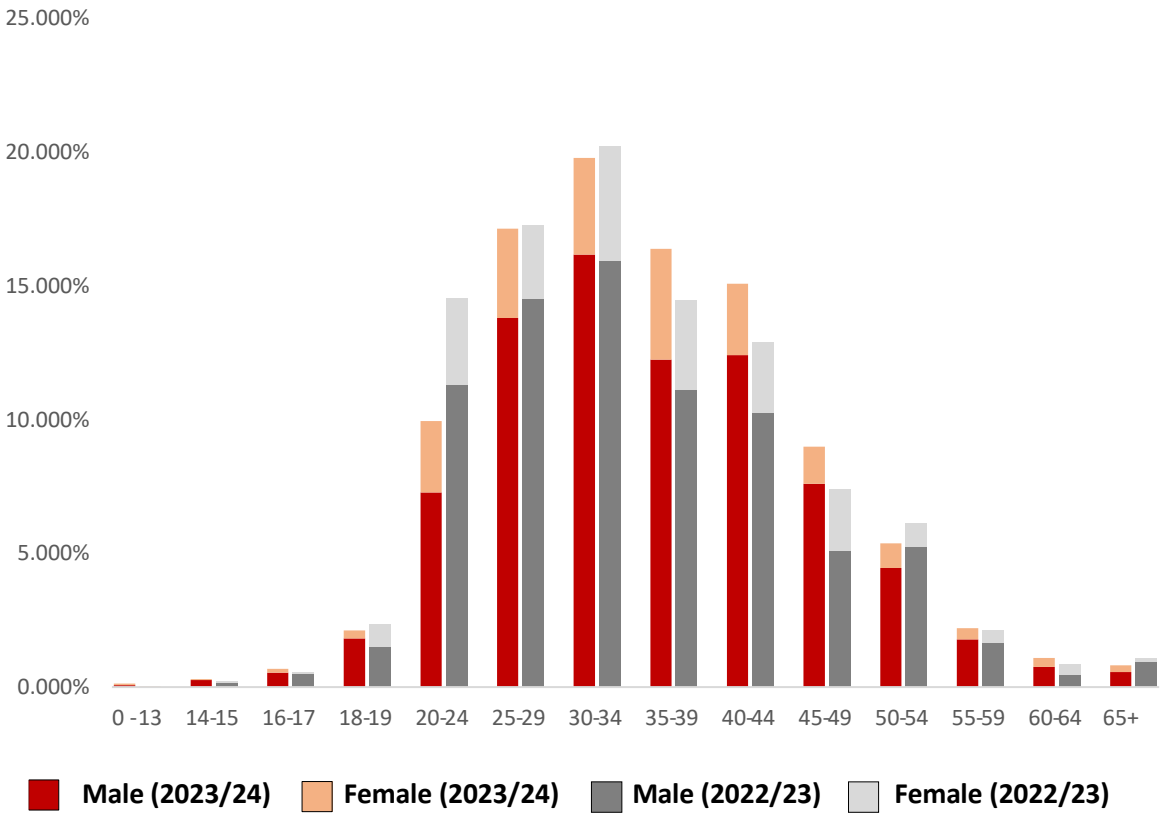


Chart 1: Demographic profile of psychoactive sample providers

WEDINOS

Community Samples Analysis

Since the launch of WEDINOS in 2013, the project has consistently evidenced the substitution of substances within the UK's illicit drug market.

In the 5,793 samples submitted via community-based sample providers, 202 substances were profiled either in isolation or combination.

Table 2 shows the changes in the "top ten most common" substances at the submission stage (purchase intent) and the post analysis stage.

Samples listed as unknown include samples submitted under a name that does not allow the substance or category of substance to be identified, samples found or unknown substances, such as those submitted by patients with acute effects within a health care setting, such as an emergency department or mental health ward.

Number	Purchase intent	Post-analysis
1	Diazepam	Diazepam
2	MDMA	Bromazolam
3	Cocaine	MDMA
4	Alprazolam	Cocaine
5	Unknown	Caffeine
6	Ketamine	Ketamine
7	THC	Pregabalin
8	Amphetamine	Paracetamol
9	Heroin	Alprazolam
10	Zopiclone	Amphetamine

Table 2 Most common substances pre (perceived) and post (actual) analysis

Table 2 demonstrates changes between the most commonly reported substances pre analysis and the most commonly identified contents post analysis.

WEDINOS

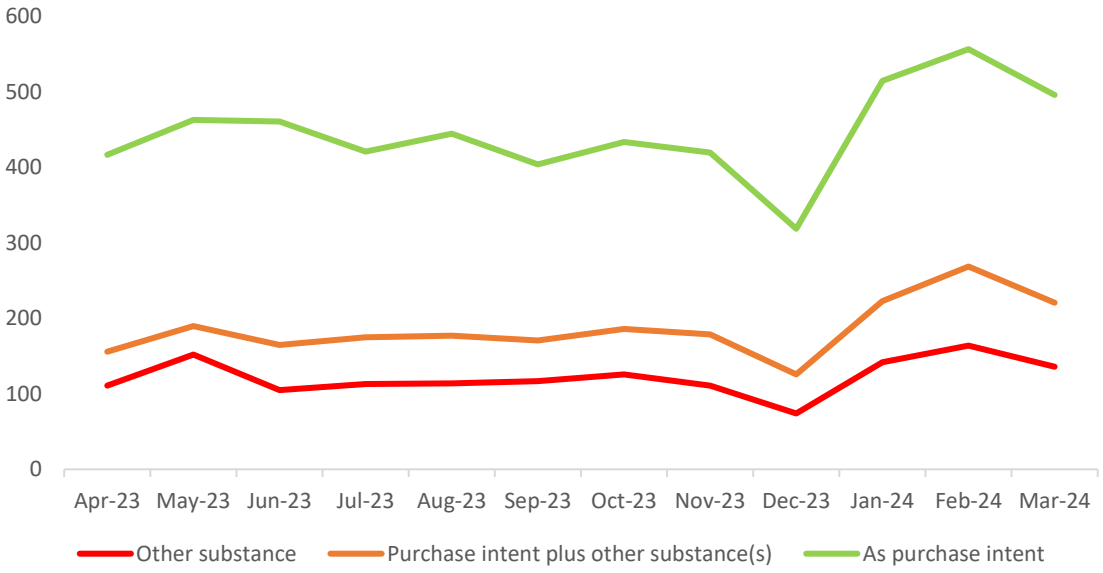
Community Samples Analysis…continued…

As in 2022-23, bromazolam is not present on the pre analysis / purchase intent list. However, is the second most commonly identified substance overall. Pre analysis bromazolam was listed only 13 times as the purchase intent, following analysis it was identified on 715 occasions.

