World Health Organization

Annex 1:
Report on WHO questionnaire for review of psychoactive substances

Expert Committee on Drug Dependence

Forty-fifth Meeting

Geneva, 10–14 October 2022

This report contains the views of an international group of experts and does not necessarily represent the decisions or the stated policy of the World Health Organization.

Contents

ADB-BUTINACA

Of the 77 countries that agreed to provide data, 34 had information on ADB-BUTINACA (Table A1).

Table A1. Numbers of countries providing information on ADB-BUTINACA

Region	No. of countries that had no information	No. of countries that had information
African	3	1
Americas	6	3
Eastern Mediterranean	5	3
European	9	21
South-East Asia	3	0
Western Pacific	3	6
Total	29	34

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for ADB-BUTINACA. No countries reported that ADB-BUTINACA was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard). None reported use for industrial purposes.

Epidemiology of non-medical use

Twenty countries (14 European, 2 Americas, 2 Western Pacific, 1 African and 1 Eastern Mediterranean) reported evidence from law enforcement and health professionals of the use of ADB-BUTINACA for non-medical purposes (outside the medical, industrial or scientific context). This evidence was derived primarily from data on seizures and customs (n=15).

Routes of administration and formulations

The most common reported route of administration was smoking, followed by oral and inhalation (Table A2).

Table A2. Reported routes of ADB-BUTINACA administration

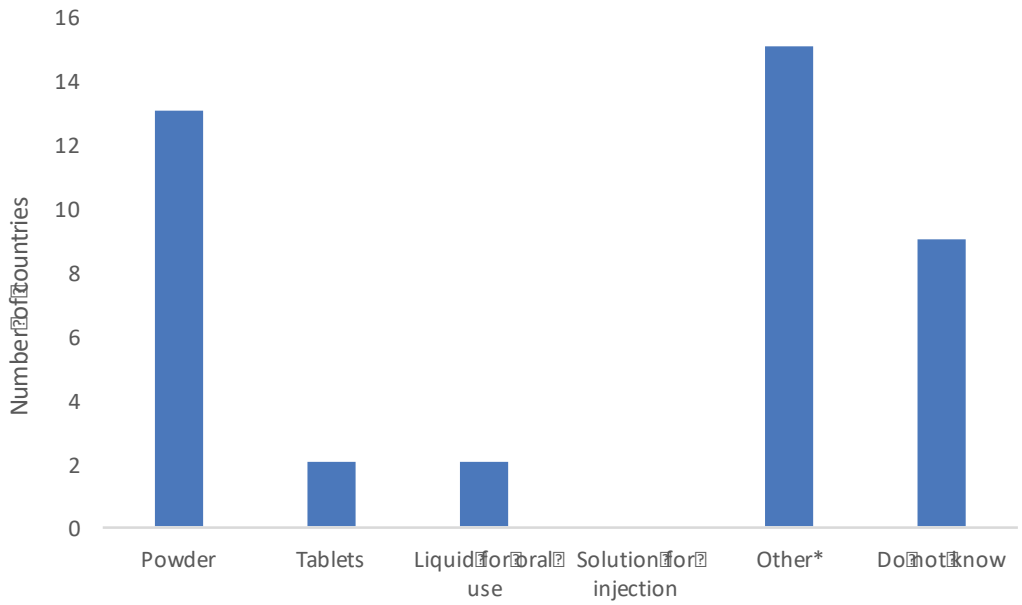
Route of administration	No. of countries
Smoking	10
Oral	6
Inhalation	2
Sniffing	0
Injection	0
Other[a]	1

Do not know	6

[a] Vaping (n=1)

The most common known formulations of ADB-BUTINACA reported were as a powder and as part of a herbal mixture (Fig. A1).

Fig. A1. Formulations of ADB-BUTINACA

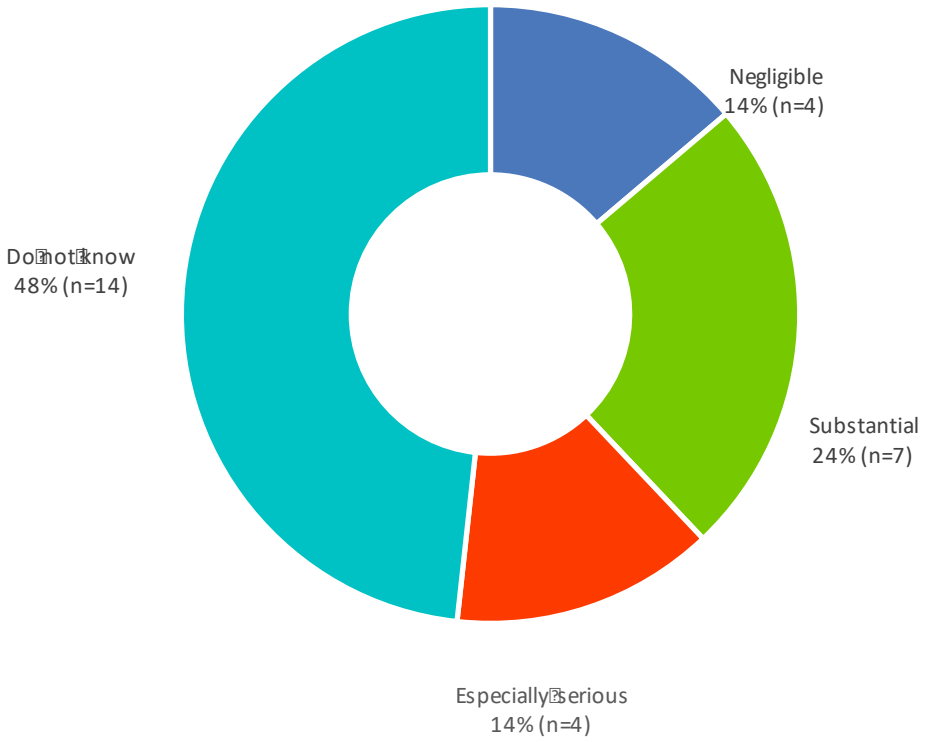


Other formulations most commonly referred to were herbal mixture or plant material (n=8) and e-liquid (n=2). One member state also referenced 'impregnated on paper' whilst another member state mentioned 'unintentional smoking of cannabis laced with ADB-BUTINACA'.

Perceived negative health impact

Ten countries (5 European, 2 Americas, 2 Eastern Mediterranean, 1 Western Pacific) reported that the negative health impact of non-medical consumption of ADB-BUTINACA was "especially serious" or "substantial" (Fig. A2). Two countries reference that ADB-BUTINACA has been involved in serious intoxications. One member state referenced that ADB-BUTINACA has been identified in a few low THC products sold as cannabis. One member state referenced that ADB-BUTINACA has been identified in 202 samples taken from persons dependent on drugs.

Fig. A2. Negative health impacts of non-medical consumption of ADB-BUTINACA



Emergency department visits

Six countries (3 European, 1 African, 1 Americas, 1 Western Pacific) were aware of emergency department visits related to ADB-BUTINACA. Two countries reported side-effects to include hallucinations, unconsciousness, altered mental state and excitement. One country in Europe noted 15 intoxications between 2021 and 2022 that were mostly reported in combination with other substances.

Deaths

Four countries (2 European, 1 Americas, 1 Western Pacific) reported a total of 16 ADB-BUTINACA related deaths in 2021. Four countries (2 European, 1 Americas, 1 Western Pacific) reported a total of 13 ADB-BUTINACA deaths in 2021 that involved other substances. Two countries (1 European, 1 Western Pacific) reported three deaths in 2021 in which ADB-BUTINACA was the only substance involved.

Drug dependence

Two countries (1 European region, 1 Eastern Mediterranean) reported that people presented for treatment of drug dependence in their country due to use of ADB-BUTINACA.

Current national controls

Twenty-six countries (16 European, 4 Western Pacific, 3 Americas, 2 Eastern Mediterranean, 1 African) responded that the availability of ADB-BUTINACA was currently regulated under national legislation.

Illicit manufacture and trafficking-related information

Table A3 shows the main reported activities for ADB-BUTINACA.

Table A3. Reported activities involving ADB-BUTINACA for purposes other than medical, scientific or industrial use

Activity	No. of countries
Trafficking	12
Smuggling (from other countries)	8
Internet sales (other or location of sellers and website unknown)	5
Direct sales	4
Internet sales (from abroad to buyers in respondent's country)	4
Internet sales (seller or website located in respondent's country)	3
Manufacture of the substance by chemical synthesis	2
Production of consumer products containing the substance	2
Manufacture of the substance by extraction from other products	1
Diversion	1
Do not know	14
Other[a]	1

[a] Includes "Several seizures".

Seizures

Eleven countries (9 European, 1 Western Pacific, 1 Americas) reported seizures in 2022. The number of seizures per country ranged from 1 to 295 and the amounts seized ranged from 0.28 g to 7.4 kg (Table A4). One European country also reported six tablets containing ADB-BUTINACA. Sixteen countries (14 European, 1 Western Pacific, 1 Americas) reported seizures in 2021. The number of seizures per country ranged from 1 to 4418 and the amounts seized from 1 g to 81 kg. One European country reported one seizure of 1960 ml of ADB-BUTINACA. Six countries (4 European, 1 Western Pacific, 1 Americas) reported seizures in 2020. The number of seizures per country ranged from 1 to 207 and the amounts seized from 12.99 g to 2.1 kg. One country (European) also reported one seizure of 528 ml in 2022 and 3 seizures totalling 505 ml in 2021. One country (European) also reported six tablets containing ADB-BUTINACA in 2022 and one tablet in 2021.

Table A4. Reported seizures of ADB-BUTINACA

Year	No. of countries that reported seizures	No. of seizures
2022	11	787
2021	16	6092
2020	6	309

Twenty-two countries (18 European, 3 Western Pacific, 2 South-East Asia, 1 Eastern Mediterranean, 1 Americas) reported that they had the laboratory capacity to analyse ADB-BUTINACA.

Adinazolam

Of the 77 countries that agreed to provide data, 17 had information on adinazolam (Table A5).

Table A5. Numbers of countries providing information on adinazolam

Region	No. of countries that had no information	No. of countries that had information
African	2	1
Americas	7	2
Eastern Mediterranean	7	0
European	17	9
South-East Asia	3	0
Western Pacific	3	5
Total	39	17

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for adinazolam. No countries reported that a dinazolam was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard). None reported use for industrial purposes.

