CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-287

Chemistry Review(s)

Memo to File

From: Suong Tran, PhD, Chemist
To: NDA 21-287 Uroxatral (alfuzosin HCl extended release tablets)
Date: 12-JUN-2003
Subject: Final, second-cycle review of the NDA

- The chemistry recommendation of APPROVAL was filed on 4-SEP-2001 (Chem. Review #2). The chemistry reviews included evaluations of labeling (container mock-up labels and physician insert- Description and How Supplied sections) for the proprietary name "Uroxatral".
- On 5-OCT-2001 an APPROVABLE action was taken on NDA 21-287 based on the clinical recommendation.
- On 12-DEC-2002 a complete response to the approvable letter was submitted by the applicant, thus triggering the second review cycle. No new chemistry information is included in the resubmission. No review of the physician insert (Description and How Supplied sections) by this chemist is necessary in the second review cycle because there is no change in the information that was found to be acceptable in the first review cycle (Chem. Review #2).
- On 16-DEC-2002, a new proprietary name [redacted] or [redacted] is proposed by the applicant.
- On 12-MAY-2003, DMETS found the name [redacted] unacceptable, while DDMAC found both [redacted] and [redacted] unacceptable.
- On 12-JUN-2003, the applicant states that the proprietary name "Uroxatral" along with all container (i.e., carton, blister, bottle) labeling reviewed by FDA in the first review cycle will be used for the drug product (refer to the 12-JUN-2003 teleconference minutes prepared by J. King, CSO). This labeling was found to be acceptable in the Chem. Review #2. Likewise, there is no change in the Description and How Supplied sections of the physician insert that were found to be acceptable in the first review cycle (Chem. Review #2).
- An "Acceptable" recommendation was obtained from the Office of Compliance on 11-JUN-2003.

CONCLUSION:
Chemistry recommends APPROVAL for NDA 21-287.

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/s/

Suong Tran
6/12/03 03:38:13 PM
CHEMIST

Moo-Jhong Rhee
6/12/03 03:59:44 PM
CHEMIST
I concur

Memo to File

From: Suong Tran, PhD, Chemist
To: NDA 21-287 (alfuzosin HCl extended release tablets)
Date: 14-MAY-2003
Subject: Second-cycle review of the NDA

On 5-OCT-2001 an APPROVABLE action was taken on NDA 21-287 based on the clinical recommendation. All chemistry reviews were finalized at the end of the first review cycle, with no pending issue. The chemistry reviews included evaluations of labeling (container mock-ups and package insert- Description and How Supplied sections). A chemistry recommendation of approval was issued on 4-SEP-2001 (Chem. Review #2).

On 12-DEC-2002 a complete response to the approvable letter was submitted by the applicant, thus triggering the second review cycle. No new chemistry information is included in the response. Therefore, no chemistry review is necessary in the second review cycle of the NDA.

One 16-DEC-2002, as part of the second review cycle, a new proprietary name [redacted] or [redacted] is proposed by the applicant. Other than the proprietary name, no other change is made to the package insert. No new container labels, including mock-ups, have been submitted pending the final decision on the new name by the Office of Drug Safety. ODS has indicated that the final review of the new name will not be completed until late May or early June, thus no container mock-up labels is available for a chemistry review because of the lack of a proprietary name.

Comments:

- The chemistry recommendation of APPROVAL was issued on 4-SEP-2001 (Chem. Review #2) for the first review cycle. No chemistry review is necessary in the second review cycle because there is no new chemistry information submitted in the second review cycle.
- No review of the physician insert (Description and How Supplied) by this chemist is necessary in the second review cycle because there is no change in the information that was found to be acceptable in the first review cycle (Chem. Review #2).
- The proprietary name of the drug product is pending the final decision from FDA (ODS and DRUDP). No container mock-up labels is available for a chemistry review in the second review cycle because of the lack of a proprietary name.

CONCLUSION:
Chemistry recommends the NDA for approval pending satisfactory container mock-up labels.

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/s/

Suong Tran
5/13/03 02:37:13 PM
CHEMIST

Moo-Jhong Rhee
5/13/03 03:38:37 PM
CHEMIST
I concur

NDA 21-287
Uroxatral (alfuzosin) Extended Release Tablets, 10 mg

CHEMISTRY DIVISION DIRECTOR REVIEW

Sanofi-Synthelabo submitted this NDA 8-DEC-2000. The indication is BPH. The product is formulated for extended release for once daily dosing.

