CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-571/S-006

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	X
Approvable Letter	
Final Printed Labeling	
Medical Review(s)	
Chemistry Review(s)	X
EA/FONSI	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative Document(s)	X
Correspondence	X
Bioresearch Monitoring	

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER(S)

NDA 20-571/S-006

Trade Name: Camptosar Injection

Generic Name(s): (irinotecan hydrochloride injection)

Sponsor: Pharmacia & Upjohn Company

Agent:

Approval Date: January 15, 1998

Indication: For the treatment of patients with carcinoma of the colon or rectum whose disease has recurred or progressed following 5-FU based therapy.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 20-571/S-006

Approval Letter(s)

(6)

N 20-571/S-006

Pharmacia & Upjohn Company
7000 Portage Road
Kalamazoo, MI 49001-0199

JAN 15 1998

Attention: John S. Walker
Regulatory Manager

Dear Mr. Walker:

Please refer to your supplemental new drug application dated July 18, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Camptosar Injection (irinotecan hydrochloride injection).

The User Fee goal date is for this application is January 21, 1998.

The supplemental application provides for the addition of a new chiral HPLC method to determine the enantiomeric purity of the active ingredient and which will also serve as an identification test for the finished product. Additionally, the supplement provides for tightening of the impurity specifications in response to the commitment outlined in the approval letter of June 5, 1997, allowing marketing of the 2 mL fill presentation.

We have completed the review of this supplemental application and it is approved as of the date of this letter.

However, we request you submit complete analytical data, such as a certificate of analysis, proof of structure, etc., on the (R)-enantiomer reference material as an NDA supplemental new correspondence.

We remind you that you must comply with the requirement for an approved NDA as set forth under 21 CFR 314.80 and 314.81.

Sincerely yours,

RHW 1-15-98

Rebecca H. Wood, Ph.D.
Chemistry Team Leader
Division of Oncology Drug Products, (HFD-150)
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: Orig. NDA 20-571
Div. File/HFD-150
HFD-150/RHWood
HFD-150/RPBarron
HFD-150/PQuinn
HFD-150/JSimmons
HFD-358/JCook

Drafted by: RBarron/January 14, 1997
Final:

Approved ~~(AE)~~ (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 20-571/S-006

Chemistry Review(s)

JAN 14 1998

CHEMIST'S REVIEW	1. ORGANIZATION HFD-150 DODP	2. NDA NUMBER 20-571	
3. NAME AND ADDRESS OF APPLICANT *(City and State)* Pharmacia & Upjohn Company 7000 Portage Road Kalamazoo, MI 49001-0199		4. AF NUMBER 5. SUPPLEMENT (S) NUMBER(S) DATES(S)	
6. NAME OF DRUG Camptosar® Injection	7. NONPROPRIETARY NAME Irinotecan hydrochloride injection	**SCF- 006**	**18-JUL-1997**
8. SUPPLEMENT PROVIDES FOR: 1) a new chiral HPLC method, with validation data, to determine enantiomeric purity and serve as an identification test and 2) new tighter impurity specifications for the drug product. This supplement also fulfills the commitments outlined in the approval letter dated 5-JUN-1997 for SCP-003 for the marketing of a 2 mL fill vial.		9. AMENDMENTS DATES	
10. PHARMACOLOGICAL CATEGORY Antineoplastic agent	11. HOW DISPENSED RX XX OTC ___	12. RELATED IND/NDA/DMF	
13. DOSAGE FORM(S) Injection	14. POTENCY 20 mg/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 hydrate** See USAN for structure		16. RECORDS AND REPORTS CURRENT YES__NO__ REVIEWED YES__NO__	

17. COMMENTS

See REVIEW NOTES on Page 2 & ff..

cc: ***Orig. NDA 20-571***
HFD-150/Div File
HFD-150/P Guinn
HFD-150/RBarron
HFD-150/RWood
R/D init. by RWood 1-14-98

18. CONCLUSIONS AND RECOMMENDATIONS

Approval is recommended. However, the applicant should provide complete information per the draft letter on the (r)-enantiomer standard utilized in the new chiral method.

