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Dear Owen and Graeme,

The Government response to the ACMD's advice on acyl piperazine opioids.

I am grateful to the ACMD for providing expedited advice on the harms of acyl piperazine opioids, including 2-methyl-AP-237, which was controlled internationally at the 66th session of the United Nations Commission on Narcotic Drugs in March 2023. I have set out each recommendation and the Government's response below.

Recommendation 1: *The following named compounds which have appeared on the international illicit drug scene, should be added to Class A of the Misuse of Drugs Act 1971, consistent with the classification of other potent opioids.*

As these materials have no medicinal use in the UK, it is recommended that they should be placed in Schedule 1 of the Misuse of Drugs Regulations 2001 (as amended) and Schedule 1 of the Misuse of Drugs (Designation) (England, Wales, and Scotland) Order 2015, to which Section 7(4) of the Misuse of Drugs Act 1971 applies. The control of the compounds should extend to include any stereoisomeric forms, any salts of such compounds and any preparation or product containing such compounds.

- (i) 2-Methyl-AP-237 (1-[2-methyl-4-[2E]-3-phenyl-2-propen-1-yl]-1-piperazinyl-1-butanone)
- (ii) AP-237 (1-[4-([2E]-3-phenyl-2-propen-1-yl)-1-piperazinyl]-1-butanone) (bucinnazine)
- (iii) para-methyl-AP-237 (1-[4-[2E]-3-(4-methylphenyl)-2-propen-1-yl]-1-piperazinyl-1-butanone)
- (iv) AP-238 (1-[2,6-dimethyl-4-[2E]-3-phenyl-2-propen-1-yl]-1-piperazinyl-1-propanone)

Recommendation 2: *Consistent with the classification of other potent opioids, the following compounds should be added to Class A of the Misuse of Drugs Act 1971 as a short-term approach, due to their potencies as μ agonists, relative ease of synthesis and potential to become drugs of misuse.*

As these materials have no medicinal use in the UK, it is recommended that they should be placed in Schedule 1 of the Misuse of Drugs Regulations 2001 (as amended) and Schedule 1 of the Misuse of Drugs (Designation) (England, Wales, and Scotland) Order 2015, to which Section 7(4) of the Misuse of Drugs Act 1971 applies.

(i) Azaprocin (1-[3-[(E)-3-phenyl-2-propen-1-yl]-3,8-diazabicyclo[3.2.1]octan-8-yl]propan-1-one)

(ii) para-nitroazaprocin (1-[3-[(E)-3-(4-nitrophenyl)-2-propen-1-yl]-3,8-diazabicyclo[3.2.1]octan-8-yl]propan-1-one)

Government response

The Government accepts recommendations 1 and 2 and intends to introduce legislation to implement them, subject to Parliamentary approval.

Recommendation 3: *The ACMD recommends that a consultation should be undertaken with stakeholders, including academia and the chemical and pharmaceutical industries on the introduction of a generic control to cover 2-methyl-AP-237-related variants, as new examples may be encountered and could present a serious risk of harm.*

Following this consultation, materials covered by the generic should be added to Class A of the Misuse of Drugs Act 1971, consistent with the classification of other potent opioids.

As these materials have no medicinal use in the UK, 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, to which 7(4) of the Misuse of Drugs Act 1971 applies.

The proposed wording for the generic for addition to the Misuse of Drugs Act is as follows:

AP-237 (bucinnazine) (1-[4-([2E]-3-phenyl-2-propen-1-yl)-1-piperazinyl]-1-butanone) and any compound structurally derived from bucinnazine by modification in any of the following ways:

(i) By substitution to any extent by methyl in the piperazine or phenyl rings.

(ii) By replacement of the butyryl group by another acyl group containing three, four or five carbon atoms.

(iii) By substitution in the phenyl ring by a nitro group.

(iv) By addition of an ethylenic bridge across the piperazine ring.

Government response

The Government accepts this recommendation.

We will consult relevant stakeholders, including academia and the chemical and pharmaceutical industries on the introduction of a generic definition for acyl piperazine opioids.

Recommendation 4: *Information should be provided in an appropriate format to the general public, including people vulnerable to drug related harms (such as through Frank) and to harm reduction services on the potential harms that acyl piperazines, such as 2-methyl-AP-237, might cause if they become available on the illicit drug markets in the UK. This should include information on the potential health effects.*

Government response

The Government accepts this recommendation.

FRANK is a trusted source of honest and impartial information on drugs, and it receives around 900,000 visits a month. The Office for Health Improvement and Disparities regularly updates FRANK in response to emerging patterns of use and trends and will continue to ensure accurate information is available on the harms of synthetic opioids as appropriate for the target audience. DHSC will provide information to harm reduction services, such as drug treatment and rehabilitation services, to increase awareness of the harms of acyl piperazine opioids. UKHSA regularly engage with the ACMD Novel Psychoactive Substances committee on issues of concern and have already updated TOXBASE to include information on acyl piperazine opioids. We will engage with the Devolved Administrations in respect of their implementation of the recommendation.

Recommendation 5: *In the view of the highly dynamic synthetic opioids landscape in the UK and the associated risks they present, responsible agencies in the devolved administrations should monitor for the appearance of acyl piperazines and other emerging new synthetic opioids in the opioid market across the UK. Adequate resources should be provided to facilitate the analysis of seized materials or submitted drug samples thought to contain opioids, as well as the analysis of patient toxicology and postmortem samples. These data should be collected, collated, and monitored by the relevant public health agencies in the UK and reviewed in a consistent and methodical manner by the UK Government, for example the newly established Synthetic Opioid Taskforce and the Early Warning System. To encourage ongoing collection of data, information about compounds appearing in the UK should be fed back to coroners / procurators fiscal and toxicology laboratories with, where necessary, information about analytical methods and access to appropriate analytical standards.*

Government response

The Government accepts this recommendation.

The HMG Synthetic Opioids Taskforce currently oversees and coordinates the Government's strategic response to the threat to the UK posed by synthetic opioids. Activity under the Taskforce should also address the risks associated with acyl piperazine opioids. Through the newly enhanced early warning and surveillance system, which will be going live in July, DHSC, Home Office and law enforcement partners, including the NCA, will continue to monitor the prevalence and harms of synthetic opioids, including through analysis of seized or submitted drug samples and patient and post-mortem toxicology. We will engage regularly with the Devolved Administrations in respect of their implementation of the recommendation.

I remain extremely grateful for the expertise and timely reports provided by the ACMD to ensure that we continue to respond appropriately to the threat from synthetic drugs such as these.

Yours sincerely,



Rt Hon Chris Philp MP

Minister of State for Crime, Policing and Fire