Drug substance manufacturing is described in DMF held by and has been found acceptable. The manufacturing site has been inspected, and received an acceptable Compliance recommendation. A retest date of 24 months was assigned.

The drug product is an extended release tablet comprised of 3 layers. The outer layers permit diffusion of the inner active layer. The manufacturing site, Sanofi-Synthelabo, Tours, France has been inspected and has received an acceptable recommendation from Compliance. Product is packaged in — bottles of 30 and 100, and in blisters. Following CMC review #1, and information request letter was sent. The response was reviewed in CMC review #2, and was found to be acceptable. All associated DMFs were found to be adequate. A tentative expiry of 24 months was found to be acceptable. The OPDRA tradename review found Uroxatral acceptable and was confirmed recently.

From a CMC perspective the application is reccomended for approval.

Eric P Duffy, PhD
Director, DNDC II/ONDC

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/s/

Eric Duffy
10/2/01 04:06:11 PM
CHEMIST

Summary of Chemistry Review of NDA 21-287 (Uroxatral)

A. Drug Substances:

Alfuzosin hydrochloride is known to be a specific and selective α_{1}-**adrenergic blocker**. It is a **new molecular entity** with one **chiral** center and manufactured as a **racemic** mixture. It is manufactured by [redacted] (DMF [redacted]) in France **in compliance with cGMP**. The chemistry, manufacturing, and controls information in the DMF [redacted] **is satisfactory**.

The **quality** of alfuzosin hydrochloride is controlled by **specifications** including characteristics, identity, water content, residue on ignition, optical rotation, pH, related substances, assay, and residual solvents. Acceptance criteria for related substances are tightened to reflect the manufacturing capability and stability data, and now all test methods and acceptance criteria are considered to be adequate.

Based on available stability data, **24-month of retest period** was proposed and deemed acceptable.

B. Drug Product:

The drug product is an **extended release** (>20 hours) tablet, which consists of **three layers** of ingredients: **top** non-active diffusible yellow layer which is debossed with "X 10" mark, **middle** white layer containing active ingredient, and **bottom** non-active erodible yellow layer. The active white layer contains **10mg** of **alfuzosin HCl** together with other excipients.

All ingredients in the layers, except for the drug substance, conformed to USP/NF monographs.

The drug product is manufactured by Sanofi-Synthelabo Group, and it is **in compliance with cGMP**.

The **quality** of tablets are controlled by specifications including appearance, identification, uniformity of content, average tablet weight, friability, dissolution, residual ethanol, degradation products, and assay. All **test methods and acceptance criteria** are considered to be **adequate** after appropriately tightened to reflect the manufacturing experience and stability data.

The tablets are **packaged** in round-opaque-twist-off bottles (30ml for 7 and 30 tablets, 75ml for 100 tablets) with cotton. They have child resistance caps with desiccant incorporated. For 1000 tablets, 500ml rectangular opaque bottle is used with desiccant insert and cotton. Also used is a **blister package** for 10 tablets using film blister and aluminum foil backing. All packaging components are deemed adequate for protecting the drug product during the shelf-life.

The sponsor proposed However, since they were not packaged in the to-be-marketed container/closure system, this proposal is not acceptable. The sponsor produced three primary

stability batches with 18-month data at 25°C/60%RH and 6-month data, which were packaged in the to-be-marketed container/closure systems.

Then the sponsor introduced another change to the product at the last stage: debossing them with "X10". The sponsor demonstrated pharmaceutical equivalence between the plain and debossed tablets with comparable dissolution profile and 6-month accelerated stability data obtained from three production batches with to-be-marketed container/closure system.

Although the drug substance is inherently stable and the drug product shows highly comparable stability data, the proposed [redacted] is denied, but based on the analysis of available data from the to-be-marketed product, **24-month of expiry date** is granted.

The tradename, **Uroxatral**, was accepted by OPDRA. The labeling information as well as labels of containers and carton are appropriately revised and deemed satisfactory.

C. Conclusion and Recommendation:

From chemistry, manufacturing, and controls point of view, as the primary reviewer recommends, this NDA may be approved.

