



European Monitoring Centre
for Drugs and Drug Addiction

This document is being made available in advance of formal layout. It will be replaced with a final version in the formal EMCDDA layout in due course.

**EMCDDA–Europol Joint Report
on a new psychoactive substance:**

N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide (ADB-CHMINACA)

In accordance with Article 5 of Council Decision 2005/387/JHA on the information exchange, risk assessment and control of new psychoactive substances

Recommended citation:

European Monitoring Centre for Drugs and Drug Addiction (2017), EMCDDA–Europol Joint Report on a new psychoactive substance: N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide (ADB-CHMINACA), Joint Reports, Publications Office of the European Union, Luxembourg.



European Monitoring Centre
for Drugs and Drug Addiction



EMCDDA–Europol Joint Report
on a new psychoactive substance:

N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1*H*-indazole-3-
carboxamide
(ADB-CHMINACA)

In accordance with Article 5 of Council Decision 2005/387/JHA on the information
exchange, risk assessment and control of new psychoactive substances

Contents

1.	Introduction	3
2.	Information collection process	3
3.	Information required by Article 5.2 of the Council Decision.....	6
3.1	Chemical and physical description, including the names under which the new psychoactive substance is known (Article 5.2(a) of the Council Decision)	6
3.2	Information on the frequency, circumstances and/or quantities in which a new psychoactive substance is encountered, and information on the means and methods of manufacture of the new psychoactive substance (Article 5.2(b) of the Council Decision)	10
3.2.1	Information provided to Europol	10
3.2.2	Information provided to the EMCDDA	11
3.3	Information on the involvement of organised crime in the manufacture or trafficking of the new psychoactive substance (Article 5.2(c) of the Council Decision)	13
3.4	A first indication of the risks associated with the new psychoactive substance, including the health and social risks, and of the characteristics of users — Article 5.2(d) of the Council Decision	14
3.4.1	Health risks	14
3.4.2	Serious adverse events.....	15
3.4.3	Characteristics of users.....	15
3.4.4	Social risks.....	16
3.5	Information on whether or not the new substance is currently under assessment, or has been under assessment, by the UN system (Article 5.2(e) of the Council Decision).....	16
3.6	The date of notification on the Reporting Form of the new psychoactive substance to the EMCDDA or to Europol (Article 5.2(f) of the Council Decision)	16
3.7	Information on whether or not the new psychoactive substance is already subject to control measures at national level in a Member State (Article 5.2(g) of the Council Decision).....	17
3.8	Further information (Article 5.2(h) of the Council Decision)	17
3.8.1	The chemical precursors that are known to have been used for the manufacture of the substance.....	17
3.8.2	The mode and scope of the established or expected use of the new substance	17
3.8.3	Other use of the new psychoactive substance and the extent of such use, the risks associated with this use of the new psychoactive substance, including the health and social risks.....	18
4.	Information from the EMA (Article 5.3 of the Council Decision)	18
5.	Conclusion	20
6.	References.....	21

1. Introduction

Article 5.1 of Council Decision 2005/387/JHA ⁽¹⁾ (hereinafter the 'Council Decision') stipulates that 'Where Europol and the EMCDDA, or the Council, acting by a majority of its members, consider that the information provided by the Member State on a new psychoactive substance merits the collection of further information, this information shall be collated and presented by Europol and the EMCDDA in the form of a Joint Report.' The Joint Report shall be submitted to the Council of the European Union, the European Medicines Agency (EMA), and the European Commission.

In March 2017, the EMCDDA and Europol examined the available information on the new psychoactive substance *N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1*H*-indazole-3-carboxamide, commonly known as ADB-CHMINACA, through a joint assessment based upon the following criteria:

1. the amount of the material seized;
2. evidence of organised crime involvement;
3. evidence of international trafficking;
4. analogy with better-studied compounds;
5. evidence of the potential for further (rapid) spread; and,
6. evidence of cases of serious intoxication or fatalities.

The EMCDDA and Europol agreed that the information collected on ADB-CHMINACA satisfied criteria 1, 4 and 6. The two agencies therefore concluded that sufficient information had been accumulated to merit the production of a Joint Report on ADB-CHMINACA as stipulated by Article 5.1 of the Council Decision.

2. Information collection process

In compliance with the provisions of the Council Decision, on 25 April 2017 the EMCDDA and Europol launched a procedure for the collection of information on ADB-CHMINACA, in order to prepare the Joint Report. The information was collected mainly through the Reitox National Focal Points in the Member States, Turkey and Norway as well as the Europol National Units. In addition, the EMA collected information through the national competent authorities responsible for human and veterinary medicinal products in the Member States as well as in Norway, Iceland and Liechtenstein. The EMA also provided information as relevant to the centralised procedure for authorising medicinal products. The information collection process was largely concluded by 6 June 2017.

⁽¹⁾ OJ L 127, 20.5.2005, p. 32.

Information collected by Europol

Europol asked the Europol National Units to provide information on:

- the level of production of ADB-CHMINACA in their country;
- the level of distribution of ADB-CHMINACA in their country;
- the level of trafficking of ADB-CHMINACA in their country, both for internal, transit or export purposes;
- the number of seizures of ADB-CHMINACA in their country, the total amount of the seizures, country of origin, details on the physical forms (including photos);
- the role of organised crime, or criminal groups, in the production, distribution and trafficking of ADB-CHMINACA in their country; and,
- any known aspect of violence and/or money laundering relating to the production and trafficking of ADB-CHMINACA.

Europol received responses from 16 Member States ⁽²⁾.

Information collected by the EMA

According to Article 5.3 of the Council Decision, the EMA requested that the national competent authorities responsible for human and veterinary medicinal products in the Member States, Norway, Iceland, and Liechtenstein, provide information on whether:

- the new psychoactive substance ADB-CHMINACA has obtained a marketing authorisation;
- the new psychoactive substance ADB-CHMINACA is the subject of an application for a marketing authorisation; and,
- a marketing authorisation that had been granted in respect of the new psychoactive substance ADB-CHMINACA has been suspended.

