CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-341

CHEMISTRY REVIEW(S)

NDA 21-341

Bextra (Valdecoxib) Tablets

G.D. Searle & Co.

Rao Puttagunta,Ph.D.
Division of Anti-inflamatory, Analgesic and Ophthalmic Drugs (HFD-550)

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Chemistry Review Data Sheet

1. **NDA #:** 21-341

2. **REVIEW #:** 1

3. **REVIEW DATE:** 14-NOV-2001

4. **REVIEWER:** Rao Puttagunta

5. **PREVIOUS DOCUMENTS:** N/A

6. **SUBMISSION(S) BEING REVIEWED:**

Submission(s) Reviewed	Document Date
Original	15-JAN-2001
Amendment 1	19-JUL-2001
Amendment 2	31-AUG-2001
Amendment 3	26-OCT-2001
Amendment 4	02-NOV-2001
Amendment 5	09-NOV-2001

7. **NAME & ADDRESS OF APPLICANT:**

Name:	G.D. Searle & Co.
Address:	4901 Searle Parkway, Skokie, IL 60077
Representative:	Peter East, Associate Director, Regulatory Affairs
Telephone:	847-982-8606

8. **DRUG PRODUCT NAME/CODE/TYPE:**

a) Proprietary Name: Bextra
b) Non-Proprietary Name: Valdecoxib Tablets
c) Code Name/#: SC-65872
d) Chem. Type/Submission Priority (ONDC only):

- **Chem. Type :** 1
- **Submission Priority:** S

9. LEGAL BASIS FOR SUBMISSION: N/A

10. PHARMACOL. CATEGORY: Relief of signs and symptoms of osteoarthriris and adult rheumatoid arthritis

11. DOSAGE FORM: Tablets

12. STRENGTH/POTENCY: 10 mg and 20 mg per Tablet

13. ROUTE OF ADMINISTRATION: Oral

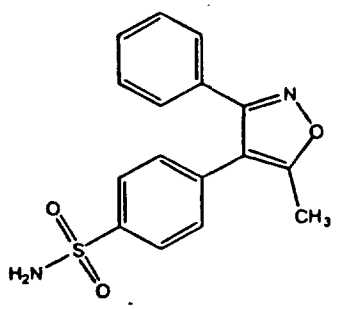
14. Rx/OTC DISPENSED: _X__Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM)

_____SPOTS product – Form Completed

__X__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



Chemical name: 4-(5-methyl-3-phenyl-4-isoxazolyl)benzenesulfonamide
Molecular Formula: $C_{16}H_{14}N_2O_3S$ **Molecular Weight**: 314.36

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

[redacted]

[1] Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 –Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	[redacted]	Valdecoxib
IND	[redacted]	Valdecoxib

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	Acceptable	24-SEP-2001	J.D. Ambrogio
Pharm/Tox	N/A		
Biopharm	N/A		
LNC	USAN	1998	
Methods Validation	Pending	Initiated on 02-NOV-2001	
OPDRA	Acceptable	10-OCT-2001	Marci Lee
EA	FONSI recommended	24-OCT-2001	Melissa J. Maust
Microbiology	N/A		

APPEARS THIS WAY
ON ORIGINAL

The Chemistry Review for NDA 21-341

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From the chemistry standpoint this NDA is recommended for approval.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance (s)

Valdecoxib (SC-65872), an isoxazole derivative, is a selective inhibitor of cyclooxygenase-2 (COX-2). The drug substance (valdecoxib) is a white to off white solid. Valdecoxib has very low solubility in water (10 mcg/mL at 25°C, pH 7.0). It is more soluble in organic solvents such as methanol (51-77 mg/mL), acetone (136-181 mg/mL), dimethyl sulfoxide (>283 mg/mL) and tetrahydrofuran (229-413 mg/mL) at ambient temperature.

Details of the drug substance manufacturing process are included. The drug substance specification was considered adequate after the acceptance criteria for

A description of the drug product manufacturing process is included. [redacted] were established to achieve consistency in product quality.

The drug product specification was considered adequate after the applicant included the test for [redacted] in response to a request for justification for omission of the test.

The tablets are packaged in [redacted] The packaging materials used were found adequate. The submitted drug product stability data include long-term stability data for [redacted] The applicant initially proposed a [redacted] expiration date. Based on the submitted data it was decided to allow a 36-moth expiration period for the bottles and a 30-month expiration period for the blister package. The applicant agreed to these expiration dates.

The proposed dissolution acceptance criterion (Q ≥ [redacted] at 45 minutes) is acceptable to the Biopharm reviewer Dr. Veneeta Tandon (discussed on 10/18/01).

The original application proposed a total of [redacted] 10, 20 [redacted] mg). Firm did not seek approval for [redacted] At the time of this review the medical reviewers indicated that only the 10 mg and 20 mg tablet strengths will be approved.

B. Description of How the Drug Product is Intended to be Used:

Bextra (valdecoxib) tablets are intended to be used orally for the relief of osteoarthritis and adult rheumatoid arthritis. The recommended maximum dose is 20 mg/day. Bextra tablets will be supplied in [redacted] bottles in 100 and 500 counts, and in a carton of 100 unit doses.

The expiration period for the drug product in [redacted] bottle is 36 months, and for the drug product in the unit dose package is 30 months.

Recommended storage conditions: 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

C. Basis for Approvability or Not-Approval Recommendation:

N/A

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

Chemist Name/Date: Rao Puttagunta/19-OCT-2001
Chemistry Team Leader Name/Date: John Smith/
Project Manager Name/Date: Carmen DeBellas/

C. CC Block

Orig. NDA # 21-341
HFD-550/Division File
HFD-550/Chem./R.Puttagunta
HFD-550/T.L./J.Smith
HFD-550/CSO/C.DeBellas
HFD-830/Dir./C.Chen

50 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

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