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Implementation of the international drug control treaties: changes in the scope of control of substances

Changes in the scope of control of substances

Note by the Secretariat**

Summary

The present document contains recommendations for action by the Commission on Narcotic Drugs pursuant to the international drug control treaties.

In accordance with article 2 of the Convention on Psychotropic Substances of 1971, the Commission will have before it for consideration a proposal from the World Health Organization concerning recommendations to place amineptine in Schedule II of that Convention.

Pursuant to the relevant provisions of the 1971 Convention, the Commission may decide on the proposal by the World Health Organization. Any decision must be taken by a two-thirds majority of the members of the Commission.

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* E/CN.7/2003/1.

** The present document includes all replies from Governments received by the Secretariat up to 3 March 2003.

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I. Consideration of a notification from the World Health Organization concerning scheduling under the Convention on Psychotropic Substances of 1971

1. Pursuant to article 2, paragraphs 1 and 4, of the Convention on Psychotropic Substances of 1971,[1] the World Health Organization (WHO) notified the United Nations on 2 October 2002 that it was of the opinion that amineptine should be placed in Schedule II of the 1971 Convention (see annex).

2. In accordance with the provisions of article 2, paragraph 2, of the 1971 Convention, the Secretary-General transmitted by a note dated 20 December 2002 to all Governments the text of the notification, together with all the information submitted by WHO in support of that notification. In response to that note, the following 17 States had provided, as of 3 March 2003, economic, social, legal, administrative or other factors relevant to the possible scheduling of amineptine: Austria, Belgium, Colombia, Croatia, Germany, Greece, Hungary, Ireland, Lithuania, Malta, Mauritius, Panama, Peru, Qatar, Republic of Korea, Spain and Turkey.

3. The Government of Austria reported that amineptine had not yet become a concern to the competent authorities in that country. No data on seizures or illicit manufacture of amineptine was available and no pharmaceutical product containing the substance was registered in Austria.

4. The Government of Belgium reported that no products containing amineptine were registered for the market in that country and that the competent authorities had not been advised that the substance had been subject to abuse.

5. The Government of Colombia reported that it had prohibited the use of amineptine because of its associated risks of dependence and abuse, especially in patients with a history of addiction to alcohol, psychoactive pharmaceutical preparations or drugs of abuse. For the above-mentioned reasons, amineptine was not available in Colombia. The Government of Colombia considered it advisable to include amineptine in Schedule II of the 1971 Convention.

6. The Government of Croatia reported that amineptine was not registered in that country. Since amineptine was not on the list of controlled substances, there were no cases involving its seizure and there was not any information available on the existence of clandestine laboratories manufacturing amineptine in Croatia. Since amineptine was not in use in Croatia, the Government would have no difficulty in placing the substance on the list of controlled psychotropic substances.

7. The Government of Germany reported that amineptine was placed on the reference list of illicit pharmaceutical doping substances and doping methods pursuant to the Anti-Doping Convention.[2] It used to be listed as an illicit class A stimulant but had been taken off the list on 1 January 2003. The federal police authority had no data on laboratories manufacturing amineptine or on possible seizures of the substance. Furthermore, no application for approval for a pharmaceutical product containing amineptine had been filed in Germany. However, the Federal Institute for Drugs and Medical Devices had found a number of medical articles on the potential of amineptine to create dependency and an overview on therapy for dysthymia in which amineptine was mentioned.

8. The Government of Greece indicated that no seizures of amineptine had been reported by the competent national authorities.

9. The Government of Hungary reported that there had been no seizures of amineptine in that country and that no clandestine laboratories manufacturing the substance had been discovered. Furthermore, there were no pharmaceutical preparations licensed to be placed on the Hungarian market. The Government noted that, despite its withdrawal from the market in several countries, amineptine continued to be available in a number of countries and that the WHO assessment and other research had indicated that the substance might be considered to be a drug of abuse and potentially addictive. Due to the likelihood of its abuse, the Government of Hungary recommended that amineptine be listed in Schedule II of the 1971 Convention. The Government also reported that new legislation in Hungary might include controls for the substance even before it was listed in Schedule II of the 1971 Convention.

10. The Government of Ireland reported that there had been no seizures of amineptine in that country.

11. The Government of Lithuania reported that amineptine was not registered for legitimate use. Furthermore, no cases of the illicit manufacture of or trafficking in amineptine or any other illicit activities involving that substance had been reported. The Government had no objection to adding amineptine to Schedule II of the 1971 Convention.

12. The Government of Malta reported that amineptine was currently not a registered medical product because it had been withdrawn from the local market in June 1999. Before June 1999 amineptine had been available as a preparation called Survector. There had not been any seizures of amineptine reported, and there had not been any reports of its abuse.

13. The Government of Mauritius reported that amineptine preparations were not marketed in Mauritius and that there had been no evidence of clandestine laboratories manufacturing the substance in that country. However, law enforcement bodies were aware of the risks of amineptine abuse.

14. The Government of Panama reported that no pharmaceutical preparations containing amineptine as the active principle were registered with the competent authorities in Panama. The Laboratory “Servier de Francia” had stopped marketing Survector tablets in Panama some years ago.

15. The Government of Peru reported that the active principle of the substance, amineptine hydrochloride, had been registered until 21 December 2000 under the name Survector. Currently, however, there were no licensed medicinal products containing the substance in Peru and amineptine was not included in any list of controlled substances. Although the substance was not commercially available in the country, the Government of Peru considered that placing it under international control would contribute to its safe use, in view of its documented risks of dependency and abuse.

