CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-157

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

UCB, Inc. – 1950 Lake Park Drive – Smyrna, Georgia 30080

PATENT CERTIFICATION

In the opinion and to the best knowledge of UCB, Inc., there are no patents, other than the patents owned by UCB, Belgium, that claim the reference listed drug or any other drug on which investigations are relied upon for approval of this application were conducted by or for someone other than applicant, or that claim a use of such drugs for which applicant is seeking approval under this subsection.

Patricia A Fritz
Vice President, Global Regulatory Affairs
UCB, Inc.

Department of Health and Human Services
Food and Drug Administration

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT

For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use

Form Approved: OMB No. 0910-0513
Expiration Date: 07/31/06
See OMB Statement on Page 3.

NDA NUMBER
22-157

NAME OF APPLICANT / NDA HOLDER
UCB, Inc.

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)
Xyzal

ACTIVE INGREDIENT(S)	STRENGTH(S)
Levocetirizine Dihydrochloride	0.5 mg/mL

DOSAGE FORM
oral solution

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4).
Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent
U.S. Patent No. 4,525,358	6/25/1985	6/25/2007

d. Name of Patent Owner	Address *(of Patent Owner)*	
Sepracor, Inc..	1950 Lake Park Drive	
	City/State: Smyrna, GA	
	ZIP Code: 30080	FAX Number *(if available)*
	Telephone Number: 770-970-7500	E-Mail Address *(if available)*

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)	Address *(of agent or representative named in 1.e.)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? ☐ Yes ☒ No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? ☐ Yes ☐ No

PSC Media Arts (301) 443-1090 EF

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1	Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?	☒ Yes	☐ No
2.2	Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement?	☒ Yes	☐ No
2.3	If the answer to question **2.2** is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).	☐ Yes	☒ No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in **2.3.**

The patent claims the form of the active ingredient that is described in the pending NDA, among others, and is submitted for listing on that basis. Accordingly, no further testing is required.

2.5	Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	☐ Yes	☒ No
2.6	Does the patent claim only an intermediate?	☐ Yes	☒ No
2.7	If the patent referenced in **2.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

3. Drug Product (Composition/Formulation)

3.1	Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	☒ Yes	☐ No
3.2	Does the patent claim only an intermediate?	☐ Yes	☒ No
3.3	If the patent referenced in **3.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

4. Method of Use

Sponsors must submit the information in section 4 separately for* each *patent claim claiming a method of using the pending drug product for which approval is being sought. For* each *method of use claim referenced, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? ☒ Yes ☐ No

4.2 Patent Claim Number *(as listed in the patent)*: 23-31

Does the patent claim referenced in **4.2** claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? ☒ Yes ☐ No

4.2a If the answer to **4.2** is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.

Use: *(Submit indication or method of use information as identified specifically in the approved labeling.)*

Treatment of seasonal allergic rhinitis due to allergens and/or perennial allergic rhinitis due to allergens according to proposed labeling

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent 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. ☐ Yes

6. Declaration/Certification

6.1 ***The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.***

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner *(Attorney, Agent, Representative or other Authorized Official) (Provide Information below)*	Date Signed
RJP	3/22/07

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

☐ NDA Applicant/Holder	☒ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☐ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name Richard J. Paris, Jr.,	
Address 1950 Lake Park Drive	City/State Smyrna, GA
ZIP Code 30080	Telephone Number 770-970-7500
FAX Number *(if available)*	E-Mail Address *(if available)*

Department of Health and Human Services
Food and Drug Administration

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1. GENERAL

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent
U.S. Patent No. 5,698,558	12/16/1997	9/24/2012

d. Name of Patent Owner	Address *(of Patent Owner)*	
Sepracor, Inc..	84 Waterford Dr.	
	City/State: Marlborough, MA	
	ZIP Code: 01752	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)	Address *(of agent or representative named in 1.e.)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? ☐ Yes ☒ No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? ☐ Yes ☐ No

PSC Media Arts (301) 443-1090 EF

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2.1	Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?	☐ Yes	☒ No
2.2	Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
2.3	If the answer to question **2.2** is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).	☐ Yes	☐ No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in **2.3.**

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2.6	Does the patent claim only an intermediate?	☐ Yes	☐ No
2.7	If the patent referenced in **2.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

3. Drug Product (Composition/Formulation)

3.1	Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	☐ Yes	☒ No
3.2	Does the patent claim only an intermediate?	☐ Yes	☐ No
3.3	If the patent referenced in **3.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

4. Method of Use

Sponsors must submit the information in section 4 separately for* each *patent claim claiming a method of using the pending drug product for which approval is being sought. For* each *method of use claim referenced, provide the following information:

4.1	Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	☒ Yes	☐ No

4.2 Patent Claim Number *(as listed in the patent)* 1-2, 4-9	Does the patent claim referenced in **4.2** claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?	☒ Yes	☐ No

4.2a If the answer to **4.2** is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.