Twenty-three countries provided a response to the EMA's request regarding human and/or veterinary medicinal products ⁽³⁾. The EMA also provided information as relevant to the centralised procedure for authorising human and veterinary medicinal products.

⁽²⁾ In alphabetical order: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, Finland, Germany, Greece, Latvia, Lithuania, Luxembourg, Romania, Slovakia, and Slovenia.

⁽³⁾ Austria, Belgium, Denmark, Estonia, Finland, Germany, Greece, Ireland, Latvia, Norway, Poland, Spain, Sweden and the United Kingdom provided a response in relation to human and veterinary medicinal products. Croatia, Czech Republic, Hungary, Italy, and the Netherlands provided a response in relation to human medicinal products. France, Portugal, Slovakia and Slovenia provided a response in relation to veterinary medicinal products.

Furthermore, in anticipation of Article 7.3 of the Council Decision in relation to the manufacturing of medicinal products in the European Union, the EMA also requested information on whether the new psychoactive substance ADB-CHMINACA is used to manufacture a medicinal product:

- which has been granted a marketing authorisation;
- for which an application has been made for a marketing authorisation; and,
- for which a marketing authorisation has been suspended by a competent authority.

Twenty-three countries ⁽⁴⁾ provided a response to the EMA's request in this regard. The EMA also provided information as relevant to the centralised procedure for authorising human and veterinary medicinal products.

Information collected by the EMCDDA

The EMCDDA collected information through:

- a structured questionnaire to the Reitox National Focal Points. The EMCDDA received replies from 27 Member States ⁽⁵⁾, as well as Turkey and Norway;
- reports previously provided to the European Union Early Warning System, including EMCDDA–Europol Reporting Forms and Progress Reports and Final Reports;
- routine monitoring of open source information;
- a specific information request to the World Health Organization on whether or not ADB-CHMINACA is under assessment by the United Nations system; and,
- a search of open source information conducted specifically for the production of the Joint Report which included: scientific and medical literature, official reports, grey literature, internet drug discussion forums and related websites (hereafter, 'user websites'), and, online vendors selling ADB-CHMINACA.

Thus, the information included in sections 3.2.1 and 3.3 of the Joint Report was provided by Europol, while the EMCDDA provided information included in sections 3.1, 3.2.2, 3.4, 3.5, 3.6, 3.7, 3.8.1, 3.8.2 and 3.8.3 (in part). The information included

⁽⁴⁾ Austria, Belgium, Denmark, Estonia, Finland, Germany, Greece, Ireland, Latvia, Norway, Poland, Spain, Sweden and the United Kingdom provided a response in relation to human and veterinary medicinal products. Croatia, Czech Republic, Hungary, Italy, and the Netherlands provided a response in relation to human medicinal products. France, Portugal, Slovakia and Slovenia provided a response in relation to veterinary medicinal products.

⁽⁵⁾ A reply was not received from Slovakia.

in sections 3.8.3 (in part), and 4 was provided by the EMA. Images of the seizures and collected samples reported to the EMCDDA are provided in Annex 1.

3. Information required by Article 5.2 of the Council Decision

The order and titles of subsections 3.1 to 3.8 and section 4, below, are as they appear in Article 5.2(a) to (h) and Article 5.3(a) to (c) of the Council Decision; sections are cross-referenced with those set down in the Council Decision.

3.1 Chemical and physical description, including the names under which the new psychoactive substance is known (Article 5.2(a) of the Council Decision)

Chemical description and names

N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1*H*-indazole-3-carboxamide carboxamide is commonly referred to as ADB-CHMINACA or MAB-CHMINACA ⁽⁶⁾.

ADB-CHMINACA is a synthetic cannabinoid receptor agonist. It has an indazole core, which is a common structural feature in many of the synthetic cannabinoids monitored by the EMCDDA.

Two synthetic cannabinoid receptor agonists have been recently controlled under Schedule II of the United Nations Convention on Psychotropic Substances of 1971: JWH-018 ⁽⁷⁾ and AM-2201 ⁽⁸⁾. In addition, MDMB-CHMICA, 5F-APINACA (5F-AKB48) and XLR-11 will be included in the same schedule.

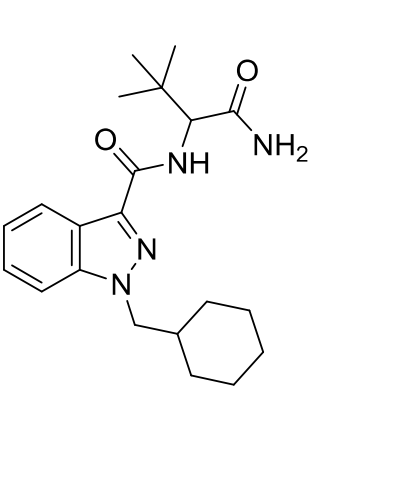
The molecular structure, molecular formula, and molecular mass of ADB-CHMINACA are provided in Figure 1.

⁽⁶⁾ The common name for the substance is derived after its structural features. Different naming systems exist and are used for applying short/code names to synthetic cannabinoids.

⁽⁷⁾ Naphthalen-1-yl(1-pentyl-1*H*-indol-3-yl)methanone

⁽⁸⁾ 1-(5-Fluoropentyl)-1*H*-indol-3-yl]-(naphthalen-1-yl)methanone

Figure 1. Molecular structure, molecular formula, and molecular mass of ADB-CHMINACA.

	
	ADB-CHMINACA
Molecular formula	C ₂₁ H ₃₀ N ₄ O ₂
Molecular mass	370.50

ADB-CHMINACA contains a stereocentre thus allowing for the existence of a pair of enantiomers, (*R*)- and (*S*)-ADB-CHMINACA. The synthesis of (*S*)-AB-CHMINACA was first described in the patent literature in 2009 (Buchler et al., 2009). Based on the literature and the most likely precursors to be used, an (*S*)-configuration of the stereocentre could be expected.

There is no representative information on the enantiomeric composition of the samples of AB-CHMINACA detected within the European Union, which in part may reflect the fact that stereochemical analysis is not routinely undertaken in forensic laboratories. Differentiation of enantiomers is possible using the following techniques: chiral chromatography, vibrational circular dichroism (VCD) spectroscopy and/or electronic circular dichroism (ECD) spectroscopy.

