

**CENTER FOR DRUG EVALUATION AND RESEARCH**

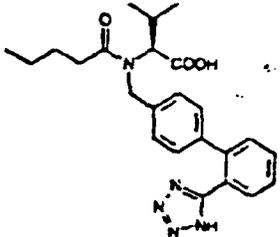
**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER**

**NDA 20-665/S-016**

**NDA 21-283/S-001**

**Chemistry Review(s)**

CHEMIST'S REVIEW		1. ORGANIZATION HFD-110	2. NDA Number 20-665
3. Name and Address of Applicant (City & State) Novartis Pharmaceuticals Corp., E. Hanover, NJ		4. Supplement(s) Number(s) Date(s) S-016 4/27/01	
5. Drug Name Diovan Capsules	6. Nonproprietary Name valsartan		8. Amendments: BZ 5/7/01 S/A 6/27/01 BL 8/1/01
7. Supplement Provides for a new indication for the treatment of heart failure.			
9. Pharmacological Category antihypertensive		10. How Dispensed <input checked="" type="checkbox"/> Rx <input type="checkbox"/> OTC	11. Related NDA(s) NDA 21-283/S-001
12. Dosage Form(s) Capsules		13. Potency(ies) 80mg & 160mg	Related DMFs: see cross reference to Above NDA 21-283.
14. Chemical Name and Structure: N-(1-Oxopentyl)-N-[[2'-(1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl]methyl]-L-valine (CGP 48933, valsartan)			15. Records/Reports Current
			
16. Comments: This is a PA supplement with a goal date of 10/27/01. The related NDA 21-283 covers the manufacturing changes involving the 40 mg tablet that will be utilized for marketing and the chemistry review dated 9/26/01 deals with the assessments involved.			
Document File: S-016(4-27-01)CR-N20665.doc			
17. Conclusions and Recommendations: May be approved from the CMC perspective.			
Name Stuart Zimmerman	Signature <i>/s/</i>		Date Completed 10/11/01

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commercial

information

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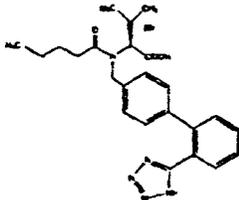
This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.

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/s/

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Stuart Zimmerman  
10/12/01 02:33:31 PM  
CHEMIST

Kasturi Srinivasachar  
10/12/01 03:38:47 PM  
CHEMIST

<b>CHEMIST'S REVIEW</b>		<b>1. ORGANIZATION</b> HFD-110	<b>2. NDA Number</b> 21-283
<b>3. Name and Address of Applicant (City &amp; State)</b> Novartis Pharmaceuticals Corp. East Hanover, New Jersey		<b>4. Supplemental New Correspondence:</b> <b>Number(s)</b> <b>Date(s)</b> S-001            7/23/01	
<b>5. Drug Name</b> Diovan Tablets	<b>6. Nonproprietary Name</b> valsartan		<b>8. Amendments &amp; Other (reports, etc.) - Dates</b> S/A            8/1/01 word copy of the package insert.
<b>7. Supplemental New Correspondence provides for a new indication for the treatment of heart failure and the use of a 40 mg tablet as a starting dose for such a new treatment.</b>			
<b>9. Pharmacological Category</b> Control of hypertensive episodes in patients (phenochromocytoma)	<b>10. How Dispensed</b> <input checked="" type="checkbox"/> Rx <input type="checkbox"/> OTC		<b>11. Related NDA(s)/DMF(s):</b> NDA 21-283/000 and DMFs, etc.; NDA 20-665/S-016
<b>12. Dosage Form:</b> tablets	<b>13. Potency(ies)</b> 40mg, 80 mg, 160 mg and 320 mg		
<b>14. Chemical Name:</b> <b>DESCRIPTION</b> Diovan® (valsartan) is a nonpeptide, orally active, and specific angiotensin II analog acting on the AT <sub>1</sub> receptor subtype. Valsartan is chemically described as N-(1-sarcosine)-N'-(2'-[1H-tetrazol-5-yl])-[1-phenyl]-4-yl(methyl)-L-valine. Its empirical formula is C <sub>26</sub> H <sub>29</sub> N <sub>5</sub> O <sub>3</sub> . Its molecular weight is 415.5, and its structural formula is 			<b>15. Records/Reports Current</b>
<b>16. Comments:</b> This is a PA efficacy supplement. See additional comments on page 2.			
<b>17. Conclusions and Recommendations:</b> The supplement may be approved from the CMC viewpoint. The action letter should include the following statement: Based on the stability data provided, we will permit the following expiration dates for the drug product: (a) 18 months for blister packaging and physician samples (b) 24 months for — bottle trade packages			
<b>18. REVIEWER:</b>		<b>FILE NAME:</b> File: S-001(7-23-01)W(9-14-01)N21283	
<b>Name:</b> Stuart Zimmerman	<b>Signature:</b>	<b>Date completed:</b> 10/12/01	

