09/17/02

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

STATISTICAL REVIEW AND EVALUATION

NDA:	19,839 / (b) (4) 044
DRUG NAME:	Zoloft ® (sertraline hydrochloride)
INDICATION:	(b) (4)
SPONSOR:	Pfizer
STATISTICAL REVIEWER:	Ohidul Siddiqui
DATE OF DOCUMENT:	Dec 14, 2001

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TABLE OF CONTENTS

Executive Summary of Statistical Findings

In this new drug application, the sponsor submitted two randomized trials' results to support the efficacy of sertraline in children (6 to 11 years of age) and adolescents (12 to 17 years of age) with major depressive disorder. (b) (4)

[redacted]

Introduction

The sponsor submitted results of two identical multicenter, randomized, double-blind, placebo-controlled, flexible dose outpatient trials of sertraline in children (6 to 11 years of age) and adolescents (12 to 17 years of age) with Major Depressive Disorder (MDD). Following a two-week screening period, eligible subjects were randomized to either sertraline or matching placebo in a 1:1 ratio with a 1:1 stratification of children to adolescents. The double-blind treatment phase was of 10 weeks duration.

Subjects were started on sertraline or matching placebo at a dose of 25 mg per day for the first 3 days followed by 50 mg per day of sertraline or matching placebo through the remainder of the first 2 weeks. Thereafter, the dose could be increased in increments of 50 mg per day at intervals of two weeks up to a maximum of 200 mg per day. Increases in dose above 50 mg per day were based on the clinical judgement of the investigator, and took into account clinical response and dose-limiting side effects. A reduction in dose for adverse events was allowed at any time but only in decrements of 50 mg/day per week. The dose could be decreased to a minimum dose of 50 mg daily. After a reduction in dose, investigators who wanted to titrate up again could do so in increments of 50 mg per day every two weeks, up to a maximum of 200 mg daily. Subjects responding well at lower doses were to be maintained on those doses until the end of the study.

The investigators were supplied with blister packs containing 25 and/or 50 mg sertraline tablets and matching placebo tablets. Separate randomization lists were generated for children and adolescents to achieve a 1:1 stratification of the age groups. Drug was packaged separately for the age groups in color-coded blister packs: blue labels for children and yellow labels for adolescents.

Children (6 to 11 years of age) and adolescents (12 to 17 years of age) diagnosed with a current episode of MDD, whose Children's Depression Rating Scale-Revised (CDRS-R) score was >=45 and Clinical Global Impression of Severity (CGI-S) score was >=4 at Screening Day 1, 7, and 14 (baseline), and who met all of the inclusion and none of the exclusion criteria as stated in the study protocols were enrolled in the studies.

At the discretion of the investigator, subjects could be discontinued from the studies at any time for reasons such as adverse events, insufficient clinical response, and noncompliance. The investigator must have determined the primary reason for discontinuation. Withdrawal due to an adverse event was to be distinguished from withdrawal due to insufficient clinical response.

In both studies, clinic visits were scheduled at Screening Day 1 and Day 7, at Baseline (Screening Day 14), and at the End of Week (EOW) 1, 2, 3, 4, 6, 8 and 10 of the study.

Study Objectives

The objectives of the two studies were to evaluate the safety and efficacy of sertraline compared with placebo in children and adolescents (6 to 17 years of age) who are outpatients with MDD.

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(b) (4)

Reviewer's Overall Conclusion:

In this new drug application, the sponsor submitted two randomized trials' results (b) (4) in children (6 to 11 years of age) and adolescents (12 to 17 years of age) with major depressive disorder. (b) (4)

(b) (4)

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/s/

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