Commonly used names:

ADB-CHMINACA

Systematic (IUPAC) name:

N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1*H*-indazole-3-carboxamide

Chemical Abstracts names:

1*H*-Indazole-3-carboxamide, *N*-[(1*S*)-1-(aminocarbonyl)-2,2-dimethylpropyl]-1-(cyclohexylmethyl)- (*S* enantiomer)

Other chemical names:

N-[1-(aminocarbonyl)-2,2-dimethylpropyl]-1-(cyclohexylmethyl)-1*H*-indazole-3-carboxamide;

N-(1-carbamoyl-2,2-dimethyl-propyl)-1-(cyclohexylmethyl)indazole-3-carboxamide;

N-(1-amino-3,3-dimethyl-1-oxo-2-butanyl)-1-(cyclohexylmethyl)-1*H*-indazole-3-carboxamide;

N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1*H*-indazole-3-carboxamide;

N-[(2*S*)-1-amino-3,3-dimethyl-1-oxobutan-2-yl]-1-(cyclohexylmethyl)-1*H*-indazole-3-carboxamide (*S* enantiomer);

N-(1-amino-3,3-dimetyl-1-oxobutan-2-yl)-1-(cyklohexylmetyl)-1*H*-indazol-3-karboxamid (Swedish)

Other names and code names:

MAB-CHMINACA

Chemical Abstracts Service (CAS) registry numbers ⁽⁹⁾:

1863065-92-2	ADB-CHMINACA racemate
1185887-13-1	(<i>S</i>)-ADB-CHMINACA

IUPAC International Chemical Identifier Key (InChI Key) ⁽¹⁰⁾:

ZWCCSIUBHCZKOY-UHFFFAOYSA-N	ADB-CHMINACA racemate
ZWCCSIUBHCZKOY-GOSISDBHSA-N	(<i>S</i>)-ADB-CHMINACA

The REACH registered substances database hosted by the European Chemicals Agency (ECHA) was searched using the CAS registry numbers listed above. The searches returned no hits.

⁽⁹⁾ The Chemical Abstract Service Registry Number (CAS RN) is a unique numeric identifier assigned by the Chemical Abstract Service Division of the American Chemical Society to a specific, single chemical substance.

⁽¹⁰⁾ InChI Key is a unique, non-proprietary structural identifier of chemical substances useful in electronic sources.

Physical description

In its pure form, ADB-CHMINACA is a white solid (SWGDRUG, 2016). It is soluble in dichloromethane (DCM), methanol (MeOH) and is poorly soluble in water (Slovenian National Forensic Laboratory, 2016). It is soluble up to approximately 1 mg/mL in ethanol, 10 mg/ml in dimethyl sulfoxide (DMSO) and 5 mg/ml in dimethyl formamide (DMF) (Cayman Chemical Company, 2016a).

The reported melting point for ADB-CHMINACA is 141.5°C (SWGDRUG, 2016).

ADB-CHMINACA has been typically seized as a herbal material and in powder form. A more detailed description of seizures and collected samples can be found in section 3.2.1 and section 3.2.2.

Chemical stability and typical reactions

For long term storage it is recommended that ADB-CHMINACA, supplied as a solid, is stored at -20°C (Cayman Chemical Company, 2016b).

Detection and analysis

Methods documented in the literature for the detection of ADB-CHMINACA include: gas chromatography – mass spectrometry (GC-MS), high performance liquid chromatography time-of-flight (HPLC-TOF), Fourier transform infrared spectroscopy attenuated total reflectance (FTIR-ATR), and gas chromatography – mass spectrometry– infrared (GC-MS-IR) condensed phase, ion chromatography (IC), and nuclear magnetic resonance spectroscopy (NMR) (Slovenian National Forensic Laboratory, 2016) ⁽¹¹⁾.

In addition, the analytical profile of ADB-CHMINACA using gas chromatography mass spectrometry (GC-MS) (Akamatsu et al., 2015 and Wurita et al., 2015), liquid chromatography – mass spectrometry (LC-MS) (Akamatsu et al., 2015), liquid chromatography tandem mass spectrometry (LC-MS-MS) (Hasegawa et al., 2015 and Wurita et al., 2015) and nuclear magnetic resonance (NMR) (Buchler et al., 2009) has been described in the literature.

Quantification of ADB-CHMINACA in products can be carried out according to the general procedure described by the UNODC (UNODC, 2013).

⁽¹¹⁾ An impurity (possibly cyclohexylmethyl) was also found.

3.2 Information on the frequency, circumstances and/or quantities in which a new psychoactive substance is encountered, and information on the means and methods of manufacture of the new psychoactive substance (Article 5.2(b) of the Council Decision)

The data reported to Europol discussed in section 3.2.1 may overlap with the data reported to the EMCDDA discussed in section 3.2.2.

3.2.1 Information provided to Europol

Europol received replies from 16 Member States (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, Finland, Germany, Greece, Latvia, Lithuania, Luxembourg, Romania, Slovakia, and Slovenia).

Eight countries reported that they have no available information on ADB-CHMINACA (Austria, Belgium, Croatia, Cyprus, Czech Republic, Greece, Luxembourg, and Slovakia).

Eight countries provided information on ADB-CHMINACA (Bulgaria, Estonia, Finland, Germany, Latvia, Lithuania, Romania, and Slovenia).

The level of production

No information was received in relation to the production of ADB-CHMINACA.

The level of distribution

At least 120 seizures were reported by 7 Member States: Bulgaria (2), Estonia (1), Finland (exact number unspecified), Germany (95), Latvia (17), Lithuania (1), and Romania (2).

- Bulgaria: 2 seizures, one of which was a crystalline substance in a bag, amounting to 9 grams, in postal package from Spain to Bulgaria, labelled 'MMB CHMINACA'; and 1 seizure made in 201
- Estonia: 1 courier seizure made in 2017, amounting to 203 grams, which came from Russia.
- Finland: unspecified number of seizures made in 2015 and 2016.
- Germany: 70 seizures made in 2016 which amounted to 2.1 kg, most of which were in the form of herbal material ('legal high' products). One of the seizures amounted to 1.66 kg; 25 seizures in 2017 which amounted to 85 grams, most of which were in powder form.
- Latvia: 11 seizures of herbal material in 2015 and 6 seizures in 2016, which amounted to 528 grams and 5.4 grams, respectively.
- Lithuania: 1 seizure containing also AD-FUBINACA, which amounted to 0.3 grams

- Romania: 2 seizures in 2015, amounting to 467 grams and 871 grams.

