Letters

The Editorial Executive Committee welcomes letters, which should be less than 250 words. Before a decision to publish is made, letters which refer to a published article may be sent to the author for a response. Any letter may be sent to an expert for comment. Letters are usually published together with their responses or comments in the same issue. The Editorial Executive Committee screens out discourteous, inaccurate or libellous statements and sub-edits letters before publication. The Committee's decision on publication is final.

Medicines Australia Code of Conduct

Editor, – I read with interest the article relating to Medicines Australia and the Committee regarding the monitoring of medications and code of conduct (Aust Prescr 2009;32:160–1). I agree the fines are enormous in terms of Australian standards although perhaps not necessarily so enormous in terms of the earning capacities of the various companies.

I would ask the following:

1. Who is involved in forming the Code of Conduct?
2. Who gets a copy of the Code of Conduct?
3. What happens to the money raised through these fines?
4. Who is represented on the Board of Medicines Australia?

David Bowman
Consultant Physician
Somerton Park, SA

Dr Brendan Shaw, Chief Executive, Medicines Australia, comments:

Dr Bowman should be assured that the 2010 edition of the Medicines Australia Code of Conduct carries appropriate sanctions. The maximum fine for a breach has increased from $200 000 to $300 000.

Importantly, however, non-monetary sanctions are often as strong a disincentive to a company as a fine. Having to send letters of retraction to doctors or take out corrective advertisements in the medical press can have an extremely negative impact on a company's reputation in the eyes of doctors, and serve as an effective deterrent.

Medicines Australia administers the Code of Conduct. An independent Code of Conduct Committee, chaired by a lawyer with extensive experience in trade practices law, adjudicates the complaints. The Committee consists of independent expert representatives of clinical, consumer and regulatory organisations. Details of the full Committee membership can be found on the website at www.medicinesaustralia.com.au/pages/page96.asp.

Medicines Australia reviews and updates the Code every three years to ensure it remains consistent with changing community standards. This is managed by an industry Code of Conduct Review Panel which seeks input from doctors and other healthcare professionals, professional associations, colleges, consumer organisations, patient groups and other groups or individuals who want to contribute.

The Code can be found on the Medicines Australia website at www.medicinesaustralia.com.au/pages/page251.asp. Hard copies are available free of charge to anyone upon request.

Revenue from fines raised through Code breaches covers the cost of administering the Code. Excess revenue is directed to a Special Purpose Fund which will be used to fund two initiatives aimed at improving outcomes in indigenous health.

The Board of Medicines Australia consists of an independent chairman and 12 managing directors of member companies, who are elected by the membership.

Nebivolol

Editor, – CSL Biotherapies is concerned by misrepresentation of data within the review of nebivolol hydrochloride in *Australian Prescriber* (2010;33:55–6). Several statements regarding nebivolol and its use in chronic heart failure are incorrect and do not accurately reflect current evidence.

The review states that the SENIORS trial 'was a *post hoc* analysis'. SENIORS (Study of the Effects of Nebivolol Intervention on Outcomes and Rehospitalisation in Seniors with Heart Failure) was a randomised, double-blind, multicentre, international trial comparing nebivolol with placebo in elderly patients with heart failure on optimal standard therapy.[1] While there are several *post hoc* analyses that have stemmed from SENIORS, the efficacy results reported in the review pertain to the original SENIORS trial. It is inaccurate and misleading to state that SENIORS is a *post hoc* analysis as the results are outcomes of pre-specified end points in a study designed and powered to determine the effects of nebivolol on mortality and morbidity in this patient population.

