Valturna
(aliskiren/valsartan) tablets
NDA 22-217

Summary Basis for Recommended Action
From Chemistry, Manufacturing, and Controls

Applicant: Novartis Pharmaceutical Corporation
East Hanover, NJ 07938-7367

Indication: Indicated for the treatment of hypertension.

Presentation: Valturna (aliskiren/valsartan) tablets are available in 150/160 mg and 300/320 mg strengths. The commercial presentation for these tablets is as follows,
HDPE bottles, 90 cc (30 count) for both strengths.
HDPE bottles, 120 cc (90 count) for 150/160 mg tablets.
HDPE bottles, 325 cc (90 count) for 300/320 mg tablets.
Both strengths are available in Al/Al blisters also.

EER Status: Acceptable, 7-Apr-09

Consults: ONDQA Biopharmaceutics: Adequate
Methods Validation – Revalidation by Agency was not requested.
EA – FONSI by Raanan Bloom as per 19-May-09

II. Summary of Chemistry Assessments
A. Description of the Drug Product(s) and Drug Substance(s)

Drug Substance:
Aliskiren and valsartan drug substances are being sourced from the currently approved sources. The CMC information for both drug substances is being referenced to currently approved NDAs and subsequent supplements. Aliskiren is a single diastereomer having 4 chiral centers, all S-configured, presented as a white to slightly yellowish crystalline powder. It is a hemifumarate salt of the corresponding amine, with a molecular weight of 609.8. Aliskiren drug substance is highly soluble in water, Acetate Buffer-pH 5.2, and Phosphate Buffer-pH 7.0 with a .

Valsartan is a white, microcrystalline powder, with a . Its solubility in water .
Conclusion: Acceptable.

Drug product:
Valturna tablets are film-coated, bilayer, immediate release tablets. The two tablet strengths are differentiated from each other based on color, size and debossing. The applicant is using a valsartan granulate that has been already approved for the monotherapy product. The compressed bilayer tablets are finally film coated. The quality of the drug product is assured through in-process controls and final drug product specification. The specification include tests and acceptance criteria for appearance, identification (HPLC and TLC), dissolution, degradation products (HPLC), microbial limits, uniformity of dosage forms by content uniformity and assay (HPLC). All analytical procedures used for the analysis are appropriately validated.

An expiration period of 24 months is being assigned to this product based on the submitted stability data when stored in the commercial packaging system at room temperature.

Overall conclusion: The application is recommended for approval from CMC perspective.

Additional Items: None

Ramesh Sood, Ph.D.
Branch Chief/DPA1/Branch 1/ONDQA
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/s/

RAMESH K SOOD
09/15/2009
NDA 22-217

CMC Review No. 2

SPV100 (Valturna)
150/160 mg, 300/320 mg
Film Coated Tablet

Novartis

Prafull Shiromani Ph.D.

Division of Pre-Marketing Assessment 1
Office of New Drug Quality Assessment
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1. NDA 22-217
2. REVIEW #: 2
3. REVIEW DATE: 25-Aug-2009
4. REVIEWER: Prafull Shiromani Ph.D.
5. PREVIOUS DOCUMENTS: N/A

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7. NAME & ADDRESS OF APPLICANT:

Name: Novartis Pharmaceutical Corporation
Address: One Health Plaza, East Hanover, NJ 07938-7367
8. DRUG PRODUCT NAME/CODE/TYPE:
   
a) Proprietary Name: Valturna
b) Non-Proprietary Name (USAN): Aliskiren/valsartan
c) Code Name/# (ONDC only): SPV100
d) Chem. Type/Submission Priority (ONDC only):
   • Chem. Type: 4
   • Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: Original NDA

10. PHARMACOL. CATEGORY: Hypertension

11. DOSAGE FORM: Tablet

12. STRENGTH/POTENCY: 150/160 mg, 300/320 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED:   _x__ Rx   ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
    ______SPOTS product – Form Completed
    _x___ Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
Aliskiren hemifumarate
Chemical name: \((2S,4S,5S,7S)-N-(2-Carbamoyl-2-methylpropyl)-5-amino-4-hydroxy-2,7-diisopropyl-8-[4-methoxy-3-(3-methoxypropoxy)phenyl]octanamide\) hemifumarate.