The level of trafficking

Information related to trafficking routes is limited to the seizures reported above.

3.2.2 Information provided to the EMCDDA

The EMCDDA received responses from 27 Member States ⁽⁵⁾, as well as from Turkey and Norway. Of these, 17 Member States (Belgium, Croatia, Estonia, Finland, France, Germany, Greece, Hungary, Latvia, Lithuania, the Netherlands, Poland, Romania, Slovenia, Spain, Sweden, and the United Kingdom), Turkey and Norway reported detections of ADB-CHMINACA ⁽¹²⁾.

It is important to note that detections of ADB-CHMINACA may be under-reported since the substance is not routinely screened for. Three Member States (Austria, Slovenia and Sweden) reported that ADB-CHMINACA is part of routine screening in some (but not all) of their laboratories.

Seizures

In total, 3794 seizures of ADB-CHMINACA were reported to the EMCDDA by 17 Member States, Norway and Turkey: Belgium (16), Croatia (2), Estonia (2), Finland (10), France (3), Germany (2), Greece (1), Hungary (75), Latvia (33), Lithuania (1), the Netherlands (1), Norway (2), Poland (233), Romania (1), Slovenia (1), Spain (1), Sweden (83), Turkey (3162) and the United Kingdom (165). The majority of the seizures comprise police and customs cases, with additional seizures taking place in custodial settings.

Seizures included herbal materials, powders, blotters and other physical forms. A summary is provided below.

Herbal material

- 485 seizures of ADB-CHMINACA in herbal material were reported by 13 countries: Croatia, Estonia, Germany, Greece, Hungary, Latvia, Lithuania, Norway, Poland, Romania, Slovenia, Sweden, and the United Kingdom, amounting to nearly 11 kg seized. In addition, Turkey reported around 3160

⁽¹²⁾ 'Detections' is an all-encompassing term and may include seizures and/or collected and/or biological samples that are analytically confirmed. Seizure means a substance available (seized) through law enforcement activities (police, customs, border guards, etc.). Collected samples are those that are actively collected by drug monitoring systems (such as test purchases) for monitoring and research purposes. Biological samples are those from human body fluids (urine, blood, etc.) and/or specimens (tissues, hair, etc.).

seizures of herbal material amounting to almost 128 kg which have not been included in the total count ⁽¹³⁾.

- The largest single seizure of ADB-CHMINACA in herbal material was reported by Germany, amounting to 1.66 kg of a mixture containing ADB-CHMINACA, 5F-AMB-PICA, EMB-FUBINACA, 5F-APP-PINACA, THC and CBD. Greece reported a seizure of 9 bags of herbal material, found to contain just over 1 kg of ADB-CHMINACA mixed with 5F-AMB. The seizure was made during a raid on a tobacco store in Drama, where a number of products containing other synthetic cannabinoids were seized.
- In herbal material, ADB-CHMINACA was commonly found mixed with other synthetic cannabinoids (33% of the cases).

Powder

- 76 seizures of powders were reported by 10 countries: Belgium, Finland, France, Hungary, Latvia, the Netherlands, Poland, Spain, Sweden and Turkey, amounting to a total of 9.8 kilograms.
- The largest single seizure of ADB-CHMINACA in powder form was reported by Belgium (3 kg seized by customs, originating in China, destined for Austria and Romania).
- Turkey reported 2 large seizures of powders: 1.84 kg, containing ADB-CHMINACA, FUBIMINA, FUB-AKB, AMB-FUBINACA and NEP; 1 kg containing ADB-CHMINACA mixed with THC, cannabiniol and cannabidiol.
- In 92% of the cases of seized powders, ADB-CHMINACA was the only substance reported.

Other physical forms

- Seizures of blotters containing ADB-CHMINACA were reported by Poland (40 cases; 25.35 grams) and Sweden (1 case; 2 blotters).
- Poland reported 19 seizures of 'agglomerated material' containing ADB-CHMINACA mixed with either caffeine (14 cases) or 5F-AKB48 (5), amounting to a total of over 235 grams of substance.
- One seizure of a 'slab' containing ADB-CHMINACA mixed with MDMB-CHMICA was reported by Estonia (13.42 grams); 1 case of a 'lump' containing ADB-CHMINACA, AB-FUBINACA, 5F-ADB-PINACA and FUB-APINACA was reported by Norway (9.7 grams) and 1 seizure of a 'paste-like substance' was reported by Finland (0.7 grams)

No quantitative information on purity was provided to the EMCDDA.

⁽¹³⁾ Minimum estimate provided by the Turkish National Focal Point for 2016.

Collected samples

Two collected samples of ADB-CHMINACA were reported to the EMCDDA: by Slovenia (5 grams of white powder purchased online as '5F-AEB' from China), and Germany (one of many substances identified in a number of powder samples collected from a scene of a death).

Biological samples

Serious adverse events with confirmed exposure to ADB-CHMINACA from biological samples are discussed in section 3.4.2.

In addition to these, 28 detections where ADB-CHMINACA was analytically confirmed in biological samples were reported by 2 Member States: Hungary (22 cases) and Poland (6) ⁽¹⁴⁾. Detections include:

- 22 cases were reported in relation to drug abuse (consumption), intoxication or non-fatal intoxication, with no further details provided.
- 6 cases related to persons suspected of driving under the influence of drugs, all reported by Hungary.

3.3 Information on the involvement of organised crime in the manufacture or trafficking of the new psychoactive substance (Article 5.2(c) of the Council Decision)

No information concerning the involvement of organised crime in the manufacture and/or trafficking of the ADB-CHMINACA was provided.

Money laundering aspects

No information was received on money laundering in connection with the production and/or trafficking of ADB-CHMINACA.

