

Abraham, Elaine G

From: Abraham, Elaine G
Sent: Friday, August 29, 2008 8:09 AM
To: 'MUOparaugo@banpharm.com'
Cc: 'DSToops@banpharm.com'
Subject: RE: Cetirizine NDA 22-429

Unfortunately 1.14.1 is not adequate for our review of the labeling. At a minimum, we need mock-up labels for all SKUs.

I will have to check with the medical officer on your response to the safety, but she is out on leave now.

When can we expect the desk copies?

*Elaine Abraham, R.Ph.
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
White Oak CDER Bldg. # 22, Room 5410
10903 New Hampshire Ave.
Silver Spring, MD 20993
Phone: (301) 796-0843
Fax: (301) 796-9899
e-mail: elaine.abraham@fda.hhs.gov*

11/14/2008

Abraham, Elaine G

From: Abraham, Elaine G

Sent: Friday, August 29, 2008 8:56 AM

To: 'MUOparaugo@banpharm.com'; 'dstoops@banpharm.com'

Subject: FW: Cetirizine NDA 22-429

Another comment on the labeling, if you are requesting hives relief as well as allergic rhinitis, we would need complete labels for both indications.

Thanks.

Elaine

11/14/2008

Abraham, Elaine G

From: Abraham, Elaine G
Sent: Thursday, September 04, 2008 3:03 PM
To: 'DSToops@banpharm.com'
Cc: 'MUOparaugo@banpharm.com'
Subject: NDA 22-429 Cetirizine

Dana,

The chemist has identified the following issue that we need a response to prior to our internal filing meeting for your NDA:

Clarify who will perform the bottling operation for the commercial batches of the proposed product. Provide the name and street address, contact information, and registration number for the facility, and a statement of readiness for GMP inspection.

Please e-mail me your response and any supporting documentation, if necessary, before September 10. You should also send a copy of this information to your NDA file at the document room.

Thanks.

*Elaine Abraham, R.Ph.
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Office of Nonprescription Products
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Silver Spring, MD 20993
Phone: (301) 796-0843
Fax: (301) 796-9899
e-mail: elaine.abraham@fda.hhs.gov*

11/14/2008

Abraham, Elaine G

From: Abraham, Elaine G
Sent: Wednesday, September 10, 2008 1:51 PM
To: 'DSToops@banpharm.com'; 'MUOparaugo@banpharm.com'
Subject: NDA 22-429 Cetirizine filing issues

Dana,

We have identified the following potential filing issues for your application.

Your NDA submission has an incomplete clinical data section as specified in 21 CFR 314.50(d)(5). Specifically, it does not contain an integrated summary of safety of the drug product. Refer to 21 CFR 314.50(d)(5)(vi).

The application does not contain a statement for the conducted clinical studies that they were conducted in compliance with the institutional review board regulations, and in compliance with the informed consent regulations [21 CFR 314.101(d)(7)].

Please refer to our previous request for clinical information dated August 25, 2008. Your response to our request sent by e-mail on August 28, 2008 is not acceptable.

In order for us to assess safety of your formulation, postmarketing safety surveillance information for cetirizine from the following databases should be submitted:

- FDA Adverse Event Reporting System (AERS) database
- World health Organization (WHO) International Drug Monitoring program
- Literature Review
- Drug Abuse and Overdose Data:
 - American Association of Poison Control Centers (AAPCC)
 - Drug Abuse Warning Network (DAWN)
 - Emergency Department reports

Time period for a safety database should start at least one year prior to your NDA submission. Data from all sources should be summarized and analyzed by formulation, marketing status (Rx vs. OTC) dose, duration of use, year of reporting, age.

The above information must be received by the Agency by September 22, 2008 before we can file your application. We acknowledge that you have a 505(b)(2) application, in which you rely on the Agency's previous finding of safety and effectiveness for cetirizine 5 and 10 mg tablet. However, you still need to submit a complete NDA application. Refer to 21 CFR 314.50 for content and format of an NDA application.

Elaine Abraham, R.Ph.
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
White Oak CDER Bldg. # 22, Room 5410
10903 New Hampshire Ave.
Silver Spring, MD 20993
Phone: (301) 796-0843
Fax: (301) 796-9899
e-mail: elaine.abraham@fda.hhs.gov

11/14/2008

Abraham, Elaine G

From: MUOparaugo@banpharm.com
Sent: Friday, September 12, 2008 1:55 PM
To: Abraham, Elaine G
Cc: VGarikipati@banpharm.com; DSToops@banpharm.com
Subject: Re: NDA 22-429 REQUEST FOR A TELECONFERENCE
Importance: High

Dear Elaine,

We have been working on the potential filing issues for our NDA 22-429 per your e-mail dated 09-12-08 and have a few concerns which we wanted to bring to your attention. In the past we have submitted 505(b)(2) applications with safety updates on the 74 days of filing as required by the regulations and/or as requested by the Agency.

We are a small pharma company and have consulted with —ifferent companies (consultants with prior experience on similar request for additional safety data from the agency) to help us with the safety assessment of our formulation, (postmarketing safety surveillance information for cetirizine) from the data bases as requested by the Agency. In summary, we need additional clarification on the following:

1. Will medical literature data and data from FDA Adverse Event Reporting System (AERS) database with a focused search criteria which includes, a time period of at least one year prior to our NDA submission summarized and analyzed by formulation, marketing status (Rx vs. OTC) dose, duration of use, year of reporting, and age be sufficient to meet your request? As from our consultants experience safety data from the various databases tends to be redundant information.
2. It would immensely help us, if you could provide a template (format) on how you would like the safety data in the ISS report be presented as we do not have prior experience.

In view of the above, we would like to request a one hour teleconference with the medical reviewer and Banner representatives for next week Thursday September 18th or Friday the 19th to obtain better clarification. In the mean time we are aggressively working on requesting access to the AERS database through Freedom of Information (FOI) and literature review of safety information.

We commit to provide information as we soon as we can before the filing date, but may not be able to meet the earlier commitment to provide you the data by September 19th. We will propose a time-line for submission of the data during the teleconference.

In addition, we commit to amend the application with mock-up labeling information and a certification statement for the conducted clinical studies per [21 CFR 314.101(d)(7)]. We respectfully request the Agency's response on our proposal by end of business today.

