

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-621**

**CHEMISTRY REVIEW(S)**



**NDA 21-621**

**Cetirizine Hydrochloride Chewable Tablets**

**Pfizer**

**Edwin Jao, Ph.D.  
Division of Pulmonary and Allergy  
Drug Products**

**APPEARS THIS WAY  
ON ORIGINAL**



# Table of Contents

<b>The Executive Summary .....</b>	<b>8</b>
I. Recommendations.....	8
A. Recommendation and Conclusion on Approvability .....	8
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable.....	8
II. Summary of Chemistry Assessments.....	8
A. Description of the Drug Product(s) and Drug Substance(s) .....	8
B. Description of How the Drug Product is Intended to be Used.....	9
C. Basis for Approvability or Not-Approval Recommendation.....	9
III. Administrative.....	10
A. Reviewer's Signature .....	10
B. Endorsement Block .....	10
<b>Chemistry Assessment.....</b>	<b>11</b>
I. Drug Substance.....	11
II. Drug Product.....	11
A. Evaluation of the Amendment dated 12/24/03 .....	11
B. Regulatory Specifications and Test Methods for the Drug Product.....	30
C. Stability Data Evaluation.....	33
1. The updated stability data:.....	33
2. Stability Protocol .....	35
3. Stability Evaluations .....	37
4. Expiry Dating .....	61
D. Labeling .....	62
<b>III. Draft Deficiency Letter .....</b>	<b>66</b>
<b>Attachment 1: Detailed Statistical Analysis .....</b>	<b>67</b>



# Chemistry Review Data Sheet

1. NDA 21-621
2. REVIEW #: 2
3. REVIEW DATE: March 5, 2004
4. REVIEWER: Edwin Jao, Ph.D.
5. PREVIOUS DOCUMENTS:

Previous Documents

Document Date

IND64570

16-Apr-2002

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>	<u>Assigned Date</u>
Amendment (BC, Electronic submission)	8-Mar-2004	8-Mar-2004
Amendment (BC, paper copy)	26-Feb-2004	26-Feb-2004
Amendment (AC, Electronic submission)	24-Dec-2003	24-Dec-2003
Amendment (BL, Electronic submission)	17-Dec-2003	17-Dec-2003
Amendment (AC, paper copy & Electronic submission )	30-Sep-2003	23-Oct-2003
Amendment (BZ, Electronic submission )	19-Sep-2003	19-Sep-2003
Amendment (BC, paper copy)	14-Oct-2003	16-Oct-2003
Amendment (BC, Electronic submission)	31-Oct-2003	31-Oct-2003
NDA21-621000 (Electronic submission)	15-May-2003	13-Jul-2003



## CHEMISTRY REVIEW #2



### Chemistry Review Data Sheet

7. NAME & ADDRESS OF APPLICANT:

Name: Pfizer Inc  
Address: 235 E. 42<sup>nd</sup> Street, New York, NY 10017  
Representative: Rita A. Wittich, VP, Worldwide Regulatory Strategy  
Telephone: (212) 573-7291

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Zyrtec (Ceterizine HCl) chewable tablets
- b) Non-Proprietary Name (USAN): Ceterizine Hydrochloride chewable tablets
- c) Code Name/# (ONDC only): N/A
- d) Chem. Type/Submission Priority (ONDC only):
  - Chem. Type: 3
  - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

10. PHARMACOL. CATEGORY: Histamine H<sub>1</sub>-receptor antagonist

11. DOSAGE FORM: Chewable tablets (Bilayer with core containing active)

12. STRENGTH/POTENCY: 5 and 10 mg

13. ROUTE OF ADMINISTRATION: oral; Max Dose 10 mg QD

14. Rx/OTC DISPENSED:  Rx  OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product – Form Completed

Not a SPOTS product

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

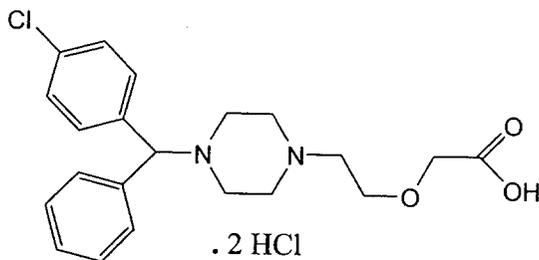
2HCl-(±)-[2-[4-(p-chloro-α-phenylbenzyl)-1-piperazinyl]ethoxy] acetic acid dihydrochloride