Violence in connection with production, wholesale and distribution

No information was received on incidents of violence in connection with the production, wholesale and/or trafficking of ADB-CHMINACA.

⁽¹⁴⁾ In addition, Turkey reported 181 samples (blood, hair and urine) which may contain duplicates and therefore have not been included in the total count.

3.4 A first indication of the risks associated with the new psychoactive substance, including the health and social risks, and of the characteristics of users — Article 5.2(d) of the Council Decision

3.4.1 Health risks

Pharmacology & Toxicology

Limited data suggests that ADB-CHMINACA is a CB₁ receptor agonist (US DEA, 2015 ⁽¹⁵⁾) that shares some similarities with the major psychoactive constituent of cannabis (–)-*trans*-Δ⁹-tetrahydrocannabinol (THC) and synthetic cannabinoids such as JWH-018 and MDMB-CHMICA (EMCDDA, 2017; Järbe and Raghav, 2017; Pertwee, 2014; Reggio, 2009).

The acute effects of THC (and consequently cannabis) include: relaxation, euphoria, lethargy, depersonalisation, distorted perception of time, impaired motor performance, hallucinations, paranoia, confusion, fear, anxiety, dry mouth, reddening of the conjunctivae of the eyes, tachycardia, and, nausea and vomiting. THC also has an abuse liability and dependence potential (Pertwee, 2014; Wiley et al., 2016). Similar effects to cannabis have been reported for synthetic cannabinoids such as ADB-CHMINACA. In some cases, the effects are reported to be more pronounced/severe (EMCDDA, 2017).

Compared to cannabis, severe and fatal poisoning appears to be more common with synthetic cannabinoids (EMCDDA, 2017; Tait et al., 2016). Poisoning may include rapid loss of consciousness/coma, cardiovascular effects (such as hypertension, tachycardia, bradycardia, chest pain, myocardial infarction, and stroke), seizures and convulsions, vomiting/hyperemesis, delirium, agitation, psychosis, and, aggressive and violent behaviour. Sudden death has also been reported. The mechanisms of this toxicity are poorly understood (Tai & Fantegrossi, 2016), but factors that are likely to play an important role are the potency of the substances and the doses that users are exposed to. In addition, some of the effects of poisoning — such as loss of consciousness or behavioural effects — may place users at additional risks such as choking on vomitus, drowning, or self-harm.

There is no antidote to poisoning caused by synthetic cannabinoids.

In general, the use of herbal smoking mixtures containing synthetic cannabinoids appears to pose a high risk of poisoning. This is because manufacturers guess the amount of cannabinoids(s) to add to the herbal material, and the manufacturing process makes it difficult to dilute them sufficiently and distribute them consistently throughout the material. This can result in mixtures that contain a large amount of highly potent cannabinoid, as well as 'hot pockets' where the cannabinoid is highly

⁽¹⁵⁾ Enantiomeric composition not specified.

concentrated within parts of the herbal material (e.g. Schäper et al., 2016). Together, this makes it difficult for users to control the dose that they are exposed to. As these mixtures are typically smoked as cigarettes ('joints'), users can inadvertently administer a toxic dose; in some cases, a small number of puffs from a cigarette have been sufficient to cause severe poisoning. Reflecting these risks, smoking mixtures have caused a large number of outbreaks of mass poisonings in recent years (Adams et al., 2017; Kasper et al., 2015; Schwartz et al., 2015; Shevyrin et al., 2015; Trecki et al., 2015; Tyndall et al., 2015).

While there is no specific data for ADB-CHMINACA, the chronic health risks might share similarities to cannabis and other synthetic cannabinoids. This may include dependence.

3.4.2 Serious adverse events

Acute intoxications

A total of 3 acute intoxications with confirmed exposure to ADB-CHMINACA were reported by the United Kingdom ⁽¹⁶⁾. The cases occurred during 2016. In 1 case, no other substances were detected. In the remaining 2 cases, another synthetic cannabinoid was detected. All the cases included clinical features of poisoning similar to those reported for synthetic cannabinoids.

Deaths

A total of 12 deaths with confirmed exposure to ADB-CHMINACA were reported by Germany (6 cases), Hungary (1), and Sweden (5). The cases occurred between 2014 and 2016.

All the deaths were male. They were aged between 17 and 38 years (mean 27.8, median 27.5). In 1 case, no other substances were detected. In the remaining cases, other substances were detected including central nervous system depressants (such as alcohol and synthetic cannabinoids). Where known, many of the cases were found dead and typically in a home environment. In at least 9 cases, ADB-CHMINACA was the cause of death or contributed to the death.

3.4.3 Characteristics of users

Similar to other synthetic cannabinoids, ADB-CHMINACA is sold and used as a 'legal' substitute for cannabis (EMCDDA, 2009; EMCDDA, 2017). The most common way of using it is by smoking a cigarette of herbal mixture that has been laced with

⁽¹⁶⁾ In addition, Germany reported 8 acute intoxications with possible exposure to ADB-CHMINACA and Sweden reported 2 acute intoxications with suspected exposure to ADB-CHMINACA. These cases are not discussed further in this report.

the substance. Because these products rarely state the ingredients, most users will be unaware that they are using ADB-CHMINACA.

People who use ADB-CHMINACA may include recreational users, high-risk drug users, and groups who experiment with the substance (such as psychonauts). This may also include individuals who are subject to drug testing (such as people in drug treatment, prisoners, and drivers) because some drug tests/screens will be unable to detect ADB-CHMINACA. In the past few years, synthetic cannabinoids have become increasingly used by vulnerable groups (such as the homeless and prisoners).

3.4.4 Social risks

While there is limited data for ADB-CHMINACA, the social risks might share some similarities with cannabis and other synthetic cannabinoids.

Of particular note is that synthetic cannabinoids are increasingly used by vulnerable groups, such as the homeless and prisoners. Reports suggest that this has caused new health and social problems as well as exacerbated existing ones for these groups. For example, in prisons, alongside the adverse health effects, the market in synthetic cannabinoids has been linked to an increase in aggression, violence, bullying, and debt. In some cases this has caused a serious threat to the overall safety and security of the prison environment (Blackman et al., 2017; HMIP, 2015; Ralphs et al., 2017; User Voice, 2016).

