CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-324

CHEMISTRY REVIEW(S)

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **NDA 21324/000** Priority: **3P** Org Code: **180**
Stamp: **24-JAN-2001** Regulatory Due: **24-JUL-2001** Action Goal: District Goal: **25-MAY-2001**
Applicant: **ASTRAZENECA**
725 CHESTERBROOK BLVD MAILST(
WAYNE, PA 190875677
Brand Name: **ENTOCORT(BUDESONIDE)3MG M-R CAPSULES**
Established Name:
Generic Name: **BUDESONIDE**
Dosage Form: **DRT (DELAYED RELEASE TABLET**
Strength: **3 MG**

FDA Contacts:

M. MCNEIL	**(HFD-180)**	**301-827-7310**	**, Project Manager**
R. FRANKEWICH	**(HFD-180)**	**301-827-7310**	**, Review Chemist**
L. ZHOU	**(HFD-180)**	**301-827-7471**	**, Team Leader**

Overall Recommendation:

ACCEPTABLE on 23-JUL-2001 by M. GARCIA (HFD-322) 301-594-0095

Establishment: **9612840** DMF No:
ASTRA PHARMACEUTICAL PRODUC AADA No:
SODERTALJE, , SW

Profile: **CRU** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **23-JUL-2001**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**
Responsibilities: **DRUG SUBSTANCE MICRONIZER**
DRUG SUBSTANCE RELEASE TESTER

Establishment: **9610565** DMF No:
ASTRA PRODUCTION CHEMICALS A AADA No:
SODERTALJE, , SW

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **26-FEB-2001**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**
Responsibilities: **DRUG SUBSTANCE MANUFACTURER**

Establishment: **9615999** DMF No:
ASTRA PRODUCTION TABLETS AB AADA No:
GARTUNAVAGAN
SODERTALJE, , SW SK102NA

Profile: **CTR** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **20-APR-2001**
Responsibilities: **FINISHED DOSAGE MANUFACTURER**
FINISHED DOSAGE RELEASE

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

TESTER

FINISHED DOSAGE STABILITY TESTER

Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Establishment: [redacted]

DMF No:
AADA No:

Profile: **CTR** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **06-MAR-2001**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE PACKAGER**

Establishment: [redacted]

DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **26-FEB-2001**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **DRUG SUBSTANCE MANUFACTURER**

APPEARS THIS WAY
ON ORIGINAL

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: July 23, 2001

FROM: Raymond P. Frankewich, Ph.D., Review Chemist, Division of Gastrointestinal and Coagulation Drug Products, HFD-180

THROUGH: Liang Zhou, Ph.D., Chemistry Team Leader, Division of Gastrointestinal and Coagulation Drug Products, HFD-180

SUBJECT: Addendum to CMC Review #2 of NDA 21-234 for Entocort® Capsules - inspection status of facilities

TO: NDA 21-234

The purpose of this memorandum is to provide the decisions of HFD-322 regarding the fitness of the facilities involved in manufacturing and testing of Entocort® Capsules.

As of July 23, 2001, the overall recommendation of HFD-322 was acceptable.

The inspection status of each of the individual facilities listed in the original Establishment Evaluation Report (submitted February 23, 2001) is provided in the table below:

Site Name	Address	Registration No. (CFN)	Operation	Inspection Status
[illegible]	[illegible]	[illegible]	[illegible]	Acceptable (based on profile) Feb. 26, 2001
AstraZeneca at AstraZeneca Bulk Production Sweden	S-151 85 Södertälje Sweden	9610565 (FCSW036)	r	Acceptable (based on profile) Feb. 26, 2001
AstraZeneca at AstraZeneca Liquid Production Sweden	S-151 85 Södertälje Sweden	9612840	t e	Acceptable (district recommendation) July 23, 2001
AstraZeneca AB at AstraZeneca Tablet Production Sweden	S-151 85 Södertälje Sweden	9615999 (FCSW093)		Acceptable (district recommendation) April 20, 2001
[illegible]	[illegible]	[illegible]		Acceptable (district recommendation) March 6, 2001
AstraZeneca AB at AstraZeneca R&D Lund	S-221 87 Lund Sweden	9614288		Inspection cancelled as of April 19, 2001*

* - see CMC review #1.

† - The AstraZeneca AB at AstraZeneca Tablet Production Sweden facility is responsible for: manufacture, testing, and release of bulk granules; manufacture, testing, release, and packaging of bulk capsules; testing and release of inactive ingredients; release of drug product; stability monitoring.

The conclusion of CMC Review #2 for NDA 21-324 is that it may be approved. At this time, there are no CMC issues with regards to this NDA.