16. The Government of Qatar reported that its competent authorities had indicated that amineptine was not registered in the country and had not been imported or used before.

17. The Government of the Republic of Korea reported that two companies had manufactured amineptine in that country from 28 December 1987 to 16 November 2000. There had been no seizures of amineptine and at present there were no facilities for the manufacture of that substance in the country.

18. The Government of Spain reported that its law enforcement and drug control authorities had reported no cases involving amineptine. The Government also reported that amineptine, marketed in Spain as a pharmaceutical preparation called Survector, had been withdrawn from sale in pharmacies on 1 September 1999, owing to a number of its side effects.

19. The Government of Turkey reported that a preparation called Survector containing amineptine had been licensed and marketed in Turkey. No other preparation containing amineptine was used for therapeutic purposes. It also reported that no seizures of amineptine had been made, nor had any cases of illicit trafficking in the substance been reported. Furthermore, no clandestine laboratory manufacturing amineptine had been identified. The Government of Turkey agreed with the proposal to put amineptine under international control.

20. The Government of Ukraine reported that, taking into consideration the addictive character of amineptine and also its use for non-medical purposes in certain States, Ukraine supported the proposal of WHO to include amineptine in Schedule II of the 1971 Convention. It also reported that the substance was not a registered pharmaceutical preparation in Ukraine. Law enforcement agencies in that country had not detected any illicit manufacture or abuse of amineptine.

II. Action by the Commission on Narcotic Drugs

21. The notification from WHO is before the Commission for consideration in accordance with the provisions of article 2, paragraph 5, of the 1971 Convention, which reads as follows:[1]

> "5. The Commission, taking into account the communication from the World Health Organization, whose assessments shall be determinative as to medical and scientific matters, and bearing in mind the economic, social, legal, administrative and other factors it may consider relevant, may add the substance to Schedule I, II, III or IV. The Commission may seek further information from the World Health Organization or from other appropriate sources."

22. With regard to the decision-making process, the attention of the Commission is drawn to article 17, paragraph 2, of the 1971 Convention, which stipulates that the "decisions of the Commission provided for in articles 2 and 3 shall be taken by a two-thirds majority of the members of the Commission".[1] From a practical point of view, that means that, for a decision to be adopted, an affirmative vote of at least 35 members of the Commission is required.

23. The Commission should therefore decide whether it wishes to add amineptine to Schedule II of the 1971 Convention or, if not, what other action, if any, is required.

Notes

[1] United Nations, *Treaty Series*, vol. 1019, No. 14956.

[2] Council of Europe, *European Treaty Series*, No. 135.

Annex

Notification dated 2 October 2002 from the World Health Organization to the United Nations concerning a proposal for international control in respect of amineptine

The World Health Organization presents its compliments to the United Nations and has the honour to submit, in accordance with article 2, paragraphs 1 and 4, of the Convention on Psychotropic Substances of 1971, assessments and recommendations of the World Health Organization, as set forth in the appendix hereto, concerning the proposed placement of amineptine in Schedule II of the 1971 Convention.

Appendix

Assessment and recommendations

Amineptine (INN)

Substance identification

Amineptine (7-[(10,11-dihydro-5*H*-dibenzo[*a,d*]cyclohepten-5-yl)amino]heptanoic acid) is available as either the free base (CAS 57574-09-1) or as the hydrochloride salt (CAS 30272-08-3). There are no chiral carbon atoms; therefore, no stereoisomers or racemates are possible.

Similarity to known substances and effects on the central nervous system

Amineptine is a synthetic, atypical tricyclic antidepressant with central nervous system stimulating effects. It is an indirect dopamine agonist, selectively inhibiting dopamine uptake and inducing dopamine release, with additional stimulation of the adrenergic system. Its antidepressant effects are similar to other tricyclic antidepressant drugs but it has a more rapid action, is better tolerated and has little cardiovascular, analgesic or anorectic effects. It produces a similar spectrum of pharmacological effects to psychomotor stimulants in Schedule II of the Convention on Psychotropic Substances of 1971.

Dependence potential

There have been few animal studies regarding the dependence or abuse potential of amineptine. However, some clinical studies indicated that amineptine has both dependence and abuse potential, particularly in patients with a previous history of substance abuse. Clinical observations of significant abuse and dependence are reported in patients treated with amineptine in France. Its dependence potential appeared to be associated with its psychomotor stimulant effect. Withdrawal has been clinically manifested by anxiety, insomnia, psychomotor agitation or bulimia. Instances of dependence have been reported in Europe and Asia.

Actual abuse and/or evidence of likelihood of abuse

Amineptine abuse has mainly been reported in Europe and Asia. It has been withdrawn from the market in France, where the drug was developed a few decades ago, for reasons of considerable hepatotoxicity and abuse. Despite this measure, medical use in developing countries, as well as abuse, still continues. The abuse-related adverse drug reaction reports for amineptine collected by the international drug monitoring programme indicate a larger number of case reports of abuse and dependence than anorectic stimulants currently placed in Schedule IV of the Convention on Psychotropic Substances of 1971, such as amfepramone. Response of Governments to the World Health Organization (WHO) questionnaire also indicated limited diversion and abuse of the drug. Some reported hospital admissions due to adverse consequences of amineptine abuse.

Therapeutic usefulness

The therapeutic usefulness of amineptine is low because of hepatotoxicity, secondary features such as acne eruption and anxiety and the availability of safer antidepressants. Of the 103 countries that responded to the WHO questionnaire, only 17 indicated amineptine use.