Use: *(Submit indication or method of use information as identified specifically in the approved labeling.)*

Treatment of seasonal allergic rhinitis due to allergens and/or perennial allergic rhinitis due to allergens according to proposed labeling

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6 Declaration Certification

6.1 ***The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.***

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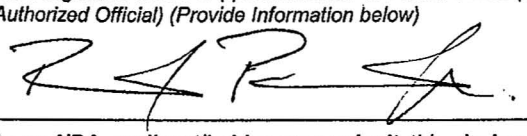
6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner *(Attorney, Agent, Representative or other Authorized Official) (Provide Information below)*	Date Signed
	3/22/07

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Check applicable box and provide information below.

☐ NDA Applicant/Holder	☒ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☐ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name Richard J. Paris, Jr.,	
Address 1950 Lake Park Drive	City/State Smyrna, GA
ZIP Code 30080	Telephone Number 770-970-7500
FAX Number *(if available)*	E-Mail Address *(if available)*

EXCLUSIVITY SUMMARY

NDA # 22-157 SUPPL # HFD # 570

Trade Name Xyzal oral solution

Generic Name levocetirizine dihydrochloride

Applicant Name UCB

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy 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 a 505(b)(1), 505(b)(2) or efficacy supplement?

YES ☒ NO ☐

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

505(b)(2)

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 ☐ 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.

The applicant conducted one clinical pharmacology study in 24 healthy volunteers to assess the bioequivalence of 10 ml levocetirizine dihydrochloride 0.5 mg/ml oral solution with levocetirizine dihydrochloride 5 mg oral tablet.

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 ☐ NO ☒

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

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

YES ☐ NO ☒

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

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

YES ☐ NO ☒

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (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 ☐

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

NDA#	19-835	Cetirizine hydrochloride oral tablets; OTC
	22-155	Cetirizine hydrochloride oral syrup, 1mg/ml: OTC
	21-621	Cetirizine hydrochloride chewable tablets; OTC
	21-150	Cetirizne hydrochloride/pseudoephedrine ER tablets; OTC
NDA#	20-346	Cetirizine oral liquid; Rx
NDA#	22-064	Levocetirizine dihydrochloride oral tablets; Rx

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 ☐

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 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs 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 8.

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.

(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 8:

(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:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

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 ☐

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

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 ☐

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

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"):

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 ☐	! NO ☐
Explain:	! Explain:

Investigation #2	!
	!
YES ☐	! NO ☐
Explain:	! 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:

==========

Name of person completing form: Lori Garcia, RPh
Title: Senior Regulatory Management Officer
Date: 1/16/08

Name of Office/Division Director signing form: Badrul A. Chowdhury, MD, PhD
Title: Division Director/DPAP

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

/s/

Badrul Chowdhury
1/28/2008 01:02:22 PM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA # : 22-157 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: March 28, 2007 PDUFA Goal Date: 1/28/08

HFD 570 Trade and generic names/dosage form: Xyzal (levocetirizine) Oral Soln

Applicant: UCB, Inc Therapeutic Class: Anithistamine

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? *

- ☐ xxYes. Please proceed to the next question.
- ☐ No. PREA does not apply. Skip to signature block.

** SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.*

Indication(s) *previously approved* (please complete this section for supplements only): _____

Each indication covered by current application under review must have pediatric studies: *Completed, Deferred, and/or Waived.*

Number of indications for this application(s): 3

Indication #1: seasonal allergic rhinitis

Is this an orphan indication?

- ☐ Yes. PREA does not apply. Skip to signature block.
- ☐ xxNo. Please proceed to the next question.