It may be argued that the high pre analysis presence of “unknown” substances would be the biggest influencer of this change. However, even following removing these samples we find that over the past year 42 per cent of samples submitted to WEDINOS with a substance listed in the purchase intent did not contain what was expected>This is up from 39 per cent 2022-23.

Some samples were found to contain the purchase intent and other substances, such as a sample purchased as heroin that was found to contain heroin and xylazine upon analysis. Other samples were found to contain a different substance or substances,. for example, a sample purchased as diazepam which was found to contain bromazolam and metonitazene.

The levels of additional substances and substitution are shown in Graph 1



Graph 1 Levels of substitution and adulteration amongst samples submitted to WEDINOS April 2023 – March 2024

Community Sample Types

Form of sample

WEDINOS requests the 'form of sample' for each submission to monitor and report the various forms in which substances appear on the market and potential differences in method of consumption.

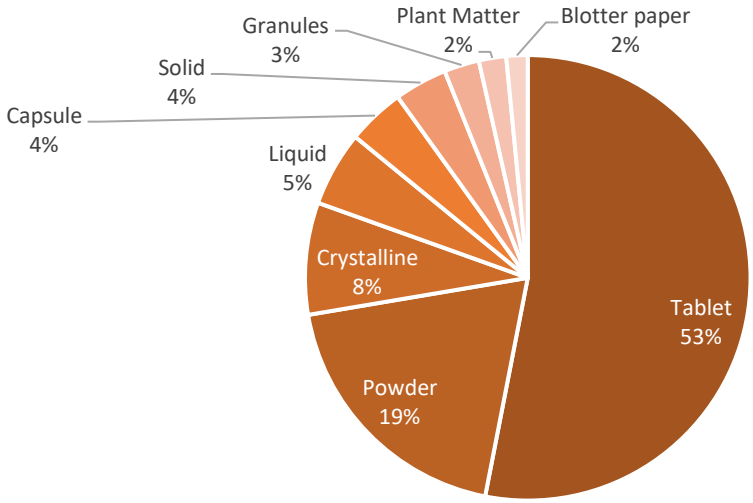


Chart 2: Forms of psychoactive substance samples submitted to WEDINOS April 2023 to March 2024

As in the previous three years, we see a high prevalence in the number of tablets submitted, this is mirrored by the high numbers of samples submitted believed to be diazepam and alprazolam.

Method of consumption and harm reduction advice

Assuming that all plant matter samples and vape liquids are smoked/vaped, the remaining samples (pills, liquids, tabs, granules etc.) were ingested through a variety of methods. The most common method of consumption (71.5 per cent) was oral (swallowing, 'bombing'). This high prevalence of oral consumption is likely linked to the high number of submissions purchased as benzodiazepines, particularly diazepam and alprazolam, alongside submissions of zopiclone and a high prevalence of MDMA tablets (n=232).

The second most common method was snorting / sniffing at 18.2 per cent, as shown in Chart 3.

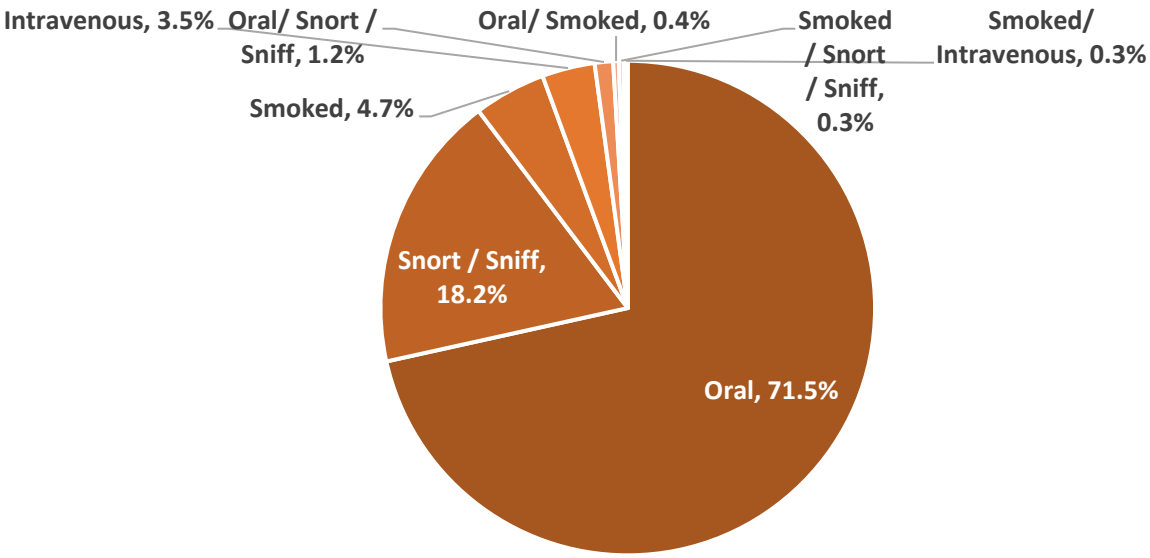


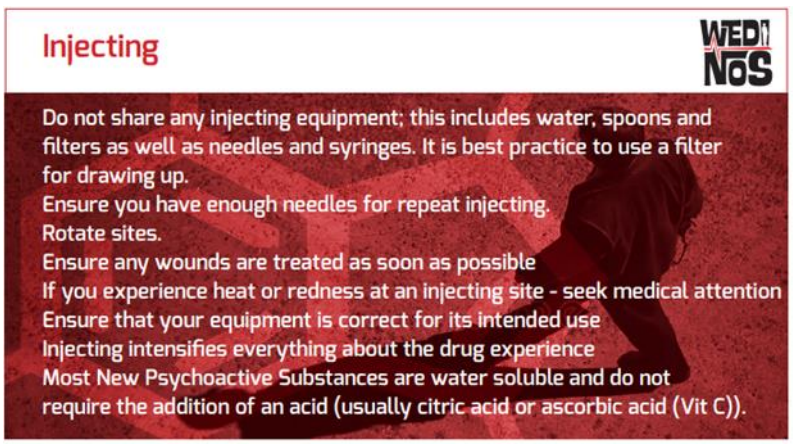
Chart 3: Method of consumption (samples submitted as tablet, powder, crystalline, capsule, solid, granules, blotter paper) April 2023 to March 2024

3.5 per cent of sample providers reported intravenous injecting of substances. This is an increase from 1.3 per cent in 2022-23.