Thank you.

XX

Marylyn Oparaugo, Bsc., RAC
Regulatory Affairs Associate
Banner Pharmacaps, Inc.
Phone: 336-812-8700 ext. 23334
Fax: 336-812-9091

11/17/2008

b(4)

Abraham, Elaine G

From: Abraham, Elaine G
Sent: Thursday, September 18, 2008 6:59 AM
To: 'MUOparaugo@banpharm.com'
Cc: 'DSToops@banpharm.com'; 'VGarikipati@banpharm.com'
Subject: RE: NDA 22-429 REQUEST FOR A TELECONFERENCE

Marylyn,

You asked for a format or template for the Integrated Summary of Safety. This is the response from the medical officer:

There is no official template for the ISS, but there is a guidance-- Reviewer Guidance Conducting a Clinical Safety Review of a New Product Application and Preparing a Report on the Review that can be found on the FDAs website (<http://www.fda.gov/cder/guidance/3580fnl.pdf>) and a Clinical Review Template (<http://www.fda.gov/cder/mapp/6010.3.pdf>). Section 7 of the latter is the integrated review of safety.

For OTC products, we rely greatly on postmarketing information from the different databases.

Elaine

Abraham, Elaine G

From: VGarikipati@banpharm.com
Sent: Thursday, September 18, 2008 8:45 AM
To: Abraham, Elaine G
Cc: DSToops@banpharm.com; MUOparaigo@banpharm.com; MECrawley@Banpharm.com
Subject: Re: FW: NDA 22-429 REQUEST FOR A TELECONFERENCE

Dear Elaine,

Thank you and we are looking forward for the Tcon at 12.30 noon tomorrow. Also we want to bring to your kind attention the other 505(b)(2) applications approved for Banner:

1. NDA 21-472 - Ibuprofen Capsules, 200 mg.
2. NDA 21-855 - Loperamide Capsules, 2 mg, 1 mg.
3. NDA 21-920 - Naproxen Sodium Capsules, 220 mg
4. NDA 22-152 - Valproic Acid Delayed Release, Capsules, 500 mg, 250 mg, 125 mg.

We sincerely appreciate the Agency's time and input on the safety information required for NDA 22-429, as we do not have prior experience about the same. Thank you once again.

Best regards
Vandana

Vandana Garikipati, MS, RAC
Manager, Regulatory Affairs
Banner Pharmacaps Inc
4125 Premier Drive
High Point 27265
Phone: 336-812-8700, Ext 23988
Fax: 336-812-9091

11/17/2008

Abraham, Elaine G

From: Abraham, Elaine G
Sent: Thursday, September 18, 2008 12:47 PM
To: 'MUOparaugo@banpharm.com'
Cc: 'VGarikipati@banpharm.com'; 'DSToops@banpharm.com'
Subject: RE: NDA 22-429 REQUEST FOR A TELECONFERENCE
Attachments: NDA 22-429 Cetirizine T-con.doc

Marylyn,

Our responses to your request for additional information are attached.

*Elaine Abraham, R.Ph.
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10903 New Hampshire Ave.
Silver Spring, MD 20993
Phone: (301) 796-0843
Fax: (301) 796-9899
e-mail: elaine.abraham@fda.hhs.gov*

11/14/2008

NDA 22-429 Cetirizine NDA Safety T-con

From: MUOparaugo@banpharm.com [mailto:MUOparaugo@banpharm.com]
Sent: Friday, September 12, 2008 1:55 PM
To: Abraham, Elaine G
Cc: VGarikipati@banpharm.com; DSToops@banpharm.com
Subject: Re: NDA 22-429 REQUEST FOR A TELECONFERENCE
Importance: High

We have been working on the potential filing issues for our NDA 22-429 per your e-mail dated 09-12-08 and have a few concerns which we wanted to bring to your attention. In the past we have submitted 505(b)(2) applications with safety updates on the 74 days of filing as required by the regulations and/or as requested by the Agency.

NDA's must be complete at the time of submission as specified in 21 CFR 314.50. This is the current standard for all NDA submissions.

We are a small pharma company and have consulted with ~~several~~ different companies (consultants with prior experience on similar request for additional safety data from the agency) to help us with the safety assessment of our formulation, (postmarketing safety surveillance information for cetirizine) from the data bases as requested by the Agency. In summary, we need additional clarification on the following:

b(4)

1. Will medical literature data and data from FDA Adverse Event Reporting System (AERS) database with a focused search criteria which includes, a time period of at least one year prior to our NDA submission summarized and analyzed by formulation, marketing status (Rx vs. OTC) dose, duration of use, year of reporting, and age be sufficient to meet your request? As from our consultants experience safety data from the various databases tends to be redundant information.

No, we do not agree. Your safety assessment report should include a separate search from the medical literature and AERS; reports from each database should be analyzed separately. Although some of the cases reported in the medical literature may also have been reported to the AERS database, this is not true for all cases.

2. It would immensely help us, if you could provide a template (format) on how you would like the safety data in the ISS report be presented as we do not have prior experience.

In general, the section on integrated summary of safety should address safety data from clinical trials, postmarketing sources, abuse and misuse potential, drug-drug interactions, and special populations.

Therefore, the integrated safety assessment (ISS) should include description, analysis and interpretation of the safety information from the studies you conducted, and from the following postmarketing safety databases for cetirizine products. Each of the following safety databases should be analyzed separately:

- FDA Adverse Event Reporting System (AERS) database
- World health Organization (WHO) International Drug Monitoring Program
- Medical Literature Review (provide references and articles)
- Drug Abuse and Overdose Data from:
 - American Association of Poison Control Centers (AAPCC)
 - Drug Abuse Warning Network (DAWN)

The analysis of the above databases should include but not be limited to the following information:

- Deaths
- Serious Adverse Events
- Common Adverse Events
- Laboratory Findings, Vital Signs, Physical Examination

- Overdose experience

Provide your own summary/conclusion and interpretation of the above information for cetirizine.

The time period for a safety database should start at least one year prior to your NDA submission. Data from all sources should be summarized and analyzed by formulation, marketing status (Rx vs. OTC) dose, duration of use, year of reporting, age. See also our email sent to you on 9/10/08.

