CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-287

Administrative Documents

ITEM 13. PATENT INFORMATION

Pursuant to § 505 of the Federal Food, Drug and Cosmetics Act (FFDCA), as amended by the Drug Price Competition and Patent Term Restoration Act of 1984, applicants hereby submit information on each patent that claims the drug, drug product, or a method of using the drug and with respect to which a claim of infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use or sale of the drug product described in this application.

United States Patent Number	Expiration Date	Type of Patent	Patent Owner
4,661,491	May 27, 2006	Method of Use	Sanofi-Synthelabo

The following party is authorized to receive notice of patent certification under § 505(b)(3) and (j)(2)(B) of the FFDCA and §§ 314.52 and 314.95 of 21 C.F.R:

Sanofi-Synthelabo Inc.
Patent Counsel
9 Great Valley Parkway
P.O. Box 3026
Malvern, Pennsylvania
19355

REQUEST FOR EXCLUSIVITY

Pursuant to §§ 505(j)(4)(D)(ii) and 505(c)(3)(D)(ii) of the Federal Food, Drug and Cosmetics Act, applicants are requesting a five-year period of marketing exclusivity from the date of approval of this NDA for alfuzosin hydrochloride.

This request for exclusivity is based upon the following:

(a) No active ingredient of the drug product for which approval is being sought has ever been approved in another drug product in the United States either as a single entity or as a part of a combination product; and

(b) No active ingredient of the drug product has ever been previously marketed in a drug product in the United States.

16. Debarment Certification

Sanofi-Synthelabo, Inc. hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug and Cosmetic Act in connection with this application.

Porter McMillian
Executive Vice President

ITEM 13. PATENT INFORMATION

Pursuant to § 505 of the Federal Food, Drug and Cosmetics Act (FFDCA), as amended by the Drug Price Competition and Patent Term Restoration Act of 1984, applicants hereby submit information on each patent that claims the drug, drug product, or a method of using the drug and with respect to which a claim of infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use or sale of the drug product described in this application.

United States Patent Number	Expiration Date	Type of Patent	Patent Owner
4,661,491	May 27, 2006	Method of Use	Sanofi-Synthelabo
— 6,149,940	August 22, 2017	Drug Product	Sanofi-Synthelabo and Jagotec AB

The following party is authorized to receive notice of patent certification under § 505(b)(3) and (j)(2)(B) of the FFDCA and §§ 314.52 and 314.95 of 21 C.F.R:

Sanofi-Synthelabo Inc.
Patent Counsel
9 Great Valley Parkway
P.O. Box 3026
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19355

REQUEST FOR EXCLUSIVITY

Pursuant to §§ 505(j)(4)(D)(ii) and 505(c)(3)(D)(ii) of the Federal Food, Drug and Cosmetics Act, applicants are requesting a five-year period of marketing exclusivity from the date of approval of this NDA for alfuzosin hydrochloride.

This request for exclusivity is based upon the following:

(a) No active ingredient of the drug product for which approval is being sought has ever been approved in another drug product in the United States either as a single entity or as a part of a combination product; and

(b) No active ingredient of the drug product has ever been previously marketed in a drug product in the United States.

ITEM 14. PATENT DECLARATION

The undersigned declares that U.S. Patent Nos. 4,661,491 and 6,149,940 cover a formulation, composition and/or method of use of alfuzosin hydrochloride. This product is the subject of this application for which approval is being sought.

Michael D. Alexander

MICHAEL D. ALEXANDER
Sr. Managing Attorney -
Intellectual Property
Sanofi-Synthelabo Inc.

NDA 21-287
Alfuzosin Hydrochloride
10 mg extended release tablet

EXCLUSIVITY SUMMARY for NDA # NDA 21-287
Trade Name pending; former tradename- Uroxatral
Generic Name alfuzosin hydrochloride
Applicant Name Sanofi-Synthelabo Research HFD- 580
Approval Date June 12, 2003

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

   a) Is it an original NDA? YES/_X__/ NO /__/

   b) Is it an effectiveness supplement? YES /__ / NO /_X__/

      If yes, what type (SE1, SE2, etc.)?

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

      YES /_X__/ NO /___/

      If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

      If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES /_X_/ NO /___/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

___ _ Five years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /_X__/

* The indicated disease/condition (BPH)does not exist in children.