The review stated that 'The target dose was reached by two-thirds of the patients in the nebivolol group and was associated with a significant reduction (relative risk reduction of 4.2%) in the composite end point of all-cause mortality or hospitalisation (due to a cardiovascular event), compared to placebo'. In SENIORS, there was a 14% relative risk reduction in the composite primary end point for nebivolol compared to placebo (hazard ratio=0.86, 95% CI 0.74–0.99, p=0.039).[1] The 4.2% reduction is the absolute, not relative, risk reduction, suggesting a number needed to treat of 24 patients for 21 months to avoid one event.[1]

The review's recommendation that 'until long-term data on its clinical use are available, it is probably better to continue to use the more established beta blockers' has the potential to mislead readers that 'more established' beta blockers have some benefit over nebivolol in heart failure. *Australian Prescriber* does not provide further information regarding these benefits or evidence to support this assertion. We are not aware of any head-to-head trials in elderly patients directly comparing the efficacy and safety of nebivolol to other beta blockers used for chronic heart failure.

SENIORS provides the best evidence to date of a treatment likely to be effective in elderly patients with a broad range of ventricular dysfunction.[1] Unlike previous beta blocker trials which excluded patients with left ventricular ejection fraction > 40%, SENIORS enrolled patients with preserved ejection fraction as well as systolic dysfunction.[1] SENIORS also enrolled patients who were older, with a mean age of 76 years, than those in previous beta blocker trials.[1] Thus, nebivolol is the only beta blocker to demonstrate proven efficacy in typical patients with chronic heart failure (aged 70 years and older with a wide range of left ventricular ejection fraction).

Nebivolol is currently approved for chronic heart failure in 72 countries worldwide (data held on file). In SENIORS the mean duration of follow-up was 21 months.[1] This is longer than the pivotal trials supporting the use of other beta blockers.[2–4]

We request that these inaccuracies regarding the efficacy of nebivolol for chronic heart failure are corrected, particularly given the potential for these errors to mislead readers.

Jane Leong

Medical Director

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References

1. Flather MD, Shibata MC, Coats AJ, van Veldhuisen DJ, Parkhomenko A, Borbola J, et al; SENIORS Investigators. Randomized trial to determine the effect of nebivolol on mortality and cardiovascular hospital admission in elderly patients with heart failure (SENIORS). Eur Heart J 2005;26:215-25.
2. CIBIS-II Investigators and Committees. The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): a randomised trial. Lancet 1999;353:9-13.
3. Packer M, Coats AJ, Fowler MB, Katus HA, Krum H, Mohacsi P, et al. Effect of carvedilol on survival in severe chronic heart failure. N Engl J Med 2001;344:1651-8.
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The Editorial Executive Committee comments:

We agree that the results of the original SENIORS trial[1] should have been quoted rather than a *post hoc* analysis.[2] This has been corrected.[3] The confusion arose partly because there were four different articles published on the SENIORS trial. We asked CSL to provide a copy of the data supporting the approval of nebivolol by the Therapeutic Goods Administration, but only received the product information.

The SENIORS trial was randomised – patients were randomised to receive nebivolol 1.25 mg or placebo at the beginning of the trial. However, our original text was referring to the fact that patients were not randomised to receive different doses of nebivolol. For example, the dose was only increased to 2.5 mg or 5 mg in patients who tolerated the lower dose. Our original sentence has been deleted to avoid confusion.[3]

Regarding the efficacy of nebivolol, the relative risk reduction of 4.2% has been corrected to read the absolute risk reduction of 4.2%.[3]

The conclusion that it is probably better to continue to use the more established beta blockers until there are more long-term data for nebivolol remains the view of the Editorial Executive Committee. In our opinion, there are currently more robust data for beta blockers such as carvedilol, bisoprolol and metoprolol succinate than for nebivolol.[4]

References

1. Flather MD, Shibata MC, Coats AJ, van Veldhuisen DJ, Parkhomenko A, Borbola J, et al; SENIORS Investigators. Randomized trial to determine the effect of nebivolol on mortality and cardiovascular hospital admission in elderly patients with heart failure (SENIORS). Eur Heart J 2005;26:215-25.
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4. National Prescribing Service (NPS). Nebivolol (Nebilet) for chronic heart failure. NPS RADAR. March 2010.