Samples injected were purchased as, and found to contain, heroin, cocaine, amphetamine, ketamine, nitazenes and xylazine.

Injecting drug use carries with it inherent risks of bacterial and viral infection over and above the risks / toxicity of the substance being injected.

All injecting, regardless of the substance, carries a significant risk of serious infection and other complications. Individuals who currently inject drugs, or have previously injected, should get tested for blood borne viruses



Powders, granules and crystalline materials

Focusing on the method of consumption for powders, granules and crystalline materials, the most common method was snorting/sniffing with 48.6 per cent reporting this as shown in Chart 4. There has been an increased number of samples of this form reported to be injected intravenously. This can be attributed to an increased number of heroin samples received during this reporting period, particularly between November 2023 and February 2024, during which time there were clusters of fatal and non-fatal drug poisonings amongst people who use heroin. With an increased level of concern we often see an increase in submissions from the population affected.

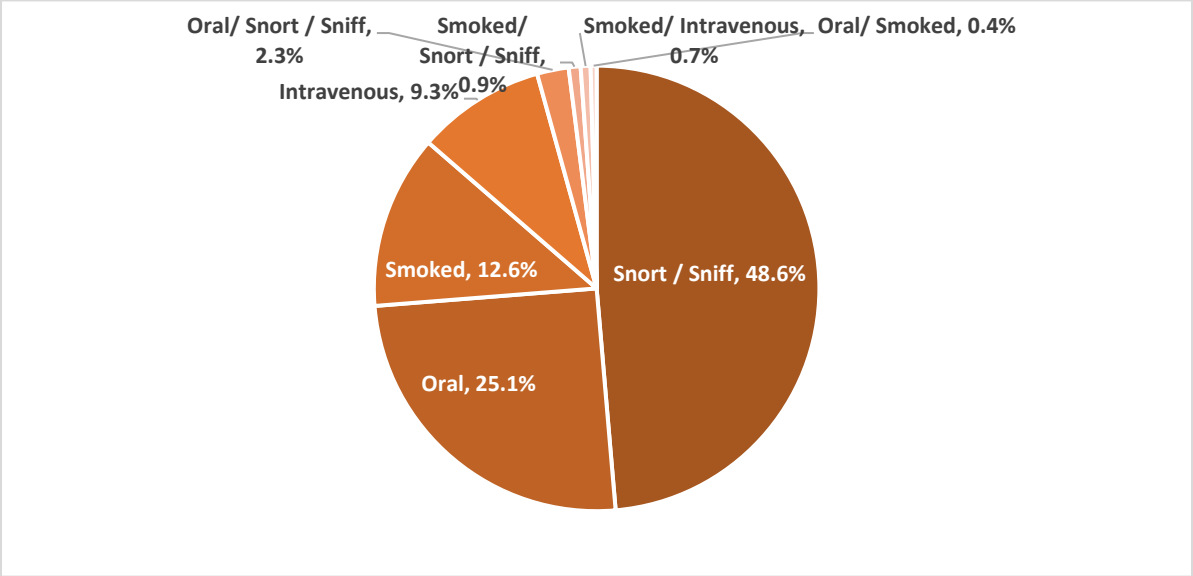
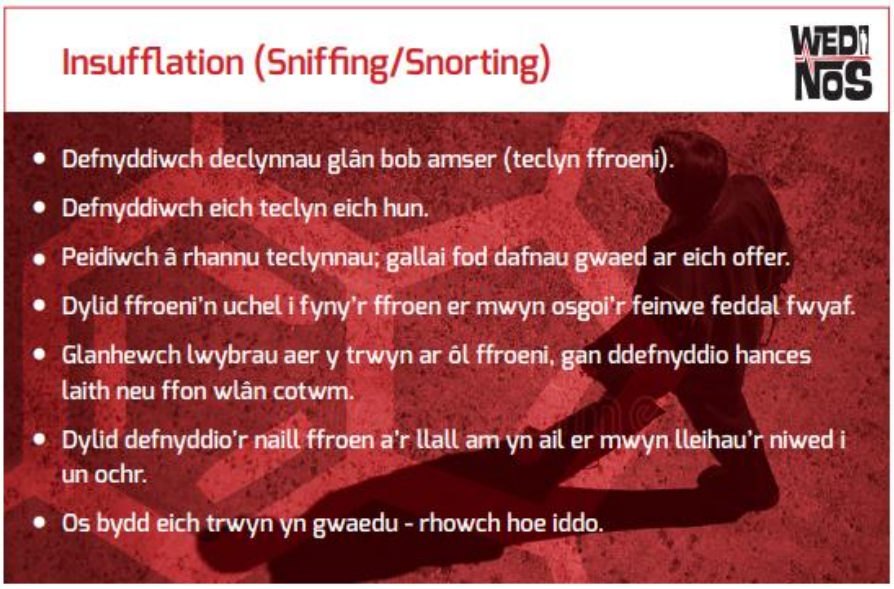


Chart 4: Method of consumption: Powders

Snorting/sniffing potentially caustic or toxic substances carries additional risks related to damage to the nasal passages, as well as potential transmission of blood borne viral infection when sharing snorting paraphernalia in the presence of nasal passage damage and blood.



Benzodiazepines

For the sixth consecutive year, benzodiazepines were the most commonly identified class of substances amongst all samples submitted to WEDINOS.

Diazepam was the most commonly reported purchase intent amongst community submitted samples, and another benzodiazepine, alprazolam, was fourth.

Post analysis the benzodiazepine diazepam was the most commonly profiled substance amongst community samples. Bromazolam was second and alprazolam ninth.

What are benzodiazepines?

Benzodiazepines are a class of sedative substances. These work by increasing the effects of a naturally occurring chemical in the brain, gamma aminobutyric acid (GABA).

GABA reduces activity in the region of the brain responsible for:

- reasoning
- memory
- emotions
- essential functions, such as breathing.