3.5 Information on whether or not the new substance is currently under assessment, or has been under assessment, by the UN system (Article 5.2(e) of the Council Decision)

The World Health Organization is the specialised United Nations agency designated for the evaluation of the medical, scientific and public health aspects of psychoactive substances under the Single Convention on Narcotic Drugs, 1961 and the Convention on Psychotropic Substances, 1971.

On 1 May 2017, the World Health Organization informed the EMCDDA that ADB-CHMINACA is currently not under assessment and has not been under assessment by the UN system.

3.6 The date of notification on the Reporting Form of the new psychoactive substance to the EMCDDA or to Europol (Article 5.2(f) of the Council Decision)

The first official EMCDDA–Europol notification of ADB-CHMINACA dates from 12 September 2014 from the Hungarian National Focal Point. The Reporting Form details a seizure of 2.07g of light brown powder that was seized in August 2014 by the Hungarian Police in Hajós. The substance was analytically confirmed by GC-MS, FT-IR and NMR.

ADB-CHMINACA was added to the list of new psychoactive substances monitored by the EMCDDA and Europol through the European Union Early Warning System. A profile of the substance was created on the European Database on New Drugs

(EDND). Since then, analytical details and other information, including a public health alert, have been exchanged between the EMCDDA, Europol, and the Member States, Turkey, and Norway, on an ad hoc basis; the European Commission and the EMA have been kept duly informed.

3.7 Information on whether or not the new psychoactive substance is already subject to control measures at national level in a Member State (Article 5.2(g) of the Council Decision)

Thirteen Member States (Belgium, Croatia, Cyprus, Czech Republic, Estonia, Finland, France, Germany, Italy, Latvia, Lithuania, Luxembourg and Sweden) reported that ADB-CHMINACA is controlled under drug control legislation.

Three Member States (Austria, Hungary, and Poland) and Turkey reported that ADB-CHMINACA is controlled under specific new psychoactive substances control legislation.

Norway reported that ADB-CHMINACA is controlled under medicinal products legislation.

Eleven Member States (Bulgaria, Denmark, Greece, Ireland, Malta, the Netherlands, Portugal, Romania, Slovenia, Spain, and the United Kingdom) reported that ADB-CHMINACA is not subject to control measures at the national level.

Slovakia did not provide information on the control status of ADB-CHMINACA.

3.8 Further information (Article 5.2(h) of the Council Decision)

3.8.1 The chemical precursors that are known to have been used for the manufacture of the substance

No information was reported by the Member States, Turkey, or Norway, about the chemical precursors or manufacturing methods used to make the ADB-CHMINACA which has been detected within Europe.

The synthesis of ADB-CHMINACA was first described in a 2009 patent (Buchler et al., 2009). The starting compound methyl 1*H*-indazole-3-carboxylate used in the 2009 patent, which is commercially available, can be prepared from 1*H*-indole-2,3-dione using the procedure of Johnson et al. (Johnson et al., 2005).

Possible synthetic routes for the production of ADB-CHMINACA could utilise L-*tert*-leucinamide (for the synthesis of the (*S*) enantiomer), 1*H*-indole-3-carboxylic acid and methyl 1*H*-indazole-3-carboxylate as potential precursors.

3.8.2 The mode and scope of the established or expected use of the new substance

No studies were identified that have examined the mode and scope of established or expected use of ADB-CHMINACA. Given the limited information currently available, the relevant information has been included in the previous sections.

3.8.3 Other use of the new psychoactive substance and the extent of such use, the risks associated with this use of the new psychoactive substance, including the health and social risks

No information was provided by the Member States, Turkey or Norway that indicated that ADB-CHMINACA had any other use apart from in analytical reference materials and scientific research.

From the available information, it does not appear that ADB-CHMINACA is used in the manufacture of a medicinal product in the European Union. However, the data collection is incomplete and some countries indicated that this information is not known. It is understood that the collection of such information is a challenge in the absence of a database on the synthetic route of all medicinal products.

Eleven countries (Austria, Belgium, Croatia, Denmark, Finland, Greece, Italy, the Netherlands, Poland, Spain and the United Kingdom) reported that ADB-CHMINACA is not used to manufacture a medicinal product for human use. Eight countries (Czech Republic, Estonia, Germany, Hungary, Ireland, Latvia, Norway and Sweden) reported that it was unknown if ADB-CHMINACA is used to manufacture a medicinal product for human use.

In addition, the EMA reported that it is not known if ADB-CHMINACA is used in the manufacture of medicinal products for human use and which are centrally authorised within the European Union.

Eleven countries (Austria, Belgium, Denmark, Finland, France, Greece, Latvia, Poland, Slovakia, Spain and the United Kingdom) provided information that ADB-CHMINACA is not used to manufacture a medicinal product for veterinary use. Seven countries (Estonia, Germany, Ireland, Norway, Portugal, Slovenia and Sweden) reported that it was unknown if ADB-CHMINACA is used to manufacture a medicinal product for veterinary use.

In addition, the EMA reported that it is not known if ADB-CHMINACA is used in the manufacture of medicinal products for veterinary use and which are centrally authorised within the European Union.

4. Information from the EMA (Article 5.3 of the Council Decision)

Nineteen countries (Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Ireland, Italy, Latvia, the Netherlands, Norway, Poland, Spain, Sweden and the United Kingdom) reported that:

- ADB-CHMINACA has not been granted a marketing authorization as a medicinal product for human use
- ADB-CHMINACA is not the subject of an application for a marketing authorization as a medicinal product for human use
- there had been no cases of suspended marketing authorization in respect to ADB-CHMINACA as a human medicine

Eighteen countries (Austria, Belgium, Denmark, Estonia, Finland, France, Germany, Greece, Ireland, Latvia, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden and the United Kingdom) reported that:

- ADB-CHMINACA has not been granted a marketing authorization as a medicinal product for veterinary use
- ADB-CHMINACA is not the subject of an application for a marketing authorization as a medicinal product for veterinary use
- there had been no cases of suspended marketing authorization in respect to ADB-CHMINACA as a veterinary medicine

The EMA also reported that ADB-CHMINACA:

- has not been granted a marketing authorization as a medicinal product for neither human nor veterinary use through the centralized procedure
- is not the subject of an application for a marketing authorization for neither human nor veterinary use through the centralized procedure
- is not the subject of a suspended marketing authorization for neither human nor veterinary use through the centralized procedure.

