ACMD

Advisory Council on the Misuse of Drugs

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Rt Hon Dame Diana Johnson DBE MP
Minister for Policing and Crime Prevention
2 Marsham Street
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13th August 2025

Dear Minister

RE: ACMD advice on the classification and schedule of zuranolone

The Advisory Council on the Misuse of Drugs (ACMD) is grateful to the Medicines and Healthcare products Regulatory Agency (MHRA) for providing a written submission and oral presentation on zuranolone (Zurzuvae®). Zuranolone is yet to be approved for marketing by the European Commission and is expecting approval in the UK, following final review by the Commission on Human Medicines, for the treatment of moderate or severe postnatal depression in adults following childbirth.

Further to these representations, the ACMD is able to provide advice regarding the appropriate classification and schedule for this medicine under the Misuse of Drugs Act 1971 (MDA) and Misuse of Drugs Regulations 2001 (MDR), respectively.

Zuranolone is an oral, synthetic neuroactive steroid (NAS) with rapid antidepressant effects. Like the endogenous NAS, allopregnanolone, zuranolone exhibits potent positive allosteric modulation of the gamma-aminobutyric acid A (GABA-A) receptor. In laboratory studies, zuranolone selectively targets GABA-A receptors, unlike benzodiazepines or barbiturates, and there was no meaningful activity at other abuse-related targets.

There are some similarities between zuranolone and several benzodiazepines already controlled under the MDA. Drug discrimination studies in animals found zuranolone showed some similarity to midazolam (a benzodiazepine included in Schedule 3 of the MDR), especially at higher doses. In self-administration studies, zuranolone showed low reinforcing potential, comparable to midazolam. Withdrawal

symptoms indicating physical dependence were mild to moderate in animals and were more pronounced in female rats.

Human studies have demonstrated effects on the central nervous system, including somnolence, euphoria, and dizziness. In a human abuse potential study, zuranolone produced dose-dependent euphoric and CNS depressant effects, similar to alprazolam (a benzodiazepine included in Schedule 4 (Part 1) of the MDR). Withdrawal symptoms (e.g., insomnia, nightmares, palpitations) of mild-to-moderate severity were reported in healthy individuals upon abrupt discontinuation.

Classification and Scheduling

It is likely that the potential harms of zuranolone would be commensurate to benzodiazepine drugs (such as alprazolam), which are controlled under Class C of the Misuse of Drugs Act 1971. The benzodiazepines to which the harms of zuranolone are considered comparable are currently scheduled under either Schedule 3 or Schedule 4 (Part 1) of the Misuse of Drugs Regulations 2001. In the United States, following an eight-factor analysis by the Department of Health and Human Services, zuranolone was placed under control of the Controlled Substances Act in 2024 as a Schedule IV material, indicating a low level of concern.

Following approval, zuranolone is intended to be a prescription-only medicine, which will only be prescribed by a healthcare professional experienced in perinatal psychiatry. Zuranolone is therefore likely to have limited use, reducing the potential for misuse.

Recommendation 1

The ACMD recommends that zuranolone should be controlled as a Class C drug under the Misuse of Drugs Act 1971.

Lead department

The Home Office.

Measure of implementation

Legislative change to the Misuse of Drugs Act 1971.

Recommendation 2

The ACMD recommends that zuranolone should be scheduled under Schedule 4 (Part 1) of the Misuse of Drugs Regulations 2001.

Lead department

The Home Office.

Measure of impact

Legislative change to the Misuse of Drugs Regulations 2001 (as amended).

Yours sincerely,

Professor Owen Bowden-Jones
Chair of the ACMD

Professor Roger Knaggs
Chair of the ACMD Technical Committee