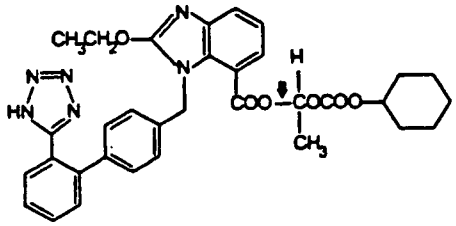
CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

20-838/S-015

Chemistry Review(s)

CHEMIST'S REVIEW	1. ORGANIZATION HFD-110	2. NDA Number 20-838
3. Name and Address of Applicant (City & State) AstraZeneca LP, Wilmington, DE		4. Supplement(s) Number(s) Date(s) S-015 9/27/01
5. Drug Name Atacand	6. Nonproprietary Name (candesartan cilexetil)	8. Amendments: None to be reviewed
7. Supplement Provides for: a change in the labeling for the drug product concerning the comparative efficacy of candesartan cilexetil and losartan.		
9. Pharmacological Category antihypertensive	10. How Dispensed [X] Rx ☐ OTC	11. Related NDA(s) in HFD-110:
12. Dosage Form(s) Oral Tablets	13. Potency(ies) 4, 8, 16 and 32 mg	
14. Chemical Name and Structure: (±)-1-[[(cyclohexyloxy)carbonyl]oxy]ethyl-2-ethoxy-1[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-benzimidazole-7-carboxylate. 		15. Records/Reports Current

16. Comments: This review is conducted to evaluate the information sent to the supplement as a Fax dated 7/10/02 that requests a categorical exclusion for an environmental assessment. In this regard, it is claimed that the total amount of candesartan cilexetil introduced into the environment is less than 1ppb of material in the aquatic environment. The content of the FAX is included in this review for the record. This is considered to be acceptable.

File: NDA 20-838-S-015

17. Conclusions and Recommendations: The supplement is considered acceptable from the standpoint of the request for an categorical exclusion for an environmental assessment.

Name	Signature	Date Completed
Stuart Zimmerman		7/19/02

AstraZeneca

Fax

To	Mr. Edward Fromm	**Fax number**	301-594-5494
CC			
Division	Cardio-Renal Drug Products		
From	Ms. Cindy M. Lancaster	**Fax number**	610-695-1828
Date	10 July 2002	**Total pages**	1(2)
Subject	ENVIRONMENTAL ASSESSMENT		

CONFIDENTIAL

NDA 20-838\S-015
ATACAND® (candesartan cilexetil) Tablets

Per your request of June 28th, please find attached information concerning the environmental assessment for this supplement. AstraZeneca requests a categorical exclusion for an environmental assessment for this supplement. AstraZeneca will submit this information in an "amendment to a pending application" to the Division for this supplement in the near future.

Please direct any questions or requests for additional information to me, or in my absence, to Pat Patterson, Associate Director, at (610) 695-1539.

Sincerely,

Cindy M. Lancaster

Cindy M. Lancaster
Director
Regulatory Affairs
Telephone: (610) 695-1348
Fax: (610) 695-1828

ENVIRONMENTAL ASSESSMENT

AstraZeneca requests categorical exclusion for an environmental assessment for the supplement to the new drug application for ATACAND in accordance with 21 CFR 25.31 (a) & (b).

This claim is in support of the proposed changes to the approved labeling. Candesartan cilexetil is the drug substance component of ATACAND.

ATACAND is currently approved in the USA for use in the treatment of hypertension (NDA 20-838 approved June 4, 1998).

Approval of this application will not result in the total amount of candesartan cilexetil introduced into the environment, as the result of this submission and all previous approvals, exceeding a concentration of 1ppb of the material in the aquatic environment.

In addition the applicant has no knowledge that any exceptional circumstances exist that would require any additional controls to be imposed on the use of ATACAND in order to protect the environment.

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

/s/

Stuart Zimmerman
7/19/02 02:22:48 PM
CHEMIST

Kasturi Srinivasachar
7/19/02 05:00:48 PM
CHEMIST

AstraZeneca

Fax

To	Mr. Edward Fromm	**Fax number**	301-594-5494
CC			
Division	Cardio-Renal Drug Products		
From	Ms. Cindy M. Lancaster	**Fax number**	610-695-1828
Date	28 August 2002	**Total pages**	1(2)
Subject	Response to CMC questions and a request for feedback		

CONFIDENTIAL

NDA 20-838\S-015
ATACAND® (candesartan cilexetil) Tablets

Please find attached information concerning the CMC questions. Per your request, AstraZeneca plans to include this information at the time of submission of FPL. Would you be so kind as to let us know if we share a common understanding concerning this CMC information?

Please direct any questions or requests for additional information to me, or in my absence, to Pat Patterson, Associate Director, at (610) 695-1539.

Sincerely,

Cindy M. Lancaster

Cindy M. Lancaster
Director
Regulatory Affairs
Telephone: (610) 695-1348
Fax: (610) 695-1828

AstraZeneca
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Wayne, PA 19087

Tel +1 610 695 1000

To facilitate review the original comments are provided in italics followed by the AstraZeneca response in bold face type.

"DESCRIPTION" – use the USAN consistent name for the compound.

Response:
Reference is made to the approvable letter dated April 28, 1998 for NDA 20-838 in which the Division provided the chemical name for the "DESCRIPTION" section of labeling. AstraZeneca accepted the Division's proposed text for the chemical name which is consistent with the USAN name, candesartan cilexetil. The Division issued an approval of NDA 20-838 on June 4, 1998.

"DOSAGE AND ADMINISTRATION" – this section makes reference to doses from 2 – 32 mg. Is the 4 mg tablet scored?

Response:
No, none of the strengths of Atacand® Tablets are scored tablets.

"HOW SUPPLIED" - the tablets are similar in color because they are light pink or pink. The sponsor should make each tablet a different color to distinguish the tablet strengths.

Response
Each tablet strength of Atacand® Tablets has a unique appearance to distinguish it from the other strengths. Differentiation is achieved by unique embossing on both sides of the tablet and by varying the color and/or size of the tablet. A summary of the four tablet strengths and their corresponding appearance is presented below. AstraZeneca believes that sufficient differentiation between tablets strengths has been achieved.

Tablet Strength	Appearance
4 mg tablets	White to off-white, circular, biconvex tablet, embossed C^{A}_{F} on one side and 004 on the other
8 mg tablets	Light pink, circular, biconvex tablet, embossed C^{A}_{G} on one side and 008 on the other
16 mg tablets	Pink, circular, biconvex tablet, embossed C^{A}_{H} on one side and 016 on the other
32 mg tablets	Pink, circular, biconvex tablet, embossed C^{A}_{L} on one side and 032 on the other

Fromm, Edward J

From: Simmons, John E
Sent: Friday, July 26, 2002 12:45 PM
To: Fromm, Edward J
Cc: Zimmerman, Stuart E; Srinivasachar, Kasturi
Subject: Re: Efficacy Supplement for Candesartan

Ed:

I took a look the e-mail package that I received. I saw a few things in the labeling that you may want to discuss with the firm.

In the description section: the chemical name is not either of the official names listed in USAN and should be changed to comply.

In the Dosage & Admin section: labeling lists a range of 2-32 mg. If the 4 mg tablet is not scored, then it should be changed.

In the How Supplied section: three strengths are pink - is this correct? No differentiation?

Hope that helps.

John