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

- ☐ Yes: Please proceed to Section A.
- ☐ xxNo: Please check all that apply: XX Partial Waiver XX Deferral ___ 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
- ☐ Disease/condition does not exist in children
- ☐ Too few children with disease to study
- ☐ There are safety concerns
- ☐ Other: _____

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 (fill in applicable criteria below):

Min_____ kg_____ mo._____ yr._<2__ 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**
- ☒ **XX Disease/condition does not exist (or is difficult to diagnose) in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☐ **Other:__**
- ☐ _____

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 (fill in applicable criteria below):

Min _____ kg_____ mo._____ yr.__2yrs_ Tanner Stage_____
Max_____ kg_____ mo._____ yr.__<6yrs__ 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**
- ☒ **xxChildren 6 years and older – studies ready for approval (NDA 22-157-Xyzal Oral Soln)**
- ☐ **Formulation needed**
- ☒ **Other: __Additional safety data needed in the 2 to <6 y.o. age group.**

_____

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

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 (fill in applicable criteria below):

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.

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: perennial allergic rhinitis

Is this an orphan indication?

- ☐ **Yes. PREA does not apply. Skip to signature block.**
- ☒ **xxNo. Please proceed to the next question.**

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

- ☐ **Yes: Please proceed to Section A.**
- ☒ **xxNo: Please check all that apply: XX Partial Waiver XX Deferral ____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**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Other:**_____

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 (fill in applicable criteria below)::

Min ____	**kg**____	**mo.** <6	**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**
- ☒ **XX Disease/condition does not exist in children (or is difficult to diagnose in this age group).**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☐ **Other:**_____

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 (fill in applicable criteria below)::

Min	**kg**	**mo.** 6	**yr**	**Tanner Stage**	
Max	**kg**	**mo.**	**yr.** <6	**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**
- ☒ **xxChildren 6 years and older – studies ready for approval (NDA 22-157 Xyzal Oral Soln)**
- ☐ **Formulation needed**
- ☒ **Other: Additional safety data needed in the 2 to <6 y.o. age group.**

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

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 (fill in applicable criteria below):

Min	**kg**	**mo.**	**yr.**	**Tanner Stage**	
Max	**kg**	**mo.**	**yr.**	**Tanner Stage**	

Comments:

Attachment A
(This attachment is to be completed for those applications with multiple indications only.)

Indication #3: chronic idiopathic urticaria
Is this an orphan indication?

- ☐ **Yes. PREA does not apply. Skip to signature block.**
- ☒ **xxNo: Please proceed to the next question.**

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

- ☐ **Yes: Please proceed to Section A.**
- ☒ **xxNo: Please check all that apply: XX Partial Waiver XX Deferral ____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**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Other:_____**

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 (fill in applicable criteria below)::

Min _____	**kg_____**	**mo.__<6__**	**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**
- ☒ **XX Disease/condition does not exist in children (or is difficult to diagnose in this age group).**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☐ **Other:_____**

f 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 (fill in applicable criteria below)::

Min ____	**kg**____	**mo.** 6	**yr** ____	**Tanner Stage**____
Max____	**kg**____	**mo.**____	**yr.** <6	**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**
- ☐ **XX Children6 years and older - studies ready for approval (NDA 22-157 Xyzal Oral Soln)**
- ☐ **Formulation needed**
- ☒ **Other: Additional safety data needed in the 6-month to <6 y.o. age group.**

Date studies are due (mm/dd/yy): **TBD**

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 (fill in applicable criteria below):

Min ____	**kg**____	**mo.**____	**yr.**____	**Tanner Stage**____
Max____	**kg**____	**mo.**____	**yr.**____	**Tanner Stage**____

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Lori Garcia, R.Ph., Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 10/10/2006)

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/s/

Lori Garcia
1/14/2008 11:58:35 AM

UCB, Inc. – 1950 Lake Park Drive – Smyrna, Georgia 30080

DEBARMENT CERTIFICATION STATEMENT

UCB, 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.

12/FEB/2007

Aaron Bartlone
Vice President, Global Preclinical/Clinical Quality Assurance
UCB, Inc.

Garcia, Lori

From: Tegtmeyer Susan [Susan.Tegtmeyer@ucb-group.com]
Sent: Monday, January 28, 2008 3:36 PM
To: Garcia, Lori
Subject: RE: Xyzal letter

Received
Thanks,
Susan

-----Original Message-----
From: Garcia, Lori [mailto:lori.garcia@fda.hhs.gov]
Sent: Monday, January 28, 2008 2:36 PM
To: Tegtmeyer Susan
Subject: Xyzal letter

<<APltrxyzal.pdf>>

Hi Susan,

Here's the action letter for Xyzal. ***Please confirm receipt.***

Contact me if you have any questions.