5. Conclusion

ADB-CHMINACA is a synthetic cannabinoid and a CB₁ receptor agonist. It shares some pharmacological similarities with Δ^9 -tetrahydrocannabinol (THC), which is responsible for the major psychoactive effects of cannabis. In humans, ADB-CHMINACA appears to cause effects that resemble those of cannabis and other synthetic cannabinoids.

ADB-CHMINACA has been available in the European Union since at least August 2014 and has been detected in 18 Member States, Turkey and Norway. More than 600 seizures have been made within the European Union, which includes 7 kg of powder and 11 kg of herbal material which has been laced with ADB-CHMINACA. This herbal material is typically sold as smoking mixtures; the products are marketed as 'legal' replacements to cannabis. Due to the way that these products are produced, it appears that users are at risk of serious poisoning. There are indications that the ADB-CHMINACA available on the market was synthesised by chemical companies based in China.

Twelve deaths with confirmed exposure to ADB-CHMINACA have been reported by 3 Member States. In at least 9 of the deaths, ADB-CHMINACA was the cause of death or contributed to the death.

ADB-CHMINACA is currently not under assessment and has not been under assessment by the UN system. ADB-CHMINACA is not subject to control measures in 11 Member States.

We conclude that the health and social risks caused by the manufacture, trafficking and use of ADB-CHMINACA, and the involvement of organised crime and possible consequences of control measures, could be thoroughly assessed through a risk assessment procedure in accordance with Article 6 of Council Decision 2005/387/JHA.

6. References

- Adams, A. J., Banister, S. D., Irizarry, L., Trecki, J., Schwartz, M., Gerona, R., (2017), '"Zombie" outbreak caused by the synthetic cannabinoid AMB-FUBINACA in New York', *New England Journal of Medicine*, 376(3), pp. 235-42. Available at: <https://doi.org/10.1056/NEJMoa1610300>
- Akamatsu, S., Yoshida, M., (2016), 'Fragmentation of synthetic cannabinoids with an isopropyl group or a tert-butyl group ionized by electron impact and electrospray', *Journal of mass spectrometry*; 51(1), pp. 28–32. Available at: <https://doi.org/10.1002/jms.3722>
- Blackman, S., Bradley, R. (2017), 'From niche to stigma-Headshops to prison: Exploring the rise and fall of synthetic cannabinoid use among young adults', *International Journal of Drug Policy*, 40, pp. 70–7. Available at: <https://doi.org/10.1016/j.drugpo.2016.10.015>
- Buchler, I. P., Hayes, M. J., Hegde, S. G., Hockerman, S. L., Jones, D. E., Kortum, S. W, et al., (2009), Indazole derivatives, International patent WO2009106980, assigned to Pfizer.
- Cayman Chemical Company, (2016a), Safety data sheet MAB-CHMINACA. Available at: <https://www.caymanchem.com/msdss/16616m.pdf>
- Cayman Chemical Company (2016b), Product information MAB-CHMINACA. Available at: <https://www.caymanchem.com/pdfs/16616.pdf>
- EMCDDA (2009), Understanding the 'Spice' phenomenon, European Monitoring Centre for Drugs and Drug Addiction, Publications Office of the European Union, Luxembourg. Available at: <http://www.emcdda.europa.eu/system/files/publications/537/Spice-Thematic-paper-final-version.pdf>
- EMCDDA (2017), Report on the risk assessment of methyl 2-[[1-(cyclohexylmethyl)-1*H*-indole-3-carbonyl]amino]-3,3-dimethylbutanoate (MDMB-CHMICA) in the framework of the Council Decision on new psychoactive substances, European Monitoring Centre for Drugs and Drug Addiction, Publications Office of the European Union, Luxembourg. Available at: <http://www.emcdda.europa.eu/publications/risk-assessments/mdmb-chmica>
- Hasegawa, K., Wurita, A., Minakata, K., Gonmori, K., Nozawa, H., Yamagishi, I., Watanabe, K., Suzuki, O., (2015), 'Postmortem distribution of MAB-CHMINACA in body fluids and solid tissues of a human cadaver', *Forensic toxicology* 33(2), pp. 380–7. Available at: <https://doi.org/10.1007/s11419-015-0272-y>
- HMIP (2015), Changing patterns of substance misuse in adult prisons and service responses. Her Majesty's Inspectorate of Prisons, London. Available at: <https://www.justiceinspectores.gov.uk/hmiprisons/wp-content/uploads/sites/4/2015/12/Substance-misuse-web-2015.pdf>
- Järbe, T. U. C., Raghav, J. G. (2017) 'Tripping with synthetic cannabinoids ("Spice"): anecdotal and experimental observations in animals and man', *Current Topics in Behavioral Neurosciences*, 32, pp. 263-281. Available at: <http://dx.doi.org/10.1007/7854201616>

