CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-571/S-008

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW	1. ORGANIZATION HFD-150 DODP	2. NDA NUMBER 20-571

3. NAME AND ADDRESS OF APPLICANT *(City and State)*
Pharmacia & Upjohn
)00 Portage Road
.alamazoo, MI 49001-0199
Attn: John S. Walker, Regulatory Affairs Manager

4. AF NUMBER

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

6. NAME OF DRUG	7. NONPROPRIETARY NAME		
Camptosar Injection	Irinotecan hydrochloride injection	SE_1-008	17-APR-1998

8. SUPPLEMENT PROVIDES FOR:
treatment of patients with metastatic carcinoma of the colon or rectum whose disease has recurred or progressed following 5-fluorouracil based therapy.

9. AMENDMENTS DATES
BC 15-July -1998

10. PHARMACOLOGICAL CATEGORY	11. HOW DISPENSED	12. RELATED IND/NDA/DMF
Antineoplastic agent	RX XX OTC __	
13. DOSAGE FORM(S) Injection	14. POTENCY 20 mg/mL as trihydrate salt (100 mg/5 mL & 40 mg/2 mL)	

15. CHEMICAL NAME AND STRUCTURE
(4S)-4,11-diethyl-4-hydroxy-9-[(4-piperidinopiperidino)carbonyloxy]-1H-pyranol](3',4':6,7)indolizino[1,2-b]quinoline-3,14(4H,12H)dione hydrochloride trihydrate $C_{33}H_{38}N_4O_6 \cdot 3H_2O$

16. RECORDS AND REPORTS
CURRENT YES__NO
REVIEWED YES__NO

17. COMMENTS

1. Irinotecan hydrochloride (CPT-11) is claimed, per se, in US Patent 4,604,463 which expires 15-Aug-2007. This supplement is in support of the transition from the present accelerated approval status under subpart H regulations to full approval status for the current second line indication for the drug.
3. The amendment dated July 15, 1998 contains CMC information confirming the clinical supplies used in the European studies are equivalent to the product marketed by Pharmacia & Upjohn in the US.

cc: Orig. NDA 20-571
HFD-150/Div File
HFD-150/RPBarron
HFD-150/PFQuinn
HFD-150/RHWood
R/D init. by RHWood 10-6-98

18. CONCLUSIONS AND RECOMMENDATIONS
The CMC aspects of this supplement are considered acceptable and approval is recommended. Minor editorial corrections to the proposed labeling are required as noted in the review notes. As required of the manufacturing facilities providing clinical supplies, a CGMP inspection of the has been requested "retrospectively." This facility has never been inspected for finished product manufacture by the Agency. This inspection remains pending but should not delay approval, if the product is otherwise deemed safe and efficacious. The product manufactured by used in the trials was terminally sterilized as opposed to sterilization by of the product currently approved for marketing in the US. The applicant should be requested to provide an explanation of this difference and justification of the continued use of aseptic techniques.

REVIEWER NAME	SIGNATURE	DATE COMPLETED
Robert P. Barron	/S/	10/2/98

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:NDA 20-571/S-008

PHARMACOLOGY REVIEW(S)

Division of Oncology Drug Products, HFD-150

REVIEW AND EVALUATION OF PHARMACOLOGY AND TOXICOLOGY DATA
NDA Supplement Review, Review # 2

NDA No.: 20-571 **SE #: 008** Type: SE

Date(s) of Submission: NDA dated: 4/17/98
CDR stamp date: 4/22/98

Information to be Conveyed to Sponsor: Yes (), No (X)

Reviewer: Sandip K. Roy, Ph.D.

Date Review Completed: 9/14/98

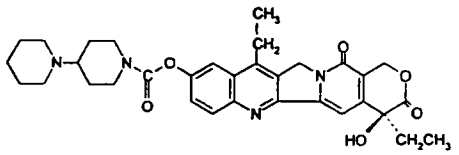
Sponsor: Pharmacia & Upjohn Company
Kalamazoo, MI

Drug Name: Camptosar® (Irinotecan Hydrochloride) **Other names:** CPT-11, PNU 101440E

Chemical Name: (4S)-4,11-diethyl-4-hydroxy-9-[(4-piperidinopiperidino)carbonyloxy]-1*H*-pyrano[3,4':6,7]indolizino[1,2-*b*]quinoline-3,14(4*H*,12*H*) dione hydrochloride.

CAS Number: 100286-90-6

Structure:



HCl • 3 H_2O

Molecular Weight: 677.1929 ($C_{33}H_{45}ClN_4O_9$)

Related INDs/NDAs/DMFs: INDs

Class: Topoisomerase I inhibitor

Indication: Metastatic carcinoma of the colon or rectum in patients whose disease has recurred or progressed following 5-FU-based chemotherapy

Clinical Formulation:

Format	Ingredient	Amount
Vial	Camptosar	100 mg
	Sorbitol	mg
	Lactic acid, USP	mg
	Water	ml (pH 3-4)

Route of Administration and dosage form: Intravenous injection

Approved Dosage: 125 mg/m^2 (90 min IV infusion) administered once weekly for 4 weeks followed by 2 weeks rest

Note: Portions of this review were excerpted directly from the sponsor's submission.

OVERALL SUMMARY AND EVALUATION

Sponsor has indicated (Amendment 1 to supplement 008) that there is no additional pharmacology/toxicology information relevant to this supplemental NDA. Please refer to the original review by Paul A. Andrews, Ph.D. (NDA 20-571, review dated: 5/24/96), for the complete pharmacology/toxicology review of the original Camptosar NDA.

RECOMMENDATION Since no additional pharmacology/toxicology information was necessary or submitted in this sNDA, this supplement is considered approvable from a pharmacology perspective.

a) Comments for further studies: none

b) Points discussed with Medical Officer: none

NDA issues: n/a

LABELING REVIEW

Due to the absence of any new pharmacology/toxicology information regarding labeling issues, we do not recommend any changes to the labeling.

Draft letter, Requests for Sponsor: none

/S/

Sandip K. Roy, Ph.D. 09/14/98
Pharmacologist/Toxicologist Date

/S/

Paul Andrews, Ph.D. 09/14/98
Pharmacology Team Leader Date

Original IND/NDA/DMF
c.c. /Division File
/PAndrews
/IChico
/PGuinn
/SRoy