As a result benzodiazepines can make people feel relaxed and sleepy (sedative effects), reduce anxiety and relax muscles.

Prevalence (licit and illicit markets)

Benzodiazepines, used as medicines, are produced by licenced pharmaceutical companies and authorised according to national legislation. In the UK, benzodiazepines are controlled under the Misuse of Drugs Act 1971 and the Psychoactive Substances Act 2016. Where they are used medicinally they are prescription only medicines.

Where prescribed, they are recommended for short-term use at the lowest possible dose. This is to reduce the risks of tolerance, dependence and withdrawal symptoms.

NHS England states that 1.1 million adults in England had received one or more prescriptions for benzodiazepines in 2020-21, showing a decrease from 1.4 million in 2017-18 (9). The most commonly prescribed benzodiazepine is diazepam.

The Crime Survey for England and Wales reports on the use of tranquilizers, a group of substances that includes barbiturates and benzodiazepines. 0.5 per cent of English and Welsh adults aged 16 to 59 years old are estimated to have used tranquilizers during the past year to March 2023, this is compared to 0.9 per cent of individuals aged 16 to 24 years old (10).

9) Optimising personalised care for adults prescribed medicines associated with dependence or withdrawal symptoms: Framework for action for integrated care boards (ICBs) and primary care, NHS England; 2nd March 2023; https://www.england.nhs.uk/long-read/optimising-personalised-care-for-adults-prescribed-medicines-associated-with-dependence-or-withdrawal-symptoms/#appendix-prescribing-patterns {accessed 2nd June 2024}
10) Drug misuse in England and Wales: year ending March 2023; Office for National Statistics; 14th December 2023; https://www.ons.gov.uk/peoplepopulationandcommunity/crimeandjustice/articles/drugmisuseinenglandandwales/yearendingmarch2023 {accessed 31st May 2024}

Benzodiazepines

Benzodiazepine toxicity

The primary toxicity of benzodiazepines is on the central nervous system. These effects can be potentially more severe when depressant drugs such as alcohol and opioids are consumed at the same time, or during the period in which benzodiazepines are still present and active in the body. The duration of effects of benzodiazepines can vary greatly depending on whether it is a short, medium or long acting benzodiazepine. For example, the duration of action for bromazolam is 5 to 8 hours (11). However the half-life* of these substances can be much longer. For example, the half-life of diazepam can be between 20 and 100 hours (12).

Benzodiazepine deaths

The Office for National Statistics reported 509 deaths involving benzodiazepines in England and Wales in 2022 (13).

The European Monitoring Council for Drugs and Drug Addiction states that the current evidence available is sufficient to indicate that these substances may have consequences for health, especially when consumed in combination with other drugs. They are often very cheap and may be used in combination with alcohol, sometimes resulting in potentially serious health reactions or uncharacteristic behaviour. They have also been linked to increasing the risk of opioid overdose death and, in the most recent data, the proportion of overdose deaths involving benzodiazepines increased in some countries (14).

However, the increased risk of adverse effects does not just lie with poly-drug use. As WEDINOS has evidenced over the past several years, there is a high rate of substitution within the illicit benzodiazepine market, with the European Monitoring Council for Drugs and Drug Addiction (EMCDDA) citing concerns over the growing crossover between the illicit drugs and the novel psychoactive substance markets In this section, we will describe this crossover in relation to samples submitted to WEDINOS as diazepam (Valium), that following analysis are found to contain other substances, primarily new / designer benzodiazepines. These substances can often be more potent than the ones they replace, have a different time of onset and duration of effects, and therefore pose an increased risk of adverse effects.

11) World Health Organisation, Critical review report: Bromazolam, Expert Committee on Drug Dependence, Forty-fifth Meeting, Geneva, 10–14 October 2022; https://cdn.who.int/media/docs/default-source/controlled-substances/45th-ecdd/bromazolam_draft.pdf?sfvrsn=f1bc761e_1#:~:text=Informational%20websites%20for%20users%20list%20a%20dosage%20range,and%20the%20duration%20of%20action%20is%205%E2%80%938%20h [accessed 4th May 2023]

*Half-life is the time taken for blood concentration of a substance to fall to half its peak value after a single dose.

12) Benzodiazepine equivalence table; https://www.benzo.org.uk/bzequiv.htm [accessed 4th May 2023]

13) Office for National Statistics (ONS), released 19 December 2023, ONS website, statistical bulletin, Deaths related to drug poisoning in England and Wales: 2022 registrations; https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/2022registrations#cite-this-statistical-bulletin {accessed 2nd June 2024}

14) European Monitoring Centre for Drugs and Drug Addiction (2023), European Drug Report 2023: Trends and Developments, https://www.emcdda.europa.eu/publications/european-drug-report/2023/drug-situation-in-europe-up-to-2023_en {accessed 2nd June 2024}

Benzodiazepines

Benzodiazepines…A Welsh perspective

In 2022-23 there were 378 benzodiazepine related admissions involving 329 individuals. The EASR was 12.6 admissions per 100,000 population. Compared to last year there has been a 25.6 per cent decrease in the number of admissions related to benzodiazepines.

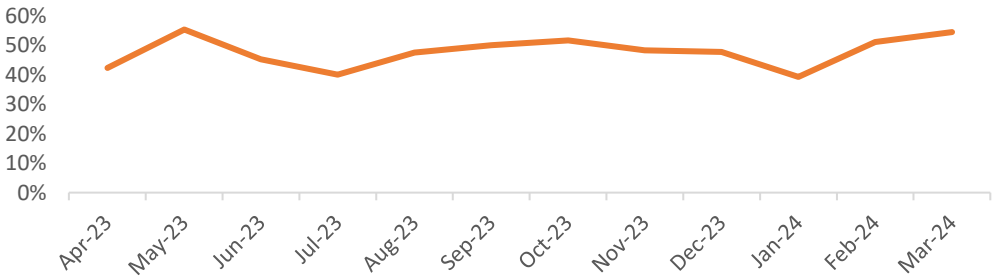
In 2022, 53 drug misuse deaths in Wales involved benzodiazepines, a decrease from 61 in the previous year, but still up from 35 in 2020.

Substitutions

In the reporting period 2023-24, WEDINOS received 1,408 samples submitted in the belief they were diazepam. Within these samples 40 substances were identified, either in isolation or combination. 34 samples were profiled as containing no active compounds.