/S/

Moo-Jhong Rhee, Ph.D.
Chemistry Team Leader
For the Division of reproductive and Urologic Drug Products
DNDC II, Office of New Drug Chemistry

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/s/

Moo-Jhong Rhee
9/27/01 03:54:03 PM
CHEMIST

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS - HFD-580

Review of Chemistry, Manufacturing and Controls

NDA #: 21-287
CHEMISTRY REVIEW #: 2

DATE REVIEWED: 4-SEP-2001

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Amendment	19-JUL-2001	20-JUL-2001	25-JUL-2001
Amendment	25-JUL-2001	26-JUL-2001	30-JUL-2001
Amendment	30-JUL-2001	31-JUL-2001	01-AUG-2001
Amendment	21-AUG-2001	22-AUG-2001	24-AUG-2001
Amendment	21-AUG-2001	22-AUG-2001	24-AUG-2001
Amendment	29-AUG-2001	30-AUG-2001	31-AUG-2001

NAME & ADDRESS OF SPONSOR:

Sanofi-Synthelabo Inc.
9 Great Valley Parkway
PO Box 3026
Malvern, PA 19355

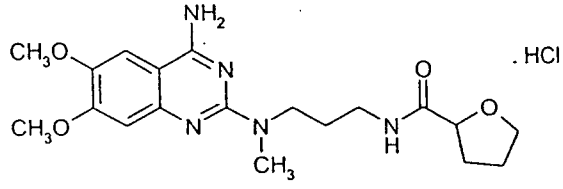
DRUG PRODUCT NAME:

Proprietary:	Uroxatral
Nonproprietary/Established/USAN:	alfuzosin HCl extended release tablets
Code Name/#:	SL77.0499-10
Chem.Type/Ther.Class:	1S

PHARMACOLOGICAL CATEGORY/INDICATION: alpha-blocker for benign prostate hyperplasia

DOSAGE FORM:	Extended release tablet
STRENGTHS:	10 mg
ROUTE OF ADMINISTRATION:	oral
DISPENSED:	__x__ Rx _____ OTC
SPECIAL PRODUCTS:	___ Yes _x_ No

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



(R,S)-N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl] tetrahydro-2-furancarboxamide hydrochloride

Molecular formula: $C_{19}H_{27}N_5O_4 \cdot HCl$
Molecular weight: 425.9
CAS # 81403-68-1

SUPPORTING DOCUMENTS:

Type/Number	Title	Holder	Status	Review Date	Letter Date
DMF	Alfuzosin HCl		Adequate	13-AUG-2001 by S. Tran	Not applicable
DMF			Adequate	8-AUG-2001 by S. Tran	Not applicable
DMF			Adequate	3-AUG-2001 by P. Peri	Not applicable
DMF			Adequate	8-AUG-2001 by S. Tran	Not applicable
DMF			Adequate	8-AUG-2001 by S. Tran	Not applicable

RELATED DOCUMENTS:

- Teleconference minutes on 4-APR-2001
- Chemistry IR letter for NDA 21-287 dated 29-JUL-2001
- Chemistry Review #1 for NDA 21-287 dated 2-JUL-2001
- Chemistry Reviews #1 and #2 for DMF dated 2-JUL-2001 and 13-AUG-2001, respectively
- Chemistry Review #1 for DMF dated 8-AUG-2001
- Chemistry Review #1 for DMF dated 8-AUG-2001
- Chemistry Review #2 for DMF dated 8-AUG-2001
- Chemistry Review #2 for DMF dated 3-AUG-2001
- FDA follow-up letter faxed on 20-AUG-2001

PATENT STATUS:

Patent No.	Type	Expiration	Patent Owner
4,661,491	Method of use	27-MAY-2006	Sanofi-Synthelabo

CONSULTS:

- The proprietary name "Uroxatral" was found to be acceptable by OPDRA on 18-MAY-2001. OPDRA reviewed the 8-DEC-2000 container labels on 23-FEB-2001 (see Chemistry IR letter dated 29-JUL-2001). OPDRA comments on the 8-DEC-2000 container labels were accepted by the applicant and reflected in the revised container labels submitted in the 30-AUG-2001 amendment. Since all issues were resolved, OPDRA has no further comment on the revised container labels. The only graphic representation on the container labels is a yellow arrow that appears in both the 8-DEC-2000 and 30-AUG-2001 labels, and OPDRA has no comment on it.
- Office of Compliance recommended "Acceptable" for facilities listed in the NDA on 3-MAY-2001 (see Chemistry Review #1 for NDA 21-287).
- The Biopharm. review (by V. Jarugula) of the dissolution acceptance criteria recommends "Acceptable" (see 28-AUG-2001 status meeting minutes).