Comments (continued):

Approval Status of Related CMC Disciplines:

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11-OCT-2001		FDA CDER EES		Page 1 of 2	
ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT					
Application:	NDA 21283/001	Priority:	3S	Org Code:	110
Stamp:	23-JUL-2001	Regulatory Due:	23-MAY-2002	Action Goal:	District Goal: 18-APR-2002
Applicant:	NOVARTIS PHARMS 59 RT 10 EAST HANOVER, NJ 079361080	Brand Name:	DIOVAN (VALSARTAN) 80/160/320MG TABLETS		
		Established Name:			
		Generic Name:	VALSARTAN		
		Dosage Form:	TAB (TABLET)		
		Strength:	80, 160, & 320 MG		
FDA Contacts:	E. FROMM (HFD-110)	301-594-5300	, Project Manager		
	S. ZIMMERMAN (HFD-110)	301-594-5300	, Review Chemist		
	K. SRINIVASACHAR (HFD-110)	301-594-5376	, Team Leader		
Overall Recommendation:					
ACCEPTABLE on 11-OCT-2001 by J. D AMBROGIO (HFD-324) 301-827-0062					
Establishment:	2416082	DMF No:			
	NOVARTIS PHARMA INC (CIBA)	AADA No:			
	OLD MILL RD				
	SUFFERN, NY 10901				
Profile:	TCM	OAI Status:	NONE		
Last Milestone:	OC RECOMMENDATION				
Milestone Date	30-AUG-2001				
Decision:	ACCEPTABLE				
Reason:	BASED ON PROFILE				
Establishment:	2210396	DMF No:			
	NOVARTIS PHARMA INC (SANDOZ)	AADA No:			
	59 RT 10				
	EAST HANOVER, NJ 079361080				
Profile:	CTL	OAI Status:	NONE		
Last Milestone:	OC RECOMMENDATION				
Milestone Date	14-SEP-2001				
Decision:	ACCEPTABLE				
Reason:	DISTRICT RECOMMENDATION				
Establishment:	9611204	DMF No:			
	NOVARTIS PHARMA INC (SANDOZ)	AADA No:			
	LICHSTRASSE 35, ST. JOHANN SITE				
	BASEL., SZ 4002				
Profile:	CTL	OAI Status:	NONE		
Last Milestone:	OC RECOMMENDATION				
Milestone Date	24 SEP 2001				

Decision:	ACCEPTABLE	
Reason:	DISTRICT RECOMMENDATION	
Establishment:	<b>I</b>	DMF No: AADA No:
Profile:	TCM	OAI Status: NONE
Last Milestone:	OC RECOMMENDATION	
Milestone Date:	30-AUG-2001	
Decision:	ACCEPTABLE	
Reason:	BASED ON PROFILE	
Establishment:	<b>I</b>	DMF No: AADA No:
Profile:	TCM	OAI Status: NONE
Last Milestone:	OC RECOMMENDATION	
Milestone Date:	30-AUG-2001	
Decision:	ACCEPTABLE	
Reason:	BASED ON PROFILE	

H. **DRAFT LETTER:** The following should be provided in the action letter based on the assumption that the EES report will eventually be positive.