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/

Ray Frankewich
7/24/01 12:14:33 PM
CHEMIST
Addendum to review describing status of facilities

Arthur B. Shaw
7/24/01 12:21:39 PM
CHEMIST
Acting for Liang Zhou

APPEARS THIS WAY
ON ORIGINAL

DIVISION OF GASTROINTESTINAL AND COAGULATION DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA#: 21-324 **CHEM REVIEW#:** 2 **REVIEW DATE:** July 10, 2001

SUBMISSION TYPE	DATES				
	DOCUMENT ST	CDER	ASSIGNED	REVIEW	NUM LETTER
ORIGINAL	1/24/01	1/24/01	1/30/01	5/11/01	
AMENDMENT	2/9/01	2/12/01	2/14/01	5/11/01	
AMENDMENT	4/6/01	4/9/01	4/11/01	5/11/01	
AMENDMENT	5/1/01	5/2/01	5/3/01	5/11/01	
AMENDMENT	6/18/01	6/19/01	6/19/01	7/10/01	
AMENDMENT	7/2/01	7/5/01	7/10/01	7/10/01	
AMENDMENT	7/10/01	7/10/01	7/10/01	7/10/01	

NAME & ADDRESS OF APPLICANT: AstraZeneca LP
725 Chesterbrook Blvd.
Mailstop E3-C
Wayne, PA 19087

DRUG PRODUCT NAME:

Proprietary: Entocort capsules

Nonproprietary/USAN: budesonide (USAN)

Code Name/#: S-1320

Chem.Type/Ther.Class: 3P/8015650

PHARMACOLOGICAL CATEGORY: Anti-inflammatory

INDICATION: Treatment of mild to moderate active Crohn's Disease involving the ileum and/or ascending colon.

DOSAGE FORM: Capsule

STRENGTH: 3 mg

ROUTE OF ADMINISTRATION: Oral

HOW DISPENSED: _X_ Rx ___ OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:
See USAN

SPECIAL PRODUCT: YES_____ NO__X__

SUPPORTING DOCUMENTS:

DMF Number	Item referenced	Holder	Status	Review Date	Letter Date
			Adequate	7/01	NA
			Adequate	7/01	NA
			Adequate	7/01	NA
			Adequate	7/01	NA
			Adequate	7/01	NA
			Adequate	7/01	7/01
			Adequate	7/01	NA
			Adequate	7/01	7/01
			Adequate	7/01	NA

RELATED DOCUMENTS (if applicable): NA

CONSULTS:

- Biopharmaceutics: complete. Recommended no references to release profile of drug in its name.
- OPDRA

REMARKS/COMMENTS:

See *Summary* below.

APPEARS THIS WAY
ON ORIGINAL

CONCLUSIONS & RECOMMENDATIONS:

This application may be approved.

Raymond P. Frankewich, Ph.D.
Review Chemist, HFD-180

Liang Zhou, Ph.D.
Chemistry Team Leader, HFD-180

cc:
NDA #21-324
HFD-180/LTalarico
HFD-180/Div File/NDA #21-324
HFD-180/LZhou
HFD-180/RFrankewich
HFD-181/CSO/MMcNeil
R/D Init by: AAlHakim 7-6-01
RF/rpf Draft 7-6-01/**F/T 7-10-01**
C:\

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

35 pages

Chemistry Summary

DIVISION OF GASTROINTESTINAL AND COAGULATION DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA#: 21-324 **CHEM REVIEW#:** 1 **REVIEW DATE:** May 11, 2001

SUBMISSION TYPE	DATES.					
	DOCUMENT	CDER	ASSIGNED	REVIEW	NUM	LETTER	ST
ORIGINAL	1/24/01	1/24/01	1/30/01	5/11/01			
AMENDMENT	2/9/01	2/12/01	2/14/01	5/11/01			
AMENDMENT	4/6/01	4/9/01	4/11/01	5/11/01			
AMENDMENT	5/1/01	5/2/01	5/3/01	5/11/01			

NAME & ADDRESS OF APPLICANT: AstraZeneca LP
725 Chesterbrook Blvd.
Mailstop E3-C
Wayne, PA 19087

DRUG PRODUCT NAME:

Proprietary:	Entocort capsules
Nonproprietary/USAN:	budesonide (USAN)
Code Name/#:	S-1320
Chem.Type/Ther.Class:	*3P*/8015650

PHARMACOLOGICAL CATEGORY: Anti-inflammatory

INDICATION: Treatment of mild to moderate active Crohn's Disease involving the ileum and/or ascending colon.

DOSAGE FORM: Capsule

STRENGTH: 3 mg

ROUTE OF ADMINISTRATION: Oral

HOW DISPENSED: _X_ **Rx** ___ **OTC**

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:
See USAN

SPECIAL PRODUCT: **YES**_____ **NO** _X_

SUPPORTING DOCUMENTS:

DMF Number	Item referenced	Holder	Status	Review Date	Letter Date
				NA	NA
				NA	NA
				NA	NA
				NA	NA
				NA	NA
				NA	NA
				NA	NA
				NA	NA
				NA	NA

RELATED DOCUMENTS (if applicable): NA

CONSULTS:

- Biopharmaceutics: pending
- OPDRA: complete, dated April 3, 2001. Recommend NOT using the proprietary name Entocort. See comments in this review under Labeling.

REMARKS/COMMENTS:

An information request letter should be addressed to the firm seeking resolution of the comments listed in Section H. of this review.

CONCLUSIONS & RECOMMENDATIONS:

Not Approvable.

Raymond P. Frankewich, Ph.D.
Review Chemist, HFD-180

Liang Zhou, Ph.D.
Chemistry Team Leader, HFD-180

cc:
NDA #21-324
HFD-180/LTalarico
HFD-180/Div File/NDA #21-324
HFD-180/LZhou
HFD-180/RFrankewich
HFD-181/CSO/MMcNeil
R/D Init by: LZhou 5-8-01
RF/rpf Draft 5-8-01/**F/T 5-11-01**
C:\

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

69 pages draft Chemistry Review

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

70 pages Chemistry