CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-303

CHEMISTRY REVIEW(S)

SLI 381, loss of appetite and nausea were more common in boys, and dyspepsia was more common in girls; however, the sponsor did not compare the relative risks for these events between boys and girls. Similarly, among subjects receiving SLI 381, insomnia was more common among Caucasians, while abdominal pain, loss of appetite, anxiety, emotional lability, and nervousness were more frequent among non-Caucasians, but here again the sponsor did not analyze these data in terms of differences in relative risk by ethnic origin.

8.6 Adequacy of safety assessment: The safety methodology was generally adequate. An analysis of weight and height, especially in the long term trial, would have been helpful. Also, the analysis of laboratory abnormalities could have been improved by selecting criterion values for significant abnormalities, and then determining the number of such abnormalities that were treatment emergent. The same comment applies to the vital sign analysis. Finally, more discussion could have been provided regarding the qualitatively abnormal ECG readings, which were simply listed in the report; presumably none were considered particularly concerning from a clinical standpoint.

8.7 Overall conclusions about safety

This is the first large clinical trial dataset available in some time for an amphetamine drug product. Overall the safety profile appears consistent with what would be expected for a sympathomimetic psychostimulant. Weight loss and anorexia were two of the the most frequent adverse reactions, which is not surprising for a drug product that was originally marketed for weight loss. The psychostimulant effects of amphetamine were reflected in the incidence of emotional lability, insomnia and nervousness. Although the findings were not entirely consistent across trials, it is evident that the drug can raise heart rate and blood pressure. There did not appear to be any findings of concern with respect to laboratory or ECG parameters.

The sponsor should provide clarification regarding the abnormalities in serum calcium that were reported in study 301. The sponsor should also provide more information on the two subjects in study 301 who developed premature atrial systoles during treatment with SLI 381.

9.0 Overall Conclusions and Recommendations

This drug product is approvable in my opinion. My suggestions for labeling are attached to this review.

Andrew D. Mosholder, M.D.
Medical Officer, HFD-120

Cc: Laughren, Wheelous, Mosholder

13 page(s) of revised draft labeling has been redacted from this portion of the review.

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

/s/

Andy Mosholder
7/24/01 02:21:23 PM
MEDICAL OFFICER

Thomas Laughren
7/28/01 12:16:17 PM
MEDICAL OFFICER
I agree that this NDA is approvable; see memo to file for more detaile
d comments.--TPL

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, HFD-120
REVIEW OF CHEMISTRY, MANUFACTURING, AND CONTROLS

NDA 21-303 CHEM REVIEW: #1 REVIEW DATE: 10/24/2000

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	10/3/2000	10/3/2000	10/10/2000
18 mo. Stability data	03/30/01		
Response to inquiry	06/19/01		

NAME AND ADDRESS OF APPLICANT
Shire Laboratories Inc.

1505 East Gude Drive
Rockville, Maryland 20850

DRUG PRODUCT NAME
Proprietary: Adderall-XR
Non proprietary/USAN: Amphetamine sulfate USA/USN, amphetamine aspartate, dextroamphetamine sulfate USP/USAN, dextroamphetamine saccharate
Code Name/Number: SLI 381
Chem. Type/Ther. Class: 3S

PHARMACOLOGICAL CATEGORY/INDICATION: 1) Treatment of ADHD 2) Treatment of narcolepsey
DOSAGE FORM: Capsules
STRENGTHS: 10 mg, 20 mg, and 30 mg
ROUTE OF ADMINISTRATION: Oral
DISPENSED: x Rx ___OTC
SPECIAL PRODUCTS: ___Yes x No

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA

Active Pharmaceutical Ingredient	Chemical Name	CAS Number
Amphetamine sulfate, USP	(±)-α-Methylphenylamine sulfate	60-13-9
Dextroamphetamine sulfate, USP	(+)-α-Methylphenylamine sulfate	617-48-8
Amphetamine aspartate	(±)-α-Methylphenylamine aspartate	51-63-8
Dextroamphetamine saccharate	(+)-α-Methylphenylamine saccharate	87-73-0

CAS for free amphetamine base is 300-62-9

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.