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC) Switches should be answered No - Please indicate as such).

YES /___/ NO /__X_/

If yes, NDA # _____ Drug Name

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /_X__/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE

NDA 21-287
Alfuzosin Hydrochloride
10 mg extended release tablet

SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /_X__/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #

NDA # _____ _____

NDA # _____ _____

2. Combination product. N/A

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not

previously approved.)

YES /___/ NO /__/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #

NDA #

NDA #

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /___/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the

Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /___/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's

conclusion? If not applicable, answer NO.

YES /___/ NO /__/

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # _____

Investigation #2, Study # _____

Investigation #3, Study # _____

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved

drug, answer "no.")

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study #
NDA # _____ Study #
NDA # _____ Study #

(b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study #

NDA # _____ Study #

NDA # _____ Study #

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #1, Study # _____

Investigation #2, Study # _____

Investigation #_3_, Study # _____

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1		
IND # _____ YES /__/	NO /___/	Explain:
Investigation #2		
IND # ____ YES /___/	NO /___/	Explain:
Investigation #3		
IND # _____ YES /_ __/	NO /___/	Explain:

Investigation #4	
IND # _____ YES /_ __/	NO /___/ Explain:
Investigation #5	
IND # _____ YES /__/	NO /___/ Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____
Investigation #2	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /__/

If yes, explain: _____

_____

_____

_____
Signature of Preparer Date
Title:

NDA 21-287
Alfuzosin Hydrochloride
10 mg extended release tablet

Signature of Office or Division Director Date

cc:
Archival NDA
HFD- /Division File
HFD- /RPM
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

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

/s/

Donna Griebel
6/12/03 07:19:53 PM

EXCLUSIVITY SUMMARY for NDA # 21-287 **SUPPL #** _____

Trade Name _____ **Generic Name** Alfuzosin HCL

Applicant Name Sanofi-Synthelabo **HFD-** 580

Approval Date _____

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

   a) Is it an original NDA? YES/ X / NO /___/

   b) Is it an effectiveness supplement? YES /___/ NO / X /

   If yes, what type(SE1, SE2, etc.)? _____

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

   YES / X / NO /___/

   If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

   _____

   _____

   If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

   _____

   _____

d) Did the applicant request exclusivity?

YES /_x_/ NO /___/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

Five years (5)

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /_X_/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC Switches should be answered No - Please indicate as such).

YES /___/ NO /_x_/

If yes, NDA # _____ Drug Name _____

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /_x_/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /X/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /___/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

_____

_____

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain: _____

_____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # _____

Investigation #2, Study # _____

Investigation #3, Study # _____

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study # _____
NDA # _____ Study # _____
NDA # _____ Study # _____

(b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study # _____

NDA # _____ Study # _____

NDA # _____ Study # _____

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #__, Study # _____

Investigation #__, Study # _____

Investigation #__, Study # _____

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1	
IND # _____ YES /___/	NO /___/ Explain: _____
	_____
	_____
Investigation #2	
IND # _____ YES /___/	NO /___/ Explain: _____
	_____
	_____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____
Investigation #2	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

_____

_____

_____ _____

Signature of Preparer Date

Title:_____

_____ _____

Signature of Office of Division Director Date

cc:
Archival NDA
HFD- /Division File
HFD- /RPM
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

Form OGD-01347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

NDA 21-287
Alfuzosin Hydrochloride
10 mg extended release tablets

PEDIATRIC PAGE

(Complete for all APPROVED original applications and efficacy supplements)

NDA/BLA # : 21-287 Supplement Type (e.g. SE5): _____

Supplement Number: Amendment #36 Complete response to Approvable Action

Stamp Date: December 8, 2000; December 12, 2002 Action Date: June 12, 2003

HFD 580

Trade and generic names/dosage form: Tradename- pending; former tradename- Uroxatral
Generic: **alfuzosin hydrochloride,** 10 mg - extended release

Applicant: Sanofi-Synthelabo Research

Therapeutic Class: 1S

Indication(s) previously approved: N/A

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 1

Indication #1: Treatment of the signs and symptoms of benign prostatic hyperplasia

Is there a full waiver for this indication (check one)?