# CHEMISTRY REVIEW #2



## Chemistry Review Data Sheet



Molecular Formula:  $C_{21}H_{25}N_2O_3 \cdot 2HCl$

Molecular Weight: 461.82

### 17. RELATED/SUPPORTING DOCUMENTS:

#### A. Supporting DMFs:

DMF #	TYP E	HOLDER	ITEM REFERENCED	CODE 1	STATUS <sup>2</sup>	DATE REVIEW COMPLETED (Reviewer)	COMMENTS
		UCB S.A.	Cetirizine Hydrochloride	1	Adequate	22-Aug-2003 (E. Jao, Ph.D.)	
					Adequate	25-Aug -2003 (E. Jao, Ph.D.)	
					Adequate	22-Oct-2002 (Dr. V. Shah)	See comment A below
					Adequate	01-Apr-2003 (R. Frankewich, Ph.D.)	
							Betadex is granted GRAS (000074) & conforms to USP27-NF22.
					Adequate	01-Sep-2003 (E. Jao, Ph.D.)	
					Adequate	29-Apr-02 2003 (R. Frankewich, Ph.D.)	The amendments dated 03-03-03 and 25-03-03 added new <u>          </u> and/or additive packages to their current product line. No changes are reported to <u>          </u> used by the applicant.



# CHEMISTRY REVIEW #2



## Chemistry Review Data Sheet

7	Adequate	29-Apr-02 (R. Frankewich, Ph.D.) Also 01-Sep-03, part of review on DMF2052 (E. Jao, Ph.D.)	Specifications & FDA statuses are included in DMF See the review on DMF
	Adequate	27-Sep-2000 (R. Lostritto)	No update for section 143 has been provided since it was deemed "Adequate" in the previous review.
	Adequate	02-Aug-2002 (A. Shaw, Ph.D.)	
	Adequate	31-Aug-2000 (P. Peri, Ph.D.)	

<sup>1</sup> Action codes for DMF Table:

1 - DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 - Type 1 DMF

3 - Reviewed previously and no revision since last review

4 - Sufficient information in application

5 - Authority to reference not granted

6 - DMF not available

7 - Other (explain under "Comments")

<sup>2</sup> Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

<sup>3</sup> Include reference to location in most recent CMC review

Comment A: In the review of DMF it was concluded that none of the ingredients of the artificial Grape Flavor poses any toxicity concerns. An IR letter was sent to the holder requesting certain supplemental information. The original "inadequate" status designated in COMIS was inappropriate and has been corrected to "adequate".

### B. Other Supporting Documents:

Doc #	OWNER	ITEM REFERENCED	STATUS	DATE REVIEW COMPLETED	COMMENTS
N19835	Pfizer	cetirizine HCl (Zyrtec®) tablets	approved	08-Dec-1995	
N20346	Pfizer	cetirizine HCl (Zyrtec®) syrup	approved	27-Sep-1996	

### C. Related Documents:

DOCUMENT	APPLICATION NUMBER	Date	OWNER	COMMENT
IND	64570	16-APR-2002	Pfizer	Safe to proceed



