CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
19-815/S-005

Correspondence

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
FOOD AND DRUG ADMINISTRATION

US Mail address:
FDA/CDER/HFD-110
5600 Fishers Lane
Rockville, MD 20857

Woodmont II
1451 Rockville Pike
Rockville, MD 20852

Transmitted to FAX Number:	(240) 453-6456
Attention:	Ms. Linda Motta
Company Name:	Shire Laboratories
Phone:	(240) 453-6445
Subject:	**Biopharm Comments for NDA 19-815, SCM-005 ProAmatine (Midodrine HCl) Tablets**
Date:	08/09/01
Pages including this sheet:	**3**
From:	**Edward Fromm**
Phone:	**301-594-5313**
Fax:	**301-594-5494**

RECOMMENDATION:
The Office of Clinical Pharmacology and Biopharmaceutics/Division of Pharmaceutical Evaluation I (OCPB/DPEI) has reviewed the information provided in NDA 19-815, Supplement SCM-005 for ProAmatine Tablets.

Although, the composition of the formulations for the 2.5, 5, and 10 mg ProAmatine Tablets are not proportional, OCPB/DPEI is of the opinion that a waiver for the requirement of an in vivo bioequivalence study for the additional strength of 10 mg for ProAmatine Tablets may be granted provided the sponsor provides additional comparative dissolution data in two additional media (i.e., pH 4.5 and 6.8 buffers) and corresponding F2 values (if appropriate).

OCPB's above recommendation is based on the following overall information for this product:

- □Previous PK studies showed linear kinetics for the 2.5, 5, and 10 mg doses of midodrine HCl
- The safety and efficacy of the 10 mg dose was evaluated in previous clinical trials
- The approved labeling recommends a dose of ProAmatine of 10 mg, 3 times daily
- □Midodrine HCl meet the requirements of a highly soluble/highly permeable drug
- □ProAmatine 2.5 and 5 mg Tablets are immediate release drug products and the comparative dissolution data for 2x5 mg and 10 mg tablets using the approved method showed that >95% is dissolved in less than 5 minutes.

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/s/

Edward Fromm
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CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA19-815

Shire Laboratories Inc.
Attention: Zohra E. Lomri
1901 Research Blvd., Suite 500
Rockville, MD 20850

Dear Ms. Lomri

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: ProAmatine (midodrine hydrochloride) Tablets

NDA Number: 19-815

Supplement number: S-005

Date of supplement: April 12, 2001

Date of receipt: April 13, 2001

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on June 12, 2001 in accordance with 21 CFR 314.101(a).

U.S. Postal Service:
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Attention: Document Room
1451 Rockville Pike
Rockville, Maryland 20852

If you have any question, please call:

Mr. Edward Fromm
Regulatory Project Manager
(301) 594-5313

Sincerely yours,

/S/

Kasturi Srinivasachar, Ph.D.
Chemistry, Team Leader
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Kasturi Srinivasachar
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