CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER(S)
NDA 20-545/S-007

Trade Name: Procanbid Tablets, 500 & 1000 mg

Generic Name(s): (procainamide hydrochloride extended release)

Sponsor: King Pharmaceuticals, Inc.

Approval Date: July 11, 2002

Indication: Provides for an alternate manufacturing, packaging, and testing site as well as a change in supplier and revised labeling

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 20-545/S-007

Administrative Documents

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*: Microbiology (HFD-805) for **Biopharm. Consult.**
Attn: Dr. Robbie Gobriel

FROM: JV Advani (HFD-110)

DATE: 10/15 /01	IND NO:	NDA NO. **20-545**	TYPE OF DOCUMENT : Supplement SCM-007	DATE OF DOCUMENT: 09/28/01

NAME OF DRUG: Procanbid (procainamide HCl extended release tablets)	PRIORITY CONSIDERATION:	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE:

NAME OF FIRM: **King Pharmaceuticals, Inc.**

REASON FOR REQUEST

I. GENERAL

NEW PROTOCOL
☐ PROGRESS REPORT
☐ NEW CORRESPONDENCE
☐ DRUG ADVERTISING
☐ ADVERSE REACTION REPORT
☐ MANUFACTURING CHANGE/ADDITION
☐ MEETING PLANNED BY
☐ PRE--NDA MEETING
☐ END OF PHASE II MEETING
☐ RESUBMISSION
☐ SAFETY/EFFICACY
☐ PAPER NDA
☐ CONTROL SUPPLEMENT
☐ RESPONSE TO DEFICIENCY LETTER
☐ FINAL PRINTED LABELING
☐ LABELING REVISION
☐ ORIGINAL NEW CORRESPONDENCE
☐ FORMULATIVE REVIEW
☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER:	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER:

III. BIOPHARMACEUTICS

☐ DISSOLUTION
☒ BIOAVAILABILTY STUDIES **(Volumes 3-6)**
☐ PHASE IV STUDIES
☐ DEFICIENCY LETTER RESPONSE
☐ PROTOCOL-BIOPHARMACEUTICS
☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
☐ SUMMARY OF ADVERSE EXPERIENCE
☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: This is King's pharmaceuticals prior approval supplement for use of new new manufacturing and testing facility for drug product and drug substance.

The Bioequivalence section of bioavailability study report is provided in volumes 3-6 of this submission.

SIGNATURE OF REQUESTER: JV Advani	METHOD OF DELIVERY (Check one): i E- MAIL X☐ HAND
SIGNATURE OF RECEIVER:	SIGNATURE OF DELIVERER:

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/s/

J. V. Advani
10/15/01 04:43:12 PM

RHPM Review of Final Printed Labeling

Application:	NDA 20-545/S-007 Procanbid (procainamide hydrochloride extended-release tablets), 500 and 1000 mg
Applicant:	King Pharmaceuticals, Inc.
Submission Date:	May 22, 2002
Receipt Date:	May 24, 2002
Type of Submission:	Final Printed Labeling for Prior Approval Chemistry Supplement

Background

King Pharmaceuticals, Inc. submitted NDA 20-545/S-007 dated September 28, 2001 as a prior approval chemistry supplement to provide for 1) the use of Catalytica Pharmaceuticals' facilities in Greenville, NC as a new manufacturing and testing (release and stability) facility for Procanbid (500 mg and 1000 mg) Tablets and 2) the change in supplier of the active drug substance (procainamide hydrochloride) from ——— to ——— This supplement was being filed due to the discontinuance of the manufacturing of both the drug substance and drug product by the currently approved manufacturer, ———

An amendment to this supplement was submitted on January 14, 2002 to provide for three items:
1) Addition of ——— testing laboratory, ——— which was used to perform a total of five tests on three different excipients used in the manufacturing of the submission batches of Procanbid 500 mg and 1000 mg.
2) Submission of revised raw material testing instructions for the excipient, magnesium stearate.
3) An additional comparative dissolution report.

An approvable letter issued for this supplement on February 1, 2002 requesting minor editorial corrections to the package insert.

