CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-114/S006

CORRESPONDENCE

Trust

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-114/S-S-006

Carter-Wallace Laboratories
Half Acre Road
P.O. Box 1001
Cranbury, New Jersey 08512-0181

DEC 3 1999

Attention: George R. Hemsworth, Ph.D.
Director, Regulatory Affairs

Dear Dr. Hemsworth:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Astelin® (azelastine hydrochloride (USAN) Nasal Spray

NDA Number: 20-114

Supplement Number: S-006

Date of Supplement: November 10, 1999

Date of Receipt: November 15, 1999

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on January 14, 2000, in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Pulmonary Drug Products, HFD-570
Office of Drug Evaluation II
Attention: Document Control Room 10B-03
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

/S/

for Sandra Barnes
Acting Chief, Project Management Staff
Division of Pulmonary and Allergy Drug Products,
HFD-570
Office of Drug Evaluation II
Center for Drug Evaluation and Research

HFD TROUT

RECORD OF TELEPHONE CONVERSATION
NDA NUMBER: 20-114, SE5-006 DATE: 7/13/00, 9:30 AM

INITIATED BY: APPLICANT:_____ FDA:_____X_____
NAME AND PERSON WITH WHOM CONVERSATION WAS HELD:

George Hemsworth, Ph.D.
Director, Regulatory Affairs
Wallace Laboratories, Cranbury, NJ 08512-0181
(609) 655-6357

Reference: Supplement to NDA (supplement to NDA)

I called Dr. Hemsworth on 7/13/00. I asked the following question:

I will need to look at the AST results for Patient 285, Study Center 980018, for baseline, Visit 4, and follow-up. I could not find the results in Table 14 Part B, pages 11.1699-11.1700. I also asked what is Table 14, Part B supposed to include.

I also requested the Case Report Forms for Patient #53, Study Center 980006.

He replied by E-Mail:

Thu, 13 Jul 2000 11:14:20

Good Morning

We are in the process of retrieving the case records for patients 98006/53 and 980018/285 and will fax them to you later on today.

With reference to Case Report TabulationTable 14 Parts A and B, Part A contains the actual by visit laboratory data for each patient sorted according to study center. The data for patient 980018/285 is on pages 11 902 through 11 904. Part B is a listing of anything written in the comment field on the original case record, sorted in the same fashion. For patient 980018/285, Table 14 Part B, pages 1699 through 1701, show comments written by the investigator for each laboratory value. Since all of the comment fields on the case record for patient 285 were blank, there are blanks also on the listing.

I hope that my description provides clarity and not confusion!! Please call if we need to talk.
Regards
George

I replied that this information answered my question.

/S/

Charles E. Lee, M.D.

cc:
Original NDA 20-114, SE5-006
HFD-570/Division File
HFD-570/Lee/Medical Reviewer
HFD-715/Elashoff/Biometrics Reviewer
HFD-570/Trout/ CSO

7 x out

RECORD OF TELEPHONE CONVERSATION
NDA NUMBER: 20-114, SE5-006 DATE: 7/11/00, 9:20 AM

INITIATED BY: APPLICANT:_____ FDA:_____X_____
NAME AND PERSON WITH WHOM CONVERSATION WAS HELD:

George Hemsworth, Ph.D.
Director, Regulatory Affairs
Wallace Laboratories, Cranbury, NJ 08512-0181
(609) 655-6357

Reference: Supplement to NDA (supplement to NDA)

I called Dr. Hemsworth on 7/11/00. I asked the following question:

Table 3, page 08.76, and Table 4, page 08.77 indicate that there were 20 patients who did not complete Study 335 and seven protocol violations. However, Table 19, pages 11.2133-11.2140 in the case report tablulations lists 22 patients that did not complete Study 335 and nine patients who were protocol violations. Please explain the discrepancy in the number of patients completing the study and the number of protocol violations.

He replied by E-Mail:
Tue, 11 Jul 2000 11:24:00

Dr. Lee

With reference to your question this morning about an apparent discrepancy between Table 4 in the clinical report and Table 19 in the Case Report Tabulations:

There are two subjects reflected in Table 19 who are not present in Table 4. Center 980006/subject 41 and center 980011/subject 145 were randomized to blinded medication and assigned a double blind code number, but were immediately identified as protocol violators and not treated with blinded medication. You will note that the line data in Table 19 for both of these subjects do not contain first or last dates for double blind medication. The title for Table 4 is 'Reason for Non-completion of Double-blind Treatment'; since neither of these two subjects received double-blind treatment, they were excluded from Table 4 by definition.

I trust that this explanation resolves this issue. Please do not hesitate to call if I can help you.

Regards,

George

I replied that this information answered my question.

/S/
Charles E. Lee, M.D.

cc:
Original NDA 20-114, SE5-006
HFD-570/Division File
HFD-570/Lee/Medical Reviewer
HFD-715/Elashoff/Biometrics Reviewer
HFD-570/Trout/ CSO

Trout

RECORD OF TELEPHONE CONVERSATION
NDA NUMBER: 20-114, SE5-006 DATE: 7/10/00, 9:30 AM

INITIATED BY: APPLICANT:_____ FDA:_____X_____
NAME AND PERSON WITH WHOM CONVERSATION WAS HELD:

George Hemsworth, Ph.D.
Director, Regulatory Affairs

Anup Dam,
Chief, Statistics

Wallace Laboratories, Cranbury, NJ 08512-0181
(609) 655-6357

Reference: Supplement to NDA (supplement to NDA)

I called Dr. Hemsworth on 7/7/00. He was not in the office. I left a voice mail request to answer the following question about Table 10, Volume 1.1, page 08.85.