Structure:

Molecular formula: \(C_{30}H_{53}N_3O_6 \cdot 0.5 C_4H_4O_4\)
MW: Salt form: 609.8 (551.8 as free base)
CAS registry #: 173334-58-2

Valsartan
Chemical Name: alternatively known as \((S)-2-\{N-(1-oxopentyl)N-[2',(1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl]methyl\}-amino\}3-methyl-butyric acid\) (chemical name) or L-Valine, \(N-(1-oxopentyl)N-[2',(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl\)- (CAS name).

Structure/Molecular Formula/MW

17. RELATED/SUPPORTING DOCUMENTS:

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1 Action codes for DMF Table:
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4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

2 Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

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18. STATUS:

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The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The applicant has provided adequate responses to the FDA IR letter sent on 30-Mar-2009 and provided an additional six months stability data; accordingly, this NDA is recommended for approval from a CMC perspective.

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

N/A

II. Summary of Chemistry Assessments

Note: CMC Review #2 focuses on the applicants response (Amendment 0009) to the Deficiencies delineated in CMC Review #1 and on the updated stability data provided in Amendment 0008. The applicants responses to the FDA CMC IR Letter have been reviewed to be adequate. This review also evaluated the applicants Amendment 0011, ‘Updated Drug Product Testing Monographs and Supporting Method Validation Reports’ and reviewed to be adequate. Additionally, this review evaluated the applicants Amendment 0018 of 24-Aug-2009, which incorporated their revised dissolution specification of the drug product, in response to ONDQA CMC/Biopharm comment; the revised specification is adequate.

A. Description of the Drug Product(s) and Drug Substance(s)

SPV100 (Valturna) film-coated tablets contain fixed combinations of the drug substances Aliskiren hemifumarate (SPP100) and Valsartan (VAL489). SPV100 film-coated tablets, 150/160 mg, 300/320 mg, are an immediate release dosage form for oral administration. Since both drug substances in this combination product are the subject of NDAs held by Novartis, all CMC information is cross-referenced to these applications and their supplements.
Aliskiren is a potent and selective inhibitor of human rennin, used in the treatment of hypertension. Valsartan is a nonpeptide, orally active, and specific angiotensin II antagonist acting on the AT1 receptor subtype.

**DRUG SUBSTANCE**

**Aliskiren hemifumarate**

The Aliskiren Hemifumarate drug substance description and characterization, manufacturers, method of synthesis and purification, raw material and process controls, test specifications and analytical methods, container/closure system and stability information are described in the approved Tekturna® (aliskiren hemifumarate) film-coated tablets NDA (#21-985) and subsequent supplements. The drug substance is a single diastereoisomer having 4 chiral centers, all S-configured, presented as a white to slightly yellowish crystalline powder. The active is the hemifumarate salt of the corresponding amine, with a molecular weight of 609.8. Aliskiren drug substance is highly soluble in water (Acetate Buffer-pH 5.2, and Phosphate Buffer-pH 7.0) with a and is therefore categorized as a class 3 compound according to the Biopharmaceutics Classification System (BCS).

**Valsartan**

The Valsartan drug substance description and characterization, manufacturers, method of synthesis and purification, raw material and process controls, test specifications and analytical methods, container/closure system and stability information are described in the approved Diovan® Capsule NDA (#20-665) and subsequent supplements. The drug substance valsartan is well known and is described in the USP. It is a white, microcrystalline and slightly bitter tasting powder, with a . Its solubility in water is .

**DRUG PRODUCT**

SPV100 film-coated tablets are immediate release dosage forms for oral administration indicated for the treatment of hypertension. The two tablet strengths are differentiated from each other in tablet color, size and debossing.