Review

When compared with the draft labeling submitted on September 28, 2001, the following changes were noted:

1) Under **WARNINGS**, in the boxed warning regarding **BLOOD DYSCRASIAS**, the hyphen has been deleted from the word "hydro-chloride" in the second sentence.

    - This change was made in accordance with the approvable letter.

2) Throughout the package insert, the font style of the section or subsection words in the parenthetical references have been made consistent with that of the actual section or subsection headers, e.g., the word "WARNINGS" in the phrase "(See WARNINGS)" has been changed to bold font style.

    - This change was made in accordance with the approvable letter.

3) Under **DOSAGE AND ADMINISTRATION**, the lines forming the table entitled "To provide up to 50 mg/kg of body weight per day*" have been removed.

- Per a June 25, 2002 conversation with Dr. Stockbridge, he stated that this change was acceptable.

4) Under **HOW SUPPLIED**, the statement "Manufactured by: Catalytica Pharmaceuticals, Inc., Greenville, NC 27834" has been changed to "Manufactured by: DSM Pharmaceuticals, Inc., Greenville, NC 27834"

- In a June 26, 2002 correspondence, the sponsor stated that the change was made to reflect the official name change of Catalytica Pharmaceuticals, Inc. to DSM Pharmaceuticals, Inc. on December 14, 2001. Per a June 26, 2002 conversation with Dr. Advani, he stated that the above change was acceptable.

The following change requested in the approvable letter was not made by the sponsor:

Under Figure 1, the hyphen should be deleted from the word "Concentra-tions" in the caption.

- The sponsor stated in the final printed labeling submission that this change was not made due to the word being separated "concentra-" on one line and "tions" being on the next line.

There are no other changes from the last approved package insert (approved on January 11, 2000/ SLR-004).

Per a June 25, 2002 conversation with Dr. Stockbridge, he concurred that the sponsor should make the following minor editorial changes to the package insert at the time of their next printing:

1) Under **DESCRIPTION**, in the first two paragraphs, "(diethylamino)" should be separated "(diethyl-" on one line and "amino)" on the next line instead of "(diethy-" on one line and "lamino)" on the next line.

2) Under **CLINICAL PHARMACOLOGY/Pharmacokinetics and Drug Metabolism/Absorption/Bioavailability**, in the third paragraph, "N-acetylprocainamide" should be separated "N-acetyl-" on one line and "procainamide" on the next line instead of "N-acetylp-" on one line and "rocainamide" on the next line.

Comments/Recommendations:

An approval letter requesting the minor editorial corrections noted above should issue for this supplement.

Quynh Nguyen, Pharm.D.
Regulatory Health Project Manager

qn/6-7-02/6-26-02

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/s/

Quynh Nguyen
7/10/02 01:56:35 PM
CSO

RHPM Review of Draft Labeling

Application:	NDA 20-545/S-007 Procanbid (procainamide hydrochloride extended-release tablets), 500 and 1000 mg
Applicant:	King Pharmaceuticals, Inc.
Submission Date:	September 28, 2001
Receipt Date:	October 3, 2001
Type of Submission:	Prior Approval Chemistry Supplement with Draft Labeling

Background

King Pharmaceuticals, Inc. submitted NDA 20-545/S-007 dated September 28, 2001 as a prior approval chemistry supplement to provide for 1) the use of Catalytica Pharmaceuticals' facilities in Greenville, NC as a new manufacturing and testing (release and stability) facility for Procanbid (500 mg and 1000 mg) Tablets and 2) the change in supplier of the active drug substance (procainamide hydrochloride) from [redacted] to [redacted] This supplement is being filed due to the discontinuance of the manufacturing of both the drug substance and drug product by the currently approved manufacturer,

An amendment to this supplement was submitted on January 14, 2002 to provide for three items:
1) Addition of [redacted] testing laboratory, [redacted], which was used to perform a total of five tests on three different excipients used in the manufacturing of the submission batches of Procanbid 500 mg and 1000 mg.
2) Submission of revised raw material testing instructions for the excipient, magnesium stearate.
3) An additional comparative dissolution report.