- Johnson, B. L., Rodgers, J. D., (2005), 'Practical Synthesis of 3-Carboxyindazoles', *Synthetic communications* 35(20), pp. 2681–4. Available at: <https://doi.org/10.1002/chin.200610134>
- Kasper, A. M., Ridpath, A. D., Arnold, J. K., Chatham-Stephens, K., Morrison, M., Olayinka, O. et al., (2015), 'Severe illness associated with reported use of synthetic cannabinoids—Mississippi, April 2015', *MMWR Morbidity and Mortality Weekly Report*, 64(39), pp. 1121–22. Available at: <https://doi.org/10.15585/mmwr.mm6439a7>
- Pertwee, R. G., (ed). (2014), *Handbook of Cannabis*, Oxford University Press, Oxford 2014.
- Ralphs, R., Williams, L., Askew, R., Norton, A. (2017), 'Adding Spice to the Porridge: The development of a synthetic cannabinoid market in an English prison', *International Journal of Drug Policy*, 40, pp. 57–69. Available at: <https://doi.org/10.1016/j.drugpo.2016.10.003>
- Reggio, P. H. (Ed). *The cannabinoids receptors*. Humana Press, New York, 2009.
- Schwartz, M. D., Trecki, J., Edison, L. A., Steck, A. R., Arnold, J., Gerona, R. R., (2015), 'A common source outbreak of severe delirium associated with exposure to the novel synthetic cannabinoid ADB-PINACA', *Journal of Emergency Medicine*, 48(5), pp. 573–80. Available at: <https://doi.org/10.1016/j.jemermed.2014.12.038>
- Schäper, J., (2016), 'Wirkstoffgehalte und inhomogene Verteilung des Wirkstoffs MDMB-CHMICA in Kräutermischungen', *Toxichem Krimtech*, 83(2), pp. 112–4. Available at: https://www.gtfch.org/cms/images/stories/media/tk/tk83_2/Schaeper_et_al_2016.pdf
- Shevyrin V., Melkozerov V., Nevero A., Eltsov O., Shafran Y., Morzherin Y., Lebedev, A. T., (2015), 'Identification and analytical characteristics of synthetic cannabinoids with an indazole-3-carboxamide structure bearing a N-1-methoxycarbonylalkyl group', *Analytical and Bioanalytical Chemistry*, 407(21), pp. 6301–15. Available at: <https://doi.org/10.1007/s00216-015-8612-7>
- Slovenian National Forensic Laboratory, (2016), 'Analytical report ADB-CHMINACA (C₂₁H₃₀N₄O₂) N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1*H*-indazole-3-carboxamide', NPS and related compounds – analytical reports. European project RESPONSE to challenges in forensic drugs analyses. Available at: http://www.policija.si/apps/nfl_response_web/0_Analytical_Reports_final/ADB-CHMINACA-ID-1380-15-report_final.pdf
- Tai, S., Fantegrossi, W. E., (2016), 'Pharmacological and toxicological effects of synthetic cannabinoids and their metabolites', *Current Topics in Behavioral Neurosciences* 32, pp. 249–262. Available at: https://doi.org/10.1007/7854_2016_60
- Tait, R. J., Caldicott, D., Mountain, D., Hill, S. L., Lenton, S. (2016), 'A systematic review of adverse events arising from the use of synthetic cannabinoids and their associated treatment', *Clinical Toxicology (Philadelphia)*, 54(1), pp. 1–13. Available at: <https://doi.org/10.3109/15563650.2015.1110590>
- Trecki, J., Gerona, R. R., Schwartz, M. D., (2015), 'Synthetic cannabinoid-related illnesses and deaths', *New England Journal of Medicine*, 373(2), pp. 103–7. Available at: <https://doi.org/10.1056/NEJMp1505328>

Tyndall, J. A., Gerona, R., De Portu, G., Trecki, J., Elie, M. C., Lucas, J., Slish, J., et al. (2015), 'An outbreak of acute delirium from exposure to the synthetic cannabinoid AB-CHMINACA', *Clinical Toxicology (Philadelphia)*, 53(10), pp. 950–6. Available at: <https://doi.org/10.3109/15563650.2015.1100306>

UNODC (2013), Recommended methods for the identification and analysis of synthetic cannabinoid receptor agonists in seized materials, United Nations Office on Drugs and Crime, Vienna. Available at: https://www.unodc.org/documents/scientific/STNAR48_Synthetic_Cannabinoids_EN_G.pdf

US DEA, (2015), N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1*H*-indazole-3-carboxamide (MAB-CHMINACA; ADB-CHMINACA). Background information and evaluation of 'three factor analysis' (factors 4, 5, and 6) for temporary scheduling. United States Drug Enforcement Administration, Washington. Available at: <https://www.regulations.gov/contentStreamer?documentId=DEA-2015-0025-0002&contentType=pdf>

User Voice (2016), 'Spice: the bird killer — what prisoners think about the use of spice and other legal highs in prison'. Available at: <http://www.uservoice.org/wp-content/uploads/2016/05/User-Voice-Spice-The-Bird-Killer-Report-Low-Res.pdf>

Wiley, J.L., Owens, R. A., Lichtman, A. H. (2016), 'Discriminative stimulus properties of phytocannabinoids, endocannabinoids, and synthetic cannabinoids, *Current Topics in Behavioral Neurosciences*. Available at: <https://doi.org/10.1007/7854201624>

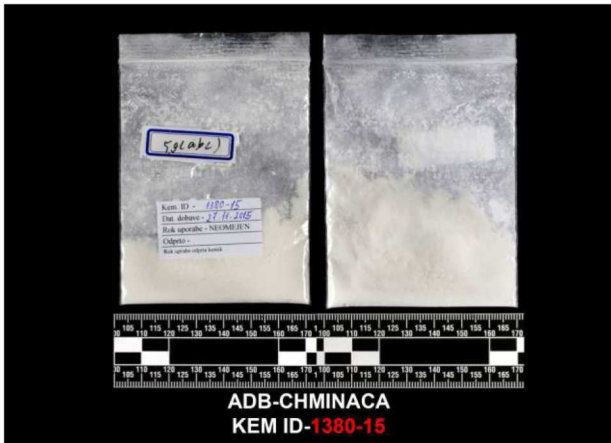
Wurita, A., Hasegawa, K., Minakata, K., Gonmori, K., Nozawa, H., Yamagishi, I., Watanabe, K., Suzuki, O., (2015), 'Identification and quantitation of 5-fluoro-ADB-PINACA and MAB-CHMINACA in dubious herbal products', *Forensic Toxicology* 33(2), pp. 213–20. Available at: <https://doi.org/10.1007/s11419-015-0264-y>



Annex 1

EMCDDA–Europol Joint Report *N*-[1-(aminocarbonyl)-2,2-dimethylpropyl]-1-(cyclohexylmethyl)-1*H*-indazole-3-carboxamide (ADB-CHMINACA)

Images from seizures and collected samples provided to the EMCDDA.

Country	Image	
Slovenia		Collected sample, 27 November 2015 White powder Collecting authority: project RESPONSE