

ACMD

Advisory Council on the Misuse of Drugs

15 December 2023

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

On 6 October 2023, the ACMD published a second addendum to its advice on 2-benzyl benzimidazole (nitazene) and piperidine benzimidazolone ('bromphine-like') opioids. This advice recommended control of a further four 2-benzyl benzimidazole compounds which had been detected in the UK: *N*-Pyrrolidino protonitazene, ethyleneoxynitazene, *N*-desethyl protonitazene and *N*-desethyl etonitazene. The ACMD also noted ethyleneoxynitazene would not be controlled by the generic definition proposed in the report.

On 18 October 2023, the Government accepted the revised ACMD recommendation to control these four compounds, including ethyleneoxynitazene. However, the ACMD have concluded it would be possible for other nitazene variants to be developed that were structurally related to ethyleneoxynitazene and could therefore fall outside the proposed generic definition.

Therefore, the ACMD recommends the proposed generic definition be updated to address other structurally related compounds similar to ethyleneoxynitazene that might appear in the future.

The ACMD has also reviewed international approaches to nitazene generic controls as they became available. The ACMD is not aware of examples of compounds which would evade the proposed generic definition and would be captured by these international controls. However, on a precautionary basis, the ACMD has considered further updates to the proposed generic definition to align with these international approaches.

Recommendation 3 has therefore been updated with a revised generic definition, intended to cover compounds structurally similar to ethyleneoxynitazene.

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 paragraph (a) above) 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, cyano, methoxy, trifluoromethyl, **trifluoromethoxy** or halogen substituents.*
- iv) By substitution at the benzylic carbon by a methyl 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.***

These modifications are subject to a maximum molecular mass of any derived compound of 500 atomic mass units.

Note: Should evidence emerge of any variants of buporphine 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.