REMARKS/COMMENTS

- Refer to the attached Chemist's Review Notes.
- The drug product to be marketed in the U.S. has "X10" debossed on the surface of the non-active-diffusible layer (thinner yellow layer).
- Outstanding issues from Chem. Review #1 of NDA 21-287 have been satisfactorily resolved (see the attached Chemist's Review Notes).
- As stated by FDA on 4-APR-2001, the expiry for the debossed tablets can be based on the unmarked tablets provided that the 6-month stability data are comparable. Results provided in the 19-JUL-2001 and 25-JUL-2001 amendments show that there is no difference between the unmarked tablets and the debossed tablets under both room temperature and accelerated conditions during the 6-month stability studies. Therefore, the expiry for the debossed tablets is based on the three plain-tablet primary stability batches. Based on data of 18 months at 25 °C/60% RH and 6 months at 40 °C/75% RH, and [redacted], the expiry for the drug product in all container/closure systems should be 24 months at room temperature. The applicant agrees to this expiry in the 21-AUG-2001 amendment.
- Container labels submitted on 30-AUG-2001 and the Physician's Package Insert (Description and How Supplied sections) submitted on 25-JUL-2001 are satisfactory.

CONCLUSIONS & RECOMMENDATIONS:

NDA 21-287 is recommended for APPROVAL from the CMC perspective.

/S/

Suong Tran, PhD
Review Chemist

cc:
Orig. NDA #21-287
HFD-580/Division File
HFD-580/STran/MRhee/EFarinas

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/s/

Suong Tran
9/5/01 10:33:10 AM
CHEMIST

your paper sign-off 9/5/01

Moo-Jhong Rhee
9/5/01 11:01:27 AM
CHEMIST
I concur

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS - HFD-580

Review of Chemistry, Manufacturing and Controls

NDA #: 21-287
CHEMISTRY REVIEW #: 1

DATE REVIEWED: 29-JUN-2001

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Original	8-DEC-2000	8-DEC-2000	14-DEC-2000
Amendment	10-APR-2001	11-APR-2001	12-APR-2001

NAME & ADDRESS OF SPONSOR:

Sanofi-Synthelabo Inc.
9 Great Valley Parkway
PO Box 3026
Malvern, PA 19355

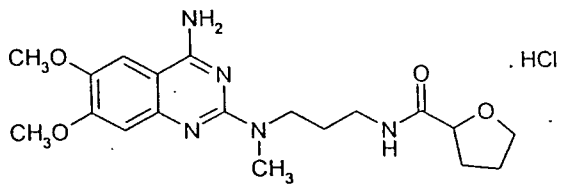
DRUG PRODUCT NAME:

Proprietary:	[to be finalized]
Nonproprietary/Established/USAN:	alfuzosin hydrochloride extended release tablets
Code Name/#:	SL77.0499-10
Chem.Type/Ther.Class:	1S

PHARMACOLOGICAL CATEGORY/INDICATION: alpha-blocker for benign prostate hyperplasia

DOSAGE FORM:	Extended release tablet
STRENGTHS:	10 mg
ROUTE OF ADMINISTRATION:	oral
DISPENSED:	___x___ Rx _____ OTC
SPECIAL PRODUCTS:	___ Yes _x_ No

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



(R,S)-N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl] tetrahydro-2-furancarboxamide hydrochloride

Molecular formula: $C_{19}H_{27}N_5O_4 \cdot HCl$
Molecular weight: 425.9
CAS # 81403-68-1

SUPPORTING DOCUMENTS:

Type/Number	Title	Holder	Status	Review Date	Letter Date
DMF [redacted]	Alfuzosin HCl	[redacted]	Not adequate	16-MAY-2001	2-JUL-2001

DMF			Under review		
DMF			Under review		
DMF			Under review		
DMF			Under review		

RELATED DOCUMENTS:

- Teleconference between FDA and the applicant on 4-APR-2001 to discuss the OPDRA's recommendation of "not acceptable" for the proposed proprietary name '