19. REVIEWER NAME	SIGNATURE	DATE COMPLETED
Robert P. Barron	Robert P Barron	1/13/98

DISTRIBUTION ORIGINAL JACKET XX DIVISION FILE XX REVIEWER XX CSO XX SUP. CHEMIST XX

5 Page(s) Withheld

X § 552(b)(4) Trade Secret / Confidential

___ § 552(b)(5) Deliberative Process

___ § 552(b)(4) Draft Labeling

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 20-571/S-006

Administrative/Correspondence

ORIGINAL

Pharmacia & Upjohn

Office of:
John S. Walker
Regulatory Affairs Manager

Mailstop: 0636-298-113
Telephone: ———
Fax: ———

SUPPL NEW CORRESP

May 1, 1998

SNC-006

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
MAY 04 1998
HFD-150

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room 3rd Floor
Woodmont II Building
1451 Rockville Pike
Rockville, MD 20852

Re: NDA 20-571
CAMPTOSAR® Injection
(Irinotecan Hydrochloride Injection)

General Correspondence
Supplemental Correspondence to S-006

Dear Sir or Madam:

Please refer to our supplement (S-006) dated July 18, 1997, which added a chiral HPLC method to determine the enantiomeric purity of the active ingredient. The assay also serves as an identification test for the finished product. Please also refer to your approval letter of January 15, 1998 for supplement 006 which requested additional analytical data on the method.

The additional analytical work has now been completed. The attached summary and study reports provide documentation on the chemical structure and chiral assignment of the (R)-enantiomer, and also summarize the basis for purity assignment of the reference material. This information supports the continued use of lot ———— as a reference material for the chiral assay, with an assigned purity of ———.

If you have questions related to this submission, please contact me at ———— or address correspondence to mailstop 0636-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

John S. Walker

John S. Walker
Regulatory Affairs Manager

JSW:SEH
Enclosures

Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, MI 49001-0199
USA

Telephone (616) 833-4000

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

Date AUG - 4 1997

NDA No. 20-571

Pharmacia & UpJohn Company
7000 Portage Road
Kalamazoo, Michigan 49001
Attention: John S. Walker
Regulatory Affairs Manager

Dear Sir/Madam:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Camptosar Injection

NDA Number: 20-571

Supplement Number: S - 006

Date of Supplement: July 18, 1997

Date of Receipt: July 25, 1997

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research, HFD-150
Attention: Document Control Room - 17B-20
5600 Fishers Lane
Rockville, MD 20857

Patrick Lucas

for Chief, Project Management Staff
Division of Oncology and Pulmonary
Drug Products

Pharmacia&Upjohn

ORIGINAL

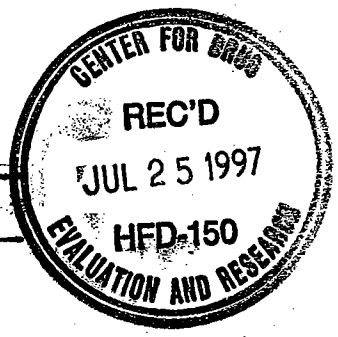
Office of:
John S. Walker
Regulatory Manager
Regulatory Affairs

Telephone No.: ————
Facsimile No.: ————

July 18, 1997

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room 3rd Floor
Woodmont II Building
1451 Rockville Pike
Rockville, MD 20852

NDA NO. 20-571 REF. NO. 006
NDA SUPPL FOR SCF



Re: NDA 20-571
CAMPTOSAR® Injection
(Irinotecan Hydrochloride Injection)

Supplement

Dear Sir or Madam:

Please refer to your Approval Letter of June 5, 1997 for a new 2 mL fill presentation of Camptosar Injection. Please also refer to our facsimile of June 4, 1997 and to our letter of June 10, 1997 in which we committed to submit information in conjunction with approval of the new presentation. The Approval Letter states this information should be submitted as a supplement for prior approval.

