# CENTER FOR DRUG EVALUATION AND RESEARCH

**APPLICATION NUMBER:** 

207620Orig1s000

**CHEMISTRY REVIEW(S)** 



# QUALITY ASSESSMENT



**Product Quality Recommendation: <u>APPROVAL</u>** 

# NDA 207620 Review # 01 Addendum Review Date: June 30, 2015

Drug Name/Dosage Form	Entresto (sacubitril and valsartan) Tablets
Strength	24 mg sacubitril and 26 mg valsartan 49 mg sacubitril and 51 mg valsartan 97 mg sacubitril and 103 mg valsartan
Route of Administration	Oral
Rx/OTC Dispensed	Rx
Applicant	Novartis Pharmaceuticals Corporation
US agent, if applicable	N/A

SUBMISSION(S) REVIEWED	DOCUMENT DATE
Amendment	25-JUN-2015
Amendment	26-JUN-2015
Amendment	15-JUN-2015
Amendment	11-JUN-2015
Amendment	04-JUN-2015
Amendment	02-JUN-2015
Amendment	26-MAY-2015
Amendment	15-MAY-2015
Amendment	15-MAY-2015

**Quality Review Team** 

DISCIPLINE	REVIEWER	BRANCH/DIVISION
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Environmental Assessment (EA)	Raanan Bloom	ONDP EA Team





# **QUALITY REVIEW**



# **Table of Contents**

Table of Contents	2
Quality Review Data Sheet	3
Executive Summary	4
Addendum to Primary Quality Review	9
List of Deficiencies To Be Communicated	
Attachments	13





### **QUALITY REVIEW**



# **Quality Review Data Sheet**

- 1. LEGAL BASIS FOR SUBMISSION: 505(b)(1)
- 2. RELATED/SUPPORTING DOCUMENTS:

#### A. DMFs:

DMF	TYPE	HOLDER	ITEM	STATUS <sup>1</sup>	REVIEW	COMMENTS
#			REFERENCED		DATE	
23902	Type II	Novartis Pharmaceutical Corporation	Valsartan	1	25-NOV-2014	

<sup>&</sup>lt;sup>1</sup> Adequate, Adequate with Information Request, Deficient, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: IND, RLD, or sister applications

DOCUMENT	APPLICATION NUMBER	DESCRIPTION	
IND	104628	LCZ696 (sacubitril/valsartan) for heart failure and chronic heart failure	
IND			(b) (4)

#### 3. CONSULTS:

No consults requested.





#### **QUALITY REVIEW**



### **Executive Summary**

#### I. Recommendations

#### A. Recommendation and Conclusion on Approvability

We recommend <u>approval of NDA 207620 from a product quality perspective</u> for Entresto<sup>TM</sup> (sacubitril/valsartan) Tablets, 97/103, 49/51, and 24/26 mg when stored in the intended packaging and stored at USP Controlled Room Temperature.

#### Additional OPQ Language for Action Letter

The comparability protocols supporting post-approval changes to 1) the drug product manufacturing site, control, batch size, and process and 2) the manufacturing site, control, batch size, and process are acceptable.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

Post-Marketing Commitment Subject to 506B: None

Post-Marketing Agreements Not Subject to 506B: Development of a new dissolution method for all strengths with demonstrated discriminating ability,

Using the new dissolution method and data from the overall multipoint dissolution profile from a minimum of 12 commercial batches per strength, manufactured under the same conditions as those used for the manufacture of the batches used in pivotal clinical trials, set the final dissolution acceptance criterion for Entresto<sup>TM</sup>

#### II. Summary of Quality Assessments

- A. Drug Substance [Sacubitril (b) (4) and Valsartan] Quality Summary
  - Chemical Name or IUPAC Name/Structure

 $\underline{Sacubitril:} \ 4-\{[(1S,3R)-1-([1,1'-Biphenyl]-4-ylmethyl)-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-methyl-4-ylmethyl-4-ethoxy-3-$ 

oxobutyl]amino}-4-oxobutanoic acid

(sacubitril/valsartan) Tablets, 97/103, 49/51, and 24/26 mg.

Valsartan: N-Pentanoyl-N-{[2'-(1Htetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl}-L-valine

2. Properties/CQAs Relevant to Drug Product Quality

The CQAs relevant to drug product quality are physical form, bulk density, and

3. List of starting materials

(b) (4)



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