



GlaxoSmithKline

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IMPORTANT PRESCRIBING INFORMATION

Dear Healthcare Professional:

GlaxoSmithKline (GSK) would like to advise you of important changes to the **Clinical Worsening and Suicide Risk** subsection of the WARNINGS section in the labels for PAXIL[®] (paroxetine HCl) and PAXIL CR[®] (paroxetine HCl Controlled-Release Tablets). These labeling changes relate to your adult patients, particularly those who are younger adults. **Please read the full text of the added WARNINGS following this letter.** Full copies of the revised package inserts for PAXIL and PAXIL CR are enclosed.

Current prescribing information for paroxetine – and for all other antidepressants – contains information in the **WARNINGS** section (**Clinical Worsening and Suicide Risk** subsection) stating that “patients with MDD, both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality), whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs.”

GSK has recently conducted a new meta-analysis (an addition to numerous prior analyses) of suicidal behavior and ideation in placebo-controlled clinical trials of paroxetine in adult patients with psychiatric disorders including Major Depressive Disorder (MDD), other depression and non-depression disorders (e.g., dysthymia, panic disorder, generalized anxiety disorder, obsessive compulsive disorder). These trials included 8958 patients treated with paroxetine and 5953 with placebo.

Results of this analysis showed a higher frequency of suicidal behavior in young adults (prospectively defined as age 18-24) treated with paroxetine compared with placebo (17/776 [2.19%] versus 5/542 [0.92%]). In the older age groups (25-64 years and ≥65 years), no such increase was observed. This finding in young adults was not statistically significant; however, the difference was observed in paroxetine-treated patients with both depressive and non-depressive conditions.

Further, in the analysis of adults with MDD (all ages), the frequency of suicidal behavior was higher in patients treated with paroxetine compared with placebo (11/3455 [0.32%] versus 1/1978 [0.05%]). This difference was statistically significant; however as the absolute number and incidence of events are small, these data should be interpreted with caution. All of the reported events of suicidal behavior in the adult patients with MDD were non-fatal suicide attempts, and the majority of these attempts (8 of 11) were in younger adults aged 18-30. These MDD data suggest that the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24.

The possible increase in risk of suicidal behavior in the MDD studies was observed despite substantial evidence for efficacy in the paroxetine-treated patients (compared with placebo) as determined by standardized disease-specific instruments (e.g., Hamilton Depression

Rating Scale and Montgomery-Asberg Depression Rating Scale for depression). Most patients had an identified social stressor at the time of the event.

It is therefore important that all patients, especially young adults and those who are improving, receive careful monitoring during paroxetine therapy regardless of the condition being treated.

It is difficult to conclude a causal relationship between paroxetine and suicidality due to the small incidence and absolute number of events, the retrospective nature of this meta-analysis, and potential for confounding by the fact that the events of interest are a symptom of the psychiatric illnesses themselves. However, GSK believes it is important to draw your attention to these findings and is voluntarily amending the paroxetine labeling to reflect this new information and to emphasize the importance of careful monitoring of all patients during paroxetine therapy. **Please read the full text of the added WARNINGS following this letter.** Full copies of the revised package inserts for PAXIL and PAXIL CR are enclosed.

GSK continues to believe that the overall risk:benefit of paroxetine in the treatment of adult patients with MDD and other non-depressive psychiatric disorders remains positive.

PAXIL is indicated for the treatment of major depressive disorder, obsessive-compulsive disorder, panic disorder, social anxiety disorder, generalized anxiety disorder, and posttraumatic stress disorder in adults; PAXIL CR is indicated for the treatment of major depressive disorder, panic disorder, social anxiety disorder, and premenstrual dysphoric disorder in adults.

The medical community can further our understanding of PAXIL and PAXIL CR by reporting adverse events to GlaxoSmithKline at 1-888-825-5249 or to FDA's MedWatch Adverse Event Reporting program online (at www.fda.gov/MedWatch/report.htm), by phone (1-800-FDA-1088), or by returning the postage-paid FDA form 3500 (which may be downloaded from www.fda.gov/MedWatch/getforms.htm) by mail (to MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787) or fax (1-800-FDA-0178).

GlaxoSmithKline encourages you to familiarize yourself with these revisions to labeling. If you have any questions about the new information, please contact our Customer Response Center at 1-888-825-5249. You can find other useful information related to this issue at gsk.com and to clinical trials involving all other GSK products at our Clinical Trial Registry website (<http://ctr.gsk.co.uk/welcome.asp>).

Sincerely,



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