Despite being the purchase intent, diazepam (in isolation) was profiled as being the sample content following analysis in 52 per cent (n=745) of submissions, meaning a substitution rate of 48 per cent. This is a decrease in the level of substitution compared with 2022-23, which stood at 55 per cent.

Throughout the year, the range of substitutions amongst samples submitted as diazepam was between to 39 per cent (January 2024) to 55 per cent (May 2023).



Graph 2 Percentage of samples submitted as diazepam that were profiled as containing other substances post-analysis

The most commonly identified substitute was the triazolobenzodiazepine, bromazolam. Bromazolam was identified in 34 per cent (n=482) of samples submitted as diazepam. Of real concern, just over 5 per cent (n=75) of all samples submitted as diazepam were found to contain metonitazene, either in combination with bromazolam (n=68) or in isolation (n=7).

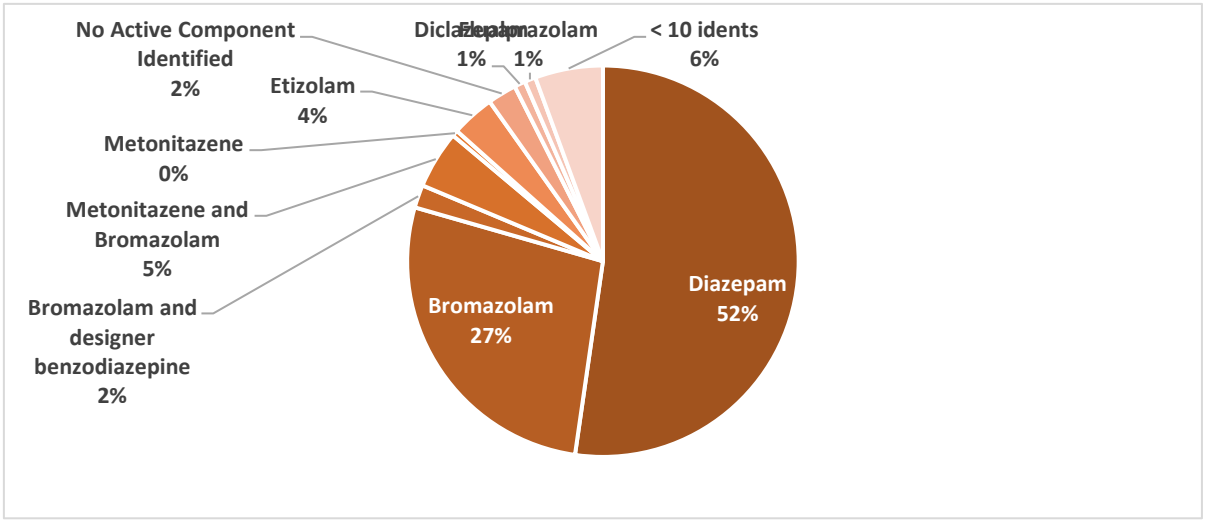


Chart 5: Substances identified in samples purchased as diazepam post analysis

Benzodiazepines

Bromazolam

Bromazolam is a triazolobenzodiazepine, structurally related to alprazolam. Originally developed as a candidate medicine, it was never approved for use. There is currently little scientific literature available relating to bromazolam.

A “common” oral dose of bromazolam, as described by users of the substance, is 1 to 3mg(15). The onset of effects is between 15 and 45 minutes, with a duration of action of 5 to 8 hours.

Self-reported effects of bromazolam consumption include hypnotic, sedative, muscle relaxing, pain relieving, euphoria, increased confidence, empathy and amnesia (16).
In the United Kingdom, bromazolam is controlled under the Psychoactive Substances Act 2016.

W051389

Date Received: 30 Apr 2024
Postcode: S8 -
Purchase Intent: Diazepam
Package Label: Bensedin (Diazepam)
Sample Colour: White, Purple
Sample Form: Tablet
Consumption Method: Not Stated
Self-Reported Effects: Not Stated
Sample Upon Analysis (Major): Bromazolam, Metonitazene
Sample Upon Analysis (Minor):

Click to Enlarge

www.wedinos.org

No data are available on the dependence and abuse potential of bromazolam. However, it can be assumed that the abuse liability and the potential to produce dependence are similar to those of other chemically related benzodiazepines, such as alprazolam.

Direct access submission of samples to WEDINOS allows capture of evidence based local and national drug market trend data, enabling drug services to provide pragmatic information on relevant drug substitutions and harms. Combining this with other data sources such as hospitalisations, toxicology and drug related death data, further enables services to provide targeted information relating to specific substances and contraindications, in this instance addressing poly-drug use involving street purchased “diazepam”.

15) European Monitoring Centre for Drugs and Drug Addiction (2021), New benzodiazepines in Europe – a review, Publications Office of the European Union, Luxembourg.
16) World Health Organisation, Critical review report: Bromazolam, Expert Committee on Drug Dependence, Forty-fifth Meeting, Geneva, 10–14 October 2022; https://cdn.who.int/media/docs/default-source/controlled-substances/45th-ecdd/bromazolam_draft.pdf?sfvrsn=f1bc761e_1#:~:text=Informational%20websites%20for%20users%20list%20a%20dosage%20range,and%20the%20duration%20of%20action%20is%205%E2%80%938%20h. [accessed 4th May 2023]

Benzodiazepines

Nitazenes identified within the illicit diazepam market

In response to the identification by WEDINOS of metonitazene within samples submitted as diazepam, Public Health Wales undertook a proactive communication approach, engaging with national media outlets with the intention of raising awareness of this substitution and the potential health risks to users of benzodiazepines who would otherwise not been aware due to not being engaged with services. This proactive communication also included guidance around naloxone (the opioid antidote) and how to get it within Wales. The following information sheet was also produced and shared amongst all stakeholders within Wales and wider, including the UK drug alerts system.

WEDINOS

Collecting • Testing • Informing

Are you getting what you think you're getting?

Over the past several years WEDINOS has been reporting on and highlighting concerns relating to *substitutions within the illicit benzodiazepine* market.

Primarily, these substitutions have involved other, albeit more potent, benzodiazepines.

Since, September 2023, WEDINOS has seen an increase in the number of samples submitted as *benzodiazepines*, particularly diazepam, that have been profiled as containing a *nitazene*, and on occasion another benzodiazepine, but *no diazepam*.



