European Monitoring Centre for Drugs and Drug Addiction

EU EARLY WARNING SYSTEM FORMAL NOTIFICATION

Date issued	20 December 2022	RCS ID	EU-EWS-RCS-FN-2022-0038
Issued by	EMCDDA	Transmitted by	Action on New Drugs Sector, EMCDDA
Subject	Formal notification of 2-(5-methoxy-2-methyl-1*H*-indol-3-yl)-*N*,*N*-dimethylethanamine (5-MeO-TMT) as a new psychoactive substance under the terms of Regulation (EC) No 1920/2006 and Council Framework Decision 2004/757/JHA		

1. Read me first

This document provides formal notification of the analytical identification of 2-(5-methoxy-2-methyl-1*H*-indol-3-yl)-*N*,*N*-dimethylethanamine (5-MeO-TMT) for the first time in Europe.

Please report any additional data you have on this substance to: ews@emcdda.europa.eu

2. Data use restrictions

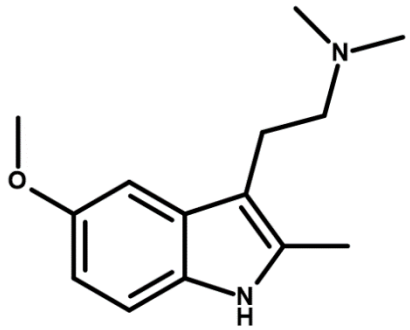
As with all formal notifications issued by the EU EWS remember that they may contain information that could be regarded as sensitive. Should you provide some of the information in this notification to other groups we would ask that you exercise your best judgment on what information needs to be provided. If you have any questions in this respect, please contact us.

3. Names of substance and other identifiers

- IUPAC name: 2-(5-methoxy-2-methyl-1*H*-indol-3-yl)-*N*,*N*-dimethylethanamine
- Chemical names: 2-(5-methoxy-2-methyl-1*H*-indol-3-yl)-*N*,*N*-dimethyl-ethanamine; 2-(5-methoxy-2-methyl-1*H*-indol-3-yl)-*N*,*N*-dimethylethan-1-amine; 2-(5-methoxy-2-methyl-1-indol-3-yl)ethyl-dimethyl-amine; methyl-2-methoxy-5-*N*-dimethyltryptamine; 3-[2-(dimethylamino)ethyl]-5-methoxy-2-methylindole; 5-methoxy-*N*,*N*,2-trimethyl-1*H*-indole-3-ethanamine; *N*,*N*-dimethyl-2-(5-methoxy-2-methyl-1*H*-indol-3-yl)ethylamine; *N*,*N*-dimethyl-2-(5-methoxy-2-methylindol-3-yl)ethylamine
- Common name: 5-MeO-TMT
- Other names: 5-MeO-2-TMT; 5-methoxy-TMT; 5-methoxy-2,*N*,*N*-trimethyltryptamine; indapex; 2-methyl-5-MeO-DMT; MMDT; 5-methoxy-2-methyl-DMT; 5-MeO-2-Me-DMT
- Chemical formula: $C_{14}H_{20}N_2O$
- Molecular weight: 232.32
- CAS Registry number: 67292-68-6
- InChIKey: ACEHBQPPDDGCGZ-UHFFFAOYSA-N

Praça Europa 1, Cais do Sodré, 1249-289 Lisbon, Portugal
Tel. (351) 211 21 02 00 | Fax (351) 211 21 03 80 | ews@emcdda.europa.eu | emcdda.europa.eu

Molecular structure



4. Substance classification

Tryptamine

5. Detection

Type: Collected sample

6. Chemistry and Analysis

Chemical classification: arylalkylamine; indole alkylamine; tryptamine

5-MeO-TMT, also known as 5-MeO-2-TMT, is a tryptamine and the 5-methoxy derivative of 2-Me-DMT, formally notified in 2013. 5-MeO-TMT differs from 5-MeO-DMT, formally notified in 2003, due to the addition of the methyl group at the 2-position on the indole. 5-MeO-TMT is also structurally related to the internationally controlled tryptamine DMT (Schedule I of the 1971 United Nations Single Convention on Psychotropic Substances). 5-MeO-TMT differs from DMT due to the addition of a methoxy group at the 5-position and addition of a methyl group on the 2-position on the indole.