The applicant developed a bilayer tablet formulation .
The 300/320 mg tablets were tested in a bioequivalence study and found to be bioequivalent to the free forms of aliskiren and valsartan. A biowaiver for the 150/160 mg tablets was submitted based on the proportionality in composition of the dosage strengths; this biowaiver was determined to be acceptable by the ONDQA Biopharm reviewer, Dr. T-M Chen. The Biopharm review also recommended that the dissolution acceptance criteria be tightened to $Q = \frac{\text{Mean} - \text{Nominal}}{\text{S.D.}}$ for aliskiren and $Q = \frac{\text{Mean} - \text{Nominal}}{\text{S.D.}}$ for valsartan. This recommendation is supported by the current stability data in all packages, both at long-term (12 months stability) and accelerated (6 months) storage conditions. This recommendation was conveyed to the applicant via an IR letter dated 16-Jun-2009. Their initial reticence (Amendment 0013 of 10-Jul-2009) towards this recommendation was eventually replaced with their full acceptance of the same (Amendment 0018) and submission of updated dissolution specification conforming to this recommendation.

The drug product will be marketed in HDPE bottles with desiccant and child resistant closures, and in blisters. A 30 count of both 150/160 mg and 300/320 mg dosage strengths will be provided in a square 90cc HDPE bottle. A 90 count will be provided in a square 120cc HDPE bottle for the 150/160 mg dosage strength, and in a square 325cc HDPE bottle for the 300/320 mg dosage strength. Both dosage strengths will also be marketed in double aluminum foil blisters.

Subsequently and as a response to the first CMC IR letter the applicant has placed additional two batches of each strength on stability in this package, the 3 month stability data review of which will not be possible due to the PDUFA goal date of 26-Sep-2009.

Six months additional satisfactory stability data in all packages have been provided in Amendment 0008. Based on current stability data of 12 months, the applicants establishment of a 24 month shelf-life for the blisters and bottles with desiccant is justified based on ICH Q1E. Their establishment of an shelf-life for bottles without a desiccant is justified based on the ICH Q1E subsection 2.4.2.1 and the ‘Decision Tree-Appendix A’. Their proposed shelf-life of 24 months is supported by their statistical analysis of the assay, through which much longer shelf-lives are calculated.

B. Description of How the Drug Product is Intended to be Used

Valturna reduces blood pressure and thereby reduces the risks of stroke and myocardial infarction. It is indicated:

- In patients not adequately controlled with monotherapy.
CHEMISTRY REVIEW

Chemistry Review Data Sheet

- May be substituted for titrated components.
- As initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals.

Dosage and Administration:
- Add-on therapy OR Initial therapy with 150/160 mg. Titrate as needed up to a maximum of 300/320 mg.
- Majority of effect attained within 2 weeks.
- Replacement therapy: may be substituted for titrated components.
- One tablet daily, with a routine pattern with regard to meals.

All proposed doses can be achieved using the proposed commercial strengths.

C. Basis for Approvability or Not-Approval Recommendation

The applicant has provided adequate responses to the FDA IR letter sent on 27-Mar-2009, accordingly, this NDA is recommended for approval from a CMC perspective.

III. Administrative

A. Reviewer’s Signature

B. Endorsement Block

ChemistName/Date: Prafull Shiromani, Ph.D.
ChemistryTeamLeaderName/Date: Ramesh Sood, Ph.D.
ProjectManagerName/Date: Lori Wachter

C. CC Block

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/s/

PRAFULL K SHIROMANI
09/01/2009

RAMESH K SOOD
09/02/2009
NDA 22-217

CMC Review No. 1

SPV100 (Valturna)
150/160 mg, 300/320 mg
Film Coated Tablet

Novartis

Prafull Shiromani Ph.D.

