CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20449/S11

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW

1. ORGANIZATION	2. NDA NUMBER
HFD-150 DODP	20-449

3. NAME AND ADDRESS OF APPLICANT *(City and State)*

Rhône-Poulenc Rorer Pharmaceuticals
500 Arcola Road
Collegeville, PA 19426-0107
Attention: Anne-Margaret Martin
Associate Director
Worldwide Regulatory Affairs
Tel: (610)-654-3037

NOV 16 1999

4. AF NUMBER

5. SUPPLEMENT (S)
NUMBER(S) DATES(S)

6. NAME OF DRUG	7. NONPROPRIETARY NAME	SE1-011	23-Jun-99
Taxotere®	docetaxel		

8. SUPPLEMENT PROVIDES FOR:

SE1-011 requests approval for the use of Taxotere® (docetaxel) for Injection Concentrate 20 mg and 80 mg for the second-line treatment of patients with locally advanced or metastatic non-small cell lung cancer with related labeling changes. The applicant has claimed a categorical exclusion for this efficacy supplement.

9. AMENDMENTS DATES

SE1-011(BC); 2-Aug-99
SE1-011(BL); 21-Oct-99
SE1-011(BL); 26-Oct-99

10. PHARMACOLOGICAL CATEGORY	11. HOW DISPENSED	12. RELATED IND/NDA/DMF
antineoplastic	RX x OTC ___	
13. DOSAGE FORM(S)	**14. POTENCY**	
for injection concentrate	20 mg and 80 mg vials	

15. CHEMICAL NAME AND STRUCTURE

16. RECORDS AND REPORTS
CURRENT YES___ NO___
REVIEWED YES___ NO___

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

Approval is recommended.

19. REVIEWER

NAME	SIGNATURE	DATE COMPLETED
Yung-Ao Hsieh, Ph.D.	/S/	11-16-99

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Summary of the Applications
This efficacy supplement provides for the use of Taxotere® (docetaxel) for Injection Concentrate 20 mg and 80 mg as a second-line treatment of patients with locally advanced or metastatic non-small cell lung cancer, based on the results of two large comparative randomized Phase III trials. The optimal dose range and schedule for this patient population is 60 mg/m^2 to 75 mg/m^2 administered as a one-hour intravenous infusion on day one of a twenty-one day cycle. In support of this submission, the applicant has submitted a claim of categorical exclusion under 21 CFR Part 25.31(b).

The applicant reported that a fifth year projection, for the United States, for all Taxotere (docetaxel), the subject of this application, and all current and expected approved applications, gives a total of kg of docetaxel drug substance. The Expected Introduction Concentration (EIC) value for docetaxel is calculated to be 2.8 ppt, far below 1 ppb for EIC.

Carton and Vial Labels [SE1-011(BL)
In an effort to address the medication errors reported through the AERS and USP voluntary reporting system, the Office of Post-marketing Drug Risk Assessment recommended that the labeling, specifically the declaration of overfills, concentration statement as well as instructions for the reconstitution and dilution of the drug product, should be revised. The proposed changes were communicated to the applicant on 9-Aug-1999. Mock-up presentations of the carton and vial labels (of the 20 mg strength) submitted in the amendment indicated that the labels have been revised following the Division's recommendations. The proposed carton and vial label revisions are acceptable.

Revision of the "PREPARATION AND Administration" Section in the Package Insert [SE1-011(BL), dated 26-Oct-99)]
The instructions for the reconstitution of the drug product and the dilution of the premixed solution provided in the **"PREPARATION AND ADMINISTRATION"** Section in the package insert have been revised in accordance with the Division's recommendations. The revised package insert is acceptable.

Conclusion and Recommendation
Adequate information has been presented to show that the requested approval of the efficacy supplement NDA 20-449 SE1-011 qualifies for a categorical exclusion from the requirement to prepare an EA under 21 CFR 25.31(b). It is recommended that the claim for a categorical exclusion for an EA should be approved. Additionally, the proposed labeling changes, as specified in amendments dated 21-Oct-99 and 26-Oct-99, are aimed to increase the safe use of the drug product and should be approved.

/S/ 11-16-99
Yung-Ao Hsieh, Ph.D.
Review Chemist, HFD-150

/S/ 11-16-99
Rebecca H. Wood, Ph.D.
Chemistry Team Leader, HFD-150