5-MeO-TMT, 4-HO-DET, 4-HO-MIPT, 5-MeO-MET, 5-MeO-NiPT and 4-HO-MPT, formally notified in 2005, 2006, 2012, 2014 and 2018, are structural isomers. The identification and discrimination of these isomers can pose analytical challenges due to the fact that these substances have the same molecular weight and similar fragmentation patterns, as a result other analysis techniques, in addition to GC-MS, such as FTIR or NMR may be required.

5-MeO-TMT was originally described in a 1959 patent on ‘1-Benzyl- and 2-methyl-5-methoxytryptamines’ [1]; a melting point of 212-215 °C (*compound 41*) and ^{1}H NMR data has been reported for the oxalate salt of 5-MeO-TMT [2]. The synthesis of 5-MeO-TMT (*compound 45*) was described in Tryptamines I have Known and Loved (TIHKAL) [3]. A fully validated method for the detection of synthetic and natural tryptamines, including 5-MeO-TMT, in human urine and plasma using liquid chromatography-linear ion trap mass spectrometry (LC-MSn), has also been reported in the literature [4].

A reference standard is available for 5-MeO-TMT and an λmax (ultraviolet wavelength of maximum absorbance) of 227 nm is reported [5]. It is soluble in DMF (30 mg/ml), DMSO (30 mg/ml), ethanol (30 mg/ml) and PBS (pH 7.2; 0.5 mg/ml) [5].

7. Pharmacology and toxicology

Pharmacological classification: hallucinogen

In a study of structure-activity relationships of *N*-arylsulfonyltryptamines for binding at the 5-HT_6 receptor in rats, 5-MeO-TMT (*compound 41*) was found to have a 5-HT_6 binding affinity of Ki = 89 nM [2]. In another study of structure affinity relationships for the binding of tryptamines at human 5-HT_6 receptors, 5-MeO-TMT (*compound 7*) was found to bind with severalfold lower affinity (Ki =60 nM) when compared to clozapine and was found to also bind at h5-HT_{1A}, h5-HT_{1D}, h5-HT_{1E}, and h5-HT_7 receptors [6]. In an examination of the ability of 5-MeO-TMT to activate adenylate cyclase, it behaved as a full agonist (K_{act} = 7.9 ± 5.0 nM) [6].

An active oral dosage of 75-150 milligrams and a duration of action of 5-10 hours has been reported [3].

8. References

[1] Dilworth W, Shaw EN, inventors; Research Corp, assignee. 1-benzyl, 2-methyl, 5-methoxy tryptamine. 1959 United States patent US 2,890,223.
[2] Russell MG, et al. *N*-Arylsulfonylindole derivatives as serotonin 5-HT6 receptor ligands. Journal of medicinal chemistry. 2001;44(23):3881-95.
[3] https://isomerdesign.com/PiHKAL/read.php?domain=tk&id=45
[4] Meyer MR, et al. A qualitative/quantitative approach for the detection of 37 tryptamine-derived designer drugs, 5 β-carbolines, ibogaine, and yohimbine in human urine and plasma using standard urine screening and multi-analyte approaches. Analytical and bioanalytical chemistry. 2014;406(1):225-37.
[5] https://www.caymanchem.com/product/32522/2-methyl-5-methoxy-dmt
[6] Glennon RA, et al. 2-Substituted tryptamines: agents with selectivity for 5-HT6 serotonin receptors. Journal of medicinal chemistry. 2000 Mar 9;43(5):1011-8.