APPLICATION NUMBER:
21-226
21-251

CHEMISTRY REVIEW(S)
DIVISION OF ANTIVIRAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls Section

NDA #: 21-226
CHEMISTRY REVIEW #: 1
DATE REVIEWED: 15-SEP-00
SUBMISSION TYPE DOCUMENT DATE CDER DATE ASSIGNED DATE
Pre-submission 31-MAR-00 01-JUN-00 06-JUN-00
Original NDA 31-MAY-00 29-JUN-00 30-JUN-00
BZ 28-JUN-00 08-SEP-00 12-SEP-00
BC 07-SEP-00 14-SEP-00
BC 13-SEP-00
NC 14-SEP-00 15-SEP-00
NC 15-SEP-00 18-SEP-00

NAME/ADDRESS OF APPLICANT: Abbott Laboratories
D-491/AP6B-1
100 Abbott Park Road
Abbott Park, IL 60064-3500

DRUG PRODUCT NAME:
Proprietary: KALETRA™
Nonproprietary: Lopinavir/Ritonavir
Code Name/#: Abbott-84387, ABT-378

CHEM.TYPE/ THER.CLASS: 1P
PHARMACOLOGICAL CATEGORY: Antiviral
INDICATION: In Combination with Other Antiretroviral Agents for the Treatment of HIV Infection

DOSAGE FORM/STRENGTH: Soft Gelatin Capsules, 133.3 mg/33.3 mg
ROUTE OF ADMINISTRATION: PO

Rx/OTC: X Rx _ OTC
SPECIAL PRODUCT: _ Yes X No

CHEMICAL NAME / STRUCTURAL FORMULA:

Lopinavir

\[1S-[1R^*, (R^*),3R^*,4R^*]}-N-[4-[[2,6-dimethylphenoxy)acetyl]amino]-3-hydroxy-5-phenyl-1-(phenylmethyl)pentyl]tetrahydro-alpha-(1-methylethyl)-2-oxo-1(2H)-pyrimidineacetamide

CAS Registry Number 192725-17-0
Formula \(C_{37}H_{49}N_{4}O_{5}\)
M.W. 628.80
Ritonavir

10-Hydroxy-2-methyl-5-(1-methylethyl)-1-[2-(1-methylethyl)-4-thiazolyl]-3,6-dioxo-8,11-bis(phenylmethyl)-2,4,7,12-tetraazatridecan-13-oic acid, 5-thiazolymethyl ester, [5S-(5R*, 8R*, 10R*, 11R*)]-

CAS Registry Number 155213-67-5
Formula C37H48N6O5S2
M.W. 720.95

SUPPORTING DOCUMENTS:
RELATED DOCUMENTS:
NDA 20-945 Chemistry Review (for ritonavir drug substance and soft gelatin capsules)
NDA 20-659 Chemistry Review (for ritonavir drug substance)
Chemistry facsimile letter dated 9/1/00
Chemistry facsimile letters dated 9/11/00
Teleconference minutes dated 9/14/00

CONSULT REVIEWS:
Trade name review by OPDRA
Pharmacology review for qualification of impurity and pertinent excipients
Product specific inspection of DS and DP manufacturing sites

CONCLUSIONS/RECOMMENDATIONS:
The NDA submission and accompanying amendments provide adequate information on the chemistry, manufacturing and controls for KALETRA Capsules. The manufacturing facilities have acceptable cGMP status. The NDA, as amended, is therefore recommended for approval from the chemistry perspective.

/Sl/
Ko-Yu Lo, Ph.D., Review Chemist

Concurrence:
HFD-530/SMiller /Sl/ 10/13/00

cc:
Orig. NDA 21-226
HFD-530/Div. File
HFD-530/KLo
HFD-530/SMiller
HFD-530/KStrubbe
HFD-530/Slynche
HFD-830/CChen