Since September 2023, 25 samples, from across the United Kingdom, submitted in the belief, they were **diazepam**, were profiled following analysis as containing the nitazene, **metonitazene** (Sept =8, Oct=12, Nov=5), and on 23 of those occasions, this was identified alongside the benzodiazepine, **bromazolam**.

Nitazenes were originally developed in the 1950s as analgesics. Found to have potent analgesic effects, the clinical development of nitazenes was abandoned due to the increased risks of adverse events. Currently, there are no drugs of this class approved as human or veterinary medicines.

Metonitazene is a high potency synthetic opioid that exceeds the potency of fentanyl and morphine.

Benzodiazepines are a class of sedative substances. These work by increasing the effects of a naturally occurring chemical in the brain gamma aminobutyric acid (GABA). Where prescribed, they are recommended for short-term use at the lowest possible dose. This is to reduce the risks of tolerance, dependence and withdrawal symptoms

Bromazolam is a triazolobenzodiazepine, structurally related to alprazolam. Originally developed as a candidate medicine, it was never approved for use. There is currently little scientific literature available relating to bromazolam. A "common" oral dose of bromazolam, as described by users of the substance, is 1 to 3mg. The onset of effects is between 15 and 45 minutes, with a duration of action of 5 to 8 hours

With the emergence of nitazenes within the illicit benzodiazepine market, we recommend, individuals who are consuming unprescribed benzodiazepines, speak to their local drug treatment service about Naloxone (often described as the opioid antidote) or visit DAN 24/7 and see their click and collect service (for those living in Wales) https://dan247.org.uk/naloxone-click-and-deliver/

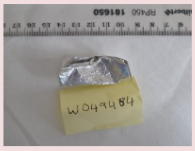
11/12/2023

Nitazenes

Nitazenes – April 2023 to March 2024, 138 samples found to contain nitazenes.

W049484

Date Received: 20 Mar 2024
Postcode: EH32 -
Purchase Intent: Heroin
Package Label: Heroin
Sample Colour: Brown
Sample Form: Solid
Consumption Method: Intravenous



Click to Enlarge

Self-Reported Effects: Relaxed, Memory Loss, Loss of consciousness
Sample Upon Analysis (Major): xylazine, Paracetamol, Noscapine, Caffeine, 6-MAM
Sample Upon Analysis (Minor): Metonitazene, Heroin, Papaverine

W049446

Date Received: 15 Mar 2024
Postcode: M20 -
Purchase Intent: Diazepam
Package Label: Accord Diazepam
Sample Colour: Blue
Sample Form: Tablet
Consumption Method: Oral

Click to Enlarge

Self-Reported Effects: Enhanced Senses, Relaxed, Nausea, Memory Loss, Loss of consciousness, Tiredness
Sample Upon Analysis (Major): Metonitazene, Bromazolam
Sample Upon Analysis (Minor):

What are nitazenes?

2-Benzyl benzimidazole (nitazene) opioids were originally developed in the 1950s as analgesics. Several were shown to have potent opioid effects, but none were subsequently marketed anywhere as human or veterinary medicines (17). This group of opioids are structurally unrelated to other opioid drug groups, including morphine and fentanyl.
They are generally highly active, with potencies and efficacies of several analogues exceeding that of fentanyl (18). However, there is very little information on their effects in humans. Animal studies have shown a wide range in potency for this group of substances, which may also vary depending on the route of administration. When administered to mice subcutaneously, potency ranged from 1 (equal to morphine) for flunitazene to 1000 for etonitazene (19).
The rank order of potency of a series of nitazenes was reported to be etonitazene >= isotonitazene > protonitazene >= metonitazene > butonitazene >= etodesnitazene >> 5-aminoisotonitazene = flunitazene > metodesnitazene (19).

United Kingdom Legal Status

On 14th May 2024, 2-benzyl benzimidazole ('nitazenes'), their variants and piperidine benzimidazolone ('brorphine-like') opioids were added to Class A of the Misuse of Drugs Act 1971, consistent with the classification of other potent opioids and other nitazenes.
As these materials have no medical use, it is recommended that they should be placed in Schedule 1 of the Misuse of Drugs Regulations 2001 (as amended) and the Misuse of Drugs (Designation) (England, Wales, and Scotland) Order 2015, Northern Ireland 2001.

Nitazenes and fatal drug related overdoses (United Kingdom)

On 24th May 2024, the National Crime Agency has revealed that a dangerous new drug has been linked to almost 176 deaths in the UK (20).

17) ACMD report – A review of the evidence on the use and harms of 2-benzyl benzimidazole ('nitazene') and piperidine benzimidazolone ('brorphine-like') opioids; July 2022; https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1091152/ACMD_advice_on_2-benzyl_benzimidazole_and_piperidine_benzimidazolone_opioids.pdf [accessed 5th May 2023]
18) Vandeputte MM, Van Uytfanghe K, Layle NK, St Germaine DM, Iula DM, Stove CP. Synthesis, Chemical Characterization, and μ-Opioid Receptor Activity Assessment of the Emerging Group of "Nitazene" 2-Benzylbenzimidazole Synthetic Opioids. ACS Chem Neurosci. 2021 Apr 7;12(7):1241-1251. doi: 10.1021/acschemneuro.1c00064. Epub 2021 Mar 24. PMID: 33759494.
19) Bromig, G. About new powerful analgesics and their clinical trials. Klin Wochenschr 36, 960–963 (1958). https://doi.org/10.1007/BF01486702
20) David Cohen: Dangerous nitazene drugs linked to rise in deaths; BBC; 24th May 2024 {accessed 3rd June 2024}

Nitazenes

Naloxone, responding to a nitazene overdose

There is a lack of research relating to the use of naloxone for specifically treating nitazene overdoses. However, there is evidence of its use reversing life-threatening respiratory depression and coma caused by subcutaneous metonitazene (21).

In the article “What are Nitazines?”, Prof. Ryan Marino of theEmergency Medicine and Psychiatry at Case Western School of Medicine, Cleveland states naloxone should be effective in treating people suffering from a nitazine overdose, although higher doses may be needed and more research is required and that thereno evidence to suggest that the new synthetic opioids are naloxone-resistant. The question is around the dose required and re-dosing (22).

