DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-760

REVIEW DATE: 10/15/97

SUBMISSION/TYPE

DOCUMENT DATE 10/3/97

AMENDMENT

NAME & ADDRESS OF APPLICANT: Pfizer Central Research
Medical Research Laboratory
Eastern Point Road
Groton, Connecticut 06340

DRUG PRODUCT NAME

Proprietary: Traven I.V.
Nonproprietary/USAN: Alatrofloxacin Mesylate, Alatrofloxacin Injection
Code Names/#'s: CP-116,517-27
Chemical Type: 1S
Therapeutic Class:

ANDA Suitability Petition/DES/Patent Status: N/A [if applicable]

PHARMACOLOGICAL CATEGORY/INDICATION:

DOSAGE FORM: Aqueous Concentrate Injection
STRENGTHS: 5 mg/mL, 100 mg, 200 mg, and 300 mg
ROUTE OF ADMINISTRATION: Intravenous Infusion
DISPENSED: X Rx OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL WT:

Structural Formula:

The structural formula of alatrofloxacin mesylate is given below:
Molecular Formulae and Weights

Molecular Formula of Alatrofloxacin Mesylate: $\text{C}_{26}\text{H}_{25}\text{F}_{3}\text{N}_{6}\text{O}_{5}\cdot\text{CH}_{3}\text{SO}_{2}\text{H}$

Molecular Formula of Alatrofloxacin: $\text{C}_{26}\text{H}_{25}\text{F}_{3}\text{N}_{6}\text{O}_{5}$

Molecular Weight of Alatrofloxacin Mesylate: 654.62

Molecular Weight of Alatrofloxacin: 558.52

Nomenclature

Chemical Abstracts Services Name:

(1α, 5α, 6α)-L-alanyl-N-[3-(6-carboxy-8-(2,4-difluorophenyl)-3-fluoro-5,8-dihydro-5-oxo-1,8-naphthyridin-2-yl]-3-azabicyclo[3.1.0]hex-6-yl]-L-alaninamide, monomethanesulfonate

Chemical Abstracts Services Number: [157605-25-9]

Proposed Proprietary or Trade Name:

TROVAN® injection

alatrofloxacin mesylate

alatrofloxacin mesylate

Laboratory Code

Pfizer Laboratory Code: CP-116,517-27
CONCLUSION:

The NDA may be approved from the chemistry, manufacturing and control point of view. The following items are acceptable.

NOTE: 1. EER is acceptable
2. Trade name approved
3. EA-FONSI has been issued
4. All chemistry deficiencies have been answered satisfactorily
5. Sterility review has been completed by HFD-805 and found acceptable, 7/3/97.

B. Vithal Shetty, Ph.D.
Review Chemist

APPEARS THIS WAY ON ORIGINAL

Orig. NDA 20-760
HFD-520/Division File
HFD-520/BVShetty
HFD-590/MO/Alivisatos
HFD-590/Pharm/Hastings
HFD-590/Micro/Lard
HFD-590/CSO/Fogarty
HFD-520/DKatagye
R/D Init by: DKatagye

/\S/ 11/26/97
DIVISION OF ANTI-INFECTION DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-760

CHEM. REVIEW #: 1

REVIEW DATE: 7/1/97

SUBMISSION/TYPe DOCUMENT DATE CDER DATE ASSIGNED DATE

ORIGINAL 12/27/96 1/02/97 6/27/97

NAME & ADDRESS OF APPLICANT: Pfizer Central Research
Medical Research Laboratory
Eastern Point Road
Groton, Connecticut 06340

DRUG PRODUCT NAME

Proprietary: Trovan I.V.
Nonproprietary/USAN: Alatrofloxacin Mesylate,
Alatrofloxacin Injection
Code Names/#'s: CP-116,517-27
Chemical Type: 1S
Therapeutic Class:  

ANDA Suitability Petition/DES/ Patent Status:

PHARMACOLOGICAL CATEGORY/INDICATION:

DOSAGE FORM: Aqueous Concentrate Injection
STRENGTHS: 5 mg/mL, 100 mg, 200 mg, and 300 mg
ROUTE OF ADMINISTRATION: Intravenous Infusion
DISPENSED: X Rx OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL. WT.

