

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

On 12 December 2023, the ACMD published a third addendum to its advice on 2-benzyl benzimidazole (nitazene) and piperidine benzimidazolone ('bromphine-like') opioids. This advice recommended the proposed generic definition be updated to address other structurally related compounds similar to ethyleneoxynitazene that might appear in the future.

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

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

- Methylenedioxy nitazene (2-(2-(benzo[d][1,3]dioxol-5-yl)methyl)-5-nitro-1H-benzo[d]imidazol-1-yl)-N,N-diethylethan-1-amine)

Methylenedioxy nitazene would not be captured by the generic published on 15 December 2023. Owing to the potential harms of methylenedioxy nitazene, the ACMD has modified Recommendation 3 to capture this compound and other structurally related compounds similar to methylenedioxy nitazene that might appear 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, 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.*
- vii) By replacement of the phenyl ring of the benzyl system by methylenedioxyphenyl.***

Note: Should evidence emerge of any variants of bromphine 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.