In view of the above, we would like to request a one hour teleconference with the medical reviewer and Banner representatives for next week Thursday September 18th or Friday the 19th to obtain better clarification. In the mean time we are aggressively working on requesting access to the AERS database through Freedom of Information (FOI) and literature review of safety information.

We commit to provide information as we soon as we can before the filing date, but may not be able to meet the earlier commitment to provide you the data by September 19th. We will propose a time-line for submission of the data during the teleconference.

In addition, we commit to amend the application with mock-up labeling information and a certification statement for the conducted clinical studies per [21 CFR 314.101(d)(7)]. We respectfully request the Agency's response on our proposal by end of business today.

Abraham, Elaine G

From: VGarikipati@banpharm.com
Sent: Thursday, September 18, 2008 4:30 PM
To: Abraham, Elaine G
Cc: DSToops@banpharm.com; MUOparaugo@banpharm.com; MECrawley@Banpharm.com
Subject: RE: NDA 22-429 REQUEST FOR A TELECONFERENCE
Attachments: NDA 22-429 Cetirizine T-con, FDA response - Banner response 9-18-08.doc

Dear Elaine,

Please find attached Banner response on the additional information. Thank you and looking forward to the T-con.

Best regards
Vandana

Vandana Garikipati, MS, RAC
Manager, Regulatory Affairs
Banner Pharmacaps Inc
4125 Premier Drive
High Point 27265
Phone: 336-812-8700, Ext 23988
Fax: 336-812-9091

11/17/2008

Therefore, the integrated safety assessment (ISS) should include description, analysis and interpretation of the safety information from the studies you conducted, and from the following postmarketing safety databases for cetirizine products. Each of the following safety databases should be analyzed separately:

- FDA Adverse Event Reporting System (AERS) database
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The analysis of the above databases should include but not be limited to the following information:

- Deaths
- Serious Adverse Events
- Common Adverse Events
- Laboratory Findings, Vital Signs, Physical Examination
- Overdose experience

Provide your own summary/conclusion and interpretation of the above information for cetirizine.

The time period for a safety database should start at least one year prior to your NDA submission. Data from all sources should be summarized and analyzed by formulation, marketing status (Rx vs. OTC) dose, duration of use, year of reporting, age. See also our email sent to you on 9/10/08.

In view of the above, we would like to request a one hour teleconference with the medical reviewer and Banner representatives for next week Thursday September 18th or Friday the 19th to obtain better clarification. In the mean time we are aggressively working on requesting access to the AERS database through Freedom of Information (FOI) and literature review of safety information.

We commit to provide information as soon as we can before the filing date, but may not be able to meet the earlier commitment to provide you the data by September 19th. We will propose a time-line for submission of the data during the teleconference.

In addition, we commit to amend the application with mock-up labeling information and a certification statement for the conducted clinical studies per [21 CFR 314.101(d)(7)]. We respectfully request the Agency's response on our proposal by end of business today.

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

/s/

Elaine Abraham
11/24/2008 07:52:48 AM
CSO

DISCUSSION: Banner stated that based on their previous submission experience, 505(b)(2) applications submitted under 314.54 make reference to and rely on the safety information submitted by the reference listed drug. FDA stated that under 314.50(d), an NDA must contain a complete technical section, at the time of submission, including a complete clinical data section, specifically safety information as required in 21 CFR 314.50(d)(5)(vi). FDA asked how quickly Banner could provide the requested safety information. Banner stated that they are working on obtaining the safety information and have gained access to AERS and WHO and need to obtain access to AAPCC and DAWN. Banner asked if FDA has specific safety concerns that they should address. FDA responded that a review of the safety data, when submitted, will determine if there are specific concerns. FDA noted that cetirizine was switched to OTC a year ago; therefore, the time period for a safety database should start at least one year prior to the NDA submission.

FDA noted that incomplete applications can be refused to file by the Agency; Banner should keep this in mind for future submissions. FDA asked about the timeframe when the safety analysis would be sent. Banner committed to submit the requested safety information by the end of October. FDA pointed out that a description, analysis and integration of all safety data will be needed. FDA also stated that the labeling and the ethics statement on the conduct of each study are needed to file the application.

FDA concluded by requesting that Banner send a letter by September 25 committing to sending in labeling and the ethics statement by September 26 and the safety section of their NDA by October 31.

N.B. Banner submitted a commitment letter dated September 25, 2008 which responded to FDA's concerns (see attached).



September 25, 2008

Banner Pharmaceps Inc.
4125 Premier Drive
High Point, NC 27265

PHONE 336.812.8700
FAX 336.812.9004

**NDA Amendment:
Letter of Commitment**

FDA, CDER
Office of Nonprescription Products
Division of Nonprescription Clinical Evaluation
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Asia/Pacific

Canada

Europe

Mexico/Latin America

► United States

**RE: NDA 22-429
Cetirizine HCl Capsules, 10 mg & 5 mg**

Banner Pharmaceps Inc. (BPI) is hereby submitting an amendment to NDA 22-429, for Cetirizine HCl Capsules, 10 mg & 5 mg capsules submitted July 31, 2008.

The purpose of this amendment is to provide a letter of commitment as requested by the Agency following the teleconference held between the agency and BPI on 9/19/08 regarding FDA's request for additional safety information.

This amendment provides for the following commitments:

- Mock-up labeling for all SKU's for each strength and both indications to be submitted by 09/26/08.
- An ethical conduct of compliance statement according to 21 CFR Part 56 and 50 (including Subpart B informed consent of human subjects) to be submitted by 09/26/08.
- An amended study report, which includes detailed safety information and the ethical conduct of compliance statement to be submitted by 10/31/08.
- Integrated safety assessment (ISS) which will include description, analysis and interpretation of the safety information from the studies Banner conducted, and from



the following postmarketing safety databases for cetirizine products by 10/31/08.

- FDA Adverse Event Reporting System (AERS) database
- World health Organization (WHO) International Drug Monitoring Program
- Medical Literature Review (provide references and articles)
- Drug Abuse and Overdose Data from:
 - American Association of Poison Control Centers (AAPCC)
 - Drug Abuse Warning Network (DAWN)

This amendment consists of one Archival copy and one Review copy. If you have any questions, comments or require any additional information in regard to this NDA, please feel free to contact me by telephone at (336) 812-8700, extension 23312, by fax at (336) 812-9091, or by email at dstoops@banpharm.com.