As committed to in our previous correspondence, validation data for the chiral HPLC assay (TA 0716) are provided in Attachment 1. The technical report of Attachment 1 demonstrates that TA 0716 is suitable for use as a limits test for determination of the chiral purity of Camptosar Injection. The assay produces adequate resolution of the (R)-enantiomer of irinotecan hydrochloride for the drug peak as well as formulation components. The method was also shown to be linear over a range of ———— of the limit level. Finally, the limit of detection is about ———— than the registration limit ———— for the (R)-enantiomer.

We have also committed to propose new impurity registration specifications. Attachment 2 contains proposed impurity limits which decrease the allowable levels of Total Impurities, as well as the individual impurities ————————

Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, MI 49001-0199
USA

Telephone (616) 833-4000

If you have any questions regarding the contents of this submission, please contact me at _____ Please send correspondence addressed to Unit 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

John S. Walker
Regulatory Manager
Regulatory Affairs

JSW:law

NDA 20-571
CAMPTOSAR® Injection

Field Copy Statement

In accord with CFR §314.70(a), this is to certify that a field copy of this Chemistry, Manufacturing and Controls section/supplement to NDA 20-571 dated July 18, 1997 has been provided to the Detroit District Office.

PHARMACIA & UPJOHN COMPANY

John S. Walker
Regulatory Manager
Regulatory Affairs

SUMMARY

Spectroscopic Proof of Structure of PNU-101,440E and Characterization of an Irinotecan Hydrochloride Trihydrate (R)-Enantiomer Reference Standard

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. *0910-0297*
Expiration Date: *November 30, 1996.*

USER FEE COVER SHEET

See Instructions on Reverse Before Completing This Form.

1. APPLICANT'S NAME AND ADDRESS

Pharmacia & Upjohn Company
7000 Portage Road
Kalamazoo, MI 49001-0199

2. USER FEE BILLING NAME, ADDRESS, AND CONTACT

Pharmacia & Upjohn Company
7000 Portage Road
Kalamazoo, MI 49001-0199

CONTACT NAME:

Daniel G. Mannix, Ph.D.
Director, Regulatory Affairs

3. TELEPHONE NUMBER *(Include Area Code)*
(616) 833-8095

4. PRODUCT NAME
CAMPTOSAR Injection

5. DOES THIS APPLICATION CONTAIN CLINICAL DATA? ☐ YES ☒ NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

6. USER FEE I.D. NUMBER

7. LICENSE NUMBER/NDA NUMBER

8. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED BEFORE 9/1/92

☐ AN INSULIN PRODUCT SUBMITTED UNDER 506

☐ THE APPLICATION IS SUBMITTED UNDER 505(b)(2) *(See reverse before checking box.)*

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGIC PRODUCT LICENSED UNDER 351 OF THE PHS ACT

9. a. HAS THIS APPLICATION QUALIFIED FOR A **SMALL BUSINESS EXCEPTION?** ☐ YES ☐ NO *(See reverse if answered YES)*

b. HAS A **WAIVER** OF APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES ☐ NO *(See reverse if answered YES)*

This completed form must be signed and accompany each new drug or biologic product, original or supplement.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Daniel G. Mannix Daniel G. Mannix, Ph.D.	Director, Regulatory Affairs	7/18/97

FORM FDA 3397 (12/93)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations; 314)

Form Approved: OMB No. 0910-0001.
Expiration Date: 12/31/95
See OMB Statement on Page 3.

FOR FDA USE ONLY

DATE RECEIVED	DATE FILED
DIVISION ASSIGNED	NDA/ANDA NO. ASS.

NOTE: No application may be filed unless a completed application form has been received *(21 CFR Part 314).*

NAME OF APPLICANT
Pharmacia & Upjohn Company

DATE OF SUBMISSION
May 1, 1998

ADDRESS *(Number, Street, City, State and Zip Code)*
7000 Portage Road
Kalamazoo, Michigan 49001

TELEPHONE NO. *(Include Area Code)*
(616) 833-8263

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER (if previously issued)
20-571