PATENT STATUS:

Patent No.	Type	Expiration	Patent Owner
4,661,491	Method of use	27-MAY-2006	Sanofi-Synthelabo

CONSULTS:

- In the original submission of the NDA, the applicant proposed the proprietary name This name was found to be unacceptable by OPDRA on 23-FEB-2001. Subsequently, the applicant proposed the name "Uroxatral" which was found to be acceptable by OPDRA on 18-MAY-2001.
- Office of Compliance recommended "Acceptable" for facilities listed in the NDA on 3-MAY-2001 (see the attached report).
- The review of dissolution acceptance criteria by the Biopharm. reviewer is currently ongoing.

REMARKS/COMMENTS

NDA 21-287 is submitted for alfuzosin hydrochloride, a new molecular entity. Reference is made to DMF for alfuzosin hydrochloride. The drug product is a 10-mg extended release tablet. The tablet has three layers compressed together. The middle layer is the drug substance. The outer layers are one diffusible inactive layer and one erodible inactive layer. The drug release is controlled by the reduction of available surface areas as a function of time. The drug product is packaged in blister packs of 10 tablets and bottles of 7, 30, 100, and 1000 tablets.

Amendment dated 10-APR-2001: The applicant requested a teleconference to discuss the implications of OPDRA's recommendation that the proposed proprietary name is unacceptable. Questions for FDA were faxed prior to the teleconference and submitted in this amendment dated 10-APR-2001. It was agreed between FDA and the applicant that stability data for unmarked tablets may be used to establish the expiration dating period, provided that the 6-month accelerated data show comparability between the unmarked tablets and the debossed tablets. Up to the date of this review, the expiration dating period is not yet determined pending the 6-month accelerated data of the debossed tablets to be provided in an amendment during the

review cycle.

CONCLUSIONS & RECOMMENDATIONS:

The NDA currently has incomplete information. Please issue an Information Request letter (refer to the attached Draft Letter).

Suong Tran, PhD
Review Chemist

cc:
Orig. NDA #21-287
HFD-580/Division File
HFD-580/STran/MRhee/EFarinas
HFD-820/EDuffy/CHoiberg
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/s/

Suong Tran
7/2/01 09:20:37 AM
CHEMIST

Moo-Jhong Rhee
7/2/01 09:29:01 AM
CHEMIST

DMF REVIEW

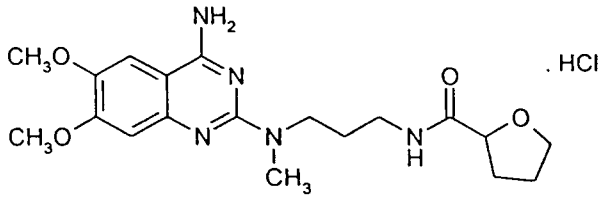
DMF # [redacted] DMF Type II

Title: Alfuzosin HCl

1. **CHEM. REVIEW # 1**

2. **REVIEW DATE:** 29-JUNE-2001

3. **ITEM REVIEWED**



Identification: Alfuzosin HCl
(R,S)-N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl] tetrahydro-2-furancarboxamide hydrochloride
CAS 81403-68-1
Molecular formula: $C_{19}H_{27}N_5O_4 \cdot HCl$
Molecular weight: 425.9

Location in DMF:

Type of Submission	Submission Date	Location	Description/Comment
Amendment	27-OCT-2000	Vol. 1.1	Fully updated DMF.
Original	18-JUN-1997	Vol. 1.1	Original submission.

4. **PREVIOUS DOCUMENTS:**
None

5. **NAME AND ADDRESS OF DMF HOLDER AND REPRESENTATIVE(S):**
DMF Holder:

DMF U.S. Agent:

Sanofi-Synthelabo, Inc.
90 Park Avenue
New York, NY 10016

6. **DMF REFERENCED FOR**

NDA # 21-287
APPLICANT NAME: Sanofi-Synthelabo, Inc.
LOA DATE: 9-OCT-2000
DRUG PRODUCT NAME: (alfuzosin HCl extended-release tablets)
DOSAGE FORM: tablet
STRENGTH: 10 mg
ROUTE OF ADMINISTRATION: oral

7. **SUPPORTING DOCUMENTS:** none

8. **CURRENT STATUS OF DMF:**
   A. This is Chem. Review #1
   B. Latest update: 27-OCT-2000
   C. Latest list of authorized companies: 27-OCT-2000

9. **CONSULTS:** none

10. **COMMENTS:** Further information is requested from the DMF holder regarding manufacturing, controls, and stability.