Epidemiology of non-medical use

Seven countries (3 European, 2 Americas and 2 Western Pacific) reported evidence from law enforcement and health professionals of the use of adinazolam for non-medical purposes (outside the medical, industrial or scientific context).

Routes of administration and formulations

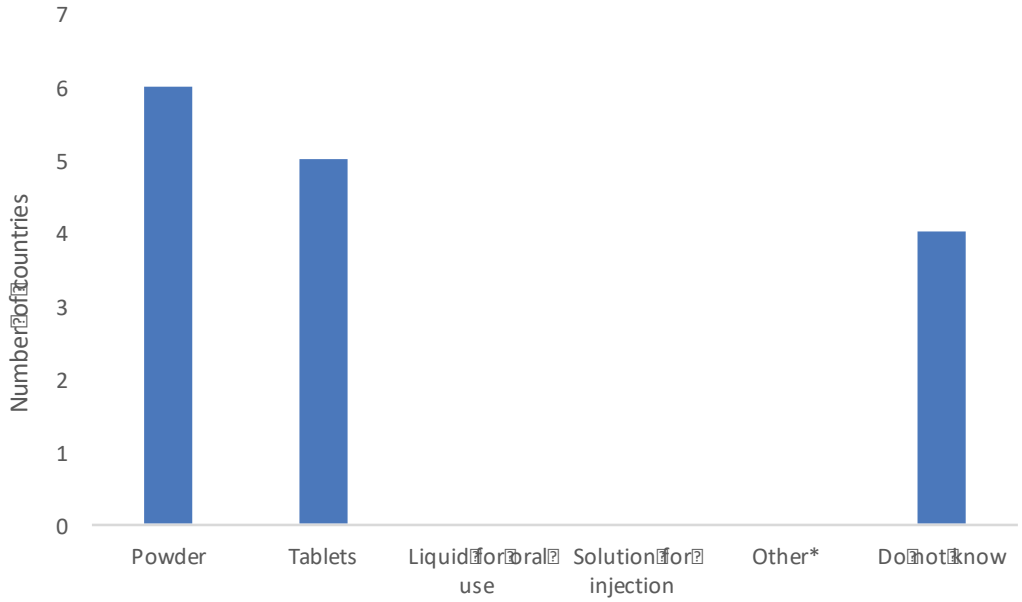
The only reported route of administration was oral (Table A6).

Table A6. Reported routes of adinazolam administration

Route of administration	No. of countries
Smoking	0
Oral	5
Inhalation	0
Sniffing	0
Injection	0
Other	0
Do not know	6

The most common known formulations of adinazolam reported were as a powder and as a tablet (Fig. A3).

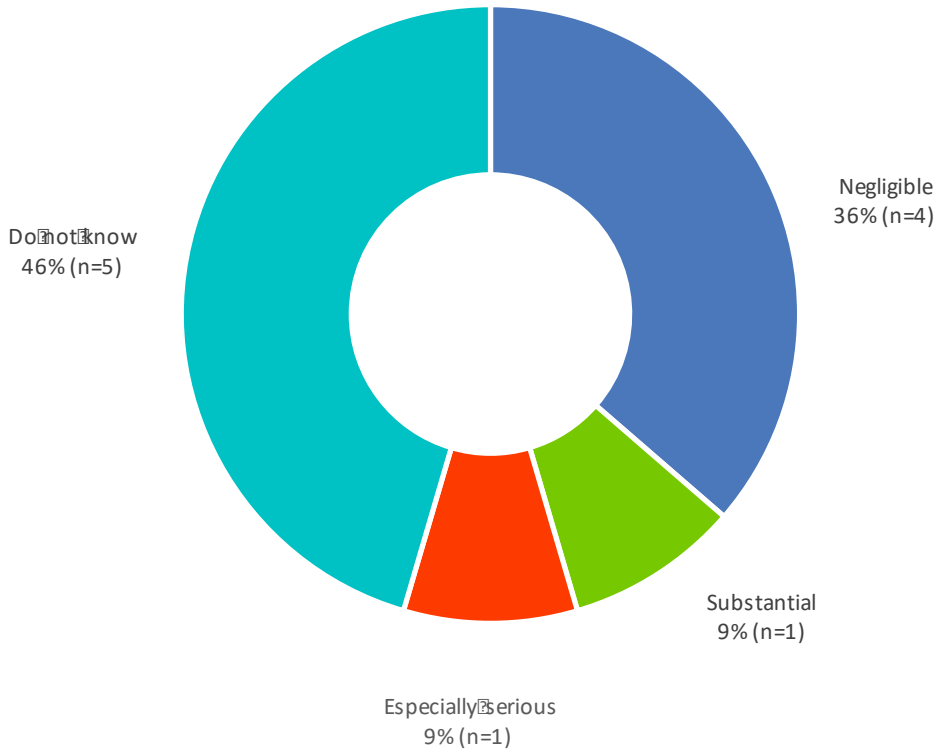
Fig. A3. Formulations of adinazolam



Perceived negative health impact

Two countries (1 European, 1 Americas) reported that the negative health impact of non-medical consumption of adinazolam was "especially serious" or "substantial" (Fig. A4). One country (Americas) described adinazolam as generally abused for its sedative/hypnotic effects and has been identified in 42 toxicology cases (a death, non-fatal overdoses and driving under the influence) between 2020 and 2021.

Fig. A4. Negative health impacts of non-medical consumption of adinazolam



Emergency department visits

Two countries (1 European, 1 Americas) were aware of emergency department visits related to adinazolam.

Deaths

One country (Americas) reported a total of 1 adinazolam-related death that involved other substances between 2020 and 2022.

Drug dependence

No countries reported that people presented for treatment of drug dependence in their country due to use of adinazolam.

Current national controls

Nine countries (5 European, 3 Western Pacific, 1 Americas) responded that the availability of a dinazolam was currently regulated under national legislation.

Illicit manufacture and trafficking-related information

Table A7 shows the main reported activities for adinazolam.

Table A7. Reported activities involving adinazolam for purposes other than medical, scientific or industrial use

Activity	No. of countries
Smuggling (from other countries)	3
Trafficking	3
Internet sales (other or location of sellers and website unknown)	3
Internet sales (from abroad to buyers in respondent's country)	1
Manufacture of the substance by chemical synthesis	1
Internet sales (seller or website located in respondent's country)	0
Direct sales	0
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Diversion	0
Do not know	4
Other[a]	1

[a] Includes "Seizures".

Seizures

Three countries (2 European, 1 Americas) reported adinazolam seizures in 2022. The number of seizures per country ranged from 1 to 30 and the amounts seized ranged from 0.27 g to 725.3 g (Table A8). Five countries (4 European, 1 Americas) reported seizures in 2021. The number of seizures per country ranged from 1 to 87 and the amounts seized from 47.4 g to 735 g. One country (European) reported 197 tablets seized in 2021. Five countries (4 European, 1 Americas) reported adinazolam, seizures in 2020. The number of seizures per country ranged from 1 to 347 and the amounts seized from 804.52 g to 2719.5 g. One country (European) reported 481 tablets seized in 2020.

Table A8. Reported seizures of adinazolam

Year	No. of countries that reported seizures	No. of seizures
2022	3	122
2020	5	125
2021	5	380

Fourteen countries (8 European, 4 Western Pacific, 2 Americas) reported that they had the laboratory capacity to analyse adinazolam.

Bromazolam

Of the 77 countries that agreed to provide data, 23 had information on bromazolam (Table A9).

Table A9. Numbers of countries providing information on bromazolam

Region	No. of countries that had no information	No. of countries that had information
African	3	2
Americas	5	3
Eastern Mediterranean	6	0
European	13	13
South-East Asia	3	0
Western Pacific	4	5
Total	34	23

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for ADB-BUTINACA. No countries reported that bromazolam was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard). None reported use for industrial purposes.

Epidemiology of non-medical use

Twelve countries (6 European, 3 Americas, 2 Western Pacific and 1 African) reported evidence from health professionals and law enforcement of the use of bromazolam for non-medical purposes (outside the medical, industrial or scientific context). This evidence was derived primarily from data on seizures and toxicology reports (n=12).

Routes of administration and formulations

The most common reported route of administration was oral, followed by sniffing and injection (Table A10).

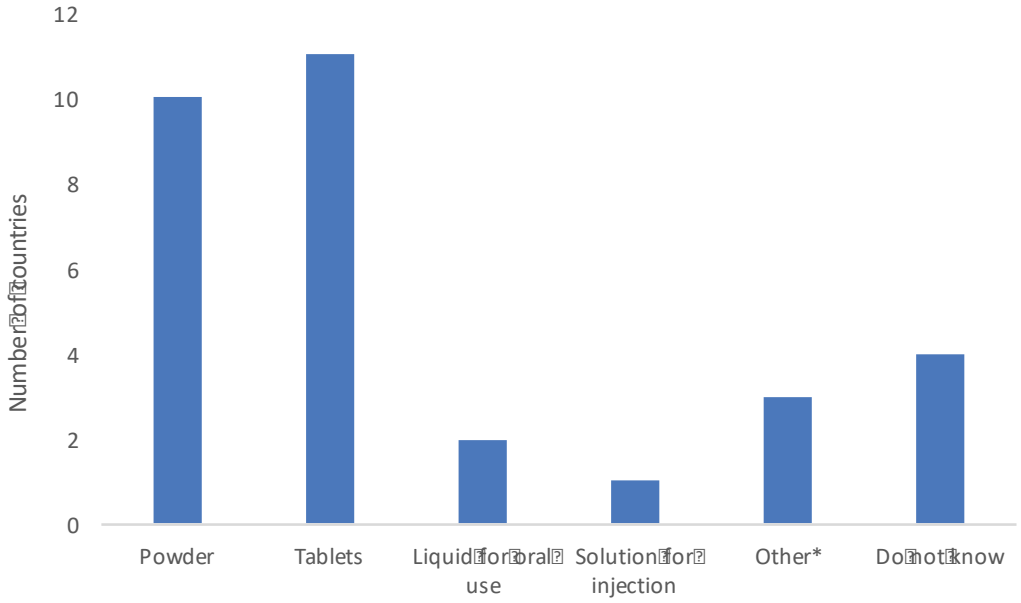
Table A10. Reported routes of bromazolam administration

Route of administration	No. of countries
Oral	11
Sniffing	1
Injection	1

Smoking	0
Inhalation	0
Other	0
Do not know	6

The most common known formulations of bromazolam reported were as a powder and as a tablet (Fig. A5).

