CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

019430Orig1s001

Trade Name: EpiPen Auto Injector and EpiPen Jr. Auto Injector

Generic or Proper Name: epinephrine injection, USP

Sponsor: Survival Technology, Inc.

Approval Date: 03/02/1989

Indication: Epinephrine is indicated in the emergency treatment of allergic reactions (anaphylaxis) to insect stings or bites, foods drugs and other allergens as well as idiopathic or exercise-induced anaphylaxis. The EpiPen and EpiPen Jr. Auto-Injectors are intended for immediate self-administration by a person with a history of an anaphylactic reaction.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

019430Orig1s001

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APPLICATION NUMBER:

019430Orig1s001

APPROVAL LETTER

MAR 02 1989

NDA 19-430/S-001

Survival Technology, Inc.
8101 Glenbrook Road
Bethesda, MD 20814

Attention: Ianthana Peterson
Senior Regulatory Specialist

Gentlemen:

Please refer to your supplemental new drug application dated February 13, 1989, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for EpiPen and EpiPen Jr. Auto-injectors (epinephrine injection).

The supplemental application provides for a change in the WARNINGS section of the package insert to alert the patient and physician to possible accidental injection into digits (S-001).

We have completed our review of the supplemental application and it is approved. We remind you that you must comply with the requirements set forth under 21 CFR 314.80 and 314.81 for approved new drugs.

Sincerely yours,

Philip G. Walters, M.D.
Acting Director
Division of Surgical-Dental
Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: NDA 19-430
HFD-160
HFD-160/Nicklas/Stone/JWWinkler
R/D JPHannan 0353H 02/27/89
R/D init by GBoyer 2/28/89 JWWinkler 2/28/89
PGWalters 2/28/89
F/T LSturdivant 3/1/89

APPROVAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

019430Orig1s001

MEDICAL REVIEW(S)

DIV.
FEB 2 1 1989

NDA 19-430 21 February 1989

Medical Officer's Review

Product- EpiPen and EpiPen Jr. (epinephrine)

Route of Administration- IM

Category of Drug- adrenergic agonist

Sponsor - Survival Technology, Inc.

Previous Medical Review- see MOR of 24 August 1988

Material Reviewed- Submission of 13 February 1989

I. In the MOR of 24 August 1988, we stated that;".....an Emergency Physician in regard to a potential hazard associated with EpiPen.....reports two patients who developed loss of blood supply to the finger after an accidental injection into the finger." The reporter recommends that this "dangerous medical device" be taken off the market.

It is unlikely that individuals will accidentally inject this medication into the digits, despite these 2 case reports. Moreover, this is a life-saving medication for many patients with severe allergies and a history of anaphylaxis, and offers an advantage over injectable epinephrine which is not packaged in an auto -injectable form, because of the ease of its use. Some patients have difficulty administering themselves epinephrine from a syringe which is not auto-injectable during an anaphylactic reaction. On the other hand, the labeling should be changed to warn physicians administering and patients using this device that injections into the digits should be avoided, and what to do if such an event accidentally occurs.

We recommend that the Warnings Section be changed to include the following statement, "Accidental injection into the hands or feet may result in loss of blood flow to the affected area and should be avoided. If there is accedental injection into these areas go immediately to the nearest emergency room for treatment. EpiPen should only be injected into the thigh or upper arm at the sites indicated in the drawing. The sponsor should then prepare a drawing of the areas where it is appropriate to inject EpiPen."

II. As a result, in the letter of 6 September 1988 to the sponsor we stated that, "We have received two (2) reports of accidental injection of Epi-Pen into the fingers with potential loss of these digits due to decreased blood supply from vasoconstriction. Therefore, we are requesting that the labeling be changed to alert the patient and physician to this possible adverse event. In this regard, an addition to the Warnings Section should read "Accidental injection into the hands or feet may result in loss of blood flow to the affected area and should be avoided. If there is an accidental injection into these areas, go immediately to the nearest emergency room for treatment. Epi-Pen should only be injected into the thigh or upper arm at the sites indicated in the drawing below." You should prepare a drawing of the areas where it should be appropriate for Epi-Pen to be injected."

III. The sponsor has made the changes requested by us and the labeling is acceptable at this time.

IV. Proposed Draft of Clinical Portion of Letter to Sponsor:

We have reviewed the labeling changes submitted by you on 13 February 1989 and they are acceptable.

Richard Nicklas MD
Richard Nicklas M.D.
2/21/89 2/22/89

cc: NDA 19,430
HFD-160
HFD-340
HFD-160/Hannan
R/D by Richard Nicklas
R/D Init by JWW 2/21/89 PGW 2/21/89
HFD-160/ Stone
FT by KAM 2/21/89 (W #4023N) (D #00253N)

AUG 24 1988

NDA 19-430 24 August 1988

Medical Officer's Review

Product- EpiPen and EpiPen Jr. (epinephrine)

Route of Administration- IM

Category of Drug- adrenergic agonist

Sponsor- Survival Technology, Inc.