Sincerely,

Dana S. Toops
Executive Director,
US Research and Development



September 25, 2008

Banner Pharmacaps Inc.
4125 Premier Drive
High Point, NC 27265

PHONE 336.812.8700
FAX 336.812.9004

Asia/Pacific

Canada

Europe

Mexico/Latin America

United States

NDA Amendment

FDA, CDER
Office of Nonprescription Products
Division of Nonprescription Clinical Evaluation
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

**RE: NDA 22-429
Cetirizine HCl Capsules, 10 mg & 5 mg**

Banner Pharmacaps Inc. (BPI) is hereby submitting an amendment to NDA 22-429, for Cetirizine HCl Capsules, 10 mg & 5 mg capsules submitted July 31, 2008.

The purpose of this amendment is to provide the following according to our commitment letter:

- A copy of the ethical conduct of compliance statement according to 21 CFR Part 56 and 50 (including Subpart B informed consent of human subjects) for BPI's clinical studies.
- Mock-up labeling for all stock keeping units (SKU's) for each strength and indication in response to request for additional information (per email dated 8/29/08 from project manager Elaine Abraham) The following labeling sections of the original NDA application have been amended.

Section 1.14.1.1	Draft Carton/Container Labels-Amended
Section 1.14.1.2	Annotated Draft Labeling Text (Container Label)-Amended
Section 1.14.1.3	Draft Labeling text-No changes (provided for information)
Section 1.14.3.1	Annotated Comparison with RLD-Amended (for clarity)
Section 1.14.3	Listed Drug Labeling-No changes

This amendment consists of one Archival copy and one Review copy. If you have any questions, comments or require any additional information



in regard to this NDA, please feel free to contact me by telephone at (336) 812-8700, extension 23312, by fax at (336) 812-9091, or by email at dstoops@banpharm.com.

Sincerely,

Dana S. Toops
Executive Director,
US Research and Development

Abraham, Elaine G

From: Abraham, Elaine G
Sent: Friday, August 22, 2008 10:39 AM
To: 'dstoops@banpharm.com'
Subject: NDA 22-429

Dana,

The medical officer could not locate the safety assessment section(s) in your NDA 22-429 cetirizine HCl. Please point us to the location or submit the following:

- (a) narrative description and analysis of adverse events from your PK studies
- (b) postmarketing safety
- (c) integrated summary of safety (ISS).

You should send me a desk copy and also send a copy to the document room. Thanks.

*Elaine Abraham, R.Ph.
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
White Oak CDER Bldg. # 22, Room 5410
10903 New Hampshire Ave.
Silver Spring, MD 20993
Phone: (301) 796-0843
Fax: (301) 796-9899
e-mail: elaine.abraham@fda.hhs.gov*

Abraham, Elaine G

From: Abraham, Elaine G
Sent: Monday, August 25, 2008 1:14 PM
To: 'dstoops@banpharm.com'
Subject: NDA 22-429

Dana,

I have more specific information about what the medical officer is looking for in your NDA. See below.

Location of safety assessments for your NDA submission including:

- (a) narrative description and analysis of adverse events from your PK studies
- (b) postmarketing safety surveillance information for the OTC marketing of cetirizine from the following databases:
 - Adverse Event Reporting System (AERS)
 - World Health Organization (WHO) International Drug Monitoring Program
 - Toxic Exposure Surveillance System (TESS) database maintained by the American Association of Poison Control Centers (AAPCC)
 - Drug Abuse Warning Network (DAWN) database
 - Medical literature
- (c) integrated summary of safety (ISS).

Again, send me a desk copy and also send a copy to the document room. Thanks.

*Elaine Abraham, R.Ph.
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
White Oak CDER Bldg. # 22, Room 5410
10903 New Hampshire Ave.
Silver Spring, MD 20993
Phone: (301) 796-0843
Fax: (301) 796-9899
e-mail: elaine.abraham@fda.hhs.gov*

Abraham, Elaine G

From: MUOparaugo@banpharm.com
Sent: Thursday, August 28, 2008 5:21 PM
To: Abraham, Elaine G
Cc: DSToops@banpharm.com
Subject: Cetirizine NDA 22-429
Attachments: Cetirizine Cover Letter.pdf

Good Afternoon Elaine,

Per your telephone conversation with Dana: This email is to confirm the shipment of the following to you:

1. (2) additional desk copies of our 505 (b)(2) New Drug Application for Cetirizine HCl Capsules, 10 mg & 5 mg.
2. (4) additional desk copies of Volume 1: Module 1 & 2

Provided below is a response to the pending requested information:

- Application missing (SKU) labeling information: **BPI's Response:** Refer to module 1 section: 1.14.1 for the draft labeling text of BPI's proposed carton/container labeling.

-(a) Narrative Description and analysis of adverse events from your PK studies:

BPI's Response: Please refer to the following sections for all AE related information in the study reports

Study 20-219-SA:

Refer to page 22 of 1545 for a narrative description of AEs for this study
Refer to page 23 of 1545 for a summary analysis of AEs for this study
Refer to page 26-35 of 1545 for the clinical listings of AEs for this study

Study 20-220-SA:

Refer to page 21 of 1590 for a narrative description of AEs for this study
Refer to page 23 of 1590 for a summary analysis of AEs for this study
Refer to page 25-34 of 1590 for the clinical listings of AEs for this study

(b) Postmarketing safety surveillance information for the OTC marketing of Cetirizine from the following

- databases:
- Adverse Event Reporting System (AERS)
 - World Health Organization (WHO) International Drug Monitoring Program
 - Toxic Exposure Surveillance System (TESS) database maintained by the American
 - Association of Poison Control Centers (AAPCC)
 - Drug Abuse Warning Network (DAWN) database
 - Medical literature

(c) integrated summary of safety (ISS).

BPI's Response for (b) and (c): Reference is made to 21 CFR 314.54(a)(3) the safety assessment of

11/14/2008

our 505 (b)(2) application relies on the Agency's finding of safety and effectiveness for the reference listed drug (RLD), Zyrtec® Tablets, 10 mg & 5 mg, the subject of NDA 19-835, held by Pfizer Labs/McNeil Consumer Healthcare.

