

**ADVICE TO  
THE EXPERT ADVISORY COMMITTEE ON DRUGS**

**Norephedrine**

**May 2009**

**Prepared by the Ministry of Health**

## **Purpose**

At the meeting of 13 November 2008, the EACD recommended that norephedrine be scheduled as a Class B2 controlled drug under the Misuse of Drugs Act 1975 (MoDA). The EACD requested that the Secretariat provide information to enable it to reach a decision on the presumption for supply. This paper provides that information where it is available. It also summarises up-to-date information under the matters on which the EACD must advise the Minister of Health.

## **Background**

### ***28 June 2007***

In 2007 the Secretariat provided the EACD with a formal assessment of norephedrine. The EACD discussed the available evidence in accordance with the criteria under Section 4B(2) of the MoDA; the matters not considered were the potential for norephedrine to cause death and its ability to cause physical or psychological dependence. The Committee considered the following options:

**Option 1:** to recommend the classification of norephedrine as a precursor substance, or

**Option 2:** to maintain the status quo and the current controls under the Medicines Act.

The Committee agreed to stay with current legislative controls and requested Police to monitor seizures over a 12 month period to determine whether there was any evidence of norephedrine being used as a precursor substance in the manufacture of amphetamine.

### ***13 November 2008***

In 2008 the Committee considered an update by the Secretariat that there has been no new evidence of norephedrine being used in New Zealand as a precursor substance in the manufacture of amphetamine.

The Committee also considered a letter from the National Drug Intelligence Bureau (NDIB) reminding the EACD of the United Nations Commission on Narcotic Drugs (UNCND) decision on norephedrine and also suggesting that New Zealand is currently in breach of its obligations under international law. NDIB requested that the Committee consider recommending norephedrine be included in Schedule 4 of the MoDA. (Schedule 4 contains a number of "precursor substances", including ephedrine and pseudoephedrine).

The EACD considered the following options:

**Option 1:** to await the information requested of Police in June 2007 in order to determine whether norephedrine is being used as a precursor substance

**Option 2:** to review norephedrine in relation to the matters set out in section 4B (2) and make a recommendation on the appropriate scheduling

**Option 3:** to request the Secretariat seek a legal opinion in regard to NZ's obligations under the 1988 Convention, irrespective of the risk and context.

The Committee agreed to recommend that norephedrine be classified in Part 2 of Schedule 2 (Class B2) and also Schedule 4 (Precursor Substances). The Committee also agreed to investigate a presumption for supply level for norephedrine for its next meeting.

## **Discussion**

### **Classification Process Under the Misuse of Drugs Act 1975**

The Chair has requested a summary of the evidence considered in 2007 with any available updates in accordance with section 4B(2) of the MoDA.

#### The likelihood or evidence of drug abuse

### **Prevalence**

Norephedrine (also known as phenylpropanolamine) is not manufactured in New Zealand and the current regulatory system under the Medicines Act 1981 makes it difficult for the substance to be brought in to New Zealand unless a prescription is written by a New Zealand registered doctor. Currently, there is no commercial or industrial use for norephedrine in New Zealand. Norephedrine is not currently marketed and is not registered as a pharmaceutical preparation (under the Medicines Act 1981). Three products containing norephedrine as an active ingredient have previously been presented to Medsafe. This includes; Nasomixin nasal spray (a prescription medicine) for which production and supply was discontinued and two other norephedrine containing products that were never approved by Medsafe.

There is currently no information with regard to the prevalence of norephedrine or consumption levels in New Zealand. In order to meet the demands for amphetamine type substances, including methamphetamine, there appears to have been an increase in the illegal importation of precursor substances rather than sourcing these domestically from commercially available pharmaceutical preparations.

### **Seizures**

There is no available evidence on current drug seizure trends and the New Zealand Customs Service informed the Ministry of Health that it does not collect formal seizure data on norephedrine. Customs considered that norephedrine appears to rarely be imported into New Zealand and is usually found as an ingredient in diet pills included in products such as: 'ThinZ',

'Eatless', 'Quickslim' and 'Realism'. All of the quantities seized would suggest that any imports are for personal use. The numbers of tablets seized have ranged from 16 to 1152, with most seizures consisting of 100 – 200 pills. In most cases the person importing the substance has not realised that the pills contain a prescription drug. No ESR testing has been completed on the diet pills as they usually have a list of ingredients on the packaging and the list of ingredients is taken as being correct. Customs has been accepting this explanation and issuing the importer with a warning. Customs reports that it has not seized any quantities of norephedrine that would suggest that people are importing it to make amphetamine.

