Dependence on Paroxetine (Paxil/Seroxat)

Statement by David Healy MD FRCPsych

Fonte *www.**seroxat**usergroup.org.uk*

I have been asked to confirm and comment on evidence relating to withdrawal reactions suggestive of physical dependence on paroxetine, observed in studies on healthy volunteers, carried out in the 1980s by SmithKline Beecham.

In the course of a recently settled legal action (Tobin v SmithKline, Wyoming, 2001), I acted as an expert witness for the Plaintiffs. As part of the discovery process I had sought and was granted access to SmithKline's Beecham's healthy volunteer archive at Harlow. My concern had been to scrutinise those records for details of possible agitation and suicidality in healthy volunteers taking paroxetine. These were present, but at least as striking was evidence from these studies about dependence on paroxetine.

A detailed expert report was prepared for the plaintiffs' lawyers in this case, which includes details of studies undertaken by SmithKline Beecham that fully substantiate concerns I communicated to the UK Medicines Control Agency in letters of 7th and 19th June 2001, the essence of which was also accurately reported in *The Guardian* newspaper (11 June 2001)

I regret that I am under a confidentiality order in regard to this material and am not able to disclose it to this appeal. However, I can confirm, and am prepared to testify to the substance of the points raised in the following exchange (in my testimony in Tobin v SmithKline) between Mr Charles Preuss, the attorney for SmithKline, and myself.

> ***Healy:*** *Yes, but there's a withdrawal syndrome from Paxil, including agitation, abnormal dreams and nightmares that comes through in spades in these healthy volunteer studies.*
>
> ***Preuss:*** *You're saying Paxil is still active for three months?*
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> ***Healy:*** *In up to 80 percent of the volunteers on this drug for only two weeks produces withdrawal syndromes in these healthy volunteers. I'm saying in my clinical experience I've seen people on this drug for short periods of time and I've seen them have troubles three months later, yes.*

My concerns about paroxetine extend far beyond the results of these studies on healthy volunteers. In the 1990s, after its release on to the market as an antidepressant, SmithKline Beecham put paroxetine into clinical trials – exemplified by the study reported by Montgomery & Dunbar,

1993 - that involved a randomised discontinuation design. The difficulties experienced by patients on randomisation to placebo were then interpreted by SmithKline Beecham as evidence of new illness episodes, and the company has subsequently responded to enquiries about the risk of withdrawal reactions and physical dependency, typically by stating that any such problems experienced by patients are simply a recrudescence of their original nervous problem. Basic pharmacological principles, epidemiological studies on depression, as well the evidence from their own healthy volunteer studies strongly suggest that such an interpretation of these data was and is quite unjustified.

Against this background SmithKline Beecham launched paroxetine in the UK with disclaimers on the datasheet to the effect that, as with any drug acting on the brain, some care needs to be taken on discontinuation. The data available to SmithKline before launch indicated problems occurring at a significantly greater rate and to a markedly more severe degree than any psychiatrist at the time would have had reason to expect either from an antidepressant or from such warnings.

Post-marketing surveillance surveys and other studies undertaken since have indicated much greater withdrawal problems with paroxetine than with the previous generation of tricyclic, MAOI and non-tricyclic or non-MAOI antidepressant drugs. A randomised controlled trial undertaken with funding provided by Eli Lilly (Rosenbaum et al, 1998), indicated rates of problems on discontinuation of paroxetine in over 30% of patients with many patients having multiple symptoms, including many novel and disturbing symptoms.

For Dr Wheadon and the company therefore to characterise paroxetine withdrawal reactions as very rare, transient, mild and/or virtually impossible to detect and distinguish from underlying psychiatric illness is simply an untenable position. It follows that I have real concerns about SmithKline promoting paroxetine for the prophylaxis of depressive disorders and other psychiatric illness, on the basis of data that are more sensibly and credibly explained in terms of physical dependence and withdrawal symptoms.
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