CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: NDA 20-553/S-002

Trade Name: OXYCONTIN 80 mg

Generic Name:(oxycodone hydrochloride controlled release tablets)

Sponsor: Purdue Pharma LP

Approval Date: December 9, 1996

Indication: Provides for 80 mg green colored tablets as a line extension to the approved 10, 20 and 40 mg tablets.

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APPLICATION: NDA 20-553/S-002

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Medical Review(s)	X			
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Pharmacology Review(s)	X			
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Microbiology Review(s)				
Clinical Pharmacology Biopharmaceutics Review(s)	X			
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Correspondence				

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Application Number: NDA 20-553/S-002

APPROVAL LETTER

NDA 20-553/S-002

DEC 9 1996

Purdue Pharma LP
100 Connecticut Ave.
Norwalk, Connecticut 06850-3590

Attention: Lee Ann Storey, RN, MPH
Assistant Director
Drug Regulatory Affairs and Compliance

Dear Ms. Storey:

Please refer to your June 24, 1996, supplemental new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for OxyContin (Oxycodone hydrochloride controlled release tablets), 80 mg.

We acknowledge receipt of your amendment dated October 24, 1996.

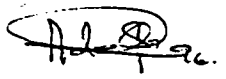
The supplemental application provides for 80 mg green colored tablets as a line extension to the approved 10, 20, and 40 mg tablets.

We have completed the review of this supplemental application, and it is approved.

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

If you have any questions, please contact Ms.Bonnie McNeal, CSO, telephone 301-443-4250.

Sincerely yours,



Albinus M. D'Sa, Ph.D.
Chemist, Team Leader, DNDC II,
Division of Anesthetic, Critical Care, and
Addiction Drug Products, HFD-170
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:
Original NDA 20-553
HFD-170 Div. Files
HFD-820/John Gibbs (only for NDAs and CMC supplements)
HFD-80
HFD-170/B.McNeal
HFD-170/P.Maturu, SDoddapaneni
HFD-170/A.D'Sa, DConner
Drafted by: P.Maturu
R/D Initials: CPMoody
F/T by

APPROVED

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-553/S-002

MEDICAL REVIEW(S)

JUL 20 1996

MEDICAL OFFICER REVIEW OF AN NDA SUPPLEMENT
DIVISION OF ANESTHETIC, CRITICAL CARE & ADDICTION DRUG PRODUCTS

NDA #: 20-553/S-002
NAME: OxyContin Controlled-Release Tablets 80 mg
APPLICANT: Purdue Pharma L.P.
TYPE: Clinical Data for NDA Supplement for 80 mg Tablet
SUBMISSION DATE: 6/24/96 Received: CDER 6/25/96 Reviewer 7/16/96
REVIEWER: Monte L. Scheinbaum PhD, MD
CSO: Bonnie McNeal

SUMMARY

Oxycodone is a well known, morphine-like opioid analgesic. A controlled-release form of oxycodone hydrochloride (OxyContin Controlled-Release Tablets, 10, 20 and 40 mg) was approved on 12/21/95. This submission seeks approval of an 80 mg strength oral controlled-release tablet for the treatment of pain in opioid tolerant patients for dosing on a q12h basis. A total of 29 adult patients received the 80 mg tablets in the course of open-label study OC92-1101 carried out from mid-1995 to March 1996. Patients were 25 to 71 years old (mean 53 years), 38% female. 66% white, 24% black and 10% hispanic. Doses ranged from 80 mg q12h daily to 960 mg (twelve tablets) in the morning and 400 mg (fivetablets) in the evening. Duration of therapy ranged from one dose to eight months treatment. No obvious changes in efficacy relative to use of the lower strengths were noted when patients were converted to 80 mg tablets or combinations of these with lower strengths or when upward or downward titrations were carried out. There were 3/29 (10%) who dropped for lack of efficacy owing to disease progression. There were three (10%) who dropped for adverse events, one with respiratory depression (a serious event), one with dizziness, confusion and ataxia, and one with severe constipation. One patient died of lung cancer, unrelated to the study drug. These findings are not unexpected. There appears to be no obvious clinical problems with the new dosage strength. Assuming it passes muster from a pharmacokinetic viewpoint, it will provide increased convenience of dosing for appropriate patients.