Review

The sponsor submitted draft labeling with changes to the **HOW SUPPLIED** section as follows:

For the 500 mg strength,
- the phrase [redacted] has been changed to "coded 'PROCANBID 500' on one side"
- the information [redacted] has been changed to "NDC 61570-069-01 Bottles of 100"

For the 1000 mg strength,
- the phrase [redacted] has been changed to "coded 'PROCANBID 1000' on one side"
- the information [redacted] has been changed to "NDC 61570-071-01 Bottles of 100"

The statement "Manufactured by: Warner-Lambert Co, Morris Plains, NJ 07950" has been changed to "Manufactured by: Catalytica Pharmaceuticals, Inc., Greenville, NC 27834"

There are no other changes from the last approved package insert (approved on January 11, 2000/ SLR-004).

In Dr. Mishina's 12/19/01 review, she noted the following: "The application is acceptable for meeting the Office of Clinical Pharmacology and Biopharmaceutics requirements and shows that the product manufactured by King Pharmaceuticals at Greenville, North Carolina is bioequivalent to the product manufactured at [redacted] The new manufacture site at Greenville may be approved from a biopharmaceutics point of view."

In Dr. Advani's 1/30/02 review, he noted the following: "The currently approved manufacturer, [redacted] has discontinued to manufacture both the drug substance and drug product Therefore firm has contracted The Catalytica facility to manufacture Procanbid Tablets according to the currently approved process. All raw materials packaging components, labeling and specifications are consistent with those currently approved. All CMC information provided including the Bioequivalence study that is reviewed by Dr. E. Mishina is satisfactory. EER for Catalytica and [redacted] sites are acceptable. Overall OC acceptance recommendation is attached with this review.
The submission is Recommended for approval."

Minor editorial errors in the package insert were noted in this draft labeling submission. Per a January 16, 2002 discussion with Dr. Stockbridge, he concurred that the sponsor should make the following editorial corrections:

1) Under Figure 1, the hyphen should be deleted from the word "Concentra-tions" in the caption.

2) Under **WARNINGS**, in the boxed warning regarding **BLOOD DYSCRASIAS**, the hyphen should be deleted from the word "hydro-chloride" in the second sentence.

3) Throughout the package insert, the font style of the section or subsection words in the parenthetical references should be made consistent with that of the actual section or subsection headers, e.g., the word "WARNINGS" in the phrase "(See WARNINGS)" should be changed to bold font style.

Comments/Recommendations:

An approvable letter should issue for this supplement requesting final printed labeling revised as indicated above.

Quynh Nguyen, Pharm.D.
Regulatory Health Project Manager

qn/1-23-02/1-30-02

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/s/

Quynh Nguyen
2/1/02 12:51:48 PM
CSO

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
FOOD AND DRUG ADMINISTRATION

US Mail address:
FDA/CDER/HFD-110
5600 Fishers Lane
Rockville, MD 20857

Woodmont II
1451 Rockville Pike
Rockville, MD 20852

Transmitted to FAX Number:	**(423) 989-6133**
Attention:	**Mr. Dean R. Cirotta, MBA**
Company Name:	**King Pharmaceuticals, Inc.**
Phone:	(423) 274-8663
Subject:	**Copy of Action Letter**
Date:	**February 4, 2002**
Pages including this sheet:	**4**

From: **Quynh Nguyen, Pharm.D.**
Phone: **(301) 594-5311**
Fax: **(301) 594-5494**

Dear Dean,

Per your request, please find attached a copy of the approvable letter for supplement 007 for NDA 20-545/Procanbid. If you have any questions, please do not hesitate to contact me at the above numbers.

Thanks,
Quynh

PLEASE LET ME KNOW YOU RECEIVED THIS. THANKS!

MESSAGE CONFIRMATION

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DIVISION OF CARDIO-RENAL DRUG PRODUCTS
FOOD AND DRUG ADMINISTRATION

US Mail address:
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5600 Fishers Lane
Rockville, MD 20857

Woodmont II
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Company Name: **King Pharmaceuticals, Inc.**

Phone: (423) 274-8663

Subject: **Copy of Action Letter**

Date: **February 4, 2002**

Pages including this sheet: **4**

From: **Quynh Nguyen, Pharm.D.**

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/s/

Quynh Nguyen
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CSO