- ☐ X Yes: Please proceed to Section A.
- ☐ No: Please check all that apply: ___Partial Waiver __ Deferred ____Completed
  NOTE: More than one may apply
  Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- ☐ Products in this class for this indication have been studied/labeled for pediatric population
- ☐ X Disease/condition does not exist in children
- ☐ Too few children with disease to study
- ☐ There are safety concerns
- ☐ Other: _____

* Alfuzosin is not indicated for use in children. A pediatric waiver has been requested and granted (August 20, 2000).

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min____ kg_____ mo._____ yr. ____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____

Reason(s) for partial waiver:

- ☐ Products in this class for this indication have been studied/labeled for pediatric population
- ☐ Disease/condition does not exist in children
- ☐ Too few children with disease to study
- ☐ There are safety concerns
- ☐ Adult studies ready for approval
- ☐ Formulation needed

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg_____ mo._____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____

Reason(s) for deferral:

- ☐ Products in this class for this indication have been studied/labeled for pediatric population
- ☐ Disease/condition does not exist in children
- ☐ Too few children with disease to study
- ☐ There are safety concerns
- ☐ Adult studies ready for approval
- ☐ Formulation needed

Other:_____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min ____ kg_____ mo._____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA
HFD-950/ Terrie Crescenzi
HFD-960/ Grace Carmouze
(revised 9-24-02)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960
301-594-7337

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

/s/

Donna Griebel
6/12/03 06:44:17 PM

NDA 21-287
Alfuzosin HCl
Sanofi-Synthelabo

Pediatric Page

Not applicable for this application.

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

/s/

Jean R. King
6/12/03 06:27:58 PM
CSO

Jean R. King
6/12/03 06:35:17 PM
CSO

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information			
NDA 21-287	Efficacy Supplement Type SE- N/A	Supplement Number:	
Drug: **alfuzosin hydrochloride**		Applicant: Sanofi-Synthelabo Research	
RPM: Jean King, M.S., R.D.		HFD-580	Phone # 301-827-4620
Application Type: (X) 505(b)(1) ( ) 505(b)(2)		Reference Listed Drug (NDA #, Drug name):	

❖ Application Classifications:	
• Review priority	(X) Standard ( ) Priority
• Chem class (NDAs only)	1S
___• Other (e.g., orphan, OTC)	N/A
❖ User Fee Goal Dates	June 12, 2003
❖ Special programs (indicate all that apply)	(X) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information	
• User Fee	(X) Paid
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (X) No
• This application is on the AIP	( ) Yes (X) No
• Exception for review (Center Director's memo)	N/A
• OC clearance for approval	N/A
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.	(X) Verified
❖ Patent	
• Information: Verify that patent information was submitted	(X) Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(*i*)(A) ( ) I ( ) II ( ) III ( ) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	( ) Verified

❖ Exclusivity (approvals only)	
• Exclusivity summary	X
• Is there an existing orphan drug exclusivity protection for the active moiety for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of sameness for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification!*	( ) Yes, Application #_____ (X) No
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	X
General Information	
❖ Actions	
• Proposed action	(X) AP ( ) TA ( ) AE ( ) NA
• Previous actions (specify type and date for each action taken)	Approvable, 10/8/2000
• Status of advertising (approvals only)	(X) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	(X) Yes ( ) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(X) None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable)	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	X
• Most recent applicant-proposed labeling	X
• Original applicant-proposed labeling	X
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	X
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	X (Flomax, Cardura, and Hytrin)
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	X
• Applicant proposed	X
• Reviews	X
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	X
• Documentation of discussions and/or agreements relating to post-marketing commitments	N/A
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	X
❖ Memoranda and Telecons	X
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	X (11/10/1999)
• Pre-NDA meeting (indicate date)	X (12/8/2000)
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	N/A

❖ Advisory Committee Meeting	
• Date of Meeting	May 29, 2003
• 48-hour alert	May 30, 2003
❖ Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	N/A
Summary Application Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	X
Clinical Information	
❖ Clinical review(s) *(indicate date for each review)*	X
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	N/A
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	X (see pages 14-23 of clinical review # 2)
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	X
❖ Statistical review(s) *(indicate date for each review)*	X
❖ Biopharmaceutical review(s) *(indicate date for each review)*	X
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	X
• Bioequivalence studies	N/A
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	X
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	X (See Chemistry Review #1)
• Review & FONSI *(indicate date of review)*	N/A
• Review & Environmental Impact Statement *(indicate date of each review)*	N/A
❖ Micro (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	N/A
❖ Facilities inspection (provide EER report)	Date completed: See pages 32-33 of Chemistry Review #1 (X) Acceptable ( ) Withhold recommendation
❖ Methods validation	( ) Completed ( ) Requested (X) Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	X
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	N/A
❖ CAC/ECAC report	X (12/11/00)