Monte L. Scheinbaum, PhD, MD

Date:7/19/96

Celia Winchell, MD

Date:
7/20/96

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-553/S-002

CHEMISTRY REVIEW(S)

20-553

DEC 5 1996

Div File

Chemistry Review	1. Division HFD-170	2. NDA Number 20-553
3. Name and Address of Applicant Purdue Pharma LP, 100 Connecticut Ave, Norwalk, CT 06850-3590, Dr. James Conover, tel 203-854-7280.		4. Supplement Number Date SCF-002 6.24.96
5. Name of Drug OxyContin 80 mg tablets (for use in opioid tolerant patients only)	6. Nonproprietary Name Oxycodone HCl CR tablets	
7. Supplement Provides for: 80 mg green colored round convex tablets, a line extension to the approved 10, 20 and 40 mg CR tablets, dated 12.12.95.		8. Amendment(s) 10.24.96 final package insert
9. Pharmacological Category	10. How Dispensed	11. Related Documents DMF
12. Dosage Form CR tablets.	13. Potency(ies) 10, 20, 40 and 80 mg	
14. Chemical Name and Structure see USAN		

15. Comments

Green colored 80 mg OxyContin tablets contain FDA approved yellow iron oxide with FDC blue no 2 dyes. Just like other approves strength tablets, 80 mg tablets are supplied as 100s and 500s in plastic bottles, and in unit dose packages of 25s per card. Added US Pat 5,508,042, for composition in the patent certification section, 505 (j)(2)(vii), and in package insert.

In the development of the composition, the first observation was a slow release rate when 40 mg tablet granulation was compressed as 80 mg tablets. In order to obtain same release rate, Eudragit RS 30D retardant level was reduced from 28 to 20 mg per tablet and a biostudy was conducted with drug product lot 6E, processed at tablets batch size, from

Processing steps, quality control standards, and expiry date were identical to the approved NDA 20-553. Executed batch records and COA were supplied 3 full size batches, 6E, 5E and 0J. 3 year expiration date request was supported with stability data for these 3 batches stored either for 12 months at 30 C/60% RH or 6 months at 40 C/75% RH. Stability test results were within the proposed acceptance standards for appearance (round biconvex green film coated tablets), oxycodone HCl (90-110%), related substances (LT 1% for highest single impurity and LT 2% for total impurities), dissolution %/ hr, %/ hr, above %/ hr). Stability test samples were packaged in opaque HDPE bottles as 100s (60 cc) and 500s (250 cc), and in unit dose PVC blisters as 25s per card. There were no specification failures.

I believe that there may not be a need for EER (supposedly acceptable till 11.17.96) and MV (green coloring agents, yellow iron oxide and FDC Blue no 2) may not interfere. 6 enclosures: For biolot 6E, COA for OxyContin 80 mg, COA for oxycodone lot, master formula/production record, process equipment/flow chart and 1 year stability data; bottle label and EER.

16. Conclusions and Recommendations

Recommends approval of the supplement upon concurrence by PK. PK concurrence review attached 12/5/96

17. Name	Signature	Date
P.Maturu, PhD	P. Maturu	12.5.96
A.D'Sa, PhD, Chemistry Team Leader	A.D'Sa	12/5/96

cc: NDA 20-553/SCF-002/6.24.96
HFD-170/Division File,PMaturu,AD'Sa, BMcNeal
Doc ID: N205532.967
APPROVED

Div File

Chemistry Review	1. Division HFD-170	2. NDA Number 20-553
3. Name and Address of Applicant Purdue Pharma LP, 100 Connecticut Ave, Norwalk, CT 06850-3590, Dr. James Conover, tel 203-854-7280.		4. Supplement Number Date SCF-002 6.24.96
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17. Name	Signature	Date
P.Maturu, PhD	P. Maturu	8.8.96
A.D'Sa, PhD, Chemistry Team Leader	AD'Sa	8/14/96

cc:

NDA 20-553/SCF-002/6.24.96
HFD-170/Division File
HFD-170/PMaturu,AD'Sa, BMcNeal
Doc ID: N205532.967
APPROVED