DRUG PRODUCT

ESTABLISHED NAME *(e.g., USP/USAN)*
Irinotecan Hydrochloride Injection

PROPRIETARY NAME *(if any)*
CAMPTOSAR® Injection

CODE NAME *(if any)*
CPT-11
U-101440E

CHEMICAL NAME
(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

DOSAGE FORM
Injection

ROUTE OF ADMINISTRATION
Intravenous

STRENGTH(S)
20 mg/mL

PROPOSED INDICATIONS FOR USE
Treatment of patients with metastatic carcinoma of the colon or rectum whose disease has recurred or progressed following 5-FU-based therapy

LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS *(21 CFR Part 312)*, NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, AND DRUG MASTER FILES *(21 CFR 314.420)* REFERRED TO IN THIS APPLICATION:

IND Nos: 35229 DMF Nos: [redacted]

INFORMATION ON APPLICATION

TYPE OF APPLICATION *(Check one)*

☐ THIS SUBMISSION IS A FULL APPLICATION *(21 CFR 314.50)* ☐ THIS SUBMISSION IS AN ABBREVIATED APPLICATION (ANDA) (21 CFR 314.55)

IF AN ANDA, IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

NAME OF DRUG	HOLDER OF APPROVED APPLICATION

TYPE SUBMISSION *(Check one)*

☐ PRESUBMISSION ☐ AN AMENDMENT TO A PENDING APPLICATION ☐ SUPPLEMENTAL APPLICATION

☐ ORIGINAL APPLICATION ☐ RESUBMISSION

SPECIFIC REGULATION(S) TO SUPPORT CHANGE OF APPLICATION *(e.g., Part 314.70(b)(2)(iv))*

PROPOSED MARKETING STATUS *(Check one)*

☐ APPLICATION FOR A PRESCRIPTION DRUG PRODUCT *(Rx)* ☐ APPLICATION FOR AN OVER-THE-COUNTER PRODUCT *(OTC)*

USER FEE DATA ENTRY/VALIDATION FORM Ver.3(2/17/9

NDA #20-571 DOCUMENT ID/LETTER DATE SOF-0010 / 7-18-97

APPLICANT NAME Pharmacia & Upjohn

PRODUCT NAME Camptosar Injection

FORM MUST BE COMPLETED ASAP

1. (YES) User Fee Cover Sheet Validated?

NOTE TO DOCUMENT ROOM:
PLEASE MAKE THE FOLLOWING CHANGES TO THE COMIS DATA ELEMENTS

2. YES (NO) CLINICAL DATA?
[Check YES if contains study reports or literature reports of what are explicitly or implicitly represented by the applicant to be adequate and well-controlled trials. "Clinical data do not include data used to modify the labelling to add a restriction that would improve the safe use of the drug (e.g., to add an adverse reaction, contraindication or warning to the labeling).]

REF IF NO CLINICAL DATA IN SUBMISSION, INDICATE IF CLINICAL DATA ARE *CROSS REFERENCED* IN ANOTHER SUBMISSION?

3. YES (NO) NDA BEING SPLIT FOR ADMINISTRATIVE CONVENIENCE (OTHER THAN BUNDLING)? IF YES, list ALL NDA numbers, review divisions & indicate those for which application fees apply.

NDA #	DIVISION		
N_____	_____	FEE	NO FEE
N_____	_____	FEE	NO FEE

4. (YES) ~~NO~~ BUNDLING POLICY APPLIED CORRECTLY? NO DATA ENTRY REQUIRED FOR ELEMENT
[Check YES if application is properly designated as one application or is properly submitted as a supplement instead of an original application. Check NO if application should be split into more than one application or submitted as an original instead of a supplement. IF NO, list resulting NDA numbers, and review divisions.]

NDA #	DIVISION	NDA #	DIVISION
N_____	_____	N_____	_____

5. P (S) PRIORITY OR STANDARD?

8/1/97
6. CSO SIGNATURE/DATE

Dotty Pease 8/1/97
SCSO CONCURRENCE SIGNATURE/DATE

COPY DISTRIBUTION: ORIGINAL TO ARCHIVAL AFTER DATA ENTRY, ONE COPY EACH TO DIVISION FILE AND CDER, ASSOCIATE DIRECTOR FOR POLICY HFD-5

27 Page(s) Withheld

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___ § 552(b)(4) Draft Labeling