Fig. A5. Formulations of Bromazolam

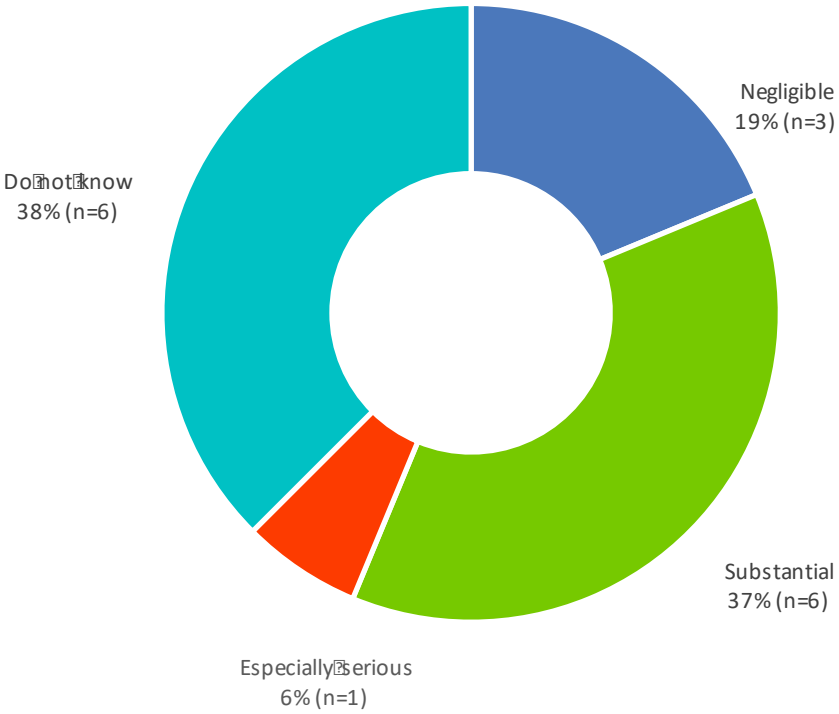


Other formulations referred to were gummy bears (n=1) or a residue, rock like solid (n=1).

Perceived negative health impact

Seven countries (6 European, 2 Western Pacific, 1 Americas, 1 Eastern Mediterranean, 1 South-East Asia) reported that the negative health impact of non-medical consumption of bromazolam was "especially serious" or "substantial" (Fig. A6). Two countries (1 European, 1 Western Pacific) reported that bromazolam was a growing concern, and had been detected in counterfeit benzodiazepine tablets. One country (African) noted that it was used by a large part of the youth population. An additional country (Americas) reported that it has been identified in at least 150 death investigations , and was commonly identified with other sedative/hypnotics.

Fig. A6. Negative health impacts of non-medical consumption of bromazolam



Emergency department visits

Four countries (3 European, 1 African) were aware of emergency department visits related to bromazolam. One country in Europe described 43 emergency presentations by people who had consumed bromazolam with other substances, with a wide range of symptoms, hypertension, hypothermia, agitation, extreme agitation, cardiac arrest, psychosis, seizure, chest pain, arrhythmia, low consciousness. Another European country reported one case of severe acute intoxication in an emergency room with dysarthria and cognitive deficit. One African country reported vomiting, nausea and drowsiness.

Deaths

Four countries (2 Americas, 2 European) reported a total of 160 bromazolam-related deaths between 2020 and 2022. One country (Americas) reported one hundred and fifty-two deaths in 2022 in which it was unknown if other substances were involved.

Drug dependence

No countries reported that people presented for treatment of drug dependence in their country due to use of bromazolam.

Current national controls

Fourteen countries (9 European, 3 Western Pacific, 1 Americas, 1 African) responded that the availability of bromazolam was currently regulated under national legislation.

Illicit manufacture and trafficking-related information

Table A11 shows the main reported activities involving bromazolam.

Table A11. Reported activities involving bromazolam for purposes other than medical, scientific or industrial use

Activity	No. of countries
Smuggling (from other countries)	7
Trafficking	6
Internet sales (from abroad to buyers in respondent's country)	3
Internet sales (other or location of sellers and website unknown)	3
Internet sales (seller or website located in respondent's country)	1
Manufacture of the substance by chemical synthesis	1
Direct sales	0
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Diversion	0
Do not know	5
Other[a]	1

[a] Includes “Seizures”.

Seizures

Eleven countries (3 European, 1 Western Pacific, 1 South-East Asia) reported seizures in 2022. The number of seizures per country ranged from 1 to 407 and the amounts seized ranged from 174.04 g to 5.1 kg. In addition, amounts seized in tablets ranged from 25 pills to 2275 pills (Table A12). One country (European) reported seizures of bromazolam as a liquid totalling 867 ml. Ten countries (8 European, 2 Americas) reported bromazolam seizures in 2021. The number of seizures per country ranged from 1 to 757 and the amounts seized from 33 g to 5.7 kg. In addition, amounts seized in tablets ranged from 9 pills to 207 pills. Nine countries (6 European, 1 African, 1 Americas, 1 Western Pacific) reported bromazolam seizures in 2020. The number of seizures per country ranged from 1 to 33 and the amounts seized from 0.9 g to 30.2 g. In addition, amounts seized in tablets ranged from 10 pills to 102 pills.

Table A12. Reported seizures of bromazolam

Year	No. of countries that reported seizures	No. of seizures
2022	11	607
2021	10	961
2020	9	59

Twenty countries (18 European, 3 Western Pacific, 2 South-East Asia, 1 Eastern Mediterranean, 1 Americas) reported that they had the laboratory capacity to analyse bromazolam.

Protonitazene

Of the 77 countries that agreed to provide data, 16 had information on protonitazene (Table A13).

Table A13. Numbers of countries providing information on protonitazene

Region	No. of countries that had no information	No. of countries that had information
African	2	1
Americas	6	2
Eastern Mediterranean	6	0
European	21	4
South-East Asia	3	0
Western Pacific	3	5
Total	41	16

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for protonitazene. No countries reported that protonitazene was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard). No country reported use for industrial purposes.

Epidemiology of non-medical use

Five countries (3 European, 2 Americas) reported evidence of the use of protonitazene for non-medical purposes (outside the medical, industrial or scientific context). This evidence was derived primarily from data on seizures (n=4), with the last country further specifying “law enforcement encounters and medical examiner reports”.

Routes of administration and formulations

The most commonly reported routes of administration were oral, sniffing and injection (Table A14).

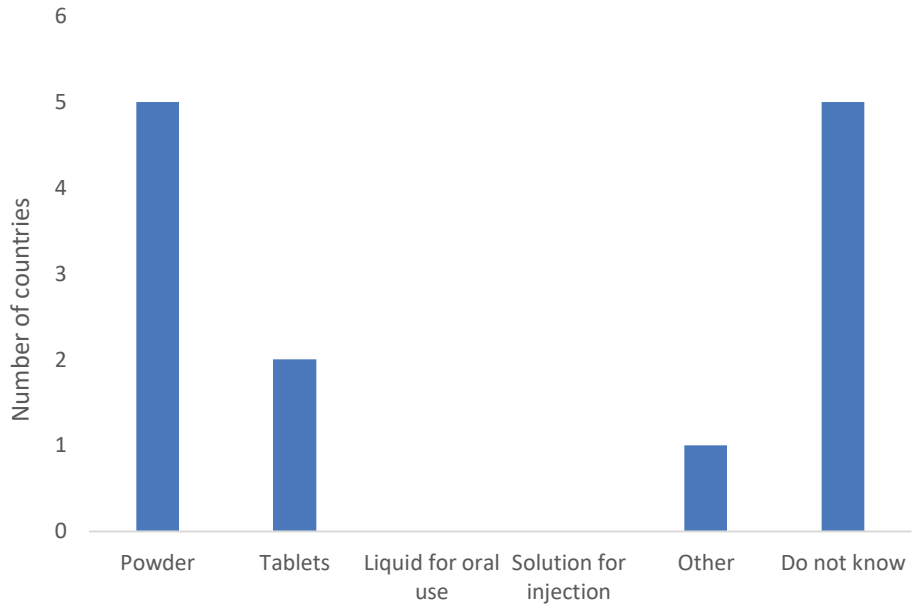
Table A14. Reported routes of Protonitazene administration

Route of administration	No. of countries
Oral	4
Sniffing	2
Injection	2
Inhalation	1
Smoking	1
Other[a]	1
Do not know	6

[a] nasal spray

The most common known formulations of protonitazene reported were as a powder and tablet (Fig. A7).

Fig. A7. Formulations of protonitazene

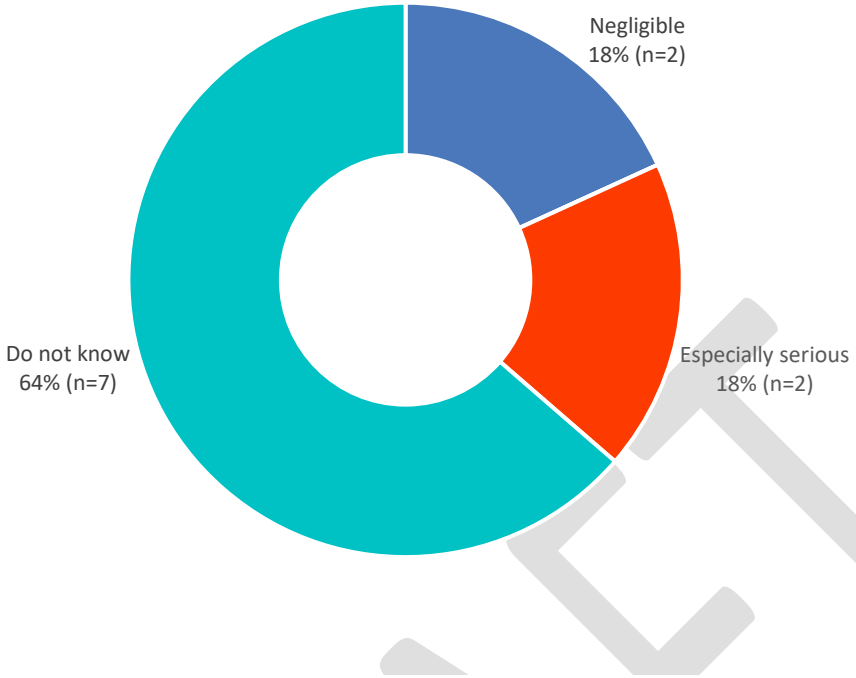


In the Other Formulation field, one country mentioned “residue, syringe”

Perceived negative health impact

Two countries (1 European, 1 Americas) reported that the negative health impact of non-medical consumption of protonitazene was “especially serious” (Fig. A8). One country (European) reported their source of evidence as being from seizures, and one country (Americas) cited protonitazene “has been identified in postmortem and toxicology cases (driving under the influence)”.