Division of Pre-Marketing Assessment 1
Office of New Drug Quality Assessment
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   A APPENDICES ................................................................................................................. 99
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III. List Of Deficiencies To Be Communicated........................................................................102
1. NDA 22-217
2. REVIEW #: 1
3. REVIEW DATE: 08-Apr-2009
4. REVIEWER: Prafull Shiromani Ph.D.
5. PREVIOUS DOCUMENTS: N/A

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7. NAME & ADDRESS OF APPLICANT:

Name: Novartis Pharmaceutical Corporation
Address: One Health Plaza, East Hanover, NJ 07938-7367
Representative: Lily Chan, PharmD, Associate Director, DRA
Telephone: (862)778-7367

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Valturna
b) Non-Proprietary Name (USAN): Aliskiren/Valsartan
c) Code Name/# (ONDC only): SPV100
d) Chem. Type/Submission Priority (ONDC only):
   • Chem. Type: 4
   • Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: Original NDA

10. PHARMACOL. CATEGORY: Hypertension

11. DOSAGE FORM: Tablet

12. STRENGTH/POTENCY: 150/160 mg, 300/320 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: _x__Rx     ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
    ______SPOTS product – Form Completed
    _x___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

   Aliskiren hemifumarate
   Chemical name: (2S,4S,5S,7S)-N-(2-Carbamoyl-2-methylpropyl)-5-amino-4-hydroxy-2,7-diisopropyl-8-[4-methoxy-3-(3-methoxypropoxy)phenyl]octanamide hemifumarate.

   Structure:
Molecular formula: $C_{30}H_{53}N_3O_6 \cdot 0.5 C_4H_4O_4$
MW: Salt form: 609.8 (551.8 as free base)
CAS registry #: 173334-58-2

Valsartan

Chemical Name: alternatively known as (S)-2-{$N$-(1-oxopentyl)-$N$-[[2'-(1Htetrazol-5-yl)-[1,1'-biphenyl]-4-yl]methyl]-amino}-3-methyl-butyric acid (chemical name) or L-Valine, $N$-(1-oxopentyl)-N-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (CAS name).

Structure/Molecular Formula/MW

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

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6 – DMF not available
7 – Other (explain under "Comments")

2 Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

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18. STATUS:

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The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This NDA in its present form cannot be recommended for approval from a CMC perspective. The approval of this application, from a CMC perspective, depends on the applicant’s response to the FDA IR letter sent to the applicant on 27-Mar-2009. Additionally, the environmental assessment, and bio-waiver and dissolution assessments have not been received at this time.

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

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

SPV100 (Valturna) film-coated tablets contain fixed combinations of the drug substances Aliskiren hemifumarate (SPP100) and Valsartan (VAL489). SPV100 film-coated tablets, 150/160 mg, 300/320 mg, are an immediate release dosage form for oral administration. Since both drug substances in this combination product are the subject of NDAs held by Novartis, all CMC information is cross-referenced to these applications and their supplements.

Aliskiren is a potent and selective inhibitor of human rennin, used in the treatment of hypertension. Valsartan is a nonpeptide, orally active, and specific angiotensin II antagonist acting on the AT1 receptor subtype.

DRUG SUBSTANCE

Aliskiren hemifumarate

The Aliskiren Hemifumarate drug substance description and characterization, manufacturers, method of synthesis and purification, raw material and process controls, test specifications and analytical methods, container/closure system and stability information are described in the approved Tekturna® (aliskiren hemifumarate) film-coated tablets NDA (#21-985) and subsequent supplements. The drug substance is a single diastereoisomer having 4 chiral centers, all S-configured, presented as a white to slightly yellowish crystalline powder. The active is the hemifumarate salt of the corresponding amine, with a molecular weight
of 609.8. Aliskiren drug substance is highly soluble in water (Acetate Buffer-pH 5.2, and Phosphate Buffer-pH 7.0) with a
and is therefore categorized as a class 3 compound according to the Biopharmaceutics Classification System (BCS).