TOXBASE and the UK National Poisons Information Service suggest the use of naloxone if a patient has been exposed to any opioid drug and develops respiratory depression, airway obstruction or vomiting with impaired consciousness.

WEDINOS and nitazenes

WEDINOS received the first sample profiled by the programme containing a nitazene on 14th April 2021. This sample (WEDINOS reference: W018254) was submitted as a found white powder from the WF1 postcode, Wakefield. This sample contained metonitazene.

Since then the programme has received and analysed 214 samples that were also profiled as containing a nitazene. To date, WEDINOS has idenified eight different nitazenes in samples submitted to the programme (up from five last year): butinitazene, etonitazepyne (N-pyrrolidino etonitazene), isotonitazene, metonitazene, protonitazene, protonitazepyne, N-desethylisotonitazene and N-pyrrolidino protonitazene.

In response to the fast moving illicit drug market and concerns over nitazenes, WEDINOS has purchased reference standards for all nitazenes notified to the National Crime Agency and validated our testing to be able to quickly and confidently identify these substances if they appear within our sample pool.

During the period April 2023 to March 2024, 138 samples were submitted that were profiled as containing a nitazene post analysis. This is up from 36 the previous year. However, as WEDINOS is a self selecting service our data is it not an indicator of prevalence.

The majority of nitazenes were profiled in samples submitted as diazepam, 54 per cent (n=75). Followed by heroin, 17 per cent (n=24) and oxycodone, 16 per cent (n=22). Only five samples were submitted with a nitazene listed as the purchase intent.

Other samples where nitazenes were identfiied were submitted as: unknown, promethazine, cannabis, flubromazolam, SCRA, temazepam and zopiclone

W032741

Date Received: 25 Apr 2023
Postcode: M11 -
Purchase Intent: Cannabis
Package Label: Not Stated
Sample Colour: Green
Sample Form: Plant Matter
Consumption Method: Not Stated
Self-Reported Effects: Not Stated
Sample Upon Analysis (Major): MDMB-4en-PINACA, ADB-4en-PINACA, ADB-BUTINACA
Sample Upon Analysis (Minor): Isotonitazene

Click to Enlarge

21) Bromig, G. About new powerful analgesics and their clinical trials. Klin Wochenschr 36, 960–963 (1958). https://doi.org/10.1007/BF01486702
22) Castaneda, R. What are Nitrazines? https://health.usnews.com/drugs/articles/nitazenes

Nitazenes

Samples containing nitazenes were submitted from throughout the UK mainland.

It must be noted that the number of heroin samples submitted was likely influenced by concern. Between December 2023 and February 2024 there were clusters of fatal and non-fatal drug poisonings involving people who inject heroin within the South Wales Police and Gwent Police areas. Fast testing of substances by those forces joint scientific investigation unit identfiied the presence of a nitazene. As a result WEDINOS and Public Health Wales worked with the local harm reduction leads and services to encourage use of the system and provided priority access of testing for samples submitted as heroin. Alongside this work, Public Health Wales held an open media day and focused on concerns relating to potent synthetic opioids, particulalrly nitazenes. The below information sheet was also produced and shared with stakeholders, alongside supporting the continued use and provision of naloxone, whilst also highlighting that due to the unknown potency and half life of nitazenes, more naloxone than normal may be required.

WEDINOS

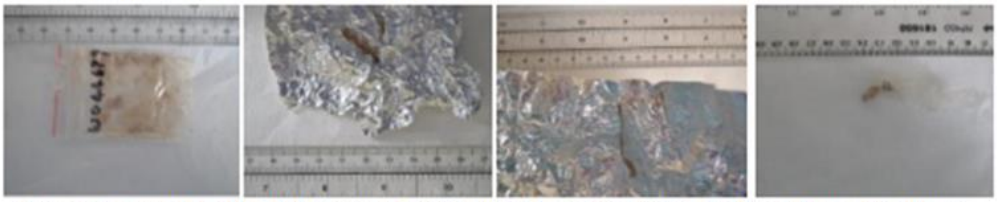
Collecting • Testing • Informing

Nitazenes within the heroin market

Public Health Wales have been notified of four suspected fatal drug poisonings and several non-fatal drug poisoning events that have occurred in the Adamsdown/Roath area of Cardiff between 23rd December 2023 - 1st January 2024.

It was reported that the individuals concerned were believed to have injected heroin.

Whilst cause of death and post-mortem toxicology remain unconfirmed, South Wales Police forensic analysis of paraphernalia seized at scene of one of the incidents has detected the presence of metonitazene, monoacetylmorphine, cocaine, paracetamol, caffeine and benzocaine.



Since January 2023, WEDINOS received and analysed seven samples, five from England and two from Wales, in the belief, they were **heroin**, that were profiled following analysis as containing nitazene(s), (Jun 23=1, Sept 23=2, Nov 23=1, Dec 23=2, Jan 24=1).

Nitazenes identified were isotonitazene and metonitazene. With one sample containing an unconfirmed nitazene (the most recent sample received in January 2024 from Cardiff, Wales).

Nitazenes were originally developed in the 1950s as analgesics. Found to have potent analgesic effects, the clinical development of nitazenes was abandoned due to the increased risks of adverse events. Currently, there are no drugs of this class approved as human or veterinary medicines.

Isotonitazene has potent analgesic effects. In mice studies isotonitazene was found to be 500 times more potent that morphine. however, studies in rodents should be interpreted with caution as they do not accurately reflect opioid toxicity in humans.

Metonitazene was around 10 times more potent than morphine as an analgesic

The import, supply, possession with the intent to supply and possession in a custodial institution of isotonitazene and metonitazene are all offences under the Psychoactive Substances Act 2016

The Advisory Council for the Misuse of Drugs (ACMD) states individuals may be unaware of the inclusion of nitazenes, the high potency of some of these compounds provides a substantial risk of severe and potentially fatal overdose.