Thanks,

Lori

Lori Garcia, R.Ph.
LCDR, U.S. Public Health Service
Senior Regulatory Project Manager
FDA/CDER/OND/DPAP
Bldg. 22, Rm. 3343
10903 New Hampshire Ave
Silver Spring, MD 20993-0002
Phone: (301) 796-1212
lori.garcia@fda.hhs.gov

From: Tegtmeyer Susan [Susan.Tegtmeyer@ucb-group.com]
Sent: Friday, November 02, 2007 10:22 AM
To: Garcia, Lori
Subject: RE: NDA 22-157 (Xyzal oral solution)

Attachments: emfinfo.txt
Dear Lori,
For the November 7 submission of the revised PI and packaging, we'll (b) (4)

Regards,
Susan

-----Original Message-----
From: Thrower Sherri
Sent: Friday, November 02, 2007 10:13 AM
To: lori.garcia@fda.hhs.gov
Cc: Tegtmeyer Susan
Subject: NDA 22-157 (Xyzal oral solution)

Good morning Lori
(b) (4)

(b) (4)

A formal letter will be submitted to the NDA in the following days.

Best regards,

Sherri N Thrower
Sr. Regulatory Affairs Associate - CMC
UCB, Inc.
770-591-0574

Garcia, Lori

From: Garcia, Lori
Sent: Thursday, January 10, 2008 1:06 PM
To: Gilbert McClain, Lydia I; Boucher, Robert
Subject: FW: DFS Email - N 022157 N 000 27-Mar-2007 - Review

Follow Up Flag: Read
Flag Status: Flagged

Attachments: 09001469801a8838.drl; 09001469801a8838.pdf; 01-09-08_NDA 22-157 Xyzal for seasonal allergies_Content Review_Final.doc



09001469801a883809001469801a8838 .drl (169 B) | .pdf (211 KB) | 01-09-08_NDA 22-157 Xyzal for ...

Here's the labeling review from SEALD. Word doc with tracked changes is attached.

-----Original Message-----
From: Furness, Melissa
Sent: Wednesday, January 09, 2008 6:19 PM
To: Garcia, Lori
Cc: Araojo, Richardae; Burke, Laurie B
Subject: FW: DFS Email - N 022157 N 000 27-Mar-2007 - Review

Hi Lori,

I just noticed that when our Word file was converted to Adobe all of our track changes comments and text were not included in the converted file in DFS. Consequently, please circulate the Word file that I sent your via e-mail, instead.

Thanks,

Melissa

-----Original Message-----
From: cderdocadmin@cder.fda.gov [mailto:cderdocadmin@cder.fda.gov]
Sent: Wednesday, January 09, 2008 6:13 PM
To: Garcia, Lori; Burke, Laurie B; Furness, Melissa; Araojo, Richardae; Delasko, Jeanne
Subject: DFS Email - N 022157 N 000 27-Mar-2007 - Review

Document room close out the following assignments:

		Personnel Code	Sup-Concur	St
N 022157 N 000	27-Mar-2007	08J	09-Jan-2008	CM
N 022157 N 000 BL	31-Jul-2007	08J	09-Jan-2008	CM
N 022157 N 000 BL	13-Nov-2007	08J	09-Jan-2008	CM

Document Type: Review
Submission Description: SEALD Labeling Review
PM activity: PM activity required

Author(s)/Discipline(s)

Melissa Furness, CSO

Signer(s)
---
1. Melissa Furness

09-Jan-2008
2. Laurie Burke
09-Jan-2008

9 pages withheld in full immediately after this page as (b)(4) draft labeling

---

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/s/

Melissa Furness
1/9/2008 05:21:27 PM
CSO

Reviewed 01-07-08 Draft Label from DPAP. Reviewed in Collaboration with Maternal Health Team.

Laurie Burke
1/9/2008 06:12:54 PM
INTERDISCIPLINARY

Garcia, Lori

From: cderdocadmin@cder.fda.gov
Sent: Tuesday, December 04, 2007 3:24 PM
To: Riley, Bryan S; Garcia, Lori
Subject: DFS Email - N 022157 N 000 27-Mar-2007 - Review (noted no comments - NAI)

Document room close out the following assignments:

		Personnel Code	Sup-Concur	St
N 022157 N 000	27-Mar-2007	66X	04-Dec-2007	NR

Document Type: Review (noted no comments - NAI)
Submission Description: NDA for Xyzal oral solution submitted for evaluation of Microbial Limits and Antimicrobial Preservative Effectiveness.