11. **CONCLUSION:** The DMF is adequate to support NDA 21-287 pending the resolution of outstanding issues delineated in the Information Request letter (attached).

cc:
DMF # [redacted] (2 copies)
HFD-580/EFarinas
HFD-580/STran/MRhee
HFD-820/EDuffy/CHoiberg

/S/ ~ 6/29/2001
Suong T. Tran, Ph.D.
Review Chemist

R/D Init by:

/S/ ~6/29/01
Moo-Jhong Rhee, Ph.D.
Team Leader

Filename: dmf[redacted].doc

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DMF REVIEW

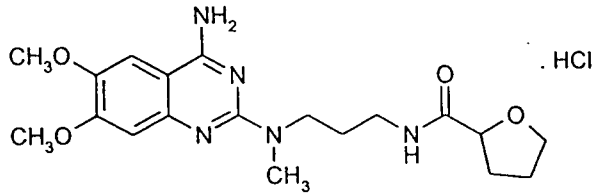
DMF # [redacted] DMF Type II

Title: Alfuzosin HCl

1. CHEM. REVIEW # 2

2. REVIEW DATE: 13-AUG-2001

3. ITEM REVIEWED



Identification: Alfuzosin HCl

(R,S)-N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl] tetrahydro-2-furancarboxamide hydrochloride

CAS 81403-68-1

Molecular formula: $C_{19}H_{27}N_5O_4 \cdot HCl$

Molecular weight: 425.9

Location in DMF:

Type of Submission	Submission Date	Location	Description/Comment
Amendment	3-AUG-2001	Vol. 1.1	Response to Deficiency Letter from Chem. Review #1.

4. PREVIOUS DOCUMENTS:

Type of Submission	Submission Date	Location	Description/Comment
Amendment	27-OCT-2000	Vol. 1.1	Fully updated DMF.
Original	18-JUN-1997	Vol. 1.1	Original submission.

5. NAME AND ADDRESS OF DMF HOLDER AND REPRESENTATIVE(S):

DMF Holder:

DMF U.S. Agent:

Sanofi-Synthelabo, Inc.
90 Park Avenue
New York, NY 10016

6. DMF REFERENCED FOR

NDA # 21-287
APPLICANT NAME: Sanofi-Synthelabo, Inc.
LOA DATE: 9-OCT-2000
DRUG PRODUCT NAME: (alfuzosin HCl extended-release tablets)
DOSAGE FORM: tablet
STRENGTH: 10 mg

ROUTE OF ADMINISTRATION: oral

7. **SUPPORTING DOCUMENTS:** none

8. **CURRENT STATUS OF DMF:**
   A. Chem. Review #1 dated 2-JUL-2001: deficient DMF.
   B. Latest update: 27-OCT-2000
   C. Latest list of authorized companies: 27-OCT-2000

9. **CONSULTS:** none

10. **COMMENTS:** The response to Chem. Review #1 Deficiency Letter is acceptable.

11. **CONCLUSION:** The DMF is adequate to support NDA 21-287.

cc:
DMF # (2 copies)
HFD-580/EFarinas
HFD-580/STran/MRhee

/S/ 8/13/01
Suong T. Tran, Ph.D.
Review Chemist

R/D Init by: 8/20/01

V
Moo-Jhong Rhee, Ph.D.
Team Leader

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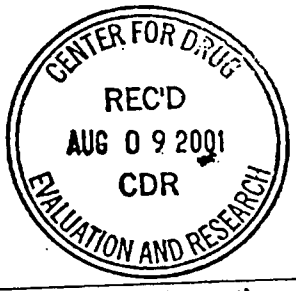
ORIGINAL

DMF REVIEW

DMF # [redacted] DMF Type III

Title: [redacted]



1. CHEM. REVIEW #1
2. REVIEW DATE: 01-AUG-2001
3. ITEM REVIEWED
   Identification: [redacted]
   Location in DMF:

Type of Submission	Date of Submission	Location of Information
Amendment	22-JUN-2000	Vol. 12.1