# CHEMISTRY REVIEW #2



## Chemistry Review Data Sheet

### 18. CONSULTS/CMC-RELATED REVIEWS:

CONSULTS	SUBJECT	DATE REQUESTED	STATUS/DATE	COMMENTS
Pharm/Tox	Qualify Betadex/ Artificial Grape Flavor	19-Aug-03	Both of them are considered save. 30-Jan-2004	
Statistician	Determination of expiry dating	28-Oct-2003	Office consult on 29-Oct-2003	
EES CFN	DS Manuf. and Testing	29-Jul-2003	Acceptable 17-Oct-2003	
EES CFN	Comm. Stability Testing	30-Jul-2003	Acceptable 30-Jul-2003	
EES CFN	Comm. Stability Testing	29-Jul-2003	Acceptable 29-Sep-2003	
EES CFN	Foil/foil Blister Packaging & Release	29-Jul-2003	Acceptable 01-Oct-2003	
EES CFN	Packaging & Release Testing	29-Jul-2003	Acceptable 01-Oct-2003	
EES	<b>Overall Approval</b>	29-Jul-2003	<b>Acceptable</b> <b>17-Oct-2003</b>	
Methods Validation				Will be forwarded once specifications and methods are finalized for the DS and DP.
OPDRA		N/A		
EA		N/A		
Microbiology		N/A		

APPEARS THIS WAY  
ON ORIGINAL





## Executive Summary Section

**B. Description of How the Drug Product is Intended to be Used**

The drug product is intended to be used orally for the symptomatic treatment of seasonal allergic rhinitis, perennial allergic rhinitis, and chronic idiopathic urticaria for adults and children 2 years of age and older. The proposed dosage for adults and children of 12 years of age and older is 10mg once daily, for children 6 to 11 years is 5 or 10 mg once daily, for children 2 to 5 years is 5 mg once daily.

**C. Basis for Approvability or Not-Approval Recommendation**

The application is currently recommended as **approval (AP)**.

## Note:

The primary stability lots (commercial scale) with twelve month stability data were manufactured by UCB S. A., Belgium, and the site-specific lots (commercial scale) with only three month stability data were manufactured by Pfizer at the intended commercial site in . The data from the intended commercial site is limited in nature.

1. A deficiency letter was sent to the applicant on 11/14/2003 after the first review of the original NDA 21-621N000.
2. A complete response to the deficiency letter dated 11/14/2003 was received on 12/24/2003. It is evaluated in this review and found satisfactory except that certain degradants acceptance criteria do not reflect the data at release and statistical analysis of the stability data, and hence needed to be tightened so as to bring the acceptance criteria in line with the data and a fair statistical treatment.
3. An amendment containing (under long and intermediate term conditions) of stability data update for the primary stability batches and of stability data for site-specific batches (under long term, intermediate term, and accelerated conditions) was received on 9/30/03. It is evaluated in this review. Based on the updated data, a **statistical analysis** is performed to support the tightening of certain degradants acceptance criteria, especially for the newly identified degradant , total specified degradant, and total degradant.
4. The 12 month stability data and statistical analyses of the primary stability lots support the proposed 24 month expiry dating, even after the tightening of the degradants acceptance criteria.
5. A FAX was sent to the applicant on 2/16/2004 in which the Agency requested the applicant a timely response to the recommended degradants "e.g." acceptance criteria.
6. A telecom was held between the Agency and the applicant on 2/18/2004 in which agreements has been reached regarding the tightening of the degradants acceptance criteria. During the telecon the Agency also expressed the concerns over the untested in-use friability of the tablets when they are pushed though the blister, taking into account that the hardness is controlled at as low as . The degradants acceptance criteria, together with the hardness acceptance criterion, are agreed to be designated as **INTERIM** which is subjected to revision pending on the actual performance of the



## CHEMISTRY REVIEW #2



### Executive Summary Section

marketed products. The result of the study will be submitted to the FDA within 12 months following approval of the NDA.