Structural Formula:

The structural formula of alatrofloxacin mesylate is given below:
Molecular Formulae and Weights

Molecular Formula of Alatrofloxacin Mesylate: \( C_{26}H_{25}F_3N_4O_5 \cdot CH_3SO_3H \)
Molecular Formula of Alatrofloxacin: \( C_{26}H_{25}F_3N_4O_5 \)
Molecular Weight of Alatrofloxacin Mesylate: 654.62
Molecular Weight of Alatrofloxacin: 558.52

Nomenclature

Chemical Abstracts Services Name: (1α, 5α, 6α)-L-alanyl-N-[3-{6-carboxy-8-(2,4-difluorophenyl)-3-fluoro-5,8-dihydro-5-oxo-1,8-naphthyridin-2-yl}-3-azabicyclo[3.1.0]hex-6-yl]-L-alaninamide, monomethanesulfonate
Chemical Abstracts Services Number: [157605-25-9]
I.N.N.: alatrofloxacin
Proposed Proprietary or Trade Name: TROVAN® injection
U.S.A.N.: alatrofloxacin mesylate
W.H.O. or B.A.N.: alatrofloxacin mesylate
Laboratory Code
Pfizer Laboratory Code: CP-116,517-27
SUPPORTING DOCUMENTS:

IND
IND
RELATED DOCUMENTS (if applicable):

NDA 20-759 (Trovafloxacin Mesylate Tablet)

This NDA was submitted simultaneously with NDA 20-759. It is being reviewed at present.
CONSULTS:

1. Environmental Assessment

3. The trade name, TROVAN I.V., has already been approved.

5. EER - The EER dated 6/9/97 was found to be acceptable.
REMARKS/COMMENTS:

Alatrofloxacin is a fluoronaphthyridone derivative, structurally similar to, and with a comparable mechanism of action to the fluoroquinolone class of antibacterial agents.
CONCLUSIONS & RECOMMENDATIONS:

The application is not approvable for manufacturing and controls under section 505 (or 507 for an antibiotic) of the Act.

B. Vithal Shetty, Ph.D.
Review Chemist

cc: Orig. NDA 20-760
HFD-520/Division File
HFD-520/BVShetty
HFD-520/MO/Alivisatos
HFD-520/Pharm/Hastings
HFD-520/Micro/Lard
HFD-520/CSO/Fogarty
HFD-520/DKatague
R/D Init by: DKatague

5/8/97
DIVISION OF ANTI-INFECTION DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-759

CHEM. REVIEW #: 2

REVIEW DATE: 9/22/97

SUBMISSION/TYPE

AMENDMENT/AC 10/09/97

DOCUMENT DATE

CDER DATE

ASSIGNED DATE

NAME & ADDRESS OF APPLICANT: Pfizer Central Research
Eastern Point Road
Groton, Connecticut 06340

DRUG PRODUCT NAME

Proprietary: Trovan

Nonproprietary/USAN: Trovafloxacin Mesylate

Code Names/#’s: CP-99, 219-27

Chemical Type: 1S

Therapeutic Class: Quinolone, antibacterial

ANDA Suitability Petition/DES/T Patent Status:

PHARMACOLOGICAL CATEGORY/INDICATION:

DOSAGE FORM: Tablets

STRENGTHS: 100 and 200 mg

ROUTE OF ADMINISTRATION: Oral

DISPENSED: X Rx ______ OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:

Structural Formula:

The structural formula of trovafloxacin mesylate is given below:

Molecular Formulae and Weights

Molecular Formula of Trovafloxacin Mesylate: C_{26}H_{3}F_{2}N_{4}O_{3} \cdot CH_{3}SO_{3}H

Molecular Formula of Trovafloxacin: C_{26}H_{12}F_{2}N_{4}O_{3}

Molecular Weight of Trovafloxacin Mesylate: 512.46

Molecular Weight of Trovafloxacin: 416.36
7 PAGES REDACTED

CONTAINED TRADE SECRETS and/or CONFIDENTIAL/COMMERCIAL INFORMATION
CONCLUSION:
The NDA may be approved from the chemistry, manufacturing and control point of view. The following items are acceptable.