Based on the stability data provided, we will permit the following expiration dates for your 40 mg drug product tablet:

- a. 18 months for blister packaging and physician samples
- b. 24 months for  bottle trade packages

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

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/s/

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Stuart Zimmerman  
10/12/01 02:57:51 PM  
CHEMIST

Kasturi Srinivasachar  
10/12/01 05:46:02 PM  
CHEMIST

**FDA CDER EES**  
**ESTABLISHMENT EVALUATION REQUEST**  
**SUMMARY REPORT**

Application: <b>NDA 21283/001</b>	Priority: <b>3S</b>	Org Code: <b>110</b>
Stamp: <b>23-JUL-2001</b> Regulatory Due: <b>23-MAY-2002</b>	Action Goal:	District Goal: <b>18-APR-2002</b>
Applicant: <b>NOVARTIS PHARMS</b>	Brand Name: <b>DIOVAN (VALSARTAN) 80/160/320MG</b>	<b>TABLETS</b>
<b>59 RT 10</b>	Established Name:	
<b>EAST HANOVER, NJ 079361080</b>	Generic Name: <b>VALSARTAN</b>	
	Dosage Form: <b>TAB (TABLET)</b>	
	Strength: <b>80, 160, &amp; 320 MG</b>	
<hr/>		
FDA Contacts: <b>E. FROMM (HFD-110)</b>	<b>301-594-5300</b>	<b>, Project Manager</b>
<b>S. ZIMMERMAN (HFD-110)</b>	<b>301-594-5300</b>	<b>, Review Chemist</b>
<b>K. SRINIVASACHAR (HFD-110)</b>	<b>301-594-5376</b>	<b>, Team Leader</b>

**Overall Recommendation:**

**ACCEPTABLE on 11-OCT-2001 by J. D AMBROGIO (HFD-324) 301-827-0062**

Establishment: <b>2416082</b>	DMF No:
<b>NOVARTIS PHARMA INC (CIBA)</b>	AADA No:
<b>OLD MILL RD</b>	
<b>SUFFERN, NY 10901</b>	

Profile: <b>TCM</b>	OAI Status: <b>NONE</b>	Responsibilities:
Last Milestone: <b>OC RECOMMENDATION</b>		
Milestone Date: <b>30-AUG-2001</b>		
Decision: <b>ACCEPTABLE</b>		
Reason: <b>BASED ON PROFILE</b>		

Establishment: <b>2210396</b>	DMF No:
<b>NOVARTIS PHARMA INC (SANDOZ)</b>	AADA No:
<b>59 RT 10</b>	
<b>EAST HANOVER, NJ 079361080</b>	

Profile: <b>CTL</b>	OAI Status: <b>NONE</b>	Responsibilities:
Last Milestone: <b>OC RECOMMENDATION</b>		
Milestone Date: <b>14-SEP-2001</b>		
Decision: <b>ACCEPTABLE</b>		
Reason: <b>DISTRICT RECOMMENDATION</b>		

Establishment: <b>9611204</b>	DMF No:
<b>NOVARTIS PHARMA INC (SANDOZ)</b>	AADA No:
<b>LICHSTRASSE 35, ST. JOHANN SITE</b>	
<b>BASEL, , SZ 4002</b>	

Profile: <b>CTL</b>	OAI Status: <b>NONE</b>	Responsibilities:
Last Milestone: <b>OC RECOMMENDATION</b>		
Milestone Date: <b>24-SEP-2001</b>		

ESTABLISHMENT EVALUATION REQUEST  
SUMMARY REPORT

Decision: ACCEPTABLE  
Reason: DISTRICT RECOMMENDATION

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Establishment: !  
DMF No:  
AADA No:

Profile: TCM OAI Status: NONE Responsibilities:  
Last Milestone: OC RECOMMENDATION  
Milestone Date: 30-AUG-2001  
Decision: ACCEPTABLE  
Reason: BASED ON PROFILE

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Establishment: !  
DMF No:  
AADA No:

Profile: TCM OAI Status: NONE Responsibilities:  
Last Milestone: OC RECOMMENDATION  
Milestone Date: 30-AUG-2001  
Decision: ACCEPTABLE  
Reason: BASED ON PROFILE

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APPEARS THIS WAY  
ON ORIGINAL

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Methods Validation

As of July 17, 2002, the Methods Validation is pending.