



Annotated Bibliography

SB SmithKline Beecham
Pharmaceuticals

EXHIBIT 21
Name: Kraws
Date: 5/20/05 JDS

ANNOTATED BIBLIOGRAPHY

Boyer WF, Blumhardt CL: The safety profile of paroxetine. *J Clin Psychiatry* 1992;53(2,Suppl):61-66.

In this article, the authors review safety data for paroxetine that have been obtained from 4,126 patients who received paroxetine. The data indicate that paroxetine has no significant cardiovascular effects, few significant drug interactions, and no significant effects on either the EEG or ECG. Paroxetine is safe in overdose and has little anticholinergic activity. Paroxetine does not impair psychomotor performance, and there is no evidence that it increases suicidal ideation. The most common side effects associated with paroxetine were nausea, somnolence, dry mouth, headache, and asthenia. These are usually well tolerated and rarely lead to drug discontinuation.

Dunner DL, Dunbar GC: Reduced suicidal thoughts and behavior (suicidality) with paroxetine. Presented at the American College of Neuropsychopharmacology, December 1991, San Juan, PR.

In this retrospective analysis of the initial 6 weeks of therapy in the worldwide database for paroxetine, the incidence of suicidal thought in patients was assessed. Measures evaluated included changes in the HAM-D suicide and retardation item scores, MADRS suicide item, emergence of suicidal ideation, and the incidence of suicidal attempts. Paroxetine was significantly superior to placebo in reducing HAM-D suicide item scores at all time points ($p < 0.05$). It was also superior to both placebo and active controls in decreasing MADRS suicide item scores at most time points ($p < 0.01$). Suicides and suicide attempts occurred less frequently with paroxetine than with either placebo or active controls. Paroxetine was also significantly superior to placebo and active controls on most measures of emergence of suicidal thoughts. This analysis shows that suicidality is inherent in depressive illness and that antidepressant therapy with paroxetine is appropriate for the integrity of depressed patients.

Please see full prescribing information for PAXIL™ (paroxetine hydrochloride) on pages 32 - 39.

27

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