Author(s)/Discipline(s)

1. Vinayak Pawar, MICROBIOLOGIST

Signer(s)

(b) (4)

NDA 22-157

UCB, Inc.
1950 Lake Park Drive
Smyrna, Georgia 30080

Attention: Patricia Fritz
Vice President
Global Regulatory Affairs

Dear Ms. Fritz:

Please refer to your new drug application dated March 27, 2007, received March 28, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Xyzal (levocetirizine dihydrochloride) 0.5mg/mL Oral Solution.

The attached Prescription Information (PI) labeling contains revisions we have made in order to comply with the Pediatric Research Equity Act of 2007 (PREA).

FDA-proposed insertions to the PI are underlined and deletions, if any, are in strike-out. Be advised that these labeling changes are not necessarily the Agency's final recommendations and that additional labeling changes may be forthcoming as the label is reviewed by other offices within the Agency.

We request that you submit your revised draft labeling and/or comments by January 8, 2008.

If you have any questions, call Lori Garcia, Senior Regulatory Management Officer, at 301-796-1212.

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/s/

Lori Garcia
10/29/2007 01:30:33 PM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

INFORMATION REQUEST LETTER

NDA 22-157

UCB, Inc.
1950 Lake Park Drive
Smyrna, Georgia 30080

Attention: Patricia Fritz
Vice President
Global Regulatory Affairs

Dear Ms. Fritz:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Xyzal (levocetirizine dihydrochloride) 0.5mg/mL Oral Solution.

We have the following comment regarding the Chemistry, Manufacturing and Controls section of your submission. We request a prompt written response in order to continue our evaluation of your NDA.

1. The 5 mg/10 mL volume of levocetirizine dihydrochloride oral solution may be dispensed in the 15 mL and 150 mL glass bottles, (b) (4)

If you have any questions, call LCDR Lori Garcia, Senior Regulatory Project Manager, at (301) 796-1212.

Sincerely,

{See appended electronic signature page}

Ali Al Hakim, Ph.D.
Chief, Branch II
Division of Pre-Marketing Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Ali Al-Hakim
9/21/2007 12:13:29 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-157

UCB, Inc.
1950 Lake Park Drive
Smyrna, Georgia 30080

Attention: Patricia Fritz
Vice President
Global Regulatory Affairs

Dear Ms. Fritz:

Please refer to your March 27, 2007, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Xyzal (levocetirizine dihydrochloride) 0.5mg/mL Oral Solution.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on May 27, 2007, in accordance with 21 CFR 314.101(a).

Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

We request that you submit the following information:

1. The analytical report submitted with Study A00318 is for the determination of cetirizine dihydrochloride in human plasma. Study A00318 is a bioequivalence study measuring levocetirizine in human plasma. Provide the correct analytical report, i.e. for levocetirizine.

2. Provide individual subject data listings indicating calendar dates of screening, discharge from the clinic, last follow-up visit and dosing (both periods).

3. In the cover letter of your March 27, 2007, NDA submission, you state that nonclinical data are not submitted in this NDA, but cross-referenced to NDA 22-064. However, in the CTD map, under Module 2, 2.6 Nonclinical Written and Tabulated Summaries, and under Module 4, Nonclinical Pharmacology and Toxicology, you state that these items are "Not Required for This Submission." This statement is not acceptable for these sections of the CTD. Revise these sections to reflect the fact that the necessary nonclinical data are provided via cross-reference to NDA 22-064.

4. Amend this NDA with content of labeling in structured product labeling (SPL) format to include the changes approved in NDA 22-064.

5. Submit patent certification(s) as required under 21 CFR 314.50(i).

Please respond to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

If you have any questions, call Lori Garcia, Regulatory Project Manager, at (301) 796-1212.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary Allergy Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

Badrul Chowdhury
6/1/2007 09:34:19 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-157

UCB, Inc.
1950 Lake Park Drive
Smyrna, Georgia 30080

Attention: Patricia Fritz
Vice President
Global Regulatory Affairs

Dear Ms. Fritz:

Please refer to your March 27, 2007, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Xyzal (levocetirizine dihydrochloride) 0.5mg/mL Oral Solution.