XX
Marylyn Oparaugo, BSc., RAC
Regulatory Affairs Associate
Banner Pharmacaps, Inc.
Phone: 336-812-8700 ext. 23334
Fax: 336-812-9091

NOTICE: This email (including attachments) is CONFIDENTIAL, may be legally privileged, and is legally protected from disclosure. If you are not the intended recipient, any retention, dissemination, distribution, or copying of this email or attachments is strictly prohibited. Please REPLY to the sender that you have received the email or attachments in error, then delete it and all attachments. Thank you.

Abraham, Elaine G

From: Abraham, Elaine G
Sent: Wednesday, September 10, 2008 1:51 PM
To: 'DSToops@banpharm.com'; 'MUOparaugo@banpharm.com'
Subject: NDA 22-429 Cetirizine filing issues

Dana,

We have identified the following potential filing issues for your application.

Your NDA submission has an incomplete clinical data section as specified in 21 CFR 314.50(d)(5). Specifically, it does not contain an integrated summary of safety of the drug product. Refer to 21 CFR 314.50(d)(5)(vi).

The application does not contain a statement for the conducted clinical studies that they were conducted in compliance with the institutional review board regulations, and in compliance with the informed consent regulations [21 CFR 314.101(d)(7)].

Please refer to our previous request for clinical information dated August 25, 2008. Your response to our request sent by e-mail on August 28, 2008 is not acceptable.

In order for us to assess safety of your formulation, postmarketing safety surveillance information for cetirizine from the following databases should be submitted:

- FDA Adverse Event Reporting System (AERS) database
- World health Organization (WHO) International Drug Monitoring program
- Literature Review
- Drug Abuse and Overdose Data:
 - American Association of Poison Control Centers (AAPCC)
 - Drug Abuse Warning Network (DAWN)
 - Emergency Department reports

Time period for a safety database should start at least one year prior to your NDA submission. Data from all sources should be summarized and analyzed by formulation, marketing status (Rx vs. OTC) dose, duration of use, year of reporting, age.

The above information must be received by the Agency by September 22, 2008 before we can file your application. We acknowledge that you have a 505(b)(2) application, in which you rely on the Agency's previous finding of safety and effectiveness for cetirizine 5 and 10 mg tablet. However, you still need to submit a complete NDA application. Refer to 21 CFR 314.50 for content and format of an NDA application.

Elaine Abraham, R.Ph.
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Office of Nonprescription Products
White Oak CDER Bldg. # 22, Room 5410
10903 New Hampshire Ave.
Silver Spring, MD 20993
Phone: (301) 796-0843
Fax: (301) 796-9899
e-mail: elaine.abraham@fda.hhs.gov

11/14/2008

Abraham, Elaine G

From: MUOparaugo@banpharm.com
Sent: Friday, September 12, 2008 1:55 PM
To: Abraham, Elaine G
Cc: VGarikipati@banpharm.com; DSToops@banpharm.com
Subject: Re: NDA 22-429 REQUEST FOR A TELECONFERENCE
Importance: High

Dear Elaine,

We have been working on the potential filing issues for our NDA 22-429 per your e-mail dated 09-12-08 and have a few concerns which we wanted to bring to your attention. In the past we have submitted 505(b)(2) applications with safety updates on the 74 days of filing as required by the regulations and/or as requested by the Agency.

We are a small pharma company and have consulted with ~~several~~ different companies (consultants with prior experience on similar request for additional safety data from the agency) to help us with the safety assessment of our formulation, (postmarketing safety surveillance information for cetirizine) from the data bases as requested by the Agency. In summary, we need additional clarification on the following:

b(4)

1. Will medical literature data and data from FDA Adverse Event Reporting System (AERS) database with a focused search criteria which includes, a time period of at least one year prior to our NDA submission summarized and analyzed by formulation, marketing status (Rx vs. OTC) dose, duration of use, year of reporting, and age be sufficient to meet your request? As from our consultants experience safety data from the various databases tends to be redundant information.
2. It would immensely help us, if you could provide a template (format) on how you would like the safety data in the ISS report be presented as we do not have prior experience.

In view of the above, we would like to request a one hour teleconference with the medical reviewer and Banner representatives for next week Thursday September 18th or Friday the 19th to obtain better clarification. In the mean time we are aggressively working on requesting access to the AERS database through Freedom of Information (FOI) and literature review of safety information.

We commit to provide information as we soon as we can before the filing date, but may not be able to meet the earlier commitment to provide you the data by September 19th. We will propose a time-line for submission of the data during the teleconference.

In addition, we commit to amend the application with mock-up labeling information and a certification statement for the conducted clinical studies per [21 CFR 314.101(d)(7)]. We respectfully request the Agency's response on our proposal by end of business today.

Thank you.

XX
Marylyn Oparaugo, Bsc., RAC
Regulatory Affairs Associate
Banner Pharmacaps, Inc.
Phone: 336-812-8700 ext. 23334
Fax: 336-812-9091

Abraham, Elaine G

From: Abraham, Elaine G
Sent: Thursday, September 18, 2008 12:47 PM
To: 'MUOparaugo@banpharm.com'
Cc: 'VGarikipati@banpharm.com'; 'DSToops@banpharm.com'
Subject: RE: NDA 22-429 REQUEST FOR A TELECONFERENCE
Attachments: NDA 22-429 Cetirizine T-con.doc

Marylyn,

Our responses to your request for additional information are attached.

*Elaine Abraham, R.Ph.
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
White Oak CDER Bldg. # 22, Room 5410
10903 New Hampshire Ave.
Silver Spring, MD 20993
Phone: (301) 796-0843
Fax: (301) 796-9899
e-mail: elaine.abraham@fda.hhs.gov*

- Overdose experience

Provide your own summary/conclusion and interpretation of the above information for cetirizine.

The time period for a safety database should start at least one year prior to your NDA submission. Data from all sources should be summarized and analyzed by formulation, marketing status (Rx vs. OTC) dose, duration of use, year of reporting, age. See also our email sent to you on 9/10/08.

In view of the above, we would like to request a one hour teleconference with the medical reviewer and Banner representatives for next week Thursday September 18th or Friday the 19th to obtain better clarification. In the mean time we are aggressively working on requesting access to the AERS database through Freedom of Information (FOI) and literature review of safety information.

We commit to provide information as we soon as we can before the filing date, but may not be able to meet the earlier commitment to provide you the data by September 19th. We will propose a time-line for submission of the data during the teleconference.

