



**THE EXPERT ADVISORY COMMITTEE ON DRUGS (EACD)  
ADVICE TO THE MINISTER ON:**

**AMINOREX**

**Released October 2002**

## Contents

<b>Executive Summary</b>	<b>3</b>
<b>Recommendations</b>	<b>3</b>
<b>Substances identification</b>	<b>3</b>
Similarity to known substances	4
<b>Current and proposed legal classification</b>	<b>4</b>
<b>Rationale for proposed classification</b>	<b>4</b>
The Misuse of Drugs Amendment Act 2000	4
Specific effects of the drug	5
Likelihood or evidence of abuse	6
Ability to create physical or psychological dependence	7
Potential to cause death	7
Risks to public health	7
Therapeutic value	7
International classification and experience	8
<b>Recommended presumption for supply</b>	<b>8</b>
Implications for harm minimisation principles	8
Other information	8
<b>References</b>	<b>9</b>

## **Executive Summary**

This paper considers the central nervous system stimulant aminorex - a drug that was used in the past as an appetite suppressant and has amphetamine-like effects.

Aminorex is not controlled under the Misuse of Drugs Act 1975 (the Act). The Expert Advisory Committee on Drugs (EACD) recommends to the Minister of Health that aminorex be classified as a Third schedule Part 5 controlled drug (Class C5). Rationale for this view is provided in this paper.

Although the EACD is not aware of aminorex being abused in New Zealand, the proposed classification for aminorex (ie. C5) would fulfil New Zealand's international obligations under the United Nations drug classification framework. Additionally, if aminorex becomes available in New Zealand in the future, appropriate domestic control will be in place.

## **Recommendations**

**After considering all of the information put to the Committee and the classification criteria in the Misuse of Drugs Act 1975, the EACD makes the following recommendations to the Associate Minister of Health:**

- (a) Aminorex should be classified in Part 5 of the Third Schedule of the Misuse of Drugs Act 1975 (ie, C5).**
- (b) This paper should be made publicly available (eg, posted on the National Drug Policy website [www.ndp.govt.nz](http://www.ndp.govt.nz)) as soon as practicable.**

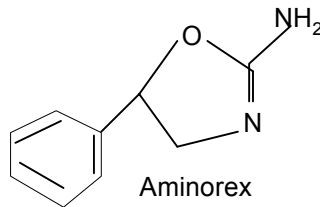
## **Substances Identification**

Aminorex is a central nervous system stimulant. The name 'aminorex' is an International Non-proprietary Name (INN) - a form of international identification. Its chemical abstracts registry service (CAS) number is CAS 2207-50-3.

Chemically, aminorex is called 2-amino-5-phenyl-2-oxazoline, 4,5-dihydro-5-phenyl-2-oxazolamine, aminoxaphen, aminozafen, and aminorex fumarate. Aminorex has an asymmetric carbon atom, so two stereoisomeric forms and one racemate are possible (WHO 1993, WHO 1995).

The Ministry of Health's Medsafe Unit advise that they have not received any application for consent to market the drug as a prescription medicine. However, it was formally marketed as Apiquel, or Monocil overseas (WHO 1995),

Aminorex's chemical structure is represented in the following figure:



### ***Similarity to Known Substances***

Aminorex is chemically and pharmacologically similar to 4-methylaminorex (WHO 1993), which has been classified in Schedule 1 of the United Nations Convention on Psychotropic Substances 1971, (“the 1971 Convention”) and in the Second Schedule (Class B), Part 2 of the Misuse of Drugs Act 1975. It also produces similar effects to amphetamine.

### **Current Classification**

Aminorex is not classified under the Act. However, it is classified as a prescription medicine in the First Schedule to the Medicines Regulations 1984.

### **Rationale for the Proposed Classification**

The following headings relate to the criteria that the EACD must use to assess the appropriateness of a classification for a drug.

#### ***Specific effects of the drug***

Aminorex produces the characteristic effects of central nervous system stimulants like amphetamine (WHO 1995). In general, amphetamine-type substances can relieve fatigue, reduce the need for sleep, increase energy and confidence levels, and bring about a psychological and physical exhilaration (Marnell 1999).

Chronic abusers of amphetamine may experience a psychosis, which may involve delusions or visual or auditory hallucinations. Marnell (1999) lists other common conditions including:

- Increased respiration and body temperature
- Increased blood pressure and heartbeat
- Weight loss
- Anxiety and tension
- Depression
- Irritability
- Mental confusion
- Aggressiveness
- Mood swings.

Aminorex is considered to increase norephedrine levels in the central nervous system and was used in Europe in the late 1960s and early 1970s as an anorectic (eg, appetite suppressant/weight reduction aid). However, it was withdrawn from use because it was considered to have caused a significant

incidence of pulmonary hypertension<sup>1</sup> (Michelakis and Weir 2001, WHO 1995). Aminorex was found on the property of three people from the same family with diagnoses of pulmonary hypertension who were subsequently discovered to have been involved in the manufacture of the designer drug 4-methyl-aminorex (Gaine et al 2000).

### ***Likelihood or evidence of drug abuse***

The Ministry of Health has never received an application to market aminorex as a prescription medicine in New Zealand. Further, the EACD is not aware of it being a drug of abuse in New Zealand. The New Zealand Customs Service also advised that they have no records of aminorex interceptions.