7. An amendment documenting those agreements is received 2/26/04. **At this point, all CMC issues have been resolved satisfactorily.**

### III. Administrative

A. Reviewer's Signature

B. Endorsement Block

C. CC Block

**APPEARS THIS WAY  
ON ORIGINAL**

WITHHOLD 75 PAGE (S)

chemistry  
notes

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

/s/

-----  
Edwin Jao  
3/12/04 01:45:41 PM  
CHEMIST

Richard Lostritto  
3/12/04 01:48:11 PM  
CHEMIST

**APPEARS THIS WAY  
ON ORIGINAL**

**NDA 21-621**

**Cetirizine Hydrochloride Chewable Tablets**

**Pfizer**

**Edwin Jao, Ph.D.  
Division of Pulmonary and Allergy  
Drug Products**

**APPEARS THIS WAY  
ON ORIGINAL**



# Table of Contents

<b>The Executive Summary .....</b>	<b>9</b>
<b>I. Recommendations.....</b>	<b>9</b>
A. Recommendation and Conclusion on Approvability .....	9
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable.....	9
<b>II. Summary of Chemistry Assessments.....</b>	<b>9</b>
A. Description of the Drug Product(s) and Drug Substance(s) .....	9
B. Description of How the Drug Product is Intended to be Used.....	10
C. Basis for Approvability or Not-Approval Recommendation.....	10
<b>III. Administrative.....</b>	<b>11</b>
A. Reviewer's Signature.....	11
B. Endorsement Block.....	11
C. CC Block .....	11
<b>Chemistry Assessment .....</b>	<b>12</b>
<b>I. DRUG SUBSTANCE .....</b>	<b>12</b>
<b>II. DRUG PRODUCT .....</b>	<b>15</b>
A/B. Components/Compositions .....	15
C. Specifications and Methods for Drug Product Ingredients.....	17
D. Manufacturer.....	20
E. Manufacturing and Packaging .....	21
F. Regulatory Specifications and Test Methods for the Drug Product .....	26
G. Containers/Closures System .....	40
H. Microbiology.....	43
I. Stability.....	44
<b>III. Investigational Formula .....</b>	<b>60</b>



**IV. Environmental Assessment.....60**

**V. Methods Validation .....60**

**VI. Labeling .....61**

**VII. Establishment Inspections .....62**

**VIII Draft Deficiency Letter .....63**

**APPEARS THIS WAY  
ON ORIGINAL**



# Chemistry Review Data Sheet

1. NDA 21-621
2. REVIEW #: 1
3. REVIEW DATE: October 5, 2003
4. REVIEWER: Edwin Jao, Ph.D.
5. PREVIOUS DOCUMENTS:

Previous DocumentsDocument Date

IND64570

16-Apr-2002

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) ReviewedDocument DateAssigned Date

Original Submission N21-621n000 15-May-2003 13-Jul-2003

7. NAME & ADDRESS OF APPLICANT:

Name: Pfizer Inc

Address: 235 E. 42<sup>nd</sup> Street, New York, NY 10017

Representative: Rita A. Wittich, VP, Worldwide Regulatory Strategy

Telephone: (212) 573-7291

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Zyrtec (Ceterizine HCl) chewable tablets
- b) Non-Proprietary Name (USAN): Ceterizine Hydrochloride chewable tablets
- c) Code Name/# (ONDC only):N/A



# CHEMISTRY REVIEW #1



## Chemistry Review Data Sheet

d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

10. PHARMACOL. CATEGORY: Histamine H<sub>1</sub>-receptor antagonist

11. DOSAGE FORM: Chewable tablets (Bilayer with core containing active)

12. STRENGTH/POTENCY: 5 and 10 mg

13. ROUTE OF ADMINISTRATION: oral; Max Dose 10 mg QD

14. Rx/OTC DISPENSED:  Rx  OTC

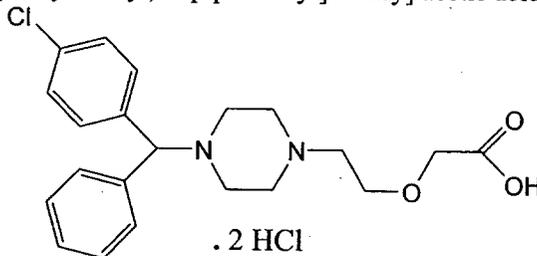
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product – Form Completed

