CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-030

MEDICAL REVIEW(S)

Financial Disclosure Review

Form FDA 3455 ("Financial Interests and Arrangements of Clinical Investigators"), dated Feb. 13th 2006, was submitted and reviewed by this clinical reviewer. In accordance with 21 CFR Part 54.4, certification and disclosure requirements, forms of clinical investigator certification and financial disclosure were also provided by Schwarz BioSciences, Inc.

In this financial disclosure submission all investigators have provided financial disclosure information via questionnaires.

No clinical investigator participating in the submitted studies from any of the study sites had any disclosures in the categories of compensation potentially affected by the outcome of the covered study [21 CFR 54.4(a)(3)(i), 54.2 (a)], significant payments of other sorts from the sponsor of the covered study [21 CFR 54.4 (a)(3)(ii), 54.2(f)], proprietary interest in the tested product [21 CFR 54.4(a)(3)(iii), 54.2(c)], or significant equity interest in the sponsor of the covered study product [21 CFR 54.4(a)(3)(iv), 54.2(b)].

Reviewer's Comment:
There is no reason to suspect that the results of any of the studies submitted in support of this NDA were compromised due to financial arrangements between the sponsor and the clinical investigators.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Suresh Kaul
10/20/2008 03:39:50 PM
MEDICAL OFFICER

NDA 22-030

Medical Officer's Review: Complete Response to Approvable

Date Submitted:	May 1, 2008
Date Received:	May 1, 2008
Date Review Completed:	October 9, 2008
PDUFA Goal Date:	November 3, 2008
Drug Product:	Toviaz (fesoterodine fumarate)
Dose and Formulation:	4mg and 8mg extended-release tablets
Sponsor:	Pfizer, Inc New York, N.Y.

Indication: Treatment of overactive bladder with symptoms of urge urinary incontinence, urgency and urinary frequency.

1. Regulatory History

NDA 22-030 was initially submitted by Schwarz Pharma and accepted for filing by the FDA on March 17, 2006 for the indication "treatment of symptoms that may occur in subjects with overactive bladder syndrome".

Under terms of an agreement with Pfizer, Inc., effective June 13, 2006, Schwarz Pharma transferred all of its rights in fesoterodine to Pfizer on an exclusive world wide basis.

In an Approvable letter to Schwarz Pharma on January 25, 2007, FDA requested: 1) that all manufacturing sites be made ready for pre-approval inspection, 2) that revised labeling be submitted, and 3) that another Safety Update be submitted, to include data from all non-clinical and clinical fesoterodine studies since the previous Safety Update.

This review focuses on the requested Safety Update submitted in the Complete Response to Approvable action. This final update includes new safety data, obtained since the cutoff date of the original NDA (October 14, 2005), from 3 long-term, open-label extension studies completed by Schwarz Pharma (Studies SP669, SP738, and SP739), and an ongoing 12-week, open-label study (A0021007), initiated by Pfizer, with data included as of January 1, 2008.

In addition, this Complete Response to Approvable includes two new Phase1 studies completed by Schwarz Pharma (Studies SP857 and SP877) and three new Phase1 studies conducted by Pfizer (Studies A0221004, A0221015 and A0221044) since the NDA. The Clinical Safety Update includes summarizes of safety from these 5 new Phase 1 studies.

1.0 2. Extent of Exposure to Fesoterodine

2.1 Overview of Extent of Exposure to Fesoterodine

The following table presents the study design, number of subjects who received fesoterodine, and duration of treatment in Study SP669, an extension of the Phase 2 study SP668, and one of the three open-label, long-term extension studies.

Table 1. Phase 2 open label studies of fesoterodine in subjects with overactive bladder (Schwarz)

Study number/study design/dosage	# Subjects receiving fesoterodine[a]	# Subjects receiving placebo[a]	Mean treatment duration on fesoterodine
SP669/Extension of SP668/ 2-phase multicenter, double-blind and open-label, long-term study to assess safety, tolerability, and efficacy in OAB/ fesoterodine SR 4mg, 8mg, and 12mg doses once daily in the double-blind phase; fesoterodine 4mg and 8mg doses once daily in the open-label phase	186 (125 new exposures[b])	0	639 days

OAB=overactive bladder, SR=sustained release

a. These subject exposures are based on the safety set (SS).

b. New exposures include 20 subjects who previously received placebo in the preceding double-blind study, and 105 "de novo" subjects who enrolled directly into SP669 without having participated in SP668.

Table 2 presents the study design, number of subjects who received fesoterodine, and durations of treatment in Studies SP738 and SP739, the two, open-label, long-term extension studies to the Schwarz Pharma Phase 3 studies SP583 and SP584, respectively.

Table 2. Phase 3 open label studies of fesoterodine in subjects with overactive bladder (Schwarz)

Study number/study design/dosage	# Subjects receiving fesoterodine[a]	# Subjects receiving placebo[a]	# Subjects receiving active control[a]	Mean treatment duration
SP738/Extension of SP583/ multicenter, open-label, long-term safety and efficacy in OAB/ fesoterodine 4mg and 8mg doses once daily	417 (218 new fesoterodine exposures)[b]	NA	NA	695 days
SP739/Extension of SP584/ multicenter, open-label, long-term safety and efficacy in OAB/ fesoterodine 4mg and 8mg doses once daily	473 (158 new fesoterodine exposures)[b]	NA	NA	584 days

OAB=overactive bladder, NA=not applicable, SR=sustained release

a. These subject exposures are based on the safety set (SS) for each study.

b. New exposures are defined as those who previously received placebo or tolterodine in the preceding double-blind studies.

The following table presents the study design, number of subjects receiving fesoterodine, and the duration of treatment in the Study A0021007, the new, open-label, Pfizer study in this report.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.