Fig. A8. Negative health impacts of non-medical consumption of protonitazene



Negligible
18% (n=2)
Especially serious
18% (n=2)
Do not know
64% (n=7)

Emergency department visits

No countries were aware of emergency department visits related to protonitazene.

Deaths

Three countries (1 African, 2 Americas) reported a total of 25 protonitazene-related deaths. One country (African) reported 1 death where protonitazene was the only substance involved, 3 where other substances were involved and 4 where it was unknown whether other substances were involved. One country (Americas) reported that in 2021 there was 1 death where protonitazene and other substances were involved and 9 where it was unknown whether other substances were involved. Another country (Americas) reported that in 2021 there were 9 deaths where protonitazene and other substances were involved.

Drug dependence

No countries were aware of people who presented for treatment of drug dependence in their country due to use of protonitazene.

Current national controls

Ten (6 European, 2 Western Pacific, 2 Americas) responded that the availability of protonitazene was currently regulated under national legislation.

Illicit manufacture and trafficking-related information

Table A15 shows the main reported activities for protonitazene.

Table A15. Reported activities involving protonitazene for purposes other than medical, scientific or industrial use

Activity	No. of countries
Trafficking	3
Smuggling (from other countries)	1
Internet sales (from abroad to buyers in respondent's country)	1
Internet sales (other or location of sellers and website unknown)	1
Internet sales (seller or website located in respondent's country)	0
Manufacture of the substance by chemical synthesis	0
Direct sales	0
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Diversion (from legal supply chain)	0
Do not know	5
Other	0

One country from the Western Pacific reported protonitazene being used for industrial or other non-medical/non-scientific purposes in their country, as a “material for synthesis of psychoactive drugs”.

Seizures

Three countries (2 European, 1 Americas) reported seizures in 2022. The number of seizures per country

ranged from 1 to 6 and the amounts seized ranged from 1.2 g to 989 g (Table A16). Two countries (1 European, 1 Americas) reported seizures in 2021. The number of seizures ranged from 1 to 21, and the amounts seized ranged from 1 g to 44 g.

Table A16. Reported seizures of protonitazene

Year	No. of countries that reported seizures	No. of seizures
2022	3	10
2021	2	22

Twelve countries (7 European, 3 Western Pacific, 2 Americas) reported that they had the laboratory capacity to analyse protonitazene.

Etazene

Of the 77 countries that agreed to provide data, 20 had information on etazene (Table A17).

Table A17. Numbers of countries providing information on etazene

Region	No. of countries that had no information	No. of countries that had information
African	2	1
Americas	6	2
Eastern Mediterranean	6	0
European	16	12
South-East Asia	3	0
Western Pacific	3	5
Total	36	20

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for etazene. No countries reported that etazene was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard).

Epidemiology of non-medical use

Five countries (3 European, 2 Americas) reported evidence of the use of etazene for non-medical purposes (outside the medical, industrial or scientific context). This evidence was derived from data on seizures/law enforcement encounters (n=5) and medical examiner reports/blood samples in cases of death (n=2).

Routes of administration and formulations

The most commonly reported routes of administration were oral, sniffing and injection (Table A18).

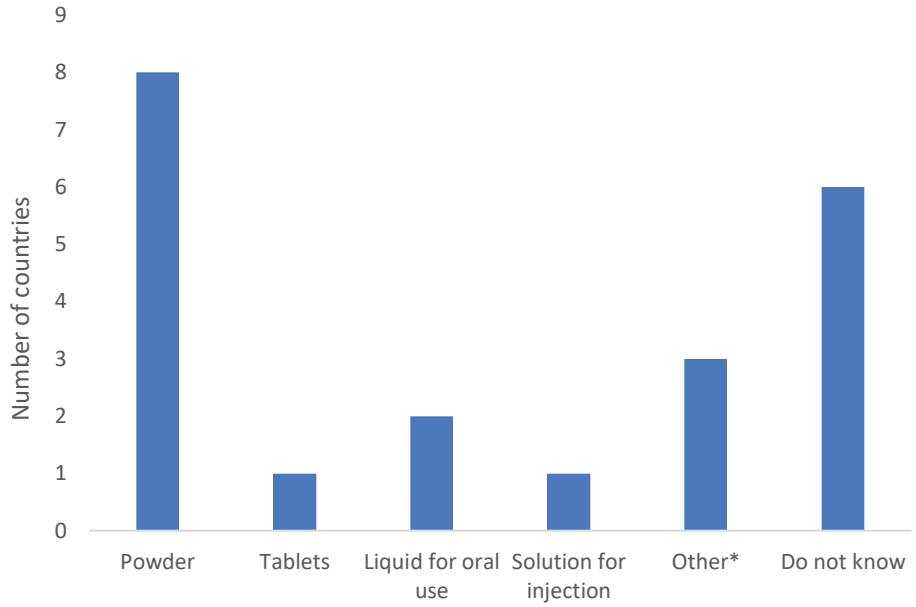
Table A18. Reported routes of etazene administration

Route of administration	No. of countries
Oral	3
Sniffing	3
Injection	3
Smoking	1
Inhalation	0
Other[a]	1
Do not know	10

[a] nasal spray

The most common known formulation of etazene reported was as a powder (Fig. A9).

Fig. A9. Formulations of etazene

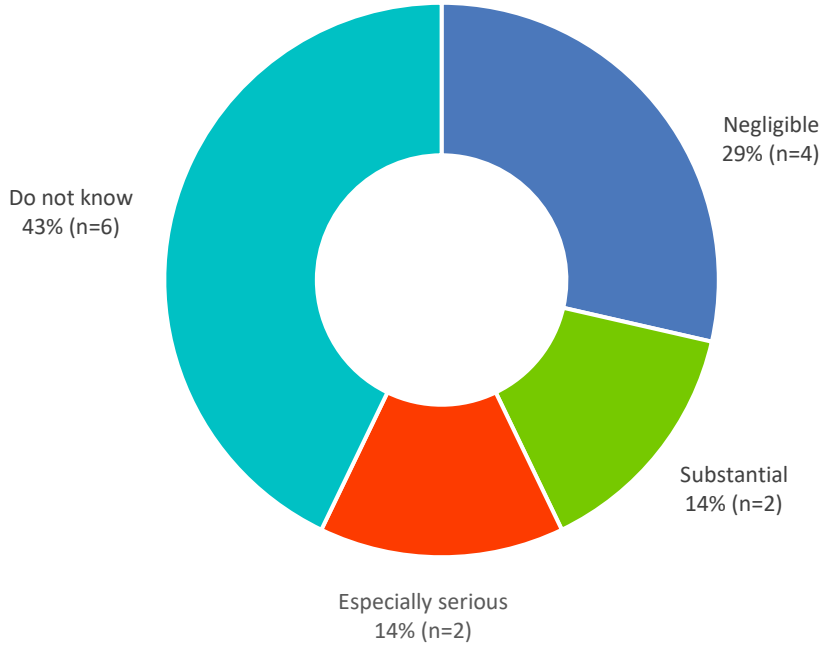


* "Seizures of liquid. No information about if the liquid/solution was for oral administration/use or for injection", "purple-red paste, residue, syringe, material", and "herbal material".

Perceived negative health impact

Two countries (1 European, 1 Americas) reported that the negative health impact of non-medical consumption of etazene was “especially serious” (Fig. A10). Two countries (2 European) reported their source of evidence as being from seizures, two countries (1 European, 1 Americas) reported postmortem investigations, and one country (1 Americas) reported one of their sources as toxicology identification as a part of driving under the influence cases.

Fig. A10. Negative health impacts of non-medical consumption of etazene



Emergency department visits

No countries were aware of emergency department visits related to etazene.

Deaths

Four countries (2 Americas, 2 European) reported a total of 10 etazene-related deaths in 2021. Two countries (1 Americas, 1 European) respectively reported 6 and 2 deaths that involved etazene and other substances. Two countries (1 Americas, 1 European) both reported 1 death for their country where it was unknown if other substances were involved.

Drug dependence

No countries were aware of people who presented for treatment of drug dependence in their country due to use of etazene.

Current national controls

Fifteen (11 European, 2 Western Pacific, 2 Americas) responded that the availability of etazene was currently regulated under national legislation.

Illicit manufacture and trafficking-related information

Table A19 shows the main reported activities involving etazene.

Table A19. Reported activities involving etazene for purposes other than medical, scientific or industrial use

Activity	No. of countries
Trafficking	5
Smuggling (from other countries)	3
Internet sales (other or location of sellers and website unknown)	2
Internet sales (seller or website located in respondent's country)	1
Internet sales (from abroad to buyers in respondent's country)	0
Manufacture of the substance by chemical synthesis	0
Direct sales	0
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Diversion (from legal supply chain)	0
Do not know	7
Other	0

One country (Western Pacific) reported etazene being used for industrial or other non-medical/non-scientific purposes in their country, as a “material for synthesis of psychoactive drugs”.

Seizures

Three countries (2 European, 1 Americas) reported etazene seizures in 2022. The number of seizures per country ranged from 1 to 2 and the amounts seized ranged from 1.5 g to 185 g (Table A20). Five countries (4 European, 1 Americas) reported etazene seizures in 2021. The number of seizures ranged from 1 to 53, and the amounts seized ranged from 0.5 g to 298 g. Five countries (4 European, 1 Americas) reported etazene seizures in 2020. The number of seizures ranged from 1 to 12, and the amounts seized ranged from 1 g to 302 g.

Table A20. Reported seizures of etazene

Year	No. of countries that reported seizures	No. of seizures
2022	3	4
2021	5	104
2020	5	25

Fifteen countries (10 European, 3 Western Pacific, 2 Americas) reported that they had the laboratory capacity to analyse etazene.

Etonitazepyne

Of the 77 countries that agreed to provide data, 19 had information on etonitazepyne (Table A21).

