

## IMPROVING ACCESS TO URINARY TRACT INFECTION TREATMENT: THE RECLASSIFICATION OF TRIMETHOPRIM

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### ABSTRACT

The recent reclassification of trimethoprim in New Zealand (NZ) will allow women with symptoms of a lower urinary tract infection (UTI) more timely access to an effective treatment. This decision contrasts with the withdrawal of similar nitrofurantoin and trimethoprim applications in the United Kingdom (UK) in 2010. Some differences between the proposed UK reclassifications and the NZ reclassification are apparent. The NZ reclassification allows supply only through 'accredited' pharmacists. Additionally, this was a 'third-party' reclassification, driven by a pharmacy retail group rather than a pharmaceutical company sponsor.

Concerns about reclassification of antibacterials include increased usage and the subsequent potential for increased resistance. In the NZ model these risks are managed by mandating training of pharmacists and limitations to the supply.

The trimethoprim reclassification in NZ provides a useful opportunity to research the effects of widening availability on the management of the condition and on resistance rates. Such evidence will help inform the debate elsewhere.

**Key words:** Nonprescription drugs; Reclassification; Pharmacy; Pharmacist; Anti-bacterial agents; Urinary tract infections.

### THE TRIMETHOPRIM RECLASSIFICATION

The recent reclassification of trimethoprim in New Zealand (NZ)<sup>1,2</sup> may revitalise the debate on antibacterial treatment of urinary tract infections (UTIs) in pharmacy. In 2010, Mann considered the withdrawal of nitrofurantoin and trimethoprim applications in the United Kingdom (UK) marked the 'probable end of a 15 year discussion'<sup>3</sup>. However, the reclassification in NZ provides an opportunity to measure effects of a reclassification on overall management and resistance, and a favourable outcome may re-open the debate in the UK.

## THE TRIMETHOPRIM SUPPLY MODEL

The model for trimethoprim supply in NZ differs in some regards from that previously proposed in the UK (Table 1), for example restriction to supply only by trained pharmacists rather than pharmacy-only status. NZ has three non-prescription categories<sup>4</sup>: general sales (sale anywhere); Pharmacy-Only Medicine (available in a pharmacy, and typically consumers can self-select); and Pharmacist-Only Medicine (self-selection is not permitted, a pharmacist consultation is required, and the supply is recorded). While trimethoprim remains a prescription medicine except under certain criteria (Table 1), this is similar to a pharmacist-only medicine, and advertising can occur. Like the reclassification of the emergency contraceptive pill in NZ<sup>5</sup>, non-prescription trimethoprim is available only through pharmacists who have successfully completed specific training<sup>1</sup>. Interest from pharmacists is high, and most community pharmacists are likely to become ‘accredited’ to supply the medicine (at their own or their employer’s expense), as occurred for the emergency contraceptive pill. Thus trimethoprim should be accessible without prescription at all, or nearly all, community pharmacies, reducing barriers to supply of this medicine to affected women who often have considerable discomfort.

The reclassification of trimethoprim continues a recent trend in NZ for third-party reclassifications, being the fourth for Pharmacybrands (a retail pharmacy group), alongside the influenza vaccination (which reclassified at the same MCC meeting)<sup>8</sup>. In NZ, anyone can apply for reclassification providing committee requirements are met, and thus Pharmacybrands, although not a sponsor for trimethoprim, could apply for reclassification. The product sponsor did not need to change packaging, or provide training or materials. Pharmacists’ tools include an algorithm for supply, a one-page checklist, and a consumer information sheet to provide with each trimethoprim supply.

**Table 1: Proposed UK reclassification and actual NZ reclassification of trimethoprim compared**

	UK proposal for reclassification <sup>6</sup>	NZ reclassification <sup>1, 7</sup>
Availability	Pharmacy Medicine for treatment of uncomplicated acute bacterial cystitis in women aged 16-70 years previously diagnosed with this condition by a doctor	Exempt from prescription* when supplied for the treatment of uncomplicated UTI in a woman aged 16-65 years, by a pharmacist who has successfully completed the College of Pharmacists’ training course
Dosage	200mg twice a day for three days†	300mg once daily for three days†
Applicant	Product sponsor	Pharmacybrands Ltd, a retail pharmacy group
Consumer information	Product would be packaged for non-prescription supply, including an approved pack insert	An approved information sheet for non-prescription supply would be provided to the consumer with the medicine
General Practitioner notification	No	Yes, with patient consent

\*Exemption from prescription through the pharmacist was discussed in *SelfCare* 3(5)<sup>8</sup>

†Strength and frequency of dosing is consistent with product licensing for each country

## CONCERNS ABOUT RECLASSIFICATION

Opposition to the reclassification primarily cited potential for increased resistance, misdiagnosis, and fragmented care. However, the Medicines Classification Committee (MCC) concluded that risks could be mitigated through pharmacist training. The MCC considered that most women with UTIs already present to general practitioners, and that '*pharmacist sale of trimethoprim may be more in line with best practice than the prescribing habits of general practitioners*'<sup>2</sup>. Oseltamivir appeared to be responsibly managed by pharmacists post-reclassification in NZ<sup>9,10</sup> and may have given the MCC confidence in pharmacy.

