REVIEW AND EVALUATION OF PHARMACOLOGY/TOXICOLOGY DATA

KEY WORDS:

REVIEWER NAME: Ita Yuen
DIVISION NAME: Division of Antiviral Drug Products
HFD#:
11/5/99
REVIEW COMPLETION DATE:
None
ELECTRONIC FILE NUMBER:
20,778 (Oral powder) & 20,779 (Tablets)
NDA NUMBERS:
SERIAL #/DATE/TYPE OF SUBMISSION: 022/January 26, 1999/Efficacy & labeling supplement

INFORMATION TO SPONSOR:
Yes ( ) No (X)
SPONSOR (OR AGENT):
Agouron Pharmaceuticals, Inc.
10350 North Torrey Pines Road
La Jolla, CA 92037-1020

MANUFACTURER OF DRUG SUBSTANCE:

DRUG:

Generic Name: Nelfinavir mesylate (AG1343)
Trade Name: VIRACEPT®
**Chemical Name:**

\[ 3S-\{2(25^\circ,\ 35^\circ),\ 3\alpha,4\alpha\beta,8\alpha\beta\}\}-N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-3-isoquinolinecarboxymaide monomethanesulfonate (salt) \]

**CAS Registry Numbers:**

- 159989-65-8 (AG1343)
- 159989-64-7 (AG1346)

**Molecular Formula/Molecular Weight:**

- C\(_{32}\)H\(_{45}\)N\(_3\)O\(_9\)S (free base)/M.W. = 567.79
- C\(_{32}\)H\(_{45}\)N\(_3\)O\(_9\)S\(\cdot\)CH\(_4\)O\(_2\)S (salt)/M.W. = 663.90

**Structure:**

![Chemical Structure Image]

**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.

Ita Yuen, Ph.D.
Reviewing Pharmacologist

CONCURRENCE

HFD-530/WDempsey
HFD-530/JFarrell

CC

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