In addition, we commit to amend the application with mock-up labeling information and a certification statement for the conducted clinical studies per [21 CFR 314.101(d)(7)]. We respectfully request the Agency's response on our proposal by end of business today.

Abraham, Elaine G

From: VGarikipati@banpharm.com
Sent: Thursday, September 18, 2008 4:30 PM
To: Abraham, Elaine G
Cc: DSToops@banpharm.com; MUOparaugo@banpharm.com; MECrawley@Banpharm.com
Subject: RE: NDA 22-429 REQUEST FOR A TELECONFERENCE
Attachments: NDA 22-429 Cetirizine T-con, FDA response - Banner response 9-18-08.doc

Dear Elaine,

Please find attached Banner response on the additional information. Thank you and looking forward to the T-con.

Best regards
Vandana

Vandana Garikipati, MS, RAC
Manager, Regulatory Affairs
Banner Pharmacaps Inc
4125 Premier Drive
High Point 27265
Phone: 336-812-8700, Ext 23988
Fax: 336-812-9091

11/17/2008

Therefore, the integrated safety assessment (ISS) should include description, analysis and interpretation of the safety information from the studies you conducted, and from the following postmarketing safety databases for cetirizine products. Each of the following safety databases should be analyzed separately:

- FDA Adverse Event Reporting System (AERS) database
- World health Organization (WHO) International Drug Monitoring Program
- Medical Literature Review (provide references and articles)
- Drug Abuse and Overdose Data from:
 - American Association of Poison Control Centers (AAPCC)
 - Drug Abuse Warning Network (DAWN)

The analysis of the above databases should include but not be limited to the following information:

- Deaths
- Serious Adverse Events
- Common Adverse Events
- Laboratory Findings, Vital Signs, Physical Examination
- Overdose experience

Provide your own summary/conclusion and interpretation of the above information for cetirizine.

The time period for a safety database should start at least one year prior to your NDA submission. Data from all sources should be summarized and analyzed by formulation, marketing status (Rx vs. OTC) dose, duration of use, year of reporting, age. See also our email sent to you on 9/10/08.

In view of the above, we would like to request a one hour teleconference with the medical reviewer and Banner representatives for next week Thursday September 18th or Friday the 19th to obtain better clarification. In the mean time we are aggressively working on requesting access to the AERS database through Freedom of Information (FOI) and literature review of safety information.

We commit to provide information as we soon as we can before the filing date, but may not be able to meet the earlier commitment to provide you the data by September 19th. We will propose a time-line for submission of the data during the teleconference.

In addition, we commit to amend the application with mock-up labeling information and a certification statement for the conducted clinical studies per [21 CFR 314.101(d)(7)]. We respectfully request the Agency's response on our proposal by end of business today.

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

/s/

Elaine Abraham
11/24/2008 07:50:03 AM
CSO

DSI CONSULT

Request for Biopharmaceutical Inspections

DATE: October 8, 2008

TO: Associate Director for Bioequivalence
Division of Scientific Investigations, HFD-48

THROUGH: Director, Division of Pharmaceutical Evaluation, HFD-560

FROM: Janice Adams-King, Regulatory Project Manager, HFD-560

SUBJECT: Request for Biopharmaceutical Inspections
NDA 22-429
cetirizine capsules, 5mg and 10mg

Study/Site Identification:

As discussed with you, the following studies/sites pivotal to approval (OR, raise question regarding the quality or integrity of the data submitted and) have been identified for inspection:

Study #	Clinical Site (name, address, phone, fax, contact person, if available)	Analytical Site (name, address, phone, fax, contact person, if available)
20-219-SA		
20-220-SA		

b(4)

b(4)

Goal Date for Completion:

We request that the inspections be conducted and the Inspection Summary Results be provided by **March 1, 2009**. We intend to issue an action letter on this application by **June 1, 2009**.

Should you require any additional information, please contact Janice Adams-King.

Concurrence: (Optional)
Wei Qiu Biopharm Team Leader
Yun Xu Biopharm Reviewer

NDA 22-429

Page 2

Request for Biopharmaceutical Inspection

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

/s/

Janice Adams-King
10/15/2008 12:43:43 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-429

Banner Pharmacaps, Inc.
Attention: Dana S. Toops
Director, Regulatory Affairs
4125 Premier Drive
High Point, NC 27265

Dear Mr. Toops,

Please refer to your new drug application (NDA) dated July 31, 2008, received August 1, 2008, pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for cetirizine HCl capsules, 5 mg and 10 mg.

We also refer to your submissions dated September 8 and 25, 2008.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is June 1, 2009.

During our filing review of your application, we identified the following potential review issues:

1. The packaging configurations are not clear.
2. A letter of authorization for DMF ~~_____~~ is not provided. **b(4)**
3. Comparative in-vitro dissolution data is not provided to support the biowaiver.
4. The clinical section is incomplete, i.e., integrated summary of safety is missing.
5. The marketing status of cetirizine in U.S. and foreign countries needs to be clarified.

We are providing the above comments to give you preliminary notice of potential review issues. 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 also request that you submit the following information:

1. Clarify the intended to-be marketed packaging configurations, especially regarding capsule counts and packaging components for each configuration or SKU.
2. Provide a letter of authorization for DMF ~~_____~~ b(4)
3. Provide comparative in-vitro dissolution data with f_2 analysis in media of pH 1 and pH 4.5 for 5 mg and 10 mg soft gelatin capsules to support the biowaiver.
4. Provide an integrated safety assessment (ISS) which will include description, analysis and interpretation of safety information from the studies Banner conducted and from the postmarketing safety databases for cetirizine products.
5. Provide information regarding whether this product has been approved, marketed, and/or withdrawn in the U.S. or any foreign countries. You should include marketing status (prescription, pharmacy-only or over-the-counter) for each country.

Additionally, we remind you of your letter of commitment, dated September 25, 2008, which provides for the following commitments:

- An amended study report, which includes detailed safety information and the ethical conduct of compliance statement.
- Integrated safety assessment (ISS) which will include description, analysis and interpretation of the safety information from the studies Banner conducted, and from the following postmarketing safety databases for cetirizine products.
 - FDA Adverse Event Reporting Systems (AERS) database
 - World Health Organization International Drug Monitoring Program
 - Medical Literature Review
 - Drug Abuse and Overdose Data from:
 - American Association of Poison Control Centers
 - Drug Abuse Warning Network

Please respond only 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.