4. PREVIOUS DOCUMENTS:

Type of Submission	Date of Submission	Location of Information
Amendments and reviews	Over decades	More than a dozen volumes

5. NAME AND ADDRESS OF DMF HOLDER AND REPRESENTATIVE(S):
   DMF Holder:

6. DMF REFERENCED FOR:
   NDA 21-287
   APPLICANT NAME: Sanofi-Synthelabo
   LOA DATE: 28-JUN-2000
   DRUG PRODUCT NAME: Uroxatral (alfuzosin HCl extended release) Tablets
   DOSAGE FORM: extended release tablet
   STRENGTH: 10 mg
   ROUTE OF ADMINISTRATION: Oral
7. SUPPORTING DOCUMENTS: None
8. CURRENT STATUS OF DMF: Active
   Date of last update (for this [redacted]): 2-MAY-2000
   Date of most recent list of companies for which LOAs have been provided: 31-JAN-2001
9. CONSULTS: none
10. COMMENTS: All information provided for [redacted] is satisfactory.
11. CONCLUSION: This DMF is adequate to support NDA 21-287.

cc:
DMF [redacted] (2 copies)
HFD-580/EFarinas/STran/MRhee

/S/ 8/1/01

Suong T. Tran, Ph.D.
Review Chemist

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Filename: dmf[redacted]1.doc

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ORIGINAL

DMF REVIEW

DMF # [redacted] DMF Type III

Title: [redacted]

1. CHEM. REVIEW #1
2. REVIEW DATE: 02-AUG-2001
3. ITEM REVIEWED

Identification: [redacted]

Location in DMF:

Type of Submission	Date of Submission	Location of Information
Amendment	17-NOV-1999	Vol. 1.1

4. PREVIOUS DOCUMENTS: none for [redacted]

5. NAME AND ADDRESS OF DMF HOLDER AND REPRESENTATIVE(S):

DMF Holder:

U.S. Agent:

6. DMF REFERENCED FOR:

NDA 21-287
APPLICANT NAME: Sanofi-Synthelabo
LOA DATE: 28-JUN-2000
DRUG PRODUCT NAME: Uroxatral (alfuzosin HCl extended release) Tablets
DOSAGE FORM: extended release tablet
STRENGTH: 10 mg
ROUTE OF ADMINISTRATION: Oral

7. SUPPORTING DOCUMENTS: None
8. CURRENT STATUS OF DMF: Active

Date of last update (for this [redacted]): 17-NOV-1999
Date of most recent list of companies for which LOAs have been provided: 30-MAY-2001

9. CONSULTS: none
10. COMMENTS: All information provided for [redacted] is satisfactory.
11. CONCLUSION: This DMF is adequate to support NDA 21-287.

cc:
DMF # [redacted] (2 copies)
HFD-580/EParinas/STran/MRhee

/S/ 8/2/01

Suong T. Tran, Ph.D.
Review Chemist

R/D Init by: /S/ 8/8/01

Filename: dmf[redacted]#1.doc

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confidential

commercial

information

ORIGINAL

DMF REVIEW

DMF # [redacted] **DMF Type III**

Title: [redacted]

1. **CHEM. REVIEW #2**
2. **REVIEW DATE: 07-AUG-2001**
3. **ITEM REVIEWED**
   Identification: [redacted] 30-mL and 75-mL twist-off [redacted] bottles, 500-mL [redacted] bottle, [redacted] cap 28 cap [redacted] and [redacted] cap [redacted]
   Location in DMF:

Type of Submission	Date of Submission	Location of Information
Amendment	14-SEP-1999	Vol. 1.1
Amendment	19-SEP-2000	Vol. 1.1

4. **PREVIOUS DOCUMENTS:** previous amendments are superseded by the latest amendment

5. **NAME AND ADDRESS OF DMF HOLDER AND REPRESENTATIVE(S):**
   DMF Holder/Contact:

