

CENTER FOR DRUG EVALUATION AND RESEARCH

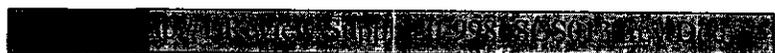
APPLICATION NUMBER:

20-998 /S-013

CHEMISTRY REVIEW(S)

Chemistry Review #1	1. Division HFD-550	2. NDA Number 20-998
3. Name and Address of Applicant G.D.Searle & Co. 4901 Searle Parkway, Skokie, IL 60077	4. Supplement Number: SCS 013 Letter Date 12/12/01 Stamp Date: 12/13/01 Due Date : 4/13/2002	
5. Name of Drug Celebrex™ Capsules	6. Nonproprietary Name Celecoxib	
7. Supplement Provides for: Manufacture of a 400 mg capsule strength		8. Amendment(s) BL Dated 1/18/02 BC Dated 2/7/02 BL Dated 4/5/02
9. Pharmacological Category To treat acute and chronic pain associated with OA and RA	10. How Dispensed Rx	11. Related Documents NDA 21156/ S 001 and S 002
12. Dosage Form Capsules	13. Potency(ies) 400 mg	
14. Chemical Name and Structure See USAN		
15. Comments This is a PA supplement. Searle wishes to manufacture a 400 mg. strength capsule so that instead of administering the approved dose of two 200 mg. capsules a single 400 mg capsule can be administered for FAP. NDA 21-156 was submitted to and approved by HFD 180 for the FAP indication. Since the 400 mg strength capsule will be used for FAP, it was decided between HFD 550 and HFD 180, that this change (submitted in S/001 and S/002 to NDA 21-156) would be reviewed by HFD 180. The HFD 550 chemistry reviewer would make reference to the HFD 180 review.		
16. Conclusions and Recommendations HFD 180 has four deficiencies that need to be addressed (see attachment). It is recommended that HFD 550 also make supplement 013 to NDA 20-998 approvable pending satisfactory resolution of these four deficiencies.		
17. Name Vispi P. Bhavnagri, Ph.D., Review Chemist	Signature	
Concurrence John Smith, Ph.D., Chemistry Team Leader		

APPROVABLE



Notes on NDA 20-998/SCS 013

- Supplement 013 for NDA 20-998 is for the same change that is submitted in supplement 001 and 002 of NDA 21-157.
- On 4/10/02 Mr. Fredrick Piskiewicz was asked why there was only one supplement (# 13) to NDA 20-998 and two supplements (# 001 and # 002) for NDA 21-157. He explained that **the same information was given to both divisions** (HFD 550 and 180), and HFD 180 chose to break down that single supplement into two supplements.
- The following table correlates the various amendments submitted to the supplements of these two NDAs

					Amend. for	Comment
20998	S 013	BL	1/18/02	1/22/02	Provided missing pg. in PI and missing equations for active and degradants for doc. 01-234-1	Noted by Dr. Frankewich
21156	S 001					
21156	S 002					
20998	S 013	BC	2/7/02	2/8/02	Replacing the stability doc. 01-239-1 dated 11/29/01 with latter version dated 1/21/02	Noted by Drs Bhavnagri and Frankewich
21156	S 001 S 002	US	3/12/02	3/12/02	IR sent by Dr. Frankewich of HFD 180 who performed the review for the 400 mg capsule proposal	
21156	S 001 S 002	BC	3/22/02	3/25/02	Response of the company to the IR of 3/12/02	Reviewed by Dr. Frankewich
20998	S 013	BL	4/5/02	4/8/02	Revised Label	Reviewed by Dr. Frankewich
21156	S 001					
21156	S 002					

- Four deficiencies were cited for S/001 and S/002 of NDA 21-157 by Dr. Raymond Frankewich of HFD 180.
- The following four deficiencies therefore also apply to supplement 013 of NDA 20-998.
 1. Provide at least three months of accelerated stability data for at least one lot of the

proposed drug product (400 mg capsules) packaged in each configuration that is proposed for market. Propose a stability commitment in which the first production batch and annual batches thereafter, packaged in each configuration, will be placed on long-term stability with results provided in the annual report.

2. Amend the Acceptance Criterion for Appearance in the Specification of the 400 mg capsule such that the description of a specific capsule imprint replaces the words _____
 3. Include information (including NDC number) in the How Supplied section of the labeling for the proposed package configurations 60 cc HDPE bottles _____
 4. Justify the change in column length in the HPLC method for Assay and determination of degradants provided in this submission _____ with respect to that which is established in NDA 20-998 _____
- The company responded to the IR sent by Dr. Frankewich, but did not send these responses to the equivalent supplements for the NDA residing in HFD 550 (NDA 20998/S 013).

Deficiency:

5. Please send any common response to supplement 013 of NDA 20-998 and supplements 001 and 002 of NDA 21-156 to both divisions in which these two NDAs reside (HFD 550 and HFD 180).

Recommendation:

It is recommended that the supplement be approvable pending satisfactory resolution of the deficiencies cited above. The company should also be told to send any common responses to all the divisions that are affected.

**APPEARS THIS WAY
ON ORIGINAL**

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Vispi Bhavnagri
4/10/02 03:14:33 PM
CHEMIST

John Smith
4/10/02 03:22:28 PM
CHEMIST

APPEARS THIS WAY
ON ORIGINAL

Chemistry Review #2	1. Division HFD-550	2. NDA Number 20-998
3. Name and Address of Applicant G.D.Searle & Co. 4901 Searle Parkway, Skokie, IL 60077	4. Supplement Number: SCS 013 Letter Date 4/26/02 Stamp Date: 4/29/02 Due Date : 8/29/02	
5. Name of Drug Celebrex™ Capsules	6. Nonproprietary Name Celecoxib	
7. Supplement Provides for: Manufacture of a 400 mg capsule strength		8. Amendment(s) Faxes submitted to HFD 180 on 6/10/02 and 8/14/02
9. Pharmacological Category To treat acute and chronic pain associated with OA and RA	10. How Dispensed Rx	11. Related Documents NDA 21156/ S 001 and S 002
12. Dosage Form Capsules	13. Potency(ies) 400 mg	
14. Chemical Name and Structure See USAN		
15. Comments This is a PA supplement. Searle wishes to manufacture a 400 mg strength capsule so that instead of administering the approved dose of two 200 mg capsules a single 400 mg capsule can be administered for FAP. NDA 21-156 was submitted to and approved by HFD 180 for the FAP indication. Since the 400 mg strength capsule will be used for FAP, it was decided that this change (submitted in S/001 and S/002 to NDA 21-156) would be reviewed by HFD 180. As a result of that review by HFD 180 four deficiencies were cited that needed to be addressed. These deficiencies have now been addressed satisfactorily in Review # 2 of supplements 001 and 002 for NDA 21-156.		
16. Conclusions and Recommendations Recommend approval based on the recommendation made by HFD 180.		
17. Name Vispi P. Bhavnagri, Ph.D., Review Chemist	Signature	
Concurrence John Smith, Ph.D., Chemistry Team Leader		

APPROVAL

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Vispi Bhavnagri
8/28/02 12:57:23 PM
CHEMIST

John Smith
8/28/02 01:04:34 PM
CHEMIST

APPEARS THIS WAY
ON ORIGINAL