We remind you to submit 4-month safety update information in accordance with 21 CFR 314.50(d)(5)(vi)(b)].

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 requirements. We acknowledge receipt of your request for waiver of pediatric studies for this application for pediatric patients less than 6 years of age.

NDA 22-429

Page 3

If you have any questions, call Janice Adams-King, Regulatory Project Manager, at (301) 796-3713.

Sincerely,

{See appended electronic signature page}

Leah Christl, Ph.D.
Acting Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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

/s/

Leah Christl
10/14/2008 03:40:01 PM

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 22-429 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: _____ Established/Proper Name: Cetirizine Dosage Form: capsules		Applicant: Banner Pharmacaps, Inc. Agent for Applicant (if applicable):
RPM: Janice Adams-King		Division: ONP/DNCE
<p>NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2)</p> <p>Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p>		<p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s)): NDA 19-835, Zyrtec®, 5 mg and 10 mg, tablets</p> <p>Provide a brief explanation of how this product is different from the listed drug. This product is in capsule dosage form and not tablet.</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p>Prior to approval, review and confirm the information previously provided in Appendix B to the Regulatory Filing Review by re-checking the Orange Book for any new patents and pediatric exclusivity. If there are any changes in patents or exclusivity, notify the OND ADRA immediately and complete a new Appendix B of the Regulatory Filing Review.</p> <p><input type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check:</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p> <p>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</p>
❖ User Fee Goal Date Action Goal Date (if different)		July 23, 2009
❖ Actions		
• Proposed action		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <input type="checkbox"/> CR
• Previous actions (specify type and date for each action taken)		<input checked="" type="checkbox"/> None
❖ Promotional Materials (accelerated approvals only) Note: If accelerated approval (21 CFR 314.510/601.41), promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see guidance www.fda.gov/cder/guidance/2197dft.pdf). If not submitted, explain _____		<input type="checkbox"/> Received

¹ The Application Information section is (only) a checklist. The Contents of Action Package section (beginning on page 5) lists the documents to be included in the Action Package.

b(4)

❖ Application ² Characteristics	
Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC NDAs: Subpart H BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart I Subpart H <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC Comments: _____	
❖ Date reviewed by PeRC (<i>required for approvals only</i>) If PeRC review not necessary, explain: _____	March 25, 2009
❖ BLAs only: <i>RMS-BLA Product Information Sheet for TBP</i> has been completed and forwarded to OBPS/DRM (<i>approvals only</i>)	<input type="checkbox"/> Yes, date
❖ BLAs only: is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Public communications (<i>approvals only</i>)	
• Office of Executive Programs (OEP) liaison has been notified of action	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Press Office notified of action (by OEP)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Indicate what types (if any) of information dissemination are anticipated	<input checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

² All questions in all sections pertain to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

❖ Exclusivity	
<ul style="list-style-type: none"> Is approval of this application blocked by any type of exclusivity? 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> NDA and BLA: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification. 	<input type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.) 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.) 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.) 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? (Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.) 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date 10-year limitation expires: _____
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	21 CFR 314.50(i)(1)(i)(A) <input checked="" type="checkbox"/> Verified (Sponsor's patent certification states that "no patent information has been submitted to FDA for the listed drug referred to in this application.") 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	<input type="checkbox"/> No paragraph III certification Date patent will expire _____
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). (If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (Summary Reviews)). 	<input type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified

- [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for each paragraph IV certification:

- (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If "Yes," skip to question (4) below. If "No," continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.

If "No," continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "No," continue with question (5).

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
---	--

CONTENTS OF ACTION PACKAGE	
❖ Copy of this Action Package Checklist ³	Yes
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) 7/23/2009; 3/31/2009; 10/14/2008
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	N/A
• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version)	
• Original applicant-proposed labeling	
• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable	
❖ Medication Guide/Patient Package Insert/Instructions for Use (<i>write submission/communication date at upper right of first page of each piece</i>)	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input checked="" type="checkbox"/> None

³ Fill in blanks with dates of reviews, letters, etc.
Version: 9/5/08

<ul style="list-style-type: none"> • Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> • Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	
<ul style="list-style-type: none"> ❖ Labels (full color carton and immediate-container labels) (write submission/communication date at upper right of first page of each submission) 	
<ul style="list-style-type: none"> • Most-recent division proposal for (only if generated after latest applicant submission) 	June 26, 2009
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling 	April 20, 2009 and May 22, 2009
<ul style="list-style-type: none"> ❖ Labeling reviews (indicate dates of reviews and meetings) 	<input type="checkbox"/> RPM <input type="checkbox"/> DMEDP <input type="checkbox"/> DRISK <input checked="" type="checkbox"/> DDMAC 6/25/2009; 5/1/2009 (Mtg – 5/18/2009) <input type="checkbox"/> CSS <input checked="" type="checkbox"/> Other reviews DNRD 5/22-2009; 4/20/2009 (Mtg – 3/31/2009 and 4/22/2009)
<ul style="list-style-type: none"> ❖ Proprietary Name <ul style="list-style-type: none"> • Review(s) (indicate date(s)) • Acceptability/non-acceptability letter(s) (indicate date(s)) 	June 25, 2009 and May 19, 2009
Administrative/Regulatory Documents	
<ul style="list-style-type: none"> ❖ Administrative Reviews (e.g., RPM Filing Review⁴/Memo of Filing Meeting) (indicate date of each review) 	March 27, 2009 and March 20, 2009
<ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (signed by Division Director) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Application Integrity Policy (AIP) Status and Related Documents www.fda.gov/ora/compliance_ref/aip_page.html 	
<ul style="list-style-type: none"> • Applicant in on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (indicate date) ○ If yes, OC clearance for approval (indicate date of clearance communication) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> ❖ Pediatric Page (approvals only, must be reviewed by PERC before finalized) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (include certification) 	<input checked="" type="checkbox"/> Verified, statement is acceptable
<ul style="list-style-type: none"> ❖ Postmarketing Requirement (PMR) Studies 	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> • Outgoing communications (if located elsewhere in package, state where located) 	
<ul style="list-style-type: none"> • Incoming submissions/communications 	
<ul style="list-style-type: none"> ❖ Postmarketing Commitment (PMC) Studies 	<input checked="" type="checkbox"/> None

⁴ Filing reviews for other disciplines should be filed behind the discipline tab.