6. **DMF REFERENCED FOR:**
   NDA 21-287
   APPLICANT NAME: Sanofi-Synthelabo
   LOA DATE: 28-JUN-2000
   DRUG PRODUCT NAME: Uroxatral (alfuzosin HCl extended release) Tablets
   DOSAGE FORM: extended release tablet
   STRENGTH: 10 mg
   ROUTE OF ADMINISTRATION: Oral
7. **SUPPORTING DOCUMENTS:** None
8. **CURRENT STATUS OF DMF:** Active (adequate per Chem.Rev. #1 on 13-JAN-1998)
   Date of last update: 19-SEP-2000
   Date of most recent list of companies for which LOAs have been provided: 19-SEP-2000
9. **CONSULTS:** none
10. **COMMENTS:** All information in the DMF is satisfactory.
11. **CONCLUSION:** This DMF is adequate to support NDA 21-287 (tablet dosage form packaged in bottles).

cc:
DMF # [redacted] (2 copies)
HFD-580/EFarinas/STran/MRhee

/s/ 8/7/01

Suong T. Tran, Ph.D.
Review Chemist

R/D Init by: /s/ 8/8/01

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NDA 21-287
Alfuzosin Hydrochloride
10 mg extended release tablets

Environmental Assessment

- Not applicable to this application cycle. See page 28 of Chemistry Review #1 addressing Environmental Assessment.

/S/
M.S. RD.
5/15/03

APPEARS THIS WAY
ON ORIGINAL

NDA 21-287
Alfuzosin hydrochloride

Environmental Assessment

See page 28 of Chemistry Review #1 addressing Environmental Assessment, attached.

D. Environmental Assessment

Satisfactory
[3: 234]

The sponsor has requested a categorical exclusion under 21 CFR § 25.31(a).

F. Labeling

NDA 21-287
Alfuzosin Hydrochloride
10 mg extended release tablets

Microbiology Review

Not applicable to this application cycle (microbiology review is not required for oral tablets).

/S/, M.S., R.D.
5/05/03

NDA 21-287
Alfuzosin hydrochloride

Microbiology Review

No microbiology review is required for oral Tablets.

NDA 21-287
Alfuzosin Hydrochloride
10 mg extended release tablets

Facilities Inspection (EES)

- Not applicable to this application cycle. Refer to pages 32-33 of Chemistry Review #1 addressing Establishment Inspections.

S

1.S. R.D.
5/15/03

NDA 21-287
Alfuzosin hydrochloride

EER

Pages 32 and 33 of Chemistry Review #1 dated July 2, 2001, addressing Establishment Inspections are attached.

G. Establishment Inspection **Satisfactory**

Office of Compliance recommended "Acceptable" for facilities listed in the NDA on 3-MAY-2001 (see the attached report).

APPEARS THIS WAY
ON ORIGINAL

16-MAY-2001

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 21287/000
Stamp: 08-DEC-2000 Regulatory Due: 08-OCT-2001
Applicant: SANOFI SYN RES
9 GREAT VALLEY PKY
MALVERN, PA 19355

Priority: S
Action Goal:
Org Code: 580
District Goal: 09-AUG-2001
Brand Name: ALFUZOSIN HCL 10MG E-R TABLEYS
Established Name:
Generic Name: ALFUZOSIN HCL 10MG E-R TABLETS
Dosage Form: EXT (EXTENDED-RELEASE TABLET)
Strength: 10 MG

FDA Contacts:			
	E. FARINAS	(HFD-580)	301-827-4260 , Project Manager
	S. TRAN	(HFD-580)	301-827-4260 , Review Chemist
	M. RHEE	(HFD-580)	301-827-4237 , Team Leader

Overall Recommendation:

ACCEPTABLE on 03-MAY-2001 by M. GARCIA (HFD-322) 301-594-0095

Establishment: 9617678
SANOFI SYNTHELABO INC
30-36 AVENUE GUSTAV EIFFEL BP 71
TOURS, CEDEX, FR 37071

DMF No:
AADA No:

Profile: TTR
OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 03-MAY-2001
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities: FINISHED DOSAGE MANUFACTURER

Establishment:

DMF No:
AADA No:

Profile: CSN
OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 05-FEB-2001
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities:

NDA 21-287
Alfuzosin Hydrochloride
10 mg extended release tablets

Methods Validation

Not applicable to this application cycle. Refer to page 28 of Chemistry Review # 1 addressing Methods Validation.

/S/

J, M.S., R.D.
5/15/03

NDA 21-287
Alfuzosin hydrochloride

Methods Validation

See page 28 of Chemistry Review #1 addressing Methods Validation, attached.

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