Meeting Minutes

Date: January 31, 2003 **Time** 11:00 AM – 12:00 PM **Location**: PKLN; 17B-43

NDA: 21,287 **Drug:** Alfuzosin hydrochloride

Indication: treatment of signs and symptoms of benign prostatic hyperplasia

Sponsor: Sanofi-Santhelabo, Inc.

Type of Meeting: Filing Meeting

Meeting Chair: George Benson, M.D., Urology Team Leader

Meeting Recorder: Jean King, M.S., R.D., Project Manager

FDA/CDER/DRUDP Attendees:
Medical Team Leader: George Benson, M.D.
Medical Officer: Marcea Whitaker, M.D.
Chemistry Reviewer: Suong Tran, Ph.D.
Clinical Pharmacology Team Leader: Ameeta Parekh, Ph.D.
Clinical Pharmacology Reviewer: Venkat Jarugula, Ph.D.
Pharmacology/Toxicology Reviewer: Laurie McLeod-Flynn, Ph.D.
Biometrics Team Leader: Mike Welch, Ph.D.

Meeting Objective: This was the 45-day internal team meeting to discuss the filing status of the sponsor's complete response submission for NDA 21-287, alfuzosin hydrochloride, 10 mg Extended Release Tablets, Chemical and Therapeutic Class 1.

Issues Discussed/Decisions Made:

Submission Date: December 8, 2000
Previous Action: Approvable on October 8, 2001
Resubmission Date: December 12, 2002
PDUFA Date: June 12, 2003

Clinical

The following is an area of concern. We will request additional clarifying information from the sponsor in the Day 74 Filing Letter:

Please refer to Study PDY 5105 entitled "Effect of supra-therapeutic doses of alfuzosin ER on QT interval, using a rate-independent method, compared to placebo and to moxifloxacin in healthy volunteers". In Table (15.2.1) on page 78 of 100 and a similar table on page 7 of 100, the "n" value representing the number of patients whose data are analyzed varies between groups. Please provide an explanation for this variation.

Clinical Pharmacology and Biopharmaceutics

No review issues noted at time of filing.

Chemistry

No review issues noted at time of filing.

Statistics

No review issues noted at time of filing. However, to facilitate review, we will request that the sponsor submit electronic SAS transport files containing the raw QT data sets from Study PDY 5105. Data dictionaries should accompany this submission.

Pharmacology/Toxicology

No review issues noted at time of filing.

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

/s/

Jean R. King
6/12/03 06:22:26 PM
CSO

Jean R. King
6/12/03 06:23:46 PM
CSO

ADMINISTRATIVE REVIEW OF NDA (review pkg)
OFFICE OF DRUG EVALUATION III

NDA: 21-287
Drug: Uroxatral (alfuzosin hydrochloride) extended release tablets
Classification: 1/S
Sponsor: Sanofi-Synthelabo
Project Manager/CSO: E. Farinas

Reviewer: M. McNeil
Review Date: 9/27/01

Review Cycle 1
Date Submitted: 12/8/00
Date Received: 12/8/00
Primary Goal Date: 10/8/01
Secondary Goal Date: 12/8/01
Extended Goal Date: N/A
Proposed Action: AE

	CONFORMS TO REGS & CDER POLICY	COMMENTS
ACTION LETTER		Letter revised to include language from CSL
PATENT STATEMENT	x	
EXCLUSIVITY CHECKLIST		Currently in draft; not needed until AP action taken
DEBARMENT STATEMENT	x	
PEDIATRIC PAGE		Not needed until approval action taken
TRADE NAME REVIEW	x	
DSI AUDITS	x	3 sites inspected: 1 NAI; 2 tentatively classified as VAI
FACILITY INSPECTIONS	x	

REVIEWS	COMPLETED	COMMENTS
DIV. DIR. MEMO		Currently in draft; finalize before action