Not a SPOTS product

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

2HCl-(±)-[2-[4-(*p*-chloro- $\alpha$ -phenylbenzyl)-1-piperazinyl]ethoxy] acetic acid dihydrochloride



Molecular Formula: C<sub>21</sub>H<sub>25</sub>N<sub>2</sub>O<sub>3</sub>·2HCl

Molecular Weight: 461.82

17. RELATED/SUPPORTING DOCUMENTS:

APPEARS THIS WAY  
ON ORIGINAL



# CHEMISTRY REVIEW #1



## Chemistry Review Data Sheet

### A. Supporting DMFs:

DMF #	TYP E	HOLDER	ITEM REFERENCED	CODE 1	STATUS <sup>2</sup>	DATE REVIEW COMPLETED (Reviewer)	COMMENTS
1		UCB S.A.	Cetirizine Hydrochloride	1	Adequate	22-Aug-2003 (E. Jao, Ph.D.)	
					Adequate	25-Aug-2003 (E. Jao, Ph.D.)	
					Inadequate	22-Oct-2002 (Dr. V. Shah)	Waiting for the holder to respond to the Deficiency letter
					Adequate	01-Apr-2003 (R. Frankewich, Ph.D.)	
					Adequate	01-Sep-2003 (E. Jao, Ph.D.)	
					Adequate	29-Apr-02 2003 (R. Frankewich, Ph.D.)	The amendments dated 03-03-03 and 25-03-03 added new _____ and/or additive packages to their current product line. No changes are reported to _____ used by the applicant.
					Adequate	29-Apr-02 (R. Frankewich, Ph.D.) Also 01-Sep-03, part of review on DMF _____ (E. Jao, Ph.D.)	Specifications & FDA statuses are included in DMF _____. See the review on DMF _____
Adequate	27-Sep-2000 (R. Lostritto)	No update for section 143 has been provided since it was deemed "Adequate" in the previous review.					
					Adequate	02-Aug-2002 (A. Shaw, Ph.D.)	



# CHEMISTRY REVIEW #1



## Chemistry Review Data Sheet

1	7	Adequate	31-Aug-2000 (P. Peri, Ph.D.)	
L	4			

<sup>1</sup> Action codes for DMF Table:

1 - DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 - Type 1 DMF

3 - Reviewed previously and no revision since last review

4 - Sufficient information in application

5 - Authority to reference not granted

6 - DMF not available

7 - Other (explain under "Comments")

<sup>2</sup> Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

<sup>3</sup> Include reference to location in most recent CMC review

### B. Other Supporting Documents:

Doc #	OWNER	ITEM REFERENCED	STATUS	DATE REVIEW COMPLETED	COMMENTS
N19835	Pfizer	cetirizine HCl (Zyrtec®) tablets	approved	08-Dec-1995	
N20346	Pfizer	cetirizine HCl (Zyrtec®) syrup	approved	27-Sep-1996	

### C. Related Documents:

DOCUMENT	APPLICATION NUMBER	OWNER	DESCRIPTION/COMMENT

### 18. CONSULTS/CMC-RELATED REVIEWS:

APPEARS THIS WAY  
ON ORIGINAL



# CHEMISTRY REVIEW #1



## Chemistry Review Data Sheet

CONSULTS	SUBJECT	DATE REQUESTED	STATUS/DATE	COMMENTS
Pharm/Tox	Qualify Betadex/ Artificial Grape Flavor	19-Aug-03	pending	
EES CFN	DS Manuf. and Testing	29-Jul-2003	Acceptable 17-Oct-2003	
EES CFN	Comm. Stability Testing	30-Jul-2003	Acceptable 30-Jul-2003	
EES CFN	Comm. Stability Testing	29-Jul-2003	Acceptable 29-Sep-2003	
EES CFN	Foil/foil Blister Packaging & Release	29-Jul-2003	Acceptable 01-Oct-2003	
EES CFN	Comm. Manuf. Packaging & Release Testing	29-Jul-2003	Acceptable 01-Oct-2003	
EES	<b>Overall Approval</b>	29-Jul-2003	<b>Acceptable 17-Oct-2003</b>	
Methods Validation				Will be forwarded once specifications and methods are finalized for the DS and DP.
OPDRA		N/A		No trademark provided for DP.
EA		N/A		
Microbiology		N/A		

APPEARS THIS WAY  
ON ORIGINAL



# The Chemistry Review for NDA 21-621

## The Executive Summary

### I. Recommendations

#### A. Recommendation and Conclusion on Approvability

The application is considered to be **approvable (AE)**.