Table A21. Numbers of countries providing information on etonitazepyne

Region	No. of countries that had no information	No. of countries that had information
African	2	1
Americas	6	2
Eastern Mediterranean	6	0
European	17	10
South-East Asia	3	0
Western Pacific	3	5
Total	37	19

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for etonitazepyne. No countries reported that etonitazepyne was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard).

Epidemiology of non-medical use

Seven countries (4 European, 2 Americas, 1 Western Pacific) reported evidence of the use of etonitazepyne for non-medical purposes (outside the medical, industrial or scientific context). This evidence was derived from data on seizures/law enforcement encounters (n=5), medical examiner reports (n=1), and drug checking services (n=1).

Routes of administration and formulations

The most commonly reported route of administration was oral (Table A22).

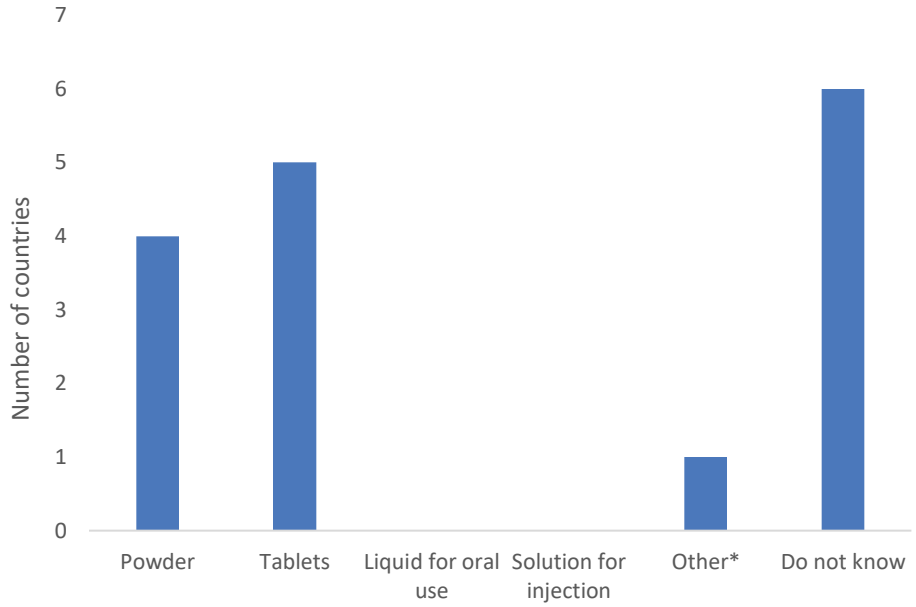
Table A22. Reported routes of etonitazepyne administration

Route of administration	No. of countries
Oral	5
Sniffing	3
Injection	2
Smoking	1
Inhalation	1
Other[a]	1
Do not know	7

[a] vaping

The most common known formulation of etonitazepyne reported was as tablets or powder (Fig. A11).

Fig. A11. Formulations of etonitazepyne

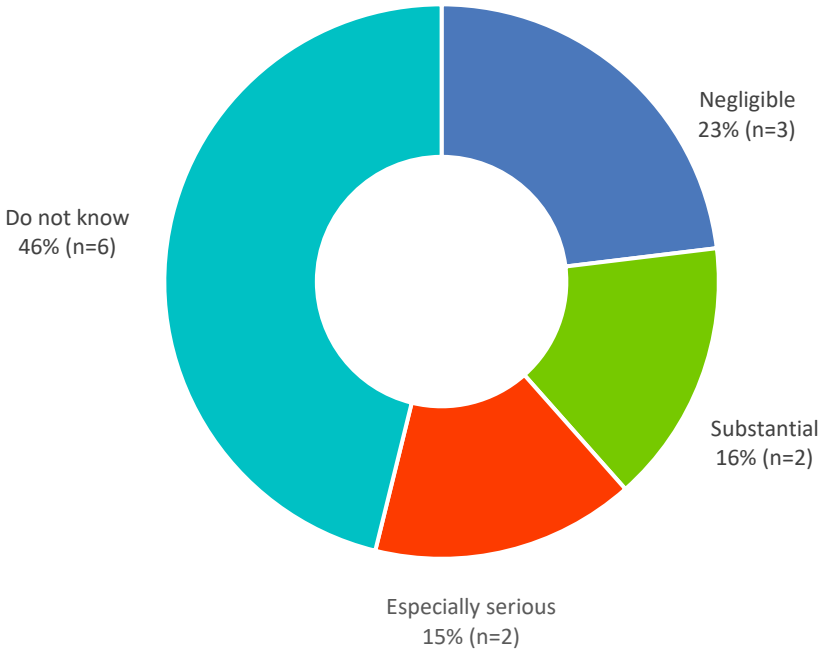


* residue in a syringe of unknown formulation

Perceived negative health impact

Two countries (1 European, 1 Americas) reported that the negative health impact of non-medical consumption of etonitazepyne was "especially serious" (Fig. A12). Two countries (2 European) reported their source of evidence as from seizures, one country (European) reported emergency department presentations and associated deaths, one country (Americas) reported evidence from toxicology identification as a part of postmortem and driving under the influence cases, and one country (Western Pacific) reported etonitazepyne as being sold as counterfeit oxycodone tablets .

Fig. A12. Negative health impacts of non-medical consumption of etonitazepyne



Emergency department visits

One country (European) was aware of emergency department visits related to etonitazepyne. This country reported 3 patients in 2022 and 2 patients in 2021 who presented to the emergency department with etonitazepyne and other substances. Their symptoms included cardiac arrest, respiratory insufficiency, loss of consciousness, tachycardia, and respiratory distress.

Deaths

Three countries (1 African, 1 Americas, 1 European) reported a total of 29 etonitazepyne-related deaths for the most recent completed year data was available (i.e. 2021 for most countries). Two countries (1 African, 1 Americas) respectively reported 3 and 17 etonitazepyne-related deaths where other substances were involved. One country (African) reported 5 deaths where it was unknown whether other substances were involved.

Drug dependence

No countries were aware of people who presented for treatment of drug dependence in their country due to use of etonitazepyne.

Current national controls

Eleven (6 European, 3 Western Pacific, 2 Americas) responded that the availability of etonitazepyne was

currently regulated under national legislation.

Illicit manufacture and trafficking-related information

Table A23 shows the main reported activities involving for etonitazepyne.

Table A23. Reported activities involving etonitazepyne for purposes other than medical, scientific or industrial use

Activity	No. of countries
Trafficking	5
Smuggling (from other countries)	3
Internet sales (from abroad to buyers in respondent's country)	2
Internet sales (other or location of sellers and website unknown)	2
Internet sales (seller or website located in respondent's country)	1
Manufacture of the substance by chemical synthesis	0
Direct sales	0
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Diversion (from legal supply chain)	0
Do not know	5
Other	0

One country (Western Pacific) reported etonitazepyne being used for industrial or other non-medical/non-scientific purposes in their country, as a “material for synthesis of psychoactive drugs”.

Seizures

Five countries (4 European, 1 Americas) reported seizures in 2022. The number of seizures per country ranged from 1 to 40 and the amounts seized ranged from 0.5 g to 29 g (Table A24). Four countries (3 European, 1 Americas) reported seizures in 2021. The number of seizures ranged from 1 to 131, and the amounts seized ranged from 5 g to 214 g.

Table A24. Reported seizures of etonitazepyne

Year	No. of countries that reported seizures	No. of seizures
2022	5	44
2021	4	135

Fifteen countries (10 European, 4 Western Pacific, 1 Americas) reported that they had the laboratory capacity to analyse etonitazepyne.

2-methyl-AP-237

Of the 77 countries that agreed to provide data, 17 had information on 2-methyl-AP-237 (Table A25).

Table A25. Numbers of countries providing information on 2-methyl-AP-237

Region	No. of countries that had no information	No. of countries that had information
African	3	0
Americas	6	2
Eastern Mediterranean	6	0
European	17	11
South-East Asia	3	0
Western Pacific	5	4
Total	40	17

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for 2-methyl-AP-237. One country (Americas) reported that 2-methyl-AP-237 was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard). No country reported other use of 2-methyl-AP-237 for industrial or other non-medical/non-scientific purposes in their country.

Epidemiology of non-medical use

Five countries (3 European, 2 Americas) reported evidence of the use of 2-methyl-AP-237 for non-medical purposes (outside the medical, industrial or scientific context). This evidence was derived from data on seizures/law enforcement encounters (n=4), medical examiner reports/detection in blood (n=2), emergency department presentations (n=1), and poison information calls (n=1).

Routes of administration and formulations

The most commonly reported route of administration was sniffing (Table A26).

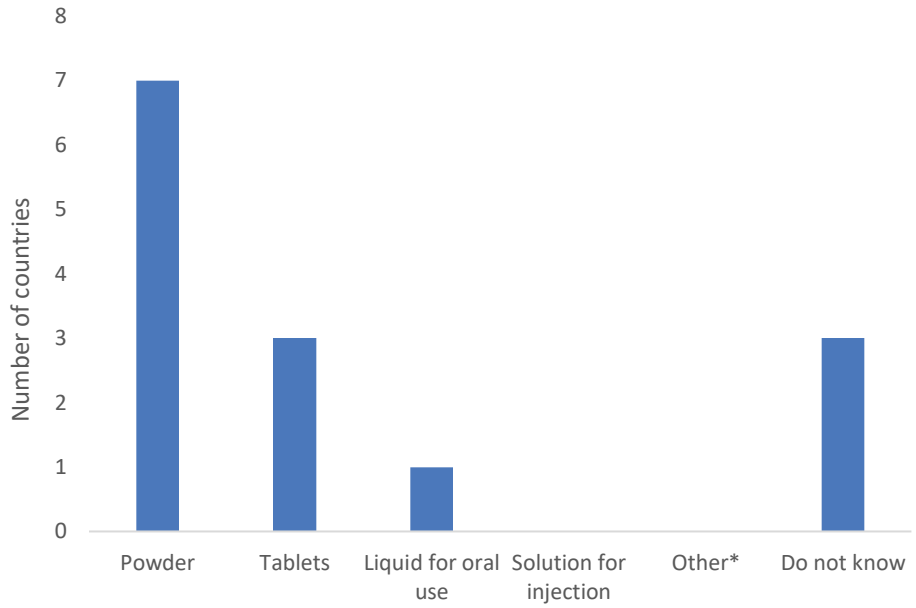
Table A26. Reported routes of 2-methyl-AP-237 administration

Route of administration	No. of countries
Sniffing	4
Oral	2
Injection	2
Smoking	2
Inhalation	0
Other[a]	2
Do not know	5

[a] Rectal administration (n=1) and as a nasal spray (n=1)

The most common known formulation of 2-Methyl-AP-237 reported was powder (Fig. A13).