TL MEMO	x	Currently in draft; finalize before action
CLINICAL	x	Currently in draft; finalize before action
SAFETY UPDATE	x	Part of draft MOR
FINANCIAL DISCLOSURE	x	
STATISTICAL	x	
BIOPHARM		Currently in draft; finalize before action
CMC	x	Team Leader memo still in draft; finalize before action
EA	x	
MICRO (validation of sterilization)		N/A
STABILITY (stats)	x	See CMC review #1 and #2
PHARM/TOX	x	
CAC (stats)	x	
CAC/ECAC REPORT	x	

Labeling: Still being negotiated with applicant
Phase 4 Commitments: None
Advisory Committee Meeting: None held
Comments:

1. All draft reviews should be finalized before taking an action.
2. The letter will be revised to use standard CSL language.
3. Consistent nomenclature for the drug product will be used throughout the letter and labeling.

Update: Division decided not to include labeling with AE letter, given that the applicant is being asked to do some PK/PD studies to characterize a safety signal (QT prolongation). This application was given an AE action on October 5, 2001. All regulatory and policy elements were met.

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

/s/

Melodi McNeil
10/5/01 03:56:47 PM
CSO

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

NDA 21-287 /SE_____ - _____

Drug Alfuzosin hydrochloride Applicant Sanofi-Synthelabo

RPM Evelyn R. Farinas Phone 301-827-4245

x☐505(b)(1)
☐505(b)(2) Reference listed drug _____

~~☐~~Fast Track ☐Rolling Review Review priority: x☐ S ☐P

Pivotal IND(s) _____

Application classifications:
Chem Class _____
Other (e.g., orphan, OTC) _____

PDUFA Goal Dates:
Primary October 8, 2001
Secondary _____

Arrange package in the following order:

Indicate N/A (not applicable), X (completed), or add a comment.

GENERAL INFORMATION:

- User Fee Information: x☐ User Fee Paid
  ☐ User Fee Waiver (attach waiver notification letter)
  ☐ User Fee Exemption

- Action Letter.....Draft..... ☐AP x☐ AE ☐NA

- Labeling & Labels
  FDA revised labeling and reviews..... X
  Original proposed labeling (package insert, patient package insert) x
  Other labeling in class (most recent 3) or class labeling..... x
  Has DDMAC reviewed the labeling? ..... x ☐ Yes (include review) ☐ No
  Immediate container and carton labels x
  Nomenclature review x

- Application Integrity Policy (AIP) ☐ Applicant is on the AIP. This application ☐ is x☐ is not on the AIP.
  Exception for review (Center Director's memo)..... _____
  OC Clearance for approval..... _____

Continued ⇨

- Status of advertising (if AP action) ☐ Reviewed (for Subpart H – attach review) ☐ Materials requested in AP letter

- Post-marketing Commitments NA
  - Agency request for Phase 4 Commitments.....
  - Copy of Applicant's commitments .....

- Was Press Office notified of action (for approval action only)?..... ☐ Yes x☐ No
  - Copy of Press Release or Talk Paper.....

- Patent
  - Information [505(b)(1)] x
  - Patent Certification [505(b)(2)].....
  - Copy of notification to patent holder [21 CFR 314.50 (i)(4)].....

- Exclusivity Summary X

- Debarment Statement X

- Financial Disclosure X
  - No disclosable information .....
  - Disclosable information – indicate where review is located .....

- Correspondence/Memoranda/Faxes X

- Minutes of Meetings X
  - Date of EOP2 Meeting August 13, 1997
  - Date of pre NDA Meeting May 24, 2000
  - Date of pre-AP Safety Conference NA

- Advisory Committee Meeting ..... NA
  - Date of Meeting .....
  - Questions considered by the committee .....
  - Minutes or 48-hour alert or pertinent section of transcript .....

- Federal Register Notices, DESI documents ..... NA

CLINICAL INFORMATION: **Indicate N/A (not applicable), X (completed), or add a comment.**

- Summary memoranda (e.g., Office Director's memo, Division Director's memo, Group Leader's memo) .....

- Clinical review(s) and memoranda x
  draft.....