Antibiotics are understandably one of the most contentious of all possible reclassifications. Antibiotics are limited in number, resistance is an important concern, and efforts usually focus on attempting to reduce use rather than making access easier<sup>11</sup>. The proposed reclassifications of trimethoprim and nitrofurantoin in the UK for UTIs generated concern, primarily around potential increase in usage and effects on resistance<sup>11-16</sup>, and one commentary stated that prescribers would '*inevitably*' move to broader-spectrum products should both medicines be reclassified<sup>11</sup>. However, data to inform the debate is lacking.

Some believe wider usage would ensue from reclassification of antibiotics for UTIs<sup>11</sup>, but the UK trimethoprim proposal suggested non-prescription supply would substitute for some prescriptions<sup>6</sup>, as echoed by the NZ MCC<sup>2</sup>. Experience shows that change in antimicrobial use post-reclassification can vary. Chloramphenicol usage in the UK increased by 48%<sup>17</sup>, despite the expectation of simply shifting supply from the doctor to pharmacist<sup>18</sup>. Sales and resistance increased post-reclassification of mupirocin in NZ in the 1990s, causing the reclassification to be reversed<sup>19</sup>. In contrast, most oseltamivir supplies remained GP-prescribed post-reclassification in NZ with modest pharmacist-supplies and no effect on resistance observed in a five year period<sup>10</sup>. Anecdotal pharmacy feedback suggests that OTC azithromycin supplies (for Chlamydia infection) in the UK are low. Usage may vary by indication and quantity, for example, 15g of topical mupirocin provides plenty of excess for (mostly inappropriate) further usage by the whole family for cuts, grazes and minor skin infections that occur frequently. In contrast, a short-course of trimethoprim for a UTI provides little opportunity for use in other household members.

A significant increase in trimethoprim usage post-reclassification requires one or more of three different scenarios to occur. The first of these could arise where UTI symptoms are currently under-treated with some self-resolving. Under this scenario a modest increase may be reasonable given the discomfort this condition can cause, that spontaneous cure is only 28% after a week<sup>20</sup>, and that it can take months for some infections to clear without antibiotics<sup>21</sup>. A second possibility is that usage would increase for conditions misdiagnosed as UTIs – clearly an undesirable outcome. A third scenario that could increase use of trimethoprim, would be significant use of other antibacterials first-line by GPs being replaced by more readily available trimethoprim. Reeves considered that there was no good current evidence on the likely change in use or on the effect any modest increase would have on resistance rates<sup>22</sup>.

## POSSIBLE BENEFITS

Like all countries, NZ is affected by increasing demand for health services alongside limited funding, and solutions include better use of the existing health workforce, and self-care<sup>23</sup>. The reclassification of trimethoprim may help to achieve this, as well as providing timely access to treatment for affected women. Logically, making a three-day course of first-line antibacterials available without prescription for UTIs could potentially improve practice, as considered by the MCC<sup>2</sup> and proposed in the UK<sup>3</sup>. Pontari stated: '*[t]he challenge in treating UTIs is to only treat those who need it, with the correct antibiotic, for as short a time as possible. This benefits the patient and limits the development of bacterial resistance as much as possible.*'<sup>24</sup>. Using more than three days of antibiotics in an uncomplicated UTI increases risk of resistant bacteria in gut flora and adverse effects without increasing the chance of success<sup>25</sup>. Prescribers have contradictory responsibilities in doing the best for the patient and the best for population health, Dryden *et al.* noting '*the latter is not usually considered.*'<sup>11</sup>. These authors may be doing prescribers a disservice, but the conflicting needs of consumers and public health probably causes suboptimal prescribing at times. Thus, a short pharmacist-supplied course of a first-line antibacterial may improve practice. Supply of a limited course minimises opportunity for further use of left-overs, reduces the need for prescribers to provide 'spare' courses to some consumers for self-management of repeat episodes, and might reduce inappropriate use of second-line agents.

## CONCLUSION

Healthcare consumers and the health system may benefit from the reclassification of trimethoprim. Given the potential risk to public health that may accompany the reclassification of antibacterials, reclassifying such medicines requires care. The ability to restrict supply to 'accredited' pharmacists enabled the reclassification in NZ, and may be worth considering elsewhere for some medicines. Research following the trimethoprim switch in NZ, including surveillance of resistance, may provide useful information for other markets considering wider availability of an antibacterial for UTIs.

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