Fig. A13. Formulations of 2-methyl-AP-237

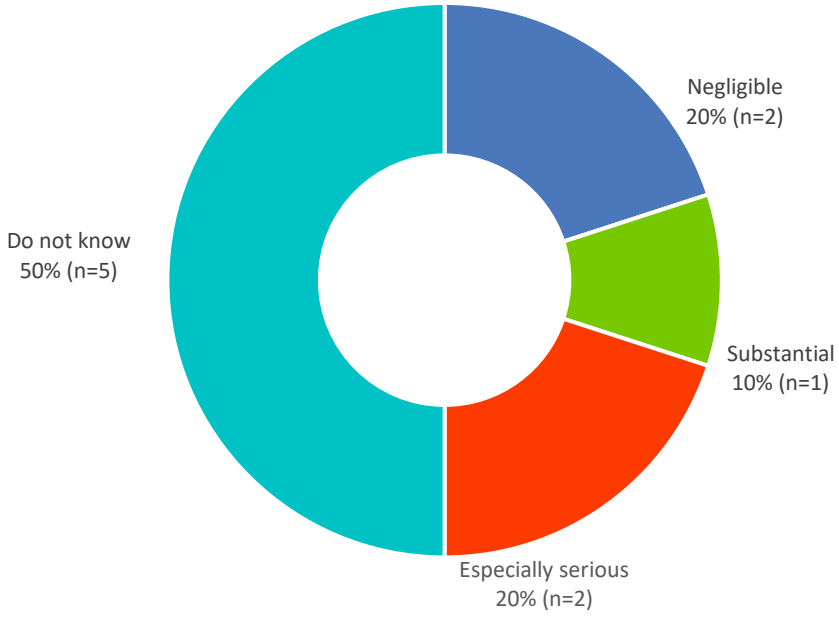


* caps

Perceived negative health impact

Two countries (1 European, 1 Americas) reported that the negative health impact of non-medical consumption of 2-methyl-AP-237 was "especially serious" (Fig. A14). One country (European) reported their sources of information as being from femoral blood, poisons information related to hospitalisations, and seizures. Another country (Americas) reported their information as from deaths related to extramedical use of drugs and medical examiner reports.

Fig. A14. Negative health impacts of non-medical consumption of 2-methyl-AP-237



Emergency department visits

Three countries (2 European, 1 Americas) were aware of emergency department visits related to 2-methyl-AP-237. The adverse effects that patients presented with at emergency departments included respiratory failure/difficulty breathing, high pulse, and miosis.

Deaths

Two countries (1 European, 1 Americas) reported a total of seven 2-methyl-AP-237-related deaths for the most recent completed year data was available. One country (European) reported one 2-methyl-AP-237-related death in 2019 where other substances were involved. One country (Americas) reported six 2-methyl-AP-237-related deaths in 2021 where other substances were involved. This country (Americas) further noted that the types of drugs co-identified in 2-methyl AP-237 associated fatal and nonfatal overdose cases were often prescription opioid analgesics, heroin, tramadol, depressants, fentanyl, and other synthetic opioid substances.

Drug dependence

No countries were aware of people who presented for treatment of drug dependence in their country due to use of 2-methyl-AP-237.

Current national controls

Eleven (8 European, 3 Western Pacific) responded that the availability of 2-methyl-AP-237 was currently regulated under national legislation.

Illicit manufacture and trafficking-related information

Table A23 shows the main reported activities involving 2-methyl-AP-237.

Table A27. Reported activities involving 2-methyl-AP-237 for purposes other than medical, scientific or industrial use

Activity	No. of countries
Trafficking	4
Smuggling (from other countries)	3
Internet sales (other or location of sellers and website unknown)	2
Internet sales (from abroad to buyers in respondent's country)	1
Internet sales (seller or website located in respondent's country)	1
Manufacture of the substance by chemical synthesis	0
Direct sales	0
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Diversion (from legal supply chain)	0
Do not know	4
Other	0

Seizures

Five countries (4 European, 1 Americas) reported seizures in 2022. The number of seizures per country ranged from 1 to 2 and the amounts seized ranged from 0.8 g to 45 g (Table A28). Two countries (1 European, 1 Americas) reported 2-methyl-AP-237 seizures in 2021. The number of seizures ranged from 2 to 47, and the amounts seized ranged from 8 g to 9 g. Two countries (1 European, 1 Americas) reported 2-methyl-AP-237 seizures in 2020. The number of seizures ranged from 3 to 5, and the amounts seized ranged from 3 g to 10 g.

Table A28. Reported seizures of 2-methyl-AP-237

Year	No. of countries that reported seizures	No. of seizures
2022	5	7
2021	2	49
2020	2	8

Twelve countries (9 European, 2 Western Pacific, 1 Americas) reported that they had the laboratory capacity to analyse 2-methyl-AP-237.

Alpha-PiHP

Of the 77 countries that agreed to provide data, 26 had information on alpha-PiHP (Table A29).

Table A29. Numbers of countries providing information on alpha-PiHP

Region	No. of countries that had no information	No. of countries that had information
African	3	0
Americas	5	3
Eastern Mediterranean	6	0
European	11	17
South-East Asia	3	0
Western Pacific	3	6
Total	31	30

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for alpha-PiHP. No countries reported that alpha-PiHP was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard). No countries reported use for industrial purposes.

Epidemiology of non-medical use

Fourteen countries (9 European, 3 Americas and 2 Western Pacific) reported evidence from law enforcement or health professionals of the use of alpha-PiHP for non-medical purposes (outside the medical, industrial or scientific context). This evidence was derived primarily from data on seizures and toxicology reports (n=14).

Routes of administration and formulations

The most common reported route of administration was sniffing, followed by oral, injection and smoking (Table A30).

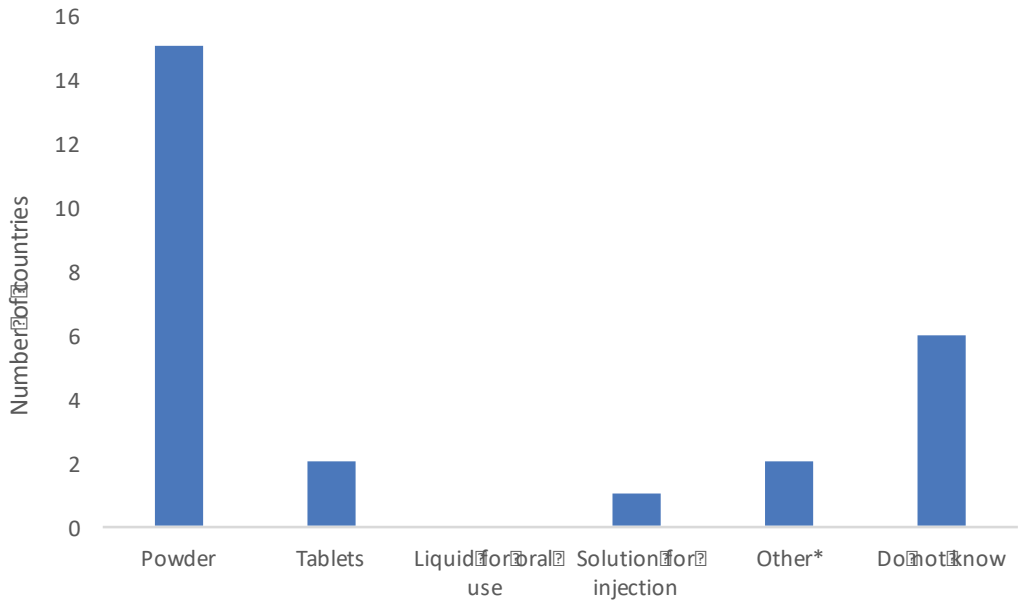
Table A30. Reported routes of alpha-PiHP administration

Route of administration	No. of countries
Sniffing	7
Oral	5
Injection	4
Smoking	4

Injection	0
Other	0
Do not know	11

The most common known formulations of alpha-PiHP reported were as a powder and as a tablet (Fig. A15).

Fig. A15. Formulations of alpha-PiHP

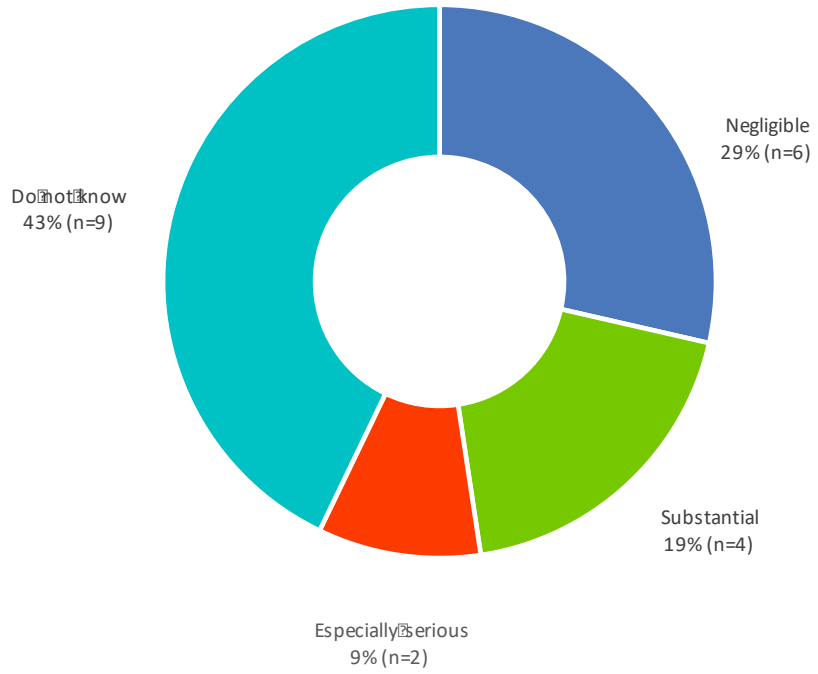


Other formulations referred to were herbal mixture or liquid (unknown if for oral use or injection).