Our review of the Chemistry, Manufacturing and Controls section of your submission is complete, and we have identified the following deficiencies:

1. The following comments pertain to the report on extractables/leachables that appears on pp. 19-46 of 3.2.P.2.

   a. It states that, with the exception of [redacted] (b) (4), the observed extractables/leachables components are compliant with the 21Code of Federal Regulations. Provide the specific references to the 21CFR for each of these eight components.

   b. Provide any information known about the origin of the various listed components, i.e., from the [redacted] (b) (4) bottles, the labels, the label adhesive.

   c. Provide more specific structural information with regard to the [redacted] (b) (4) extractables that are merely referred to as [redacted] (b) (4)

   d. Considering the nine extractables/leachables that were included in table 3 on p. 23 in the P.2 section, clarify the significance of the [redacted] (b) (4)

e. Additional comments may be forthcoming based upon your responses to the above four inquiries and our subsequent evaluation in view of the other information contained in your extractables/leachables report.

2. Additional comments regarding the microbiological testing, preservative effectiveness studies, and associated specifications may be forthcoming.

3. Revise the chiral and achiral HPLC methods to include a list of typical or expected retention times for the various potential degradants, process impurities, and excipient-related compounds.

4. (b) (4)

5. Provide the reason(s) for the development of (b) (4) as an alternate method to the current (b) (4).

6. Provide validation data for (b) (4)

7. Reduce the acceptance criterion for drug product total related substances to a level that is more consistent with your data and the proposals that have been made for the individual identified and unidentified impurities. A limit of NMT 1.0%, for example, would still allow sufficient flexibility in terms of future expected manufacturing and analytical variability, as well as allow for expiry extension.

8. (b) (4)

9. Drug Master File (b) (4) from (b) (4) was reviewed and was found

to be deficient. A deficiency letter was forwarded to the holder.

10. We have the following preliminary comments regarding the labels/labeling.

    a. Revise the chemical structure in the DESCRIPTION section of the package insert such that the correct stereochemistry is displayed.

    b. Revise the HOW SUPPLIED/STORAGE AND HANDLING section of the prescribing information to specifically list (b) (4) the (b) (4) glass 5 ounce bottles.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call Lori Garcia, Regulatory Project Manager, at 301-796-1212.

Sincerely,

{See appended electronic signature page}

Blair A. Fraser, Ph.D.
Chief, Branch II
Division of Pre-Marketing Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Blair Fraser
5/23/2007 07:47:00 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-157

NDA ACKNOWLEDGMENT

UCB, Inc.
1950 Lake Park Drive
Smyrna, Georgia 30080

Attention: Patricia Fritz
Vice President
Global Regulatory Affairs

Dear Ms. Fritz:

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

Name of Drug Product:	Xyzal (levocetirizine dihydrochloride) 0.5mg/mL oral solution
Review Priority Classification:	Standard (S)
Date of Application:	March 27, 2007
Date of Receipt:	March 28, 2007
Our Reference Number:	NDA 22-157

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on May 27, 2007, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be January 28, 2008.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirement. We acknowledge receipt of your request for a deferral of pediatric studies for this application. Once the application has been filed, we will notify you whether we have deferred the pediatric study requirement for this application.

Please cite the NDA number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Pulmonary and Allergy Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, call Lori Garcia, Regulatory Project Manager, at (301) 796-1212.

Sincerely,

{See appended electronic signature page}

Sandy Barnes
Supervisory CSO
Division of Pulmonary and Allergy Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

Lori Garcia
4/9/2007 06:00:46 PM
signed for Sandy Barnes

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	REQUEST FOR CONSULTATION
TO: *(Division/Office)* James McVey, Ph.D., New Drug Microbiology Staff Team Leader (OPS), WO21 RM3652	FROM: Lori Garcia, R.Ph., Regulatory Project Manager, Division of Pulmonary and Allergy Products

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
06-APR-2007	N/A	N22-157	Original NDA [505(b)(2)]	27-MAR-2007

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Xyzal (levocetirizine dihydrochloride) oral solution	S	3	05-JUL-2007

NAME OF FIRM: UCB, Inc.