NOTE:
1. EER is acceptable
2. FONSI has been issued
3. All chemistry deficiencies have been answered satisfactorily
4. Trade name has been approved.

PENDING:

/S/ 10/8/97

B. Vithal Shetty, Ph.D.
Review Chemist

CC: Orig. NDA 20-795
HFD-590/Div. Files
HFD-520/Shetty
HFD-590/Albrecht
HFD-590/Alivisatos
HFD-590/Hastings
HFD-590/Schnuff
HFD-520/Katague
HFD-590/Lard
HFD-590/Fogarty
R/D Init by: DKatague /S/ 10/20/97
DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-759
CHEM. REVIEW #: 1
REVIEW DATE: 3/26/97
SUBMISSION/TYPENOCOMMISSION DATE CDER DATE ASSIGNED DATE
ORIGINAL 12/27/96 1/02/97 1/7/97

NAME & ADDRESS OF APPLICANT:
Pfizer Central Research
Eastern Point Road
Groton, Connecticut 06340

DRUG PRODUCT NAME
Proprietary: Trovan
Nonproprietary/USAN: Trovafloxacin Mesylate
Code Names/#’s: CP-99,219-27
Chemical Type: 1S
Therapeutic Class: Quinolone, antibacterial

ANDA Suitability Petition/DESIPatent Status:
N/A [if applicable]

PHARMACOLOGICAL CATEGORY/INDICATION:

DOSAGE FORM: Tablets
STRENGTHS: 100 and 200 mg
ROUTE OF ADMINISTRATION: Oral
DISPENSED: X Rx OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT.:
Structural Formula:
The structural formula of trovafloxacin mesylate is given below:

\[
\text{Molecular Formulae and Weights} \\
\text{Molecular Formula of Trovafloxacin Mesylate: } C_{20}H_{15}F_3N_4O_3\cdot CH_3SO_3H \\
\text{Molecular Formula of Trovafloxacin: } C_{20}H_{15}F_3N_4O_3 \\
\text{Molecular Weight of Trovafloxacin Mesylate: } 512.46 \\
\text{Molecular Weight of Trovafloxacin: } 416.36
\]
Nomenclature

Chemical Abstracts Services Name: (1α, 5α, 6α)-7-(6-
amino-3-
azabicyclo[3.1.0]hex-
3-yl)-1-(2,4-
difluorophenyl)-6-
fluoro-1,4-dihydro-
4-oxo-1,8-
naphthyridine-3-
carboxylic acid, monomethanesulfonate

Chemical Abstracts Services Number: [147059-75-4]

L.N.N.: trovafloxacin

Proposed Proprietary or Trade Name: TROVAN®

U.S.A.N.: trovafloxacin mesylate

W.H.O. or B.N.F.: trovafloxacin mesylate

Laboratory Code

Pfizer Laboratory Code: CP-99,219-27

SUPPORTING DOCUMENTS:
3. Trade Name, TROVAN, already approved.

4. EER - Requested on January 29, 1997. It was found to be acceptable.

REMARKS/COMMENTS:

Trofloxacin is a fluoronaphthridone derivative similar to, and with a comparable mechanism of action to the fluoroquinolone class of antibacterial agents. The tablets are 100 and 200 mg in weight. The firm states that Trovan has demonstrated activity against certain resistant pathogens including penicillin-resistant streptococcus pneumonia and methicillin-resistant staphylococcus aureus. It is stated that this is the only antibacterial agent (trovan) to date that can be administered orally for the treatment of infections caused by these pathogens including serious infections of the respiratory tract, epidemic meningococcal meningitis in children and for the prophylaxis of infection following abdominal or vaginal hysterectomy.

CONCLUSIONS & RECOMMENDATIONS:

The application is not approvable for manufacturing and controls under section 505 (or 507 for an antibiotic) of the Act. Specific items which are not approvable are identified under the

B. Vithal Shetty, Ph.D.
Review Chemist

cc: Orig. NDA 20-759
HFD-520/Division File
HFD-520/BVShetty
HFD-520/MA/Aliments
HFD-520/Pharm/Hasoso
HFD-520/Micro/Und
HFD-520/CSO/Fogarty
HFD-520/DRatague
R/D Init by: DRatague