

## Linezolid-induced neuropathy

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TO THE EDITOR: Linezolid is the first of a new class of oxazolidinone antibacterials which was first registered in Australia in September 2001. It represents an important advance in the treatment of infections caused by some enterococci resistant to vancomycin and staphylococci resistant to methicillin.<sup>1</sup> In clinical trials, the most commonly reported drug-related adverse events which led to discontinuation of linezolid therapy were headache, diarrhoea, nausea and vomiting.<sup>2</sup> We describe a patient who developed peripheral and optic neuropathy while being treated with linezolid.

A 76-year-old man was hospitalised in November 2000 for the third revision of a left total hip joint prosthesis. This was complicated by infection with methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from hip joint washout. The organism was sensitive to vancomycin, teicoplanin, rifampicin and fusidic acid, and resistant to ciprofloxacin. Vancomycin therapy was commenced, but had to be replaced by rifampicin and fusidic acid when the patient developed fever (40°C), rigors, rash and eosinophilia. However, the patient developed severe, generalised pruritus. Therapy with rifampicin and fusidic acid was ceased and oral linezolid (600 mg twice daily) was given.

Linezolid was initially well tolerated. However, about six months after starting treatment with the antibiotic, the patient presented to his general practitioner with numbness of his hands, feet and legs below the knee, intermittent sharp pain in both feet and blurred vision. He was hospitalised and linezolid therapy ceased. On admission, peripheral sensory loss in a glove-and-stocking distribution was noted. Nerve-conduction studies showed severe sensory-motor axonal neuropathy, more severe in

the lower limbs than the upper limbs. Formal visual field testing showed patchy field damage, suggestive of drug-induced toxicity.

The patient declined further ophthalmological review. Five months after he stopped taking linezolid, he reported subjective resolution of visual impairment, but the peripheral neuropathy persists. The patient's alcohol intake had been negligible. Ongoing medications include digoxin, irbesartan, frusemide, omeprazole, piroxicam and diazepam.

We are not aware of any published articles describing peripheral or optic neuropathy associated with linezolid therapy. This information was not included in the original product information, but has been added to the revised version under the heading "Post-marketing surveillance".<sup>3</sup>

Up to June 2002 there had been only 13 reports of adverse reactions to linezolid to the Australian Adverse Drug Reactions Advisory Committee (ADRAC). Four of these, including our report, describe peripheral neuropathy and involve adult males who had received 1.2 g of linezolid daily for six to nine months. No patient's neuropathy had resolved at the time of reporting. Moreover, linezolid was the sole suspected drug in all four reports. It is important to note that the maximum duration of treatment with linezolid in clinical trials has been 28 days. Reports of neuropathy received by the manufacturer have primarily involved patients treated for longer than 28 days.<sup>3</sup>

Our report highlights the importance of postmarketing surveillance and reporting of adverse drug reactions, especially when a drug is used outside original indications or duration.

1. Hussar DA. New drugs of 2000. *J Am Pharm Assoc (Wash)* 2001; 41: 229-272.

2. Zyvox (linezolid) product information. Rydalmere, New South Wales: Pharmacia Australia Pty Limited, 24 August 2001.

3. Zyvox (linezolid) product information. Rydalmere, New South Wales: Pharmacia Australia Pty Limited, 21 February 2002. □

## Cervical screening: time to change the policy

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TO THE EDITOR: I read with interest the article on cervical screening by Dickinson.<sup>1</sup> Cervical screening has been the most successful public health measure introduced for the prevention of cancer, and the Pap test has been highly effective in reducing cervical cancer mortality and morbidity.

In New South Wales, between 1972 and 1999, the age-standardised incidence and mortality of cervical cancer fell by 49% and 66.6%, respectively.<sup>2</sup> The overseas experience is similar, with the best screening programs reporting a 70% reduction in mortality rates, with slight annual mortality increases since 1986.<sup>3</sup>

That women continue to die from this potentially preventable disease emphasises the limitations of the current screening method and highlights the need for new directions. The conventional Pap test is "yesterday's tool for today's world", let alone tomorrow's! The Pap test is prone to errors at all levels, but, most importantly, at specimen collection and cytological interpretation. Consequently, relatively high numbers of false negative results are associated with the test. Further, the Pap test is only partially successful in predicting the biological behaviour of the cytological abnormality.

As Dickinson states, minor abnormalities that come and go are unimportant, and can cause unnecessary alarm. These minor and transient abnormalities often lead to colposcopy, biopsy, surgical treatment and subsequent cytological and clinical or colposcopic follow-up, at a considerable cost to individual women, the screening program and taxpayers.<sup>4</sup>

Recent developments in cervical cytology and molecular biology have opened up new horizons.<sup>5</sup> Liquid-based cytology, human papillomavirus (HPV) DNA testing and new molecular markers will help us to accurately select the patients who are likely to have biologically aggressive disease with a high probability of progression.<sup>4,5</sup> With refinements, these new technologies will not only dramatically reduce the frequency of Pap test screening, but they may postpone the age for starting screening from 18 years to perhaps 25 or even 30 years.

These new technologies come at a price. Liquid-based cytology costs about \$30 and HPV DNA testing is about \$90, and no

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