#### B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

No recommendations for phase 4 studies are proposed or agreed upon at this time.

### II. Summary of Chemistry Assessments

Page location in this electron submission and numbering system used in this review:

1. Open "ndatoc.pdf" to display the first layer table of content.
2. Open the *modules* (e.g. labeling, module 1, CMC, module 3) through the hyperlink. This will display all the *sections* (e.g. 3.2 P Drug Product) and *subsections* (e.g. 3.2.P.8 Stability). All the sections/subsections **with hyperlinks** under "Electronic Archive File Location" are *electronically* independently numbered. For example, 3.2 P Drug Product is numbered from 1-379 at the bottom of the screen, but **NOT** on the print out, which has their own confusing numbering system. Clicking any of those hyperlinks will display the table of content of this section/subsection on the left of the screen which links to all the topics therewith.
3. In this review, the referenced page in the submission is indicated by *subsection* number followed by the *electronic page number* showing at the bottom of the screen. For example, 3.2.P.2.1.2., p. 11 locates in subsection 3.2.P.2.1.2. Excipient, Page 11.

#### A. Description of the Drug Product(s) and Drug Substance(s)

##### Drug Substance

- The drug substance, Cetirizine Hydrochloride, is a histamine H<sub>1</sub>-receptor antagonist. According to the applicant, it is a white or practically white powder. It is manufactured and supplied by UCB S. A., Belgium and referenced to DMF         , which has been reviewed and deemed "Adequate" (the latest amendments dated October 15, 2002 & May 14, 2003, E. Jao, 22-Apr-2003). The drug substance has been approved for use as immediately release tablet (N19-835), oral syrup (N20346), and extended release oral tablet (N21150).

**Drug Product**

- Cetirizine hydrochloride chewable tablets will be provided as round, purple, grape flavored, bilayer tablets in both 5 mg and 10 mg strengths packaged in aluminum foil/foil blisters. The weight for 5mg tablet is 225 mg and for 10 mg tablet is 450 mg (2.3.P.1., p.4). The 5 mg tablets are engraved with "ZYRTEC C5" on one side. The 10 mg tablets are engraved with "ZYRTEC C10" on one side. Based on the solubility profile provided (3.2.p.2.2. pp.44-45) and according to BCS guidance this drug product is classified as "rapidly dissolving".
- The bilayer design (with mannitol in the outside layer and Cetirizine HCl in the inside layer) and Cetirizine (3.2.P.2.1.2., p. 11). This design plus the process are also to (3.2.P.2.1.2., p. 11) (3.2.P.5.5., p.221).
- The novel excipient Betadex (betacyclodextrin, BCD) is referenced in NF (NF20, p.2215). But it has not been approved for use in drug product in this country. The 10 mg tablet contains mg of Betadex. LOA and COAs from the manufacturer will be requested.
- The novel excipient Artificial Grape Flavor is referenced to DMF, which is under Pharm/Tox's review.
- The excipient Carmine Dye is reported to cause anaphylaxis in very small populations who consumed Carmine containing food (Ann Allergy Asthma Immunol, 1997, (79), 414-419).

**B. Description of How the Drug Product is Intended to be Used**

The product is intended to be used orally for the symptomatic treatment of seasonal allergic rhinitis and for perennial allergic rhinitis and chronic idiopathic urticaria for adults and children 2 years of age and older. The proposed dosage for adults and children of 12 years of age and older is 10mg once daily, for children 6 to 11 years is 5 or 10 mg once daily, and , for children 2 to 5 years is 5 mg once daily (1.5.3.2.).

