

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-998

CHEMISTRY REVIEW(S)

**DIVISION OF ANTI-INFLAMMATORY, ANALGESIC AND OPHTHALMIC
DRUG PRODUCTS**

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-998

REVIEW # 1

DATE REVIEWED: 11/24/98

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE DATE</u>	<u>ASSIGNED DATE</u>
Original (000)	6/29/98	6/30/98	7/1/98
NC (000)	9/02/98	9/03/98	9/03/98
BC (000)	9/02/98	9/03/98	9/4/98
BC (000)	9/24/98	9/25/98	9/28/98
BC (000)	9/28/98	10/01/98	10/05/98
BL (000)	10/02/98	10/05/98	10/05/98
BC (000)	10/14/98	10/15/98	10/19/98
BC (000)	10/23/98	10/26/98	10/28/98
BC (000)	10/30/98	11/02/98	11/24/98
BC (000)	11/04/98	11/05/98	11/09/98

NAME & ADDRESS OF APPLICANT:

G.D. Searle and Co.,
4901 Searle Parkway,
Skokie, IL 60077

DRUG PRODUCT NAME

Proprietary: CELEBREX™ Capsules

Established: Celecoxib

Code Name/#: SC-58635

Chem.Type/Ther.Class: COX-2 Inhibitor as per Searle. To be determined
by Agency (Modified NSAID ?)

PHARMACOL. CATEGORY: Antiinflammatory

DOSAGE FORM: Capsules

STRENGTHS: 100 and 200 mg.

ROUTE OF ADMINISTRATION: Oral

DISPENSED: Rx OTC

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA
AND WEIGHT:**

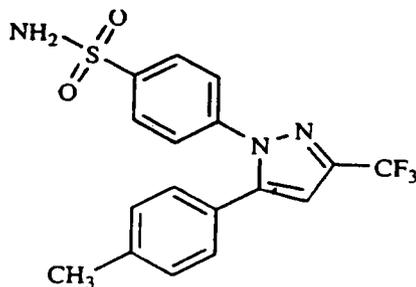
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CHEMICAL NAME: 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide.

MOLECULAR WEIGHT: 381.38

MOLECULAR FORMULA: $C_{17}H_{14}F_3N_3O_2S$

STRUCTURAL FORMULA:



SUPPORTING DOCUMENTS:

IND #

DMFs

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RELATED DOCUMENTS

None

REMARKS:

This is a new molecular entity. The drug substance is synthesized in two steps, and found to be very stable in the stability studies that were conducted. Details of the starting material controls, synthesis, release and stability controls are provided and found to be adequate.

The drug product will be in 100 and 200 mg strengths. It will be packaged in two types of blister packs and in HDPE bottles.

Details of the composition, manufacture and controls, release and stability specifications and stability results are provided and found to be adequate.

In some stability studies the drug product showed a marked reduction in dissolution values. This is attributed to _____ formation, which the Agency and the USP has

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started to recognize.

The drug product has demonstrated very good stability in all cases. No degradation products could be detected or quantitated in most of the stability studies conducted.

The environmental assessment and the establishment evaluation reports were satisfactory.

The methods validation packages have been sent to the FDA laboratories for evaluation.

The company has proposed a two year expiration period for this drug product, which is acceptable.

CONCLUSIONS & RECOMMENDATIONS:

Most of the information provided in the CMC section is satisfactory. A few deficiencies need to be addressed and some additional information needs to be provided (see page 51). It is recommended that this NDA be approvable pending the resolution of the minor deficiencies.

Hasmukh B Patel
Hasmukh Patel Ph. D., Team Leader

12/9/98
Date

Vispi P. Bhavnagri
Vispi P. Bhavnagri Ph. D., Review Chemist

12/8/98
Date

NDA 20-998

CC:

NDA # 20-998
HFD-550/Division File
HFD-550/V.Bhavnagri
HFD-550/H.Patel
HFD-550/V.Lutwak

HFD-550/J.Hyde
HFD-550/S.Lee
HFD-550/J.Witter
HFD-550/J.Yang
HFD-830/Chi Wan Chen

APPROVABLE

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**DIVISION OF ANTI-INFLAMMATORY, ANALGESIC AND OPHTHALMIC
DRUG PRODUCTS**

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-998

REVIEW # 2

DATE REVIEWED: 12/10/98

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE DATE</u>	<u>ASSIGNED DATE</u>
Fax	12/8/98		12/8/98
Fax	12/10/98		12/10/98

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G.D. Searle and Co.,
4901 Searle Parkway,
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AND WEIGHT:**

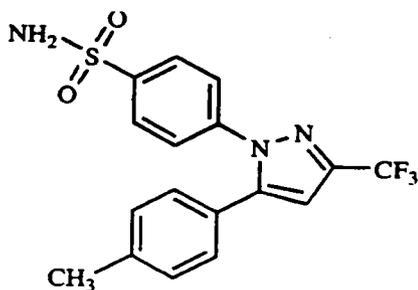
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MOLECULAR FORMULA: C₁₇H₁₄F₃N₃O₂S

NDA 20-998

STRUCTURAL FORMULA:



SUPPORTING DOCUMENTS:

Review # 1

RELATED DOCUMENTS

Review # 1

REMARKS:

The company has addressed all the deficiencies satisfactorily and provided all the information requested in Review # 1.

CONCLUSIONS & RECOMMENDATIONS:

It is recommended that this NDA be approved.

Hasmukh B. Patel
Hasmukh Patel Ph. D., Team Leader

12-11-98
Date

Vispi P. Bhavnagri
Vispi P. Bhavnagri Ph. D., Review Chemist

12/10/98
Date

NDA 20-998
Review #2

CC:

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APPROVE

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