It should be noted that clandestine laboratory seizures have not discovered norephedrine, as a potential precursor substance, at these illegal manufacturing sites.

There is no evidence of the potential for norephedrine itself to appeal to vulnerable populations.

#### Specific effects of the drug

Norephedrine acts directly on the alpha and, to a lesser degree, beta-adrenergic receptors in the mucosa of the respiratory tract. Norephedrine functions as a vasoconstrictor via innervation of the vascular smooth muscle. Stimulation of alpha-adrenergic receptors produces vasoconstriction, reduces tissue hyperemia, oedema, and nasal congestions, and increases nasal airway patency. Norephedrine indirectly stimulates beta-receptors, producing tachycardia and a positive inotropic effect. Norephedrine may result in reduced bioavailability (about 38%) from gastrointestinal tract because of first pass metabolism by monoamine oxidase in the stomach and liver. Norephedrine may induce premature ventricular contraction (extrasystoles) and short paroxysms (spasm) of ventricular tachycardia, and/or sensation of fullness in the head and tingling of the extremities.

#### Risks to public health

In 2000, the United States Food and Drug Administration (FDA) requested that all drug companies discontinue marketing products containing phenylpropanolamine (norephedrine), due to an increased risk of hemorrhagic strokes in women. The British National Formulary (BNF) reports that UK studies on the effects of phenylpropanolamine do not substantiate the claim by the FDA, but the BNF recognises the associated risk with large doses.

#### Therapeutic value of the drug

Norephedrine has previously been used in the treatment of nasal congestion; and was included in several over the counter decongestants and prescription medicines. Norephedrine may also be found in appetite suppressant formulations as a treatment for obesity and with guaifenesin in cough-cold formulations. It also has been used for the treatment and control of urinary incontinence and priapism (prolonged and painful erection).

### Potential for use of the drug to cause death

Norephedrine does not lead to psychosis or death.

### Ability of the drug to create physical or psychological dependence

It is not dangerous in itself, nor is it addictive.

### International classification and experience of the drug in other jurisdictions

The International Narcotic Control Board produced the report entitled 'Implementation of the international drug control treaties: changes in the scope of control of substances' (Vienna, 2000). Recommendations made in this report by the Board were as follows:

*The Board is of the opinion that the international control of norephedrine is required to limit its availability to traffickers and reduce the quantity of amphetamine manufactured illegally. Furthermore, those controls would have no adverse effect on the legitimate trade in that substance or on its availability for legal medical requirements. In view of the above, the Board recommends that norephedrine be placed under the control of the 1988 Convention.*

At its 1184<sup>th</sup> meeting on 7 March 2000 the Commission on Narcotic Drugs, on the recommendation of the INCB, decided to include norephedrine in Table I of the UN Convention against Illicit Drug Traffic in Narcotic Drugs & Psychotropic Substances of 1988. The purpose of this Convention is to promote co-operation among the parties to address illicit traffic in narcotic drugs and psychotropic substances. In carrying out their obligations under the Convention, the parties are to take necessary measures, including legislative and administrative measures, in conformity with the fundamental provisions of their respective domestic legislative systems.

In the UK, the BNF classifies phenylpropanolamine (norephedrine) as a discontinued drug substance. In the USA, the FDA does not list this drug substance as a pharmaceutical in the 'orange book' – approved drug products.

### **Presumption for Supply under the Misuse of Drugs Act 1975**

Section 4B (4) outlines the matters which the EACD must give advice with regard to presumption for supply. The Secretariat has assessed the drug against the criteria for presumption for supply.

### Amount of the drug that could reasonably be possessed for personal use, including levels of consumption

There is currently no firm data on this and levels of use in New Zealand are not known.

The ability of the drug to create physical or psychological dependence and specific effects of the drug

The EACD has noted that norephedrine is neither addictive nor dangerous in itself.

Presumption for supply in other jurisdictions

It has not been possible to obtain information on other jurisdictions' presumption for supply levels.

The Secretariat has examined similar substances such as norpseudoephedrine for a comparison. The classification of Norpseudoephedrine was considered by the EACD when recommending a B2 classification. Norpseudoephedrine does not have a specific presumption for supply (Schedule 5) and therefore the recommended presumption for supply would be the 'default' option of 56 grams.

**Recommended Presumption for Supply**

It is recommended that the presumption for supply be set at the default 56 grams.