

4 April 2008

Hon Jim Anderton  
Associate Minister of Health  
Parliament Buildings  
Wellington

Dear Minister

### **Advice of the Expert Advisory Committee on Drugs regarding Tramadol and Thalidomide**

The Expert Advisory Committee on Drugs (the Committee) considered thalidomide at its meeting on 29 November 2007. At its meeting of 19 February 2008, the Committee discussed the medicine tramadol. The minutes from these meetings are attached, in addition to a strategic assessment of tramadol.

#### **Tramadol**

##### **Background**

Tramadol is a synthetic opioid analogue of codeine. It has been available in New Zealand since 1997 as a prescription-only medicine for the relief of moderate to severe pain. Tramadol products available in New Zealand include: Tramadol®, Tramal®, and Zytram®. Whilst it is an opioid-type analgesic, tramadol is not currently classified as a controlled drug.

Tramadol is not subsidised through PHARMAC in the primary care setting, although it is scheduled for hospital use, where it is widely used. The Committee noted that tramadol is also prescribed as a substitute for morphine both by general practitioners and increasingly in emergency departments. It is used to treat postoperative, dental, cancer and acute musculoskeletal pain and as an adjuvant to non-steroidal anti-inflammatory drug (NSAID) therapy in patients with osteoarthritis. The Committee noted that it is likely that tramadol will be subsidised by PHARMAC in the future, increasing its availability.

##### **Illicit use of Tramadol**

Unlike other opioid-type analgesics, tramadol acts through several different mechanisms (including the  $\mu$ -opioid receptor, serotonin and noradrenaline uptake mechanisms) and does not produce the same euphoric effects as heroin, morphine or oxycodone. Whilst anecdotal evidence suggests that tramadol creates a sense of euphoric release, it is likely that more potent opioids would be drugs of choice over tramadol.

##### **Harm Potential**

International experience would suggest that, compared with other opioids such as morphine, tramadol is relatively safe and is not as highly addictive. However, long-

term use can result in tolerance particularly for those with a history of opioid dependence. As with other opioids, withdrawal effects can include a degree of craving.

Adverse outcomes are in line with other opioids and include the risk of cardiovascular collapse, coma and respiratory arrest. The risk of harm is increased in the case of poly-drug use or when used intravenously. The Committee also discussed the potential for harm given the slow release pharmacokinetics of tramadol and the risk that some patients could overdose by taking more tablets when the onset of effect is delayed.

There are no hospital admission data available in New Zealand citing tramadol overdose. International evidence reports low numbers of people experiencing adverse effects and no deaths from tramadol use/misuse. Pre-clinical data indicate that central nervous manifestations only occur after taking doses considerably above the therapeutic range or large intravenous doses.

### **The Committee's Advice regarding Tramadol**

The Committee considered two options for addressing the potential misuse of tramadol. These were that:

- tramadol remains a prescription-only drug but prescribers are made more aware of the misuse potential of the drug;
- tramadol is classified in Schedule 3 of the Misuse of Drugs Act (1975) as a Class C(2) controlled drug, in line with codeine.

After consideration of the options, the Committee agreed that the level of risk posed by tramadol is similar to that of codeine. The Committee considered that classifying tramadol would provide greater safeguards over supply, would alert prescribers to the potential risks, and prohibit prescribing to drug-dependent persons. Whilst codeine is available in over-the-counter preparations, the Committee agreed that tramadol should not be available in low-dose preparations to be sold over the counter.

Therefore the Committee's advice to you is:

- **That tramadol be classified as a Class C(2) controlled drug (without any exemption for preparations containing amounts below a certain level).**
- **That the "default" presumption for supply of 56 grams (the equivalent of a three month prescription) is appropriate, as currently provided for in Schedule 5(2) of the Misuse of Drugs Act.**

In line with other Class C(2) drugs, the penalty for possession and supply would be three months imprisonment, a \$500 fine or both.

The Committee also noted that PHARMAC and Medsafe should be advised of the potential for diversion and misuse of tramadol and I will write to these organisations on this matter.

## **Thalidomide**

### **Background**

Thalidomide was prescribed during the 1950s and 1960s as an anti-emetic/anti-nausea agent for the treatment of morning sickness in pregnant women. It has also been used as a sedative. In response to the effects on the foetus noted during the 1960s, thalidomide was classified in Schedule 1 (Class A) of the Misuse of Drugs Act.

Thalidomide has since been approved as a prescription medicine for the treatment of cancer and leprosy. Thalidomide is currently used for the treatment of multiple myeloma both in the hospital and community setting.

Robust and strict guidelines for the prescription and dispensing of thalidomide have been established in New Zealand. The guidelines place strict controls on the appropriate use of concurrent contraception and pregnancy testing, registration of prescribing physicians and registered hospital pharmacy dispensing.

### **Illicit use of Thalidomide**

Thalidomide has no reported addictive potential nor does it have the potential to be an illicit drug of abuse or be diverted for illicit purposes.

### **The Committee's Advice regarding Thalidomide**

The Committee discussed the historical circumstances surrounding the placement of thalidomide into the Misuse of Drugs Act. All members agreed that it is an anomaly and that, in retrospect, it should not have been scheduled in the Act.

The Committee agreed that thalidomide should be removed from the Misuse of Drugs Act in due course and controlled solely under the Medicines Act (1981). The availability, distribution and use of thalidomide continue to require stringent monitoring, which the current arrangements provide for.

The Committee recommends:

- **That the removal of thalidomide from Schedule 1 of the Misuse of Drugs Act should be considered during the forthcoming review of the Misuse of Drugs Act.**

Yours sincerely,

Ashley Bloomfield (Dr)  
**Chair**  
**Expert Advisory Committee on Drugs**

- enc: 1. Minutes of the Expert Advisory Committee on Drugs meeting of 29 November 2007 and 19 February 2008 (draft)  
2. Assessment of tramadol.