REASON FOR REQUEST

I. GENERAL

NEW PROTOCOL PROGRESS REPORT NEW CORRESPONDENCE DRUG ADVERTISING ADVERSE REACTION REPORT MANUFACTURING CHANGE/ADDITION MEETING PLANNED BY	PRE-NDA MEETING END OF PHASE II MEETING RESUBMISSION SAFETY/EFFICACY PAPER NDA CONTROL SUPPLEMENT	RESPONSE TO DEFICIENCY LETTER FINAL PRINTED LABELING LABELING REVISION ORIGINAL NEW CORRESPONDENCE FORMULATIVE REVIEW X OTHER *(Specify below)*

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
TYPE A OR B NDA REVIEW END OF PHASE II MEETING CONTROLLED STUDIES PROTOCOL REVIEW OTHER	CHEMISTRY PHARMACOLOGY BIOPHARMACEUTICS OTHER

III. BIOPHARMACEUTICS

DISSOLUTION BIOAVAILABLITY STUDIES PHASE IV STUDIES	DEFICIENCY LETTER RESPONSE PROTOCOL-BIOPHARMACEUTICS *IN-VIVO* WAIVER REQUEST

IV. DRUG EXPERIENCE

PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES CASE REPORTS OF SPECIFIC REACTIONS *(List below)* COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP	REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY SUMMARY OF ADVERSE EXPERIENCE POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

CLINICAL	PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: **Please evaluate, from the microbiological perspective, the adequacy of the preservative assay, microbial limits, and antimicrobial effectiveness acceptance criteria (see p. 107 of 1016 in 3.2.P.2). The formulation (p. 8 of 1016 in 3.2.P.2) has methylparaben and propylparaben** (b) (4) **The preservative challenge study results are on pp. 530-551 of 1016 in 3.2.P.2. The application is on the EDR.**

cc: Orig. NDA # 22-157
ONDQA/DIV I/CBertha
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OPS/JMcVey
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Lori Garcia
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Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: February 1, 2007

To: Susan Tegtmeyer	**From:** LCDR Lori Garcia Regulatory Project Manager
Company: UCB, Inc.	Division of Pulmonary and Allergy Products
Fax number: 770-970-8345	**Fax number:** 301-796-9718
Phone number: 770-970-8654	**Phone number:** 301-796-1212
Subject: PIND 72,233	
Total no. of pages including cover: 11	
Comments:	

Document to be mailed: **YES** xNO

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Meeting Type:	Type B
Meeting Category:	Pre-NDA
Meeting Date and Time:	January 26, 2007, 8:30am-9:30am EST
Meeting Location:	Teleconference
Application Number:	PIND 72,233
Product Name:	levocetirizine dihydrochloride
Received Briefing Package	November 28, 2006
Sponsor Name:	UCB, Inc.
Meeting Requestor:	UCB, Inc.
Meeting Chair:	Badrul A. Chowdhury, M.D., Ph.D.
Meeting Recorder:	Lori A. Garcia, R.Ph.
Meeting Attendees:	

FDA Attendees
Division of Pulmonary and Allergy Drug Products
Badrul Chowdhury, M.D., Ph.D., Division Director
Lydia Gilbert-McClain, M.D., Clinical Team Leader
Emmanuel Fadiran, Ph.D., ClinPharm Team Leader
Partha Roy, Ph.D., ClinPharm Reviewer
Prasad Peri, Ph.D., ONDQA Pharmaceutical Assessment Lead
Donald Collier, Regulatory Information Specialist
Lori Garcia, RPh., Regulatory Project Manager

Sponsor Attendees
UCB, Inc.
Patty Fritz, Regulatory Affairs
Catherine Arendt, Clinical Development
Susan Tegtmeyer, Regulatory Affairs

1.0 BACKGROUND

UCB, Inc. submitted a meeting request and meeting package dated November 28, 2006, for a Pre-NDA meeting to discuss UCB's plans to submit a 505(b)(2) NDA for pediatric liquid formulations of levocetirizine dihydrochloride. Upon review of the briefing package, the Division responded to UCB's questions via fax on January 22, 2007. The content of that fax is printed below. Any discussion that took place at the meeting is captured directly under the relevant original response including any changes in our original position. UCB's questions are in ***bold italics***; FDA's response is in *italics*; discussion is in normal font.

The purpose of this meeting is to further clarify and discuss the FDA's responses to UCB's questions which were faxed on January 22, 2007, particularly Introductory Comment #2, and Responses #2 and #6. UCB sent a clarification in response to the Intruductory Comment #2 to FDA via email on January 23, 2007 (see Attachment 1).

