

# Australia reschedules naloxone for opioid overdose

The Therapeutic Goods Administration has changed naloxone scheduling to make it available over the counter

On 24 November 2015, the Therapeutic Goods Administration (TGA) announced its final decision to place “naloxone when used for the treatment of opioid overdose” on Schedule 3, thereby allowing over-the-counter (OTC) purchase.<sup>1</sup> This measure came into effect on 1 February 2016, making Australia the second country, after Italy (in 1995), to have naloxone formally available OTC.

## Background

With much recent media focus on problems due to crystalline methamphetamine use in Australia, few may be aware that deaths from opioid overdose have been increasing over recent years.<sup>2</sup> Following the “heroin drought” of late 2000, accidental deaths from heroin and other opioids among Australians aged 15–54 years dropped from 1116 deaths in 1999 (10.19 deaths per 100 000 population) to 386 deaths in 2001 (3.46 deaths per 100 000 population). However, opioid-related deaths have been rising steadily since 2007 — the most recent confirmed data indicate that 617 Australians aged 15–54 years died in 2011 (4.95 deaths per 100 000 population). Estimates for 2012 and 2013 suggest that this trend continues.<sup>2</sup>

Take-home naloxone (THN) programs are designed to help manage opioid overdose events in the pre-hospital setting.<sup>3</sup> These programs involve training potential overdose witnesses (typically opioid users, and their friends and families) in overdose response (including naloxone administration), and then prescribing and distributing naloxone to potential overdose victims for later use in an overdose situation. Training typically includes education on risk factors for opioid overdose, signs of opioid overdose, basic life support and overdose response, including resuscitation techniques, calling for an ambulance, administration of naloxone, and post-naloxone management. Training addresses the possibility of rebound opioid toxicity due to the relatively short half-life of naloxone (mean, 60 min; range, 30–80 min)<sup>4</sup> compared with many opioids and the need to monitor the person and administer another dose of naloxone if required. However, the evidence indicates that rebound toxicity is rare.<sup>5</sup> To date, naloxone kits provided to trainees in Australian THN programs have typically comprised between 2 and 5 minijets of naloxone 400 µg/mL plus intramuscular needles, swabs, gloves and instructional materials.

Reports on THN programs, including successful reversals with few adverse effects, emerged in the late 1990s and

programs have expanded since that time. A survey of programs in the United States in 2010 found that, since 1996, 53 000 kits containing naloxone were distributed through 188 programs across 16 US states, and naloxone was administered in over 10 000 successful overdose reversals.<sup>6</sup> In November 2010, Scotland became the first jurisdiction to implement a national THN program<sup>7</sup>; however, like most current programs, this program involves prescription. Many advocates of THN programs have called for better access to naloxone by making it available OTC.<sup>8</sup> To our knowledge, only Italy and some US states have naloxone available OTC (the US has inconsistent policy across state pharmacy boards, and at least one pharmacy chain in the US recently began offering naloxone OTC),<sup>9</sup> and recent initiatives will further expand OTC naloxone availability in the US.<sup>10</sup> There are no published accounts of the extent and consequences of naloxone use in Italy.

Timely naloxone administration is crucial for preventing morbidity and mortality associated with opioid overdose. Wider access, through making the drug available OTC, is a positive step towards reducing morbidity and mortality.<sup>11</sup>

## The TGA's decision

The TGA's decision creates a new listing for OTC naloxone, under Schedule 3, while keeping the original listing under Schedule 4 (requiring prescription). This dual system means that the drug will be government-subsidised, but only when on prescription. The decision was made in response to a Melbourne community pharmacist's rescheduling application, which resulted in 96 individual submissions to the TGA in the subsequent consultation process. According to the TGA, all submissions supported the proposal to down-schedule naloxone; the main points were that: making it OTC will remove barriers to access; naloxone is safe and has no effect on anyone without opioids in their system; and it has little to no misuse potential. The TGA's reasons for the recommendation included that: naloxone is a well tolerated life-saving medicine with minimal adverse effects, and the benefits outweigh the risks; and overseas experience and the outcomes of a program conducted in the Australian Capital Territory<sup>12</sup> show that easier availability of naloxone will likely decrease the proportion of opioid overdoses that result in fatality. The TGA further suggested that OTC naloxone would need to be supplied with full and clear instructions for use, understandable by lay people (rather than only for trained health care professionals, as is currently the case),

*“We recommend ... regulatory changes that allow current THN programs to dispense naloxone directly to their clients”*

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and emphasised that naloxone does not replace other resuscitation treatments.<sup>1</sup>

### Further considerations

Several matters must be addressed before OTC supply of naloxone is effectively implemented. Currently available products do not include needles for administration (the kits are assembled by individual programs), and product instructions need to be modified for lay people using the minijet to give the intramuscular injection. These issues are typically addressed in THN programs that involve extensive training, but recent research found no significant differences between trained and untrained lay rescuers using naloxone to manage an overdose.<sup>13</sup> As a Schedule 3 medication, the most important requirements for THN are therefore: an easily used product with appropriately designed information materials and needles to administer the drug within the package; pointers to online and other training resources; and brief advice from pharmacy staff.

A major issue regarding OTC availability is the cost to consumers. Naloxone is currently listed (exclusive of dispensing fee) at A\$16.90 per minijet, distributed by UCB Australia. However, under the Pharmaceutical Benefits Scheme, five minijets cost A\$37.70, or A\$6.10 on concession. Although the dual listing means that naloxone will be available at the discounted price on prescription, it is important that the retail price per OTC unit is kept as low as possible as price will be a significant barrier to initial access, and any subsequent replacement of expired naloxone, especially for opioid users who are financially disadvantaged.

Another issue regarding OTC availability is the implications for THN programs, such as those operating in the ACT, New South Wales, Western Australia and Victoria. These programs may be run by specialist drug treatment or other services but often involve community services or groups such as drug user organisations and community health services. These programs have access to particularly marginalised and financially disadvantaged drug users. They currently provide naloxone via prescription, typically engaging a doctor to

attend small-group training sessions. The doctor must then review participants, and both prescribe and dispense the medication. While OTC access removes the need for a doctor's prescription, the requirement for dispensing by a doctor or pharmacist remains. Access to naloxone will be maximised when those providing instructions for use (including, for example, allied health or peer workers) also provide the medication. Thus rescheduling to Schedule 3 does little to simplify dispensing arrangements for current THN programs. We note that in other countries where THN programs operate, health authorities have put in place arrangements such that approved programs which meet defined training and other criteria can dispense naloxone to their participants. We hope that the rescheduling of naloxone to make it available OTC will lead to state and territory health officials exploring ways to similarly allow Australian THN programs to dispense this medication directly and cost-effectively to their clients.

### Implications

The TGA decision sets a new precedent for other countries exploring ways to make naloxone available OTC. We recommend that the rescheduling of naloxone be followed by regulatory changes that allow current THN programs to dispense naloxone directly to their clients for later use in an overdose situation.

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