Correspondence

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SSRIs and deliberate self-harm

Markowitz (2001), commenting on a study by Donovan *et al* (2000), which indicated that selective serotonin reuptake inhibitors (SSRIs) were more associated with presentations of deliberate self-harm to accident and emergency departments than were other antidepressants, suggested that it was 'astounding' that Donovan *et al* had not taken into account the fact that their results might stem simply from a preferential prescribing of SSRIs to patients with borderline personality disorder – a patient group particularly prone to self-harm. Dr Markowitz's points about the Donovan *et al* study come down essentially to two – that this study was not randomised and that there was no placebo control. There are, however, data in the public domain bearing on these points to which he may not have had access.

Khan *et al* (2000) published a meta-analysis of randomised controlled trials submitted to the US Food and Drug Administration (FDA) showing suicides and suicide attempts on a number of recently licensed antidepressants. Requests to the FDA under freedom of information provisions (further details available from the author upon request) indicate that three of five suicide attempts characterised as placebo suicide attempts in the sertraline trial programme reported by Khan *et al* occurred during washout rather than while on placebo. Similarly, in the paroxetine trial programme reported by Khan *et al*, both suicides and three of six suicide attempts characterised as placebo suicides and attempts appear to have been washout rather than placebo suicides or attempts. Taking this information into account and analysing the drug *v.* 'true placebo' data for absolute numbers of patients reveals a statistically significant general increase in the risk of suicide acts on novel antidepressants compared with placebo and a specific increase for paroxetine.

In the light of these randomised, placebo-controlled findings it would seem that Dr Donovan *et al* were cautious and understated in their discussion of their results.

Declaration of interest

I have had consultancies with, been a principal investigator or clinical trialist for, been a chairman or speaker at international symposia for or been in receipt of support to attend foreign meetings from a number of pharmaceutical companies with interests in the manufacture of antidepressants, including SmithKline Beecham and Pfizer. I have been an expert witness for the plaintiffs (US) and claimants (UK) in legal actions involving SSRIs.

Donovan, S., Clayton, A., Beeharry, M., *et al* (2000) Deliberate self-harm and antidepressant drugs. Investigation of a possible link. *British Journal of Psychiatry*, **177**, 551–556.

Khan, A., Warner, H. A. & Brown, W. A. (2000) Symptom reduction and suicide risk in patients treated with placebo in antidepressant clinical trials. *Archives of General Psychiatry*, **57**, 311–317.

Markowitz, J. C. (2001) Antidepressants and suicide risk. *British Journal of Psychiatry*, **178**, 477.

Montgomery, S. A., Montgomery, D. B. & Rani, J. (1993) Pharmacological differences between brief and major depressions. *European Neuropsychopharmacology*, **3** (suppl. 3), 214–215.

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Response from Pfizer: The possible association between SSRIs and suicidal behaviour has been the subject of intense discussion throughout the 1990s, following the publication of case reports of suicidal behaviour suspected to be associated with fluoxetine.

Healy states that three of five suicide attempts characterised as placebo suicide attempts in the sertraline trial programme reported by Khan *et al* occurred during the washout period rather than while on placebo. All of the five suicide attempts to which he refers occurred while patients were on placebo, three of which occurred during the washout period. Healy similarly states that three of six suicide attempts and two completed suicides also occurred during washout rather than while on placebo in the paroxetine trial programme. Pfizer does not have access to data regarding other companies' products and cannot therefore comment whether this is accurate or not. Healy concludes that taking this information into account and reanalysing the data, there is a statistically significant general increase in the risk of suicidal acts in patients taking novel antidepressants when compared with placebo. However, since this is based on inaccurate information, at least as regards sertraline, it is not a justifiable conclusion.

Pfizer has submitted information specific to when deaths occurred to the Medicines Control Agency (MCA) as well as other regulatory bodies, in compliance with worldwide regulatory requirements.

As with all medicines, the safety of the SSRIs is continually monitored by the MCA and the independent expert advisory body, the Committee on Safety of Medicines (CSM). Since 1992 a number of epidemiological studies and analyses of clinical trial data have failed to establish a causal association between the SSRIs and suicidal behaviour, and the CSM has reviewed this issue on a number of occasions. The most recent review, conducted in 2001 and discussed at the CSM on 12 December 2001, concluded that 'the current evidence is insufficient to confirm a causal association between SSRIs and suicidal behaviour' (Commons Hansard Written Answers, 2002) and advised that the issue should be kept under review.

The product information and the *British National Formulary* warn that patients should be closely monitored for suicidal impulses, and an article emphasising this advice was also published in the MCA/CSM drug safety bulletin in September 2000.

Commons Hansard Written Answers (2002) 4 February, Vol. 379, part no. 94, column 780W.

MCA/CSM (2000) Selective serotonin reuptake inhibitors (SSRIs). *Current Problems in Pharmacovigilence*, **26**, 11–12.

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