Continued ⇨

- Safety Update review(s) x

- Pediatric Information
  ☐ Waiver/partial waiver (Indicate location of rationale for waiver) ☐ Deferred
  Pediatric Page..... _____
  ☐ Pediatric Exclusivity requested? ☐ Denied ☐ Granted ☐ Not Applicable

- Statistical review(s) and memoranda x

- Biopharmaceutical review(s) and memoranda..... x

- Abuse ~~Lia~~bility review(s) ..... NA
  Recommendation for scheduling ..... _____

- Microbiology (efficacy) review(s) and memoranda ..... NA

- DSI Audits X
  x☐Clinical studies ☐ bioequivalence studies ..... _____

CMC INFORMATION: **Indicate N/A (not applicable), X (completed), or add a comment.**

- CMC review(s) and memoranda x

- Statistics review(s) and memoranda regarding dissolution and/or stability ..... NA

- DMF review(s) x

- Environmental Assessment review/FONSI/Categorical exemption x

- Micro (validation of sterilization) review(s) and memoranda ..... NA

- Facilities Inspection (include EES report)
  Date completed May 3, 2001 ..... x☐ Acceptable ☐ Not Acceptable

- Methods Validation ..... ☐ Completed x☐ Not Completed

PRECLINICAL PHARM/TOX INFORMATION: **Indicate N/A (not applicable), X (completed), or add a comment.**

- Pharm/Tox review(s) and memoranda x

- Memo from DSI regarding GLP inspection (if any) ..... NA

Continued ⇨

- Statistical review(s) of carcinogenicity studies x
- CAC/ECAC report x

ITEM 18. User Fee Cover Sheet (Form FDA 3397)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS

Sanofi-Synthelabo Inc.
90 Park Ave.
NY, NY 10016

2. TELEPHONE NUMBER *(Include Area Code)*

( )

3. PRODUCT NAME

Alfuzosin hydrochloride

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?
IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:

☒ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____ (APPLICATION NO. CONTAINING THE DATA).

5. USER FEE I.D. NUMBER

4010

6. LICENSE NUMBER / NDA NUMBER

NDA 21-287

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 *(Self Explanatory)*

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY *(Self Explanatory)*

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES ☒ NO *(See reverse side if answered YES)*

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Richard P. Gural, Ph.D.	Vice President Regulatory Affairs	8/25/00

OCT. 3 2000 7:36AM

This is Manhattan Bank
Funds Transfer
4 New York Plaza
New York, NY 10004

Date 00/09/25
Our Ref. (TRN NO.) 0014700269GP
Please mention our Reference No. (TRN) in any correspondence.
Originator's Date 00/09/25
Related Ref. No. PHN OF 00/09/25

ORIGINAL
ADVICE OF DEBIT

WE DEBIT YOUR ACCOUNT NO [redacted]
FOR PAYMENT INDICATED SAME DAY FUNDS

$285,740.00**

SANOFI-SYNTHELABO
ATTN: MR. MICHAEL WILLIAMS
90 PARK AVENUE - 5TH FLOOR
NEW YORK NY 10016-

BENEFICIARY:
FOOD AND DRUG ADMINISTRATION

PAID THRU FED TO:
MELLON BANK N.A.
PITTSBURGH PA 15259-0001

IMAD:0925 B1QGC05C 001793
OMAD:

DETAILS OF PAYMENT
INV. NBR. NDA21-287, USER FEE ID
NBR. 4010

Authorized Signature

Confirmation Report – Memory Send

Page : 001
Date & Time: Jun-12-03 08:01pm
Line 1 : 301-827-4267
Line 2 :
Machine ID : FDA/CDER/OND/ODE3/DRUDP

Job number : 207

Date : Jun-12 07:57pm

To : ☎916108896993

Number of pages : 025

Start time : Jun-12 07:57pm

End time : Jun-12 08:01pm

Pages sent : 025

Status : OK

Job number : 207 *** SEND SUCCESSFUL ***

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE III

FACSIMILE TRANSMITTAL SHEET

DATE: June 12, 2003

To: Jon Villaume, Ph.D.
Company: Sanofi-Synthelabo, Inc.
Fax number: 610-889-6993
Phone number: 610-889-6028

From: Jean King
Division of Division of Reproductive and Urologic Drug Products
Fax number: 301-827-4267
Phone number: 301-827-4260

Subject: NDA 21-287: approval letter

Total no. of pages including cover:

Comments: Please see below.

Document to be mailed: YES NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-4260. Thank you.

Dear Dr. Villaume,

Please find attached the final approval letter for NDA 21-287 for Uroxatral (alfuzosin hydrochloride) extended release tablets, 10 mg per day.