Previous Medical Review- see MOR of 3 Nov 1987

Material Reviewed- Letter to FDA from outside physician of 23 May 1988

I. This letter was sent by an Emergency Physician in regard to a potential hazard associated with EpiPen. He reports two patients who developed loss of blood supply to the finger after an accidental injection into the finger. The reporter recommends that this "dangerous medical device" be taken off the market.

II. It is unlikely that individuals will accidentally inject this medication into the digits, despite these 2 case reports. Moreover, this is a life-saving medication for many patients with severe allergies and a history of anaphylaxis, and offers an advantage over injectable epinephrine which is not packaged in an auto-injectable form, because of the ease of its use. Some patients have difficulty administering themselves epinephrine from a syringe which is not auto-injectable during an anaphylactic reaction. On the other hand, the labeling should be changed to warn physicians administering and patients using this device that injections into the digits should be avoided, and what to do if such an event accidentally occurs.

III. We recommend that the Warnings Section be changed to include the following statement, "Accidental injection into the hands or feet may result in loss of blood flow to the affected area and should be avoided. If there is accidental injection into these areas go immediately to the nearest emergency room for treatment. EpiPen should only be injected into the thigh or upper arm at the sites indicated in the drawing." The sponsor should then prepare a drawing of the areas where it is appropriate to inject EpiPen.

IV. Proposed Draft of Medical Portion of Letter to Sponsor:

We have received two (2) reports of accidental injection of EpiPen into the fingers with potential loss of these digits due to decreased blood supply from vasocontriction. Therefore, we are requesting that the

labeling be changed to alert the patient and physician to this possible adverse event. In this regard, an addition to the Warnings Section should read, "Accidental injection into the hands or feet may result in loss of blood flow to the affected area and should be avoided. If there is accidental injection into these areas go immediately to the nearest emergency room for treatment. EpiPen should only be injected into the thigh or upper arm at the sites indicated in the drawing below." You should prepare a drawing of the areas where it would be appropriate for EpiPen to be injected.

Richard A. Nicklas MD
Richard A. Nicklas, M.D.
8/24/88

NDA 19-430
HFD-160
HFD-160/Winkler/Stone/Hannan
HFD-340
R/D RANicklas 8-24-88
R/D init by JWWinkler 8-24-88;PGWalters 8-24-88
FT/MPD/8-24-88/D#0243N/W#3817N

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019430Orig1s001

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA No. 19-430/S-001

Date February 16, 1989

Survival Technology, Inc.
8101 Glenbrook Road
Bethesda, Maryland 20814

Attention: Iantha Peterson
Senior Regulatory Specialist

Gentlemen:

We acknowledge receipt of your supplemental application(s) for the following:

Name of Drug: EpiPen and Epi-Pen Jr. Auto-injectors (epinephrine injection)

NDA Number: 19-430

Supplement Number: S-001

Date of Supplement: February 13, 1989

Date of Receipt: February 14, 1989

File Date: April 14, 1989

All communications concerning this NDA should be addressed as follows:

Center for Drugs and Biologics, HFN-160
Attention: Document Control Room 18B-03
5600 Fishers Lane
Rockville, MD 20857

Sincerely Yours,

Gary H. Boyer

Gary H. Boyer
Supervisory Consumer Safety Officer
Division of Surgical-Dental Drug Products
Center for Drugs and Biologics

FORM FDA 3217f (3/87)

SEP 6 1988

NDA 19-430

Survival Technology, Inc.
8101 Glenbrook Road
Bethesda, MD 20814

Attention: Gary W. Leyland
Director
Regulatory Affairs

Gentlemen:

Please refer to your approved new drug application for Epi-Pen and Epi-Pen Jr. Auto-Injector (epinephrine injection).

We have received two (2) reports of accidental injection of Epi-Pen into the fingers with potential loss of these digits due to decreased blood supply from vasoconstriction. Therefore, we are requesting that the labeling be changed to alert the patient and physician to this possible adverse event. In this regard, an addition to the WARNINGS section should read, "Accidental injection into the hands or feet may result in loss of blood flow to the affected area and should be avoided. If there is an accidental injection into these areas, go immediately to the nearest emergency room for treatment. Epi-Pen should only be injected into the thigh or upper arm at the sites indicated in the drawing below." You should prepare a drawing of the areas where it would be appropriate for Epi-Pen to be injected.

This labeling change should be implemented during the next printing and submitted as a supplemental application to this NDA.

Sincerely yours,

Philip G. Walters, M.D.
Acting Director
Division of Surgical-Dental
Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: NDA 19-430
HFD-160
HFD-160/Nicklas/Hoiberg
R/D JPHannan 0215H 08/30/88
R/D Init by GBoyer 8/31/88 JWWinkler 8/31/88
CPHoiberg for PGWalters 8/31/88
F/T MJO 9/1/88

INFORMATION REQUEST