The ACMD report – A review of the evidence on the use and harms of 2-benzyl benzimidazole ('nitazene') and piperidine benzimidazolone ('brorphine-like') opioids can be found here: https://www.gov.uk/government/publications/acmd-advice-on-2-benzyl-benzimidazole-and-piperidine-benzimidazolone-opioids

Clinical management of toxicity with nitazenes recommends the use of Naloxone as an antidote. Individuals using heroin, or those concerned in the care of individuals using heroin should speak to their local drug treatment service about Naloxone or visit DAN 24/7 and see their click and collect service (for those living in Wales) https://dan247.org.uk/naloxone-click-and-deliver/

THC / CBD / Cannabis Vapes

Synthetic Cannabinoid Receptor Agonists (SCRAs) identfiied in products purchased as THC / CBD or Cannabis vapes

Between April 2023 and March 2024 WEDINOS received 211 samples that were submitted as THC / CBD or Cannabis vapes. Of those samples, 41 per cent (n=86) contained one or more Synthetic Cannabinoid Receptor Agonist **(**SCRA).

The term 'synthetic cannabinoids' covers all synthetic substances that bind to one of the two known cannabinoid receptors (CB1 or CB2) (23).

Most SCRAs have higher affinities for the CB1 receptor than tetrahydrocannabinol (THC) and are full agonists of this site. THC in comparison acts as a partial agonist (24).

In their 2014 report, the European Monitoring Council for Drugs and Drug Addiction stated *'that these substances can be extremely potent, but are not chemically similar to cannabis, and therefore may result in different and potentially more serious health consequences. Although our current understanding of the health implications of consuming these substances remains limited, there is increasing concern about reports of acute adverse consequences associated with their use'* (25).

In the WEDINOS annual report 2014-2015 some of the evidenced health harms relating to SCRAs were discussed, primarily concerns relating to psychosis. Where individuals were presenting with psychosis, these events were characterised by paranoid delusions, ideas of reference and a disorganised, confused mental state (26).

Vape liquids are for use with devices that allow the user to inhale a substance in a vapour rather than smoke. They work by heating a liquid that (27), in terms of WEDINOS results, typically contains one or a combination of the following substances: nicotine, cannabidiol (CBD), tetrahydrocannabinol (THC), cannabinol (CBN) or Synthetic Cannabinoid Receptor Agonists (SCRAs).

Where a substance was named in the purchase intent, all samples were related to cannabis, either named as THC (n=189), cannabis (n=16) or CBD (n=6).

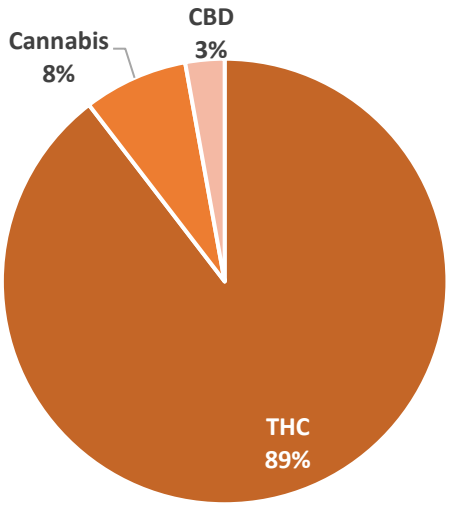


Chart 6: Purchase intent (where reported) for samples submitted as vape liquids to WEDINOS 2023-2024

23) Auwärter V., Dargan P., Wood D., Novel Psychoactive Substances, Chapter 13 - Synthetic Cannabinoid Receptor Agonists, Academic Press, 2013,Pages 317-343, ISBN 9780124158160,https://doi.org/10.1016/B978-0-12-415816-0.00013-4.
24) WEDINOS annual report 2013-2014, Public Health Wales, Cardiff, 2014; https://www.wedinos.org/resources/downloads/WN%20Annual%20Report%205012015.pdf {accessed 3rd June 2024}
25) European Monitoring Centre for Drugs and Drug Addiction (2014), European Drug Report 2014: Trends and Developments, Publications Office of the European Union, Luxembourg https://www.emcdda.europa.eu/publications/edr/trends-developments/2014_en {accessed 3rd June 2024}
26) Abdulrahim D et al (NEPTUNE Expert Group).(2015). Guidance on the Management of Acute and Chronic Harms of Club Drugs and Novel Psychoactive Substances. Novel Psychoactive Treatment UK Network. London, NEPTUNE
27) Using e-cigarettes to stop smoking-Quit smoking, NHS, https://www.nhs.uk/live-well/quit-smoking/using-e-cigarettes-to-stop-smoking/ {accessed 3rd June 2024}

THC / CBD / Cannabis Vapes

Synthetic Cannabinoid Receptor Agonists (SCRAs) identfiied in products purchased as THC / CBD or Cannabis vapes

Of serious concern is the finding that of the 211 samples submitted with stated purchase intent, 41 per cent (n=86) were found to contain SCRAs.

Within the 86 vape liquid samples found to contain SCRAs, seven SCRAs were identified either in isolation or combination: MDMB-4en-PINACA (n=56), ADB-BUTINACA (n=20), 4F-MDMB-BINACA (n=13), 5F-ADB (n=9), MDMB-BUTINACA (n=7), ADB-4en-PINACA (n=3) and 4F-MDMB-BUTINACA (n=1)

Five samples contained three SCRAs in combination.

W031411

Date Received: 07 Mar 2023
Postcode: CM13 -
Purchase Intent: THC vape oil
Package Label: Strawberry
Sample Colour: Red
Sample Form: Liquid
Consumption Method: Not Stated
Self-Reported Effects: Not Stated
Sample Upon Analysis (Major): MDMB-4en-PINACA
Sample Upon Analysis (Minor): 4F-MDMB-BINACA, ADB-4en-PINACA

Click to Enlarge

MDMB-4en-PINACA was subject to an EMCDDA risk assessment in March 2021. There is limited information on the pharmacological properties of MDMB-4en-PINACA. It is a full agonist of the CB1 receptor, and has high potency. “Adverse effects from overdosing MDMB-4en-PINACA might include gastrointestinal (e.g. nausea and vomiting (including hyperemesis)), neurological (e.g. hallucination, seizures, convulsions, agitation, anxiety, paranoia, confusion, delusions, catatonia, lethargy, psychosis (including susceptible individuals) and severe central nervous system depression (such as rapid loss of consciousness/coma), cardiovascular (e.g. tachycardia, hypertension, acute myocardial infarction and sudden cardiac death) and renal (e.g. acute kidney failure) clinical features, and respiratory depression”.

With respect to smoking mixtures and vape liquids, MDMB-4en-PINACA and other SCRAs consumed in this way are rapidly absorbed into the blood stream. This alongside the high potency of this SCRA makes it difficult for individuals to control their dosage.