2.0 DISCUSSION

2.1 INTRODUCTORY COMMENTS

1. *Your development program for levocetirizine liquid formulations is based on the premise that the efficacy and safety of levocetirizine tablets have been established. We remind you that the efficacy and safety of levocetirizine tablets for the treatment of the symptoms of seasonal and perennial allergic rhinitis and chronic idiopathic urticaria in adults and children 6 years of age and older is currently under review (NDA 22-064). Be advised that in the absence of the Agency's final determination on the efficacy and safety of levocetirizine tablets, the Division cannot comment on the adequacy of your proposed bioequivalence approach to support the efficacy of levocetirizine* (b) (4) *oral solution in children* (b) (4) *6 years of age.*

(b) (4)

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(b) (4)

[redacted]

2.5 QUESTION 4

The planned NDA will include a Module 2 Quality Overall Summary which addresses Drug Product only (Module 2.3.P). It is proposed that the Drug Substance sections (Module 2.3.S, 3.2.S) will consist of a cross-reference to the pending NDA 22-064. The Quality content of the planned NDA is described in Section 4 of this document. UCB requests the Division's concurrence regarding the plan to cross-reference the Drug Substance information (Modules 2.3.S and 3.2.S) in pending NDA 22-064.

FDA Response:

Your plan to cross-reference the Drug Substance information (Modules 2.3.S and 3.2.S) in pending NDA 22-064 is acceptable.

2.6 QUESTION 5

In the planned NDA, UCB plans to cross-reference, and not resubmit, the Nonclinical information provided in the pending NDA 22-064. No new levocetirizine Nonclinical studies have been performed, and to date no levocetirizine safety issues specific to the pediatric population have been identified. UCB requests the Division's concurrence regarding the plan to cross-reference the Nonclinical information (Modules 2.4, 2.6 and 4) in pending NDA 22-064.

FDA Response:

Your plan to cross-reference the Nonclinical information (Modules 2.4, 2.6 and 4) in pending NDA 22-064 is acceptable.

2.7 QUESTION 6

Two bioequivalence studies in healthy adult subjects, four safety/efficacy studies of levocetitizine in (b) (4) ***of age, and a retrospective population pharmacokinetics analysis will form the basis of the Clinical and Biopharmaceutics content of the planned NDA. Safety and efficacy information from sources other than UCB-sponsored studies will also be summarized. These sources include reference the approved cetirizine NDA(s) that include data in children*** (b) (4) ***of age, spontaneously reported adverse events for levocetirizine (limited to children*** (b) (4)***) and published literature on levocetirizine and cetirizine (also limited to children*** (b) (4) ***The safety and efficacy information in the pending NDA 22-064 will be cross-referenced, as appropriate, to provide additional evidence of levocetirizine safety/efficacy in the pediatric population. The planned Biopharmaceutics and Clinical content is described in Section 6 of this document. UCB requests the acceptability of the proposed Biopharmaceutics and Clinical content of the planned NDA.***

FDA Response:

Refer to the introductory comments 1 and 2 above.

In addition to your proposal, we recommend that you conduct a population pharmacokinetics (PK) data analysis to evaluate the effect of covariates (e.g. age, bodyweight, body surface area) on systemic exposure of levocetirizine to justify the age-stratified dosing recommendation. All available levocetirizine PK data, both in adult and different age/weight groups of pediatric population, may be pooled together to conduct this analysis.

As a guidance, refer to the "Pediatric Study Decision Tree" attached as an appendix (Appendix B) with the Guidance for Industry "Exposure-Response Relationships — Study Design, Data Analysis, and Regulatory Applications". Also refer to the Guidance for Industry "Population Pharmacokinetics (Final-1999)" for further details on population pharmacokinetics data analysis.

Discussion:

UCB agreed to perform the recommended analysis.

3.0 ISSUES REQUIRING FURTHER DISCUSSION

None.

4.0 ACTION ITEMS

None.

5.0 ATTACHMENTS AND HANDOUTS

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Drafted: LGarcia/January 26, 2007

Initialed: PRoy/1.29.07
EFadiran/1.29.07
DCollier/1.29.07
LGilbert-McClain/1.29.07
BChowdhury/1.29.07

Finalized: LGarcia/February 1, 2007

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/s/

Lori Garcia
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