

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER for: 020778, S011

PHARMACOLOGY REVIEW(S)

REVIEW AND EVALUATION OF PHARMACOLOGY/TOXICOLOGY DATA

KEY WORDS:

REVIEWER NAME:

DIVISION NAME:

HFD#:

REVIEW COMPLETION DATE:

ELECTRONIC FILE NUMBER:

NDA NUMBERS:

SERIAL #/DATE/TYPER OF SUBMISSION:

INFORMATION TO SPONSOR:

SPONSOR (OR AGENT):

MANUFACTURER OF DRUG SUBSTANCE:

Ita Yuen

Division of Antiviral Drug Products

530

11/5/99

None

20,778 (Oral powder) & 20,779 (Tablets)

022/January 26, 1999/Efficay & labeling supplement

Yes () No (X)

Agouron Pharmaceuticals, Inc.

10350 North Torrey Pines Road

La Jolla, CA 92037-1020

[Large empty rectangular box for handwritten notes]

DRUG:

Generic Name:

Trade Name:

Nelfinavir mesylate (AG1343)

VIRACEPT®

Chemical Name:

[3*S*-[2(2*S*^{*}, 3*S*^{*}), 3 α ,4 α β ,8 α β]]-*N*-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-3-isoquinolinecarboxamide monomethanesulfonate (salt)

CAS Registry Numbers:

159989-65-8 (AG1343)

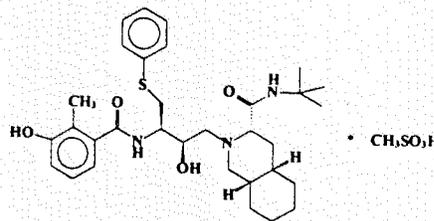
159989-64-7 (AG1346)

Molecular Formula/Molecular Weight:

C₃₂H₄₅N₃O₄S (free base)/M.W. = 567.79

C₃₂H₄₅N₃O₄S·CH₄O₃S (salt)/M.W. = 663.90

Structure:



RELEVANT INDS/NDAS/DMFS:

IND []

DRUG CLASS:

HIV protease inhibitor

INDICATION:

Treatment of HIV infection

CLINICAL FORMULATION:

VIRACEPT Tablets are supplied as a light blue, capsule-shaped tablet in a 250 mg strength (the weight of free base) containing calcium silicate, crospovidone, magnesium stearate, and FD&C blue #2 powder. VIRACEPT Oral Powder is available in a 50 mg/g strength (the weight of free base) containing microcrystalline cellulose, maltodextrin, dibasic potassium phosphate, crospovidone, hydroxypropyl methylcellulose, aspartame, sucrose palmitate, and natural and artificial flavor.

ROUTE OF ADMINISTRATION:

Oral

PROPOSED CLINICAL USE:

Treatment of HIV infection

INTRODUCTION AND DRUG HISTORY:

Nelfinavir is a protease inhibitor which has demonstrated significant *in vitro* and clinical activity against HIV. Clinical studies have shown the drug to be relative safe, especially compared to previously marketed HIV protease inhibitors. In addition, nelfinavir appears to produce a different pattern of viral resistance compared to other protease inhibitors. Like other drug in this class, nelfinavir is extensively metabolized. VIRACEPT received accelerated

approval for marketing on March 14, 1997 for the treatment of HIV infection. The approval was based on results of changes in surrogate markers (CD₄ count and plasma HIV RNA) in patients for up to 24 weeks of therapy from 2 well controlled Phase III clinical trials: AG1343-506 and AG1343-511. The present NDA supplement contains 48 week follow-up data from these 2 trials and 48 week results from a trial evaluating twice-a-day dose administration (AG1343-542). The sponsor seeks to obtain full approval status for the twice-a-day dosing regimen.

There is no new nonclinical pharmacology/toxicology information submitted with the present 2 NDA's. No changes are made in the "Carcinogenesis and Mutagenesis," "Pregnancy, Fertility, and Reproduction," and "Nursing Mothers" sections of the Label.

CONCLUSION

Since no change was made in the "Carcinogenesis and Mutagenesis," "Pregnancy, Fertility, and Reproduction," and "Nursing Mothers" sections of the Label and no new nonclinical pharmacology/toxicology information was submitted, there is no regulatory action associated with this review from the nonclinical pharmacology/toxicology perspective.

[Handwritten signature box containing "IS/"]

Ita Yuen, Ph.D.
Reviewing Pharmacologist

CONCURRENCE

HFD-530/WDempsey [Handwritten initials and date 11/26/99]
HFD-530/JFarrell [Handwritten initials and date 11/24/99]

CC

- HFD-530/NDA 20,778 [redacted]
- HFD-530/NDA 20,779 (022)
- HFD-530/Division File
- HFD-530/SLynch
- HFD-345
- HFD-530/TWu
- HFD-530/LIaconno-Connors
- HFD-530/GLunn
- HFD-530/RKumi
- HFD-530/THammerstrom