Perceived negative health impact

Six countries (4 European, 2 Americas) reported that the negative health impact of non-medical consumption of alpha-PiHP was "especially serious" or "substantial" (Fig. A16). Three countries (2 European, 1 Americas) reported the occurrence of seizures and identification in toxicology cases.

Fig. A16. Negative health impacts of non-medical consumption of alpha-PiHP



Emergency department visits

One country (European) were aware of emergency department visits related to alpha-PiHP and described side-effects to include headache, sweating, vertigo, anxiety, reduced blood pressure, tremors, overactivity, anxiety and increased body temperature. Two cases report on individuals that injected the substance and had discomfort at the injection site or high pulse, increased blood pressure and chest pain.

Deaths

Four countries (3 European, 1 Americas) reported a total of 18 alpha-PiHP-related deaths between 2020 and 2022. Two countries (1 European, 1 Americas) reported ten deaths in 2021 in which it was unknown if other substances were involved. One country (European) reported 3 alpha-PiHP-related deaths in which another substance was also involved, also in 2021.

Drug dependence

No countries reported that people presented for treatment of drug dependence in their country due to use of alpha-PiHP.

Current national controls

Twenty-one countries (13 European, 5 Western Pacific, 3 Americas) responded that the availability of alpha-PiHP was currently regulated under national legislation.

Illicit manufacture and trafficking-related information

Table A31 shows the main reported activities involving alpha-PiHP.

Table A31. Reported activities involving alpha-PiHP for purposes other than medical, scientific or industrial use

Activity	No. of countries
Trafficking	10
Smuggling (from other countries)	6
Internet sales (from abroad to buyers in respondent's country)	2
Internet sales (other or location of sellers and website unknown)	2
Internet sales (seller or website located in respondent's country)	1
Manufacture of the substance by chemical synthesis	1
Direct sales	1
Diversion	1
Manufacture of the substance by extraction from other products	0
Production of consumer products containing the substance	0
Do not know	6
Other	0

Seizures

Nine countries (8 European, 1 Americas) reported alpha-PiHP seizures in 2022. The number of seizures per country ranged from 1 to 181 and the amounts seized ranged from 3 g to 1.3 kg (Table A32). Eight countries (6 European, 1 Western Pacific, 1 Americas) reported alpha-PiHP seizures in 2021. The number of seizures per country ranged from 1 to 341 and the amounts seized from 11 g to 35.7 kg. Seven countries (6 European, 1 Americas) reported alpha-PiHP seizures in 2020. The number of seizures per country ranged from 1 to 200 and the amounts seized ranged from below 1 g to 613.2 g.

Table A32. Reported seizures of alpha-PiHP

Year	No. of countries that reported seizures	No. of seizures
2022	9	318
2021	8	409
2020	7	280

Twenty-two countries (15 European, 5 Western Pacific, 2 Americas) reported that they had the laboratory capacity to analyse alpha-PiHP.

3-MMC

Of the 77 countries that agreed to provide data, 31 had information on 3-MMC (Table A33).

Table A33. Numbers of countries providing information on 3-MMC

Region	No. of countries that had no information	No. of countries that had information
African	2	0
Americas	5	3
Eastern Mediterranean	6	0
European	7	22
South-East Asia	3	0
Western Pacific	3	6
Total	26	31

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for 3-MMC. No countries reported that 3-MMC was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard). No countries reported use for industrial purposes.

Epidemiology of non-medical use

Nineteen countries (14 European, 3 Americas and 2 Western Pacific) reported evidence from health professionals, law enforcement or drug checking services of the use of 3-MMC for non-medical purposes (outside the medical, industrial or scientific context).

Routes of administration and formulations

The most common reported route of administration was oral, followed by sniffing and injection (Table A34).

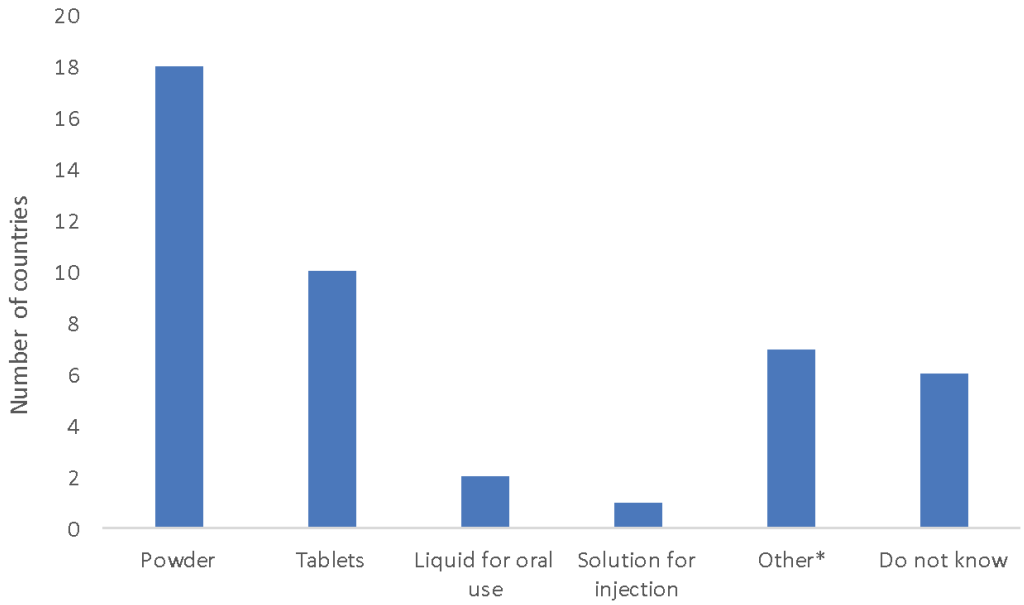
Table A34. Reported routes of 3-MMC administration

Route of administration	No. of countries
Oral	10
Sniffing	9
Injection	3
Smoking	1
Inhalation	0
Other[a]	1
Do not know	13

[a] Rectal

The most common known formulations of 3-MMC reported were as a powder and as a tablet (Fig. A17).

Fig. A17. Formulations of 3-MMC

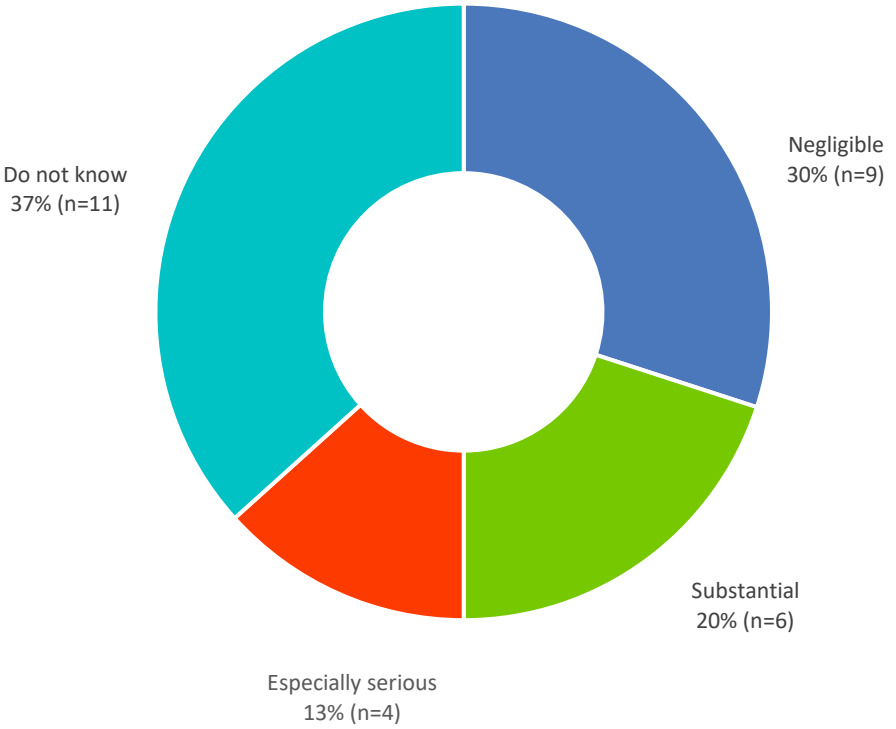


Other formulations referred to were a crystalline substance (n=3) and blotters or paper (n=2).

Perceived negative health impact

Ten countries (8 European, 2 Americas) reported that the negative health impact of non-medical consumption of 3-MMC was "especially serious" or "substantial" (Fig. A18). One European country reported that 3-MMC had been found in tablets or powders sold as MDMA at festivals and nightclubs. Two European countries mentioned that 3-MMC had been detected in intoxications. One European country mentions that 3-MMC is used by various user groups and is readily, freely available and sold at a low price.

Fig. A18. Negative health impacts of non-medical consumption of 3-MMC



Emergency department visits

Four European countries were aware of emergency department visits related to 3-MMC. One European country reported side-effects from 3-MMC to include confusion, dissociation and paraesthesia. Another European country described three intoxications with a number of side effects to include increased heart rate (2 cases), increased body temperature, hallucinations, change in behaviour, tight chest, and anxiety .

Deaths

Five countries (4 European, 1 Western Pacific) reported a total of 18 3-MMC-related deaths between 2018 and 2020. One country (European) reported six deaths during 2021 and 2022 that involved other substances as well as six deaths during 2021 and 2022 in which 3-MMC was the only substance involved.

Drug dependence

Two European countries reported that people presented for treatment of drug dependence in their country due to use of 3-MMC.

Current national controls

Twenty-nine countries (17 European, 6 Western Pacific, 3 Americas) responded that the availability of 3-MMC was currently regulated under national legislation.

Illicit manufacture and trafficking-related information

Table A35 shows the main reported activities involving 3-MMC.

Table A35. Reported activities involving 3-MMC for purposes other than medical, scientific or industrial use

Activity	No. of countries
Trafficking	13
Smuggling (from other countries)	9
Internet sales (other or location of sellers and website unknown)	5
Internet sales (from abroad to buyers in respondent's country)	3
Direct sales	2
Manufacture of the substance by chemical synthesis	2
Internet sales (seller or website located in respondent's country)	1
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Diversion	0
Do not know	8
Other	0

Seizures

Thirteen countries (3 European, 1 Western Pacific, 1 South-East Asia) reported 3-MMC seizures in 2021. The number of seizures per country ranged from 1 to 34 and the amounts seized ranged from 0.5 g to 5.9 kg (Table A36). In addition, one European country seized 15,297 tablets. Sixteen countries (14 European, 1 Western Pacific, 1 Americas) reported 3-MMC seizures in 2021. The number of seizures per country ranged from 1 to 89 and the amounts seized from 6 g to 610 kg. Twelve countries (11 European, 1 Americas) reported 3-MMC seizures in 2020. The number of seizures per country ranged from 1 to 87 and the amounts seized from 2 g to 613.5 kg.