<ul style="list-style-type: none"> Outgoing Agency request for postmarketing commitments (<i>if located elsewhere in package, state where located</i>) 	
<ul style="list-style-type: none"> Incoming submission documenting commitment 	
❖ Outgoing communications (<i>letters (except previous action letters), emails, faxes, telecons</i>)	
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
<ul style="list-style-type: none"> PeRC (<i>indicate date; approvals only</i>) 	<input type="checkbox"/> Not applicable March 25, 2009
<ul style="list-style-type: none"> Pre-Approval Safety Conference (<i>indicate date; approvals only</i>) 	<input checked="" type="checkbox"/> Not applicable
<ul style="list-style-type: none"> Regulatory Briefing (<i>indicate date</i>) 	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> Pre-NDA/BLA meeting (<i>indicate date</i>) 	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> EOP2 meeting (<i>indicate date</i>) 	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> Other (e.g., EOP2a, CMC pilot programs) 	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
<ul style="list-style-type: none"> Date(s) of Meeting(s) 	
<ul style="list-style-type: none"> 48-hour alert or minutes, if available 	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None July 1, 2009
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None
Clinical Information⁵	
❖ Clinical Reviews	
<ul style="list-style-type: none"> Clinical Team Leader Review(s) (<i>indicate date for each review</i>) 	
<ul style="list-style-type: none"> Clinical review(s) (<i>indicate date for each review</i>) 	April 8, 2009
<ul style="list-style-type: none"> Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> None
❖ Safety update review(s) (<i>indicate location/date if incorporated into another review</i>)	April 8, 2009
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, review/memo explaining why not	April 8, 2009
❖ Clinical reviews from other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not needed
❖ Risk Management <ul style="list-style-type: none"> Review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>) REMS Memo (<i>indicate date</i>) REMS Document and Supporting Statement (<i>indicate date(s) of submission(s)</i>) 	<input checked="" type="checkbox"/> None
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input type="checkbox"/> None requested March 11, 2009

⁵ Filing reviews should be filed with the discipline reviews.

Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Biostatistics <input checked="" type="checkbox"/> None	
❖ Statistical Division Director Review(s) (indicate date for each review)	<input type="checkbox"/> None
Statistical Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
Statistical Review(s) (indicate date for each review)	<input type="checkbox"/> None
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	<input type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
Clinical Pharmacology review(s) (indicate date for each review)	<input type="checkbox"/> None March 30, 2009
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)	<input type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	<input type="checkbox"/> None
• Supervisory Review(s) (indicate date for each review)	<input type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	<input type="checkbox"/> None April 10, 2009
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	<input type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	<input type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (include copies of DSI letters)	<input type="checkbox"/> None requested
CMC/Quality <input type="checkbox"/> None	
❖ CMC/Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (indicate date for each review)	<input type="checkbox"/> None
• Branch Chief/Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
• CMC/product quality review(s) (indicate date for each review)	<input type="checkbox"/> None Jan 22, 2009 and April 29, 2009
• BLAs only: Facility information review(s) (indicate dates)	<input type="checkbox"/> None
❖ Microbiology Reviews	
• NDAs: Microbiology reviews (sterility & pyrogenicity) (indicate date of each review)	<input checked="" type="checkbox"/> Not needed
• BLAs: Sterility assurance, product quality microbiology (indicate date of each review)	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)	<input checked="" type="checkbox"/> None
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion (indicate review date)(all original applications and all efficacy supplements that could increase the patient population)	April 29, 2009

<input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>)	
<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	
❖ NDAs: Methods Validation	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed
❖ Facilities Review/Inspection	
<ul style="list-style-type: none"> • NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>) 	Date completed: Dec 6, 2008 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
<ul style="list-style-type: none"> • BLAs: <ul style="list-style-type: none"> ○ TBP-EER ○ Compliance Status Check (approvals only, both original and all supplemental applications except CBEs) (<i>date completed must be within 60 days prior to AP</i>) 	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation Date completed: <input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold

Appendix A to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.



NDA 22-429

NDA ACKNOWLEDGMENT

Banner Pharmacaps, Inc.
Attention: Dana S. Toops
Director, Regulatory Affairs
4125 Premier Dr.
High Point NC, 27265

Dear Mr. Toops:

We have received your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Cetirizine HCl capsules, 5 and 10 mg

Date of Application: July 31, 2008

Date of Receipt: August 1, 2008

Our Reference Number: NDA 22-429

The NDA number provided above should be cited 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 Nonprescription Clinical Evaluation
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/cder/ddms/binders.htm>.

If you have any questions, call me at (301) 796-0943.

Sincerely,

{See appended electronic signature page}

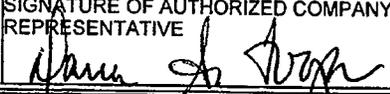
Elaine Abraham, R.Ph.
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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

/s/

Elaine Abraham

8/18/2008 09:57:51 AM

Form Approved: OMB No. 0910 - 0297 Expiration Date: January 31, 2010 See instructions for OMB Statement, below.		
DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION		PRESCRIPTION DRUG USER FEE COVERSHEET
A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm		
1. APPLICANT'S NAME AND ADDRESS BANNER PHARMACAPS INC Dana Toops 4125 Premier Drive High Point NC 27265 US	4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER	
2. TELEPHONE NUMBER 336-812-8700 23312	5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO 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: <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO: NDA 19-835	
3. PRODUCT NAME Cetirizine HCl, Capsules 10 mg & 5 mg	6. USER FEE I.D. NUMBER PD3008531	
7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION. <input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory) <input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE <input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act <input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY		
8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO		
OMB Statement: Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: Department of Health and Human Services Food and Drug Administration An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Food and Drug Administration CDER, HFD-94 CBER, HFM-99 12420 Parklawn Drive, Room 3046 1401 Rockville Pike Rockville, MD 20852 Rockville, MD 20852-1448		
SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 	TITLE Director, RA	DATE 7/29/08
9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION \$589,000.00		
Form FDA 3397 (03/07)		

Close Print Cover sheet