Sincerely,

Jean King, M.S., R.D.
Regulatory Project Manager

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE III

FACSIMILE TRANSMITTAL SHEET

DATE: June 12, 2003

To: Jon Villaume, Ph.D.

Company: Sanofi-Synthelabo, Inc.

Fax number: 610-889-6993

Phone number: 610-889-6028

From: Jean King

Division of Division of Reproductive and Urologic Drug Products

Fax number: 301-827-4267

Phone number: 301-827-4260

Subject: NDA 21-287: approval letter

Total no. of pages including cover:

Comments: Please see below.

Document to be mailed: **YES** **NO**

Dear Dr. Villaume,

Please find attached the final approval letter for NDA 21-287 for Uroxatral (alfuzosin hydrochloride) extended release tablets, 10 mg per day.

Sincerely,

Jean King, M.S., R.D.
Regulatory Project Manager

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: October 5, 2001

To: Jon Villaume	**From:** Evelyn R. Farinas
Company: Sanofi-Synthelabo	Division of Division of Reproductive and Urologic Drug Products
Fax number: 9.1.-610-889-6910	**Fax number:** 301-827-4267
Phone number: 9-1-610-889-6028	**Phone number:** 301-827-4260

Subject: action letter - Approvable letter NDA 21287, alfuzosin hydrochloride

Total no. of pages including cover: 3

Comments: Dear Jon: As mentioned by Dr. Houn, attached is the approvable letter for NDA 21-287. If you have any questions, please call me at 301-827-4260. Evelyn

Document to be mailed: ☑ YES ☐ NO

TRANSMISSION VERIFICATION REPORT

TIME : 10/05/2001 13:04
NAME :
FAX :
TEL :

DATE,TIME	10/05 13:03
FAX NO./NAME	916108896910
DURATION	00:01:04
PAGE(S)	04
RESULT	OK
MODE	STANDARD ECM

Confirmation Report – Memory Send

Page : 001
Date & Time: Jun-12-03 03:26pm
Line 1 : 301-827-4267
Line 2 :
Machine ID : FDA/CDER/OND/ODE3/DRUDP

Job number	:	203
Date	:	Jun-12 03:23pm
To	:	☎916108896993
Number of pages	:	019
Start time	:	Jun-12 03:23pm
End time	:	Jun-12 03:26pm
Pages sent	:	019
Status	:	OK

Job number : 203 *** SEND SUCCESSFUL ***

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE III

FACSIMILE TRANSMITTAL SHEET

DATE: June 12, 2003

To: Jon Villaume, Ph.D.
Company: Sanofi-Synthelabo, Inc.
Fax number: 610-889-6993
Phone number: 610-889-6028

From: Jean King
Division of Division of Reproductive and Urologic Drug Products
Fax number: 301-827-4267
Phone number: 301-827-4260

Subject: NDA 21-287: revised PI containing FDA comments and revised phase 4 commitment proposal for alfuzosin HCL

Total no. of pages including cover: 19

Comments: Please see below.

Document to be mailed: YES NO

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE III

FACSIMILE TRANSMITTAL SHEET

DATE: June 12, 2003

To: Jon Villaume, Ph.D.

Company: Sanofi-Synthelabo, Inc.

Fax number: 610-889-6993

Phone number: 610-889-6028

From: Jean King

Division of Division of Reproductive and Urologic Drug Products

Fax number: 301-827-4267

Phone number: 301-827-4260

Subject: NDA 21-287: revised PI containing FDA comments and revised phase 4 commitment proposal for alfuzosin HCL

Total no. of pages including cover: 19

Comments: Please see below.

Document to be mailed: YES NO

Dear Dr. Villaume,

Please find attached the Division's revised PI for discussion on our continued teleconference this afternoon.

Additionally, our Phase 4 commitment proposal for NDA 21-287 (alfuzosin hydrochloride) has been revised as follows:

Commitment # 1

Sanofi-Synthelabo, Inc. will conduct a study to evaluate the impact on QT interval prolongation of combining a phosphodiesterase-5 inhibitor (sildenafil or vardenafil) with alfuzosin at steady state drug levels.

The timeline is as follows:

- Draft protocol submission — within six months of the date of this letter
- Study initiation — within 12 months of the date of this letter
- Submission of Clinical Study Report — within 18 months of the date of this letter

We will also discuss this on the conference call to be resumed this afternoon. A letter of acceptance that includes the agreed upon Phase 4 commitment must be sent via fax to us for incorporation into a final action letter.