**C. Basis for Approvability or Not-Approval Recommendation**



Executive Summary Section

The application is currently recommended as **approvable (AE)** pending the corrections of the CMC deficiencies of the drug product.

1. The application does not include sufficient stability data for a comprehensive review on such issues as specification, stability, and expiry dating. Specifically, the only **12-month** stability data for the drug product is from a 10mg development batch ( — ) of commercial scale, manufactured at a non commercial site (UCB S. A., Belgium)). No stability data from the qualifying batches manufactured at the intended commercial site is provided. No statistical analysis on the submitted data is provided.
2. The acceptance criteria of drug product specification are not reflective of the data and hence need to be tightened.
3. The stability protocol needs to be revised to support of the current proposed specification and expiration dating period, and to assure continuity of product stability in the future during routine commercial production.
4. Additional information, modification, and clarification are required with regard to the container closure systems used for the drug product.

**III. Administrative**

**A. Reviewer's Signature**

**B. Endorsement Block**

**C. CC Block**

**APPEARS THIS WAY  
ON ORIGINAL**

WITHHOLD 54 PAGE(S)

chem r/w  
notes

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

/s/

-----  
Edwin Jao  
10/23/03 02:26:34 PM  
CHEMIST

Craig Bertha  
10/23/03 03:00:09 PM  
CHEMIST

**APPEARS THIS WAY  
ON ORIGINAL**

ESTABLISHMENT EVALUATION REQUEST

SUMMARY REPORT

Application : NDA 21621/000 Sponsor: PFIZER  
Org Code : 570 BOX 800202  
Priority : 3S CHARLOTTESVILLE, VA 22908020

Stamp Date : 16-MAY-2003 Brand Name : ZYRTEC(CETIRIZINE CHEWA  
PDUFA Date : 16-MAR-2004 TABLET)5/10MG  
Action Goal : Estab. Name:  
District Goal: 16-JAN-2004 Generic Name: CETIRIZINE HCL CHEWABLE  
TABLET  
Dosage Form: (TABLET, ORALLY DISINTE  
Strength : 5 & 10 MG

FDA Contacts: C. JACKSON Project Manager (HFD-570) 301-8  
50 E. JAO Review Chemist (HFD-570) 301-8  
17-1097 G. POOCHIKIAN Team Leader (HFD-800) 301-8  
17-5918

Overall Recommendation: ACCEPTABLE on 17-OCT-2003 by S. ADAMS (HFD-322) 3  
01-827-9051

Establishment : CFN : FEI :

DMF No: AADA:

Responsibilities:

Profile : TCM OAT Status: NONE



ESTABLISHMENT EVALUATION REQUEST

SUMMARY REPORT

Responsibilities: FINISHED DOSAGE RELEASE TESTER

Profile : CTL OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 29-SEP-03

Decision : ACCEPTABLE

Reason : DISTRICT RECOMMENDATION

-----  
Establishment :

PFIZER PHARMACEUTICAL INC  
UNION ST RD 195 KM 11  
FAJARDO, PR 00648

DMF No:

AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER  
FINISHED DOSAGE PACKAGER  
FINISHED DOSAGE RELEASE TESTER

Profile : TCM OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 01-OCT-03

Decision : ACCEPTABLE

Reason : DISTRICT RECOMMENDATION

-----  
Establishment :

CFN : \_\_\_\_\_ FEI :  
UCB BIOPRODUCTS SA  
BRAINE L'ALLEUD, , BE

DMF No: \_\_\_\_\_

AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Profile : CSN OAI Status: NONE  
Last Milestone: OC RECOMMENDATION  
Milestone Date: 17-OCT-03  
Decision : ACCEPTABLE  
Reason : DISTRICT RECOMMENDATION

---

APPEARS THIS WAY  
ON ORIGINAL