Table A36. Reported seizures of 3-MMC

Year	No. of countries that reported seizures	No. of seizures
2022	13	119
2021	16	327
2020	12	252

Twenty-nine countries (22 European, 5 Western Pacific, 2 Americas) reported that they had the laboratory capacity to analyse 3-MMC.

Zopiclone

Of the 77 countries that agreed to provide data, 43 had information on zopiclone (Table A37).

Table A37. Numbers of countries providing information on zopiclone

Region	No. of countries that had no information	No. of countries that had information
African	2	2
Americas	3	8
Eastern Mediterranean	4	3
European	7	21
South-East Asia	3	1
Western Pacific	1	8
Total	20	43

Approved medical, scientific or industrial use

Medical use

Forty-one of the countries (21 European, 8 Americas, 8 Western Pacific, 3 Eastern Mediterranean, 2 African, 1 South-East Asia) reported approved therapeutic indications for zopiclone. Thirty-six countries (17 European, 8 Western Pacific, 7 Americas, 3 Eastern Mediterranean, 2 African, 1 South-East Asia) reported that zopiclone was used in the treatment of insomnia or sleep disorders. One country (European) reported that zopiclone was used for post-acute withdrawal syndrome.

Veterinary use

No countries reported that zopiclone was approved as a veterinary product.

Scientific research

Three countries (2 European, 1 Western Pacific) reported that zopiclone is used in medical or scientific research, including two countries reporting ongoing clinical trials.

Industrial use

One country (Western Pacific) reported industrial use of zopiclone.

Epidemiology of non-medical use

Eleven countries (5 European, 3 Americas and 3 Western Pacific) reported evidence from law enforcement or health professionals of the use of zopiclone for non-medical purposes (outside the medical, industrial or scientific context).

Routes of administration and formulations

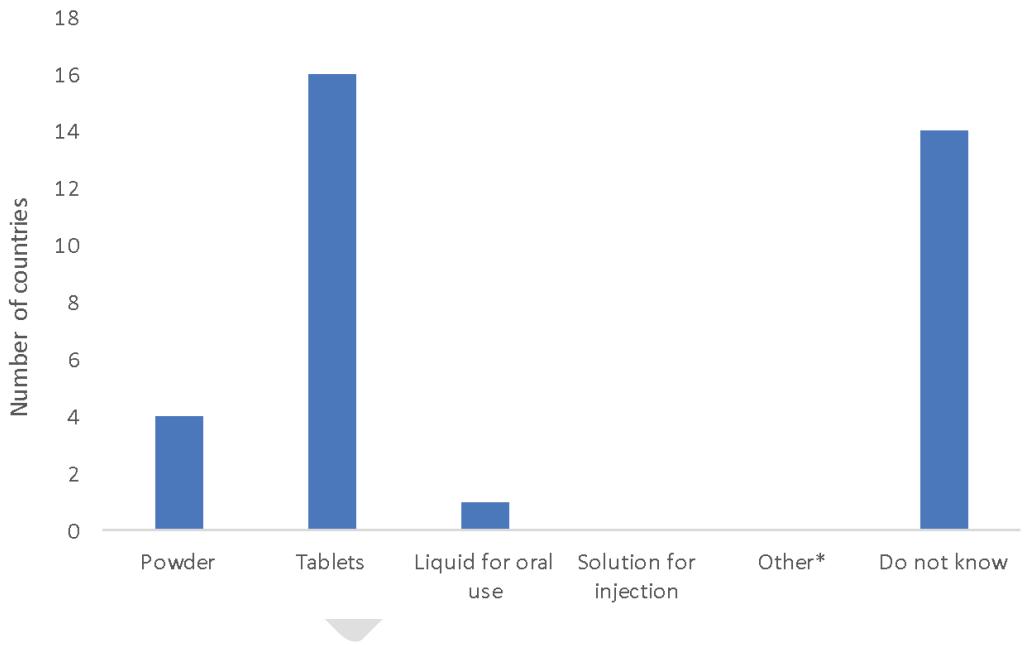
The most common reported route of administration was oral (Table A38).

Table A38. Reported routes of zopiclone administration

Route of administration	No. of countries
Oral	17
Sniffing	1
Injection	1
Smoking	0
Inhalation	0
Other	0
Do not know	16

The most common known formulations of zopiclone reported were as a tablet (Fig. A19).

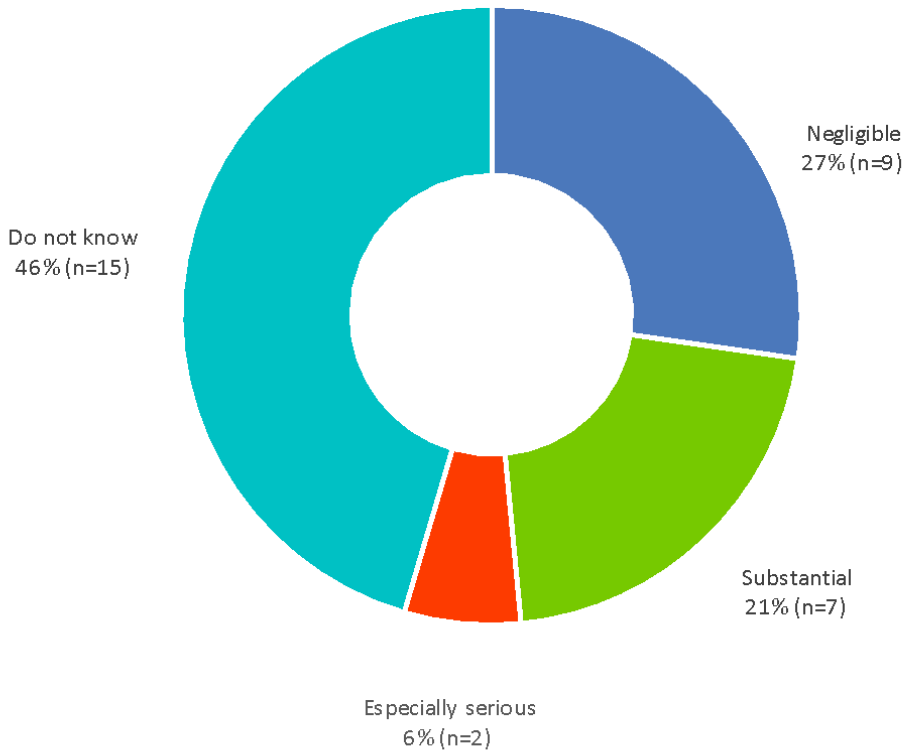
Fig. A19. Formulations of zopiclone



Perceived negative health impact

Nine countries (3 European, 2 Western Pacific, 3 Americas, 1 Eastern Mediterranean) reported that the negative health impact of non-medical consumption of zopiclone was “especially serious” or “substantial” (Fig. A20). Two countries (1 European, 1 Western Pacific) reported hospital admissions as a result of zopiclone use. One country (Western Pacific) reported evidence of oversupply and overprescribing of zopiclone as well as evidence of zopiclone for sale on social media platforms.

Fig. A20. Negative health impacts of non-medical consumption of zopiclone



Emergency department visits

Five countries (2 European, 2 Western Pacific, 1 Americas) were aware of emergency department visits related to zopiclone. Three countries (2 European, 1 Americas) reported side-effects to include amnesia, memory loss, anxiety, agitation, decreased consciousness, chest pain, respiratory insufficiency or psychosis. One Western Pacific country mentioned that zopiclone had been used in self-harm or suicide attempts. One Western Pacific country reported 12 cases of drug dependence and two overdoses.

Deaths

Four countries (1 European, 1 Western Pacific, 1 Americas) reported a total of 155 zopiclone-related deaths between 2020 and 2022. One European country reported one hundred and fifteen deaths in 2020.

Drug dependence

Seven countries (3 Western Pacific, 2 European region, 1 Americas, 1 Eastern Mediterranean) reported that people presented for treatment of drug dependence in their country due to use of zopiclone.

Current national controls

Thirty-two countries (15 European, 7 Western Pacific, 5 Americas, 3 Eastern Mediterranean, 2 African) responded that the availability of zopiclone was currently regulated under national legislation. Table A40 shows the main reported control activities for zopiclone.

Illicit manufacture and trafficking-related information

Table A40. shows the main reported activities involving zopiclone.

Activity	No. of countries
Trafficking	6
Smuggling (from other countries)	3
Diversion	3
Direct sales	3
Internet sales (from abroad to buyers in respondent's country)	2
Internet sales (other or location of sellers and website unknown)	2
Internet sales (seller or website located in respondent's country)	1
Manufacture of the substance by chemical synthesis	0
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Do not know	21
Other	0

Seizures

Six countries (4 European, 1 Western Pacific, 1 Americas) reported zopiclone seizures in 2022. The number of seizures per country ranged from 1 to 71 and the amounts seized ranged from 9 tablets to 1426 tablets (Table A4). In addition, two countries (1 European, 1 Americas) reported 28.06 g and 20 g of powder seized. Eleven countries (6 European, 3 Western Pacific, 1 Eastern Mediterranean, 1 Americas) reported zopiclone seizures in 2021. The number of seizures per country ranged from 1 to 191 and the amounts seized from 13 tablets to 25,390 tablets. In addition, four countries (2 European, 1 Western Pacific, 1 Americas) reported amounts seized from 0.67 g to 817.6 g. Six countries (4 European, 2 Western Pacific) reported zopiclone seizures in 2020. The number of seizures per country ranged from 1 to 129 and the amounts seized ranged from 14 tablets to 9026 tablets. In addition, one country (European) reported 125.21 g of powder seized.

Table A4. Reported seizures of zopiclone

Year	No. of countries that reported seizures	No. of seizures
2022	6	110
2021	11	336
2020	6	258

Thirty-eight countries (20 European, 7 Western Pacific, 6 Americas, 2 Eastern Mediterranean, 2 African, 1 South-East Asia) reported that they had the laboratory capacity to analyse zopiclone.