Sincerely,

Jean King, M.S., R.D.
Regulatory Project Manager

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: 6/3/03	
To: Jon Villarreal	**From:** Jean Kings
Company: Sanofi - Santaris Labs	Division of Reproductive and Urologic Drug Products
Fax number: 610-889-6993	**Fax number:** (301) 827-4267
Phone number: 610-889-6028	**Phone number:** (301) 827-4260
Subject: FDA comments regarding Uroxatral labeling	
Total no. of pages including cover: 17	

Document to be mailed: YES (NO)

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Page	: 001
Date & Time	: Jun-03-03 10:10am
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Line 2	:
Machine ID	: FDA/CDER/OND/ODE3/DRUDP
Job number	: 101
Date	: Jun-03 10:07am
To	: 916108869693
Number of pages	: 017
Start time	: Jun-03 10:07am
End time	: Jun-03 10:10am
Pages sent	: 017
Status	: OK
Job number	: 101 *** SEND SUCCESSFUL ***

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: 6/3/03

To: Jon Villaume	**From:** Jean King
Company: Sanofi - Santrelabs	Division of Reproductive and Urologic Drug Products
Fax number: 610-889-6993	**Fax number:** (301) 827-4267
Phone number: 610-889-6028	**Phone number:** (301) 827-4260

Subject: FDA comments regarding Uroxatral labeling

Total no. of pages including cover: 17

Document to be mailed: YES (NO)

Confirmation Report – Memory Send

Page : 001
Date & Time: Jun-12-03 03:58pm
Line 1 : 301-827-4267
Line 2 :
Machine ID : FDA/CDER/OND/ODE3/DRUDP

Job number : 205

Date : Jun-12 03:57pm

To : ☎916108896993

Number of pages : 005

Start time : Jun-12 03:57pm

End time : Jun-12 03:58pm

Pages sent : 005

Status : OK

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Center for Drug Evaluation and Research
Office of Drug Evaluation ODE III

FACSIMILE TRANSMITTAL SHEET

DATE: June 12, 2003

To: Jon Villaume, Ph.D.

Company: Sanofi-Synthelabo, Inc.

Fax number: 610-889-6993

Phone number: 610-889-6028

From: Jean King
Division of Division of Reproductive and Urologic Drug Products

Fax number: 301-827-4267

Phone number: 301-827-4260

Subject: NDA 21-287: revised PPI containing FDA comments

Total no. of pages including cover: 5

Comments: Please see below.

Document to be mailed: YES NO

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Dear Dr. Villaume,

Please find attached the Division's revised PPI for discussion on our continued teleconference this afternoon.

Sincerely,

Jean King, M.S., R.D.
Regulatory Project Manager

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE III

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Confirmation Report – Memory Send

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DATE: 6/5/03	
To: Jon Villaume, Ph.D.	**From:** Jean King
Company: Sanofi-Synthelabo	Division of Reproductive and Urologic Drug Products
Fax number: (610) 889-6993	**Fax number:** (301) 827-4267
Phone number: (610) 889-6028	**Phone number:** (301) 827-4260
Subject: FDA Comments regarding Alfuzosin HCL PPI	
Total no. of pages including cover: 9	

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Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: 6/5/03

To: Jon Villaume Ph.D.	**From:** Jean King
Company: Sanofi-Synthelabo	Division of Reproductive and Urologic Drug Products
Fax number: 610 889 6993	**Fax number:** (301) 827-4267
Phone number: 610-889-6028	**Phone number:** (301) 827-4260

Subject: FDA Comments regarding Alfuzosin HCL PPI

Total no. of pages including cover: 9

Document to be mailed: YES (NO)

NDA 21-287
Alfuzosin Hydrochloride
10 mg extended release tablets

FDA Revised Carton Labels

Not applicable for this application; carton and container labels submitted August 30, 2001 (see action packet) remain unchanged. See Chemistry Memo to File, dated June 12, 2003.

/S/
6/12/03

NDA 21-287
Alfuzosin Hydrochloride

FDA revised Carton Labels

See page 3 of Chemistry Review # 2, attached.

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] supportive stability data, 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.

Suong Tran, PhD
Review Chemist

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