

# ACMD

## Advisory Council on the Misuse of Drugs

8 November 2024

### **Fifth addendum to ACMD report on the use and harms of 2-benzyl benzimidazole ('nitazene') and piperidine benzimidazolone ('bromphine-like') opioids**

On 5 April 2024, the ACMD published a fourth addendum to its advice on 2-benzyl benzimidazole (nitazene) and piperidine benzimidazolone ('bromphine-like') opioids.

Following publication of this addendum the ACMD has continued to review international approaches to nitazene generic controls as they became available.

The ACMD has been made aware of evidence to suggest that the carbamoyl derivative of etonitazene retains high opioid potency [Ujváry et al., 2021]. Therefore, on a precautionary basis, the ACMD has considered further updates to the proposed generic definition to capture carbamoyl derivatives.

The ACMD has also recently been alerted to a further 2-benzyl benzimidazole compound which has been detected in the UK:-

- Aminoisotonitazene (1-[2-(diethylamino)ethyl]-2-[(4-(propan-2-yloxy)phenyl)methyl]benzimidazole-5-amine)

Aminoisotonitazene would not be captured by the generic published on 5 April 2024. Owing to the potential harms of aminoisotonitazene, the ACMD has modified Recommendation 3 to capture this compound and other structurally related compounds similar to aminoisotonitazene that might appear in the future.

Therefore, the ACMD recommends the proposed generic definition (Recommendation 3) be updated to address further 2-benzyl benzimidazoles (nitazenes) that might emerge in the future.

### **Updated 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 on 2-benzyl benzimidazole 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 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. The proposed wording for the generic for addition to the Misuse of Drugs Act is as follows (amended text in bold):

*Any compound (not being a compound for the time being specified in subparagraph (a) above), with a maximum molecular mass of 500 atomic mass units, structurally derived from 2-(2-benzyl-benzimidazol-1-yl)ethanamine by modification in any of the following ways, that is to say:*

- i) By substitution at the nitrogen of the ethanamine to any extent by alkyl substituents containing up to three carbon atoms or alkenyl substituents containing up to three carbon atoms or by inclusion of the nitrogen atom (and no other atoms of the side chain) in a cyclic structure.*
- ii) By substitution in the phenyl ring of the benzyl system to any extent by alkyl or haloalkyl containing up to six carbon atoms, alkoxy or haloalkoxy containing up to five carbon atoms, acetyloxy, hydroxy, cyano, halogen, thioalkyl containing up to five carbon atoms or alkylsulphonyl containing up to five carbon atoms.*
- iii) By substitution at the 5- or 6- positions of the benzimidazole system by nitro, acetyl, **amino**, cyano, methoxy, trifluoromethyl, trifluoromethoxy or halogen substituents.*
- iv) By substitution at the benzylic carbon by a methyl group **or by a carbamoyl group**.*
- v) By replacement of the benzylic carbon by a nitrogen, oxygen or sulphur atom.*
- vi) By substitution in the phenyl ring of the benzyl system by an ethoxy group linked back to the phenyl ring to form a dihydrobenzofuran structure.*
- vii) By replacement of the phenyl ring of the benzyl system by methylenedioxyphenyl.*

Note: Should evidence emerge of any variants of bromophine appearing, a further generic control, requiring a similar consultation, should be considered.

Lead: Home Office.

Measure of outcome: The inclusion of the revised generic definition in the Misuse of Drugs Act 1971, following appropriate consultation.

## REFERENCES

1. Ujváry I, Christie R, Evans-Brown M, Gallegos A, Jorge R, de Morais J, Sedefov R. DARK Classics in Chemical Neuroscience: Etonitazene and Related Benzimidazoles. ACS Chem Neurosci. 2021 Apr 7;12(7):1072-1092. doi: 10.1021/acscchemneuro.1c00037. Epub 2021 Mar 24. PMID: 33760580.