The World Health Organization's ("WHO") Expert Committee on Drug Dependence published its review of aminorex in 1995. The WHO noted that police and forensic reports indicated that aminorex was illicitly distributed in the United States, as well as Germany to a limited degree (WHO 1995). Such reports document its distribution as amphetamine or methamphetamine, suggesting that the population using aminorex is primarily composed of stimulant abusers.

In 1995, the United States Drug Enforcement Administration ("DEA") uncovered three illicit aminorex laboratories (Marnell 1999). However, the significance of this fact should be put in context with the 327 methamphetamine laboratories uncovered in the same year. Between 1991 and 1998, no other DEA uncovered aminorex laboratories are recorded. Methamphetamine laboratories have been far and above the most commonly uncovered clandestine laboratories in the United States. Of the 1621 clandestine laboratories uncovered by the DEA in 1998, 1596 (or 98.6%) were methamphetamine, whereas there were no DEA uncovered aminorex laboratories (Marnell 1999). This would tend to suggest that illicit manufacturers of amphetamine-type drugs are significantly less likely to manufacture aminorex, than they would be to produce methamphetamine.

Interestingly, Gaine et al (2000) recently noted that DEA officials had confirmed that the aminorex derivative 4-methyl-aminorex had appeared on the United States illicit drug market as a designer drug alternative to methamphetamine. The authors report that one of the street names for 4-methylaminorex in the United States is 'U-4-E-uh' (pronounced euphoria). This may be a signal of a potential widening of the drugs produced in clandestine laboratories, in the United States to include aminorex-related compounds. However, there is little information available in this regard, especially in New Zealand.

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<sup>1</sup> Primary pulmonary hypertension refers to raised pulmonary arterial pressure. Symptoms include breathlessness on exertion, fatigue, and chest discomfort or pain. In advanced disease right ventricle hypertrophy (the ventricle becomes enlarged in a response to "cope") may progress to right sided heart failure. Primary pulmonary hypertension is a progressive and incurable disease and patients appear to be prone to sudden death. Secondary pulmonary hypertension is more prevalent, i.e. the pulmonary hypertension occurs as a consequence of conditions such as:

- Left ventricular failure (common after myocardial infarction (heart attacks)) which leads to pulmonary hypertension by increasing pulmonary venous pressure, which in turn increases pulmonary arterial pressure.
- Diseases affecting the pulmonary vessels e.g. thrombo-embolic disease (blockages in vessels due to clots).
- Chronic obstructive pulmonary disease.

Despite the limited level of abuse, the WHO assessed aminorex as having a moderate abuse liability, particularly in view of the simplicity of its manufacture in clandestine laboratories (WHO 1995).

### ***Ability to create physical or psychological dependence***

The WHO has reported that in drug discrimination studies, aminorex generalises to amphetamine and cocaine. Animal self-administration studies indicate that the drug has some reinforcing effects and suggest that it has moderate dependence potential (WHO 1995).

### ***Potential to cause death***

The WHO report did not discuss any deaths attributable to aminorex abuse. However, aminorex use has been attributed to a significance of pulmonary hypertension - a potentially fatal condition (Michelakis and Weir 2001).

### ***Therapeutic value***

The WHO concluded that because of its serious adverse effects aminorex is assessed to have, on balance, very little therapeutic usefulness (WHO 1995). In the past, aminorex was used clinically for its anorectic effects. However, due to a potential to cause pulmonary hypertension that was noted in Austria, Switzerland, and Germany in the late 1960s to early 1970s when used as a weight-reduction drug, it was withdrawn from the market (Michelakis and Weir 2001).

### ***Risks to public health***

The 1995 World Health Organisation review concluded that on the basis of the available data concerning its pharmacological and toxicological profile, dependence potential and the likelihood of abuse, the public health and social problems associated with the abuse of aminorex are 'significant'.

Although Aminorex does not appear to be a drug of abuse in New Zealand, it is not unreasonable to assume that if the drug became available its abuse potential could be similar to prescription amphetamines, which are abused for their euphoric effects.

### ***International classification and experience***

#### ***New Zealand's international obligations under the United Nations Conventions***

In 1995, the WHO Expert Committee on Drug Dependence submitted an assessment of aminorex to the United Nations, along with a recommendation that the drug be classified under Schedule 4 of the 1971 Convention (WHO 1995). This followed a pre-review by the WHO in 1993 (WHO 1993).

In May 1995, the United Nations Commission on Narcotic Drugs voted to include aminorex in Schedule 4 of the 1971 Convention. New Zealand has ratified the 1971 Convention and is thus obligated to include aminorex within its domestic drug control regime. However, New Zealand has discretion as to how it classifies substances under its national legislation.

In 2000, the International Narcotic Control Board wrote to the Ministry of Health requesting that aminorex be classified under adequate domestic control (INCB 2000). The proposed classification for aminorex (ie. C5) will fulfil New Zealand's international obligations under the United Nations drug classification framework.

*Other countries' classification of Aminorex*

In the United Kingdom aminorex is classified as a Class C controlled drug under the Misuse of Drugs Act 1971.

In the United States, it is classified in Schedule 1 of the Federal Controlled Substances Act 1970.

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