In the "Period" column, please define how the "Endpoint" period was calculated.

He returned my call on the date and time noted above. Mr. Dam gave this clarification:

"Overall" represents the difference between the mean Total Vasomotor Rhinitis Symptom Score (TVRSS) over the entire treatment period and the baseline period. This is calculated with available data.

"Endpoint" represents the difference between the mean Total Vasomotor Rhinitis Symptom Score (TVRSS) over the entire treatment period and the baseline period. This is calculated with data handled as last observation carried forward.

/S/

Charles E. Lee, M.D.

cc:
Original NDA 20-114, SE5-006
HFD-570/Division File
HFD-570/Lee/Medical Reviewer
HFD-715/Elashoff/Biometrics Reviewer
HFD-570/Trout/ CSO

TROUT

RECORD OF TELEPHONE CONVERSATION
NDA NUMBER: 20-114, SE5-006 DATE: 2/07/00, 11:35 AM

INITIATED BY: APPLICANT:_____ FDA:_____X_____
NAME AND PERSON WITH WHOM CONVERSATION WAS HELD:

Ana Fontana, Secretary for:
George Hemsworth, Ph.D.
Director, Regulatory Affairs
Wallace Laboratories, Cranbury, NJ 08512-0181

(609) 655-6357

Reference: Efficacy supplement to NDA

I called Dr. Hemsworth's office on 2/07/00 at 11:45 AM. I spoke with Ms. Fontana because Dr. Hemsworth was out of the office at a meeting. I requested the following information for this submission be faxed to DPADP at (301) 827-1271:

Address, telephone numbers, fax numbers
If available, E-mail addresses for the following investigators:

1. William E. Berger, M.D., Carter Wallace Site number 980006
2. Jonathan Matz, M.D., Carter Wallace Site number 980025

She indicated that the above information would be sent.

/S/

Charles E. Lee, M.D.

cc:
Original NDA 20-114, SE5-006
HFD-570/Division File
HFD-570/Chowdhury/Acting Team Leader
HFD-570/Lee/Medical Reviewer
HFD-715/Wilson/Biometrics Team Leader
HFD-570/Trout/ CSO

Trout

RECORD OF TELEPHONE CONVERSATION
NDA NUMBER: 20-114, SE5-006 DATE:01/10/00, 8:30 AM

INITIATED BY: APPLICANT:_____ FDA:_____X_____
NAME AND PERSON WITH WHOM CONVERSATION WAS HELD:
George Hemsworth, Ph.D.
Director, Regulatory Affairs
Wallace Laboratories, Cranbury, NJ 08512-0181

Reference: Supplement to NDA (supplement to NDA)

I called Dr. Hemsworth on 01/07/00 at 2:45 PM. He returned my call on the date and time noted above. I requested the following information for this submission:

- A foreign marketing and regulatory history for azelastine nasal spray with a focus on vasomotor rhinitis
- A listing of serious adverse events and deaths in Studies 335 and 336 (or a statement that there were no SAEs or deaths in Studies 335 and 336
- A plan to meet the pediatric study requirement
- A subgroup analysis of the ISS and ISE by gender (subgroup analysis by age is not necessary as subjects were 12-65 years of age)
- An electronic copy of the proposed label
- An electronic copy of study reports, protocols and SAS data files for Studies 335 and 336

He indicated that the above materials would be sent.

/S/
Charles E. Lee, M.D.

cc:
Original NDA 20-114, SE5-006
HFD-570/Division File
HFD-570/Chowdhury/Acting Team Leader
HFD-570/Lee/Medical Reviewer
HFD-715/Wilson/Biometrics Team Leader
HFD-570/Trout/ CSO

APPEARS THIS WAY
ON ORIGINAL

To minimize the potential bias of clinical study results by any of the participating investigators, the following steps were taken:

- As a randomized, double-blind, multicenter, and placebo-controlled trial, the study design minimized the ability of any individual investigator to introduce a bias which could influence the overall outcome of the study.
- For each investigational site, the computer-generated random code was used to allocate subjects evenly balanced between blinded treatment groups.
- The Case Report Form information was validated against investigator source documents in a blinded fashion.
- A lack of treatment-by-center interaction during data analysis, with regard to outcome of the study, is further supportive.

WITHHOLD 11 PAGES

Draft

Labeling

WITHHOLD 12 PAGES

Draft

Labeling

ANNOTATED PRODUCT LABELING

Revisions to current Astelin® (azelastine hydrochloride) Nasal Spray, 137 mcg, product labeling based on clinical efficacy and safety data contained in this supplement are highlighted in yellow on the following pages. Annotations referencing technical sections in this supplement are shown for each labeling revision.

WITHHOLD 8 PAGES

DRAFT

Labeling