CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
19-979/S-018

Chemistry Review(s)
DIVISION OF CARDIO-RENAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 19-979 SE1-018  Review #1  REVIEW DATE: March 28, 2001

<table>
<thead>
<tr>
<th>Submission Type</th>
<th>Document Date</th>
<th>CDER Date</th>
<th>Content / Topics Covered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amendment to Supplement</td>
<td>January 5, 2001</td>
<td>January 8, 2001</td>
<td>(1) Response to FDA’s letter dated Nov 22, 2000</td>
</tr>
<tr>
<td>(BL)</td>
<td></td>
<td>(HFD-110)</td>
<td>(2) Revised draft labeling</td>
</tr>
<tr>
<td>Amendment to</td>
<td>March 20, 2001</td>
<td>March 21, 2001</td>
<td>Final Printed Labeling</td>
</tr>
<tr>
<td>Supplement (BF)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NAME & ADDRESS OF APPLICANT:
Hoffmann-La Roche Inc
340 Kingsland Street
Nutley, New Jersey 07110-1199
Phone (973) 562-3550
Fax (973) 562-3554

Lynn DeVenezia-Tobias
Program Manager, Drug Regulatory Affairs
Phone (973) 562-5539
Fax (973) 562-3554

DRUG PRODUCT NAME
Trade Name: Ticlid ® Tablets
Nonproprietary name (USAN): ticlopidine hydrochloride
Code Name: RS-99847
CAS Number: 53885-35-1
Chemical Name: 5-(2-chlorobenzyl)-4,5,6,7-tetrahydrothieno-[3,2-c]pyridine HCl

AMENDMENT TO SUPPLEMENT contains Final Printed Labeling.

PHARMACOLOGICAL CATEGORY / INDICATION: Platelet inhibitor

DOSE FORM: Oral Tablet
STRENGTH: 250 mg

ROUTE OF ADMINISTRATION: Oral
DISPENSED: Rx

SUPPORTING DOCUMENT: CMC Review & T-con dated October 6, 2000 (attached)

REMARKS AND COMMENTS:
1) There are no CMC issues that require evaluation prior to approval of this efficacy supplement.
2) There are no changes to the How Supplied & Description Sections of the labeling.
3) Categorical exclusion from the requirement to prepare an Environmental Assessment is granted because entry concentration into the aquatic environment is not more than 1 ppb. [Reference: 21 CFR § 25.31 (b)]

CONCLUSION & RECOMMENDATION:
The supplement may be approved from a CMC perspective.


Distribution:
Orig. NDA 19-979 S-018
HFD-110 Division File
HFD-110 CSO, Colleen LoCicero

Initialed by Kasturi Srinivasachar
NDA #19-979 SEI-018                  CMC Review and T-Con: Oct. 6, 2000

Submission Type               Date Received @ FDA              Content / Topics Covered
Efficacy Supplement          January 24, 2000                Exemption from EA requirement

NAME & ADDRESS OF APPLICANT:
Hoffmann-La Roche Inc
340 Kingsland Street
Nutley, New Jersey 07110-1199

Debra Iorio, Program Manager, Drug Regulatory Affairs, (973) 562-3550
Lynn DeVenezia-Tobias, Program Manager, Drug Regulatory Affairs, (973) 562-5539
Fax (973) 562-3700

DRUG PRODUCT NAME: Trade Name: Ticlid ® Tablets

SUPPLEMENT 18 provides for a new indication.

PHARMACOL. CATEGORY / INDICATION: Antiplatelet agent (Platelet inhibitor)

DOSAGE FORM: Oral Tablet             STRENGTHS: 250 mg

ROUTE OF ADMINISTRATION: Oral       DISPENSED: Rx

SUMMARY OF REMARKS/COMMENTS FROM THE T-CON: Hoffmann-La Roche Inc., Nutley, NJ requested and qualifies for, categorical exclusion from the requirement to prepare an EA. Approval of the Efficacy Supplement will increase the amount of active moiety used. However, the estimated concentration of the drug substance at the point of entry into the aquatic environment is less than 1 part per billion. Reference: CFR 21 § 25.31 (b)

CONCLUSIONS & RECOMMENDATIONS:
(1) The supplement, SEI-018, requests approval of a new indication for the drug product based on a review of the medical literature. As a result, there are no CMC issues that require evaluation prior to approval of this Supplement.
(2) Grant categorical exclusion from the requirement to prepare an Environmental Assessment

/Sl/                                      Oct 6, 2000
Florian W. Zielinski, Review Chemist
October 6, 2000

Distribution:
Orig. NDA 19-979 S-018
HFD-110 Division File
HFD-110 Florian Zielinski
HFD-110 CSO, LoCicero
Initiated by: K Srinivasachar