Valsartan

The Valsartan drug substance description and characterization, manufacturers, method of synthesis and
purification, raw material and process controls, test specifications and analytical methods, container/closure
system and stability information are described in the approved Diovan® Capsule NDA (#20-665) and
subsequent supplements. The drug substance valsartan is well known and is described in the USP. It is a
white, microcrystalline and slightly bitter tasting powder, with a
solubility in water

DRUG PRODUCT

SPV100 film-coated tablets are immediate release dosage forms for oral administration indicated for the
treatment of hypertension. The two tablet strengths are differentiated from each other in tablet color, size
and debossing.

The applicant developed a bilayer tablet formulation

The applicant employed a ‘Design-of-
Experiments’ study to optimize the process parameters, for which no details were provided and hence, is the
subject of a deficiency in the first FDA IR letter.

The 300/320 mg tablets were tested in a bioequivalence study and found to be bioequivalent to the free
forms of aliskiren and valsartan. A biowaiver for the 150/160 mg tablets has been submitted based on the
proportionality in composition of the dosage strengths, the acceptability of which is being determined by the
ONDQA biopharm reviewer.

The drug product will be marketed in HDPE bottles with desiccant and child resistant closures, and in
blisters. A 30 count of both 150/160 mg and 300/320 mg dosage strengths will be provided in a square 90cc
HDPE bottle. A 90 count will be provided in a square 120cc HDPE bottle for the 150/160 mg dosage
strength, and in a square 325cc HDPE bottle for the 300/320 mg dosage strength. Both dosage strengths will
also be marketed in double aluminum foil blisters.

Six months satisfactory stability data in all packages has been provided. The applicant states that they will
provide an additional 6 months stability data during this review.
An ‘Overall Recommendation’ was issued by OC on 0-Apr-2009, a summary report of which is included in this review.

### B. Description of How the Drug Product is Intended to be Used

Valturna reduces blood pressure and thereby reduces the risks of stroke and myocardial infarction. It is indicated:

- In patients not adequately controlled with monotherapy.
- May be substituted for titrated components.
- As initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals.

**Dosage and Administration:**

- Add-on therapy OR Initial therapy with 150/160 mg. Titrate as needed up to a maximum of 300/320 mg.
- Majority of effect attained within 2 weeks.
- Replacement therapy: may be substituted for titrated components.
- One tablet daily, with a routine pattern with regard to meals.

All proposed doses can be achieved using the proposed commercial strengths.

### C. Basis for Approvability or Not-Approval Recommendation

Approvability will be based on the applicant’s response to FDA comments submitted through an IR letter dated 27-Mar-2009. These comments are the following:

1. **P.2.2.1 Formulation Development**

   Since hydroxypropyl cellulose is an important component of the product (b) (4) include appropriate limits for attributes such as molecular weight, viscosity, etc., that can impact the final product quality.

2. **P.2.2.3 Physicochemical and Biological Properties**

   i. Provide a summary with supporting data of your development efforts to demonstrate the homogeneity of the tabletting mixture and of the tablets, as stated, in this section.

   ii. How is this demonstration at the developmental stage related to consistent commercial manufacturing?

3. **P.2.3 Manufacturing Process Development**

   Provide a summary of the design of experiments employed by you, as stated in your section (b) (4) to optimize the parameters and the associated statistical analyses. The statistical analysis should include the polynomial model used, the regression coefficients for main and interacting independent variables, the standard error, the statistical method to determine
Executive Summary Section

significance, information on any established design space. Describe verification of the design space at commercial scale.

4. P.3.3 Description of Manufacturing Process and Process Controls

Clarify why tablet hardness, thickness, disintegration time, and friability for the core tablets are not included as in-process controls. Tablet hardness may affect tablet dissolution.

5. P.3.4 Controls of Critical Steps and Intermediates

Identify critical process parameters and how they will be controlled.

6. P.5.1 Specification

Provide clarification as to why a test and a limit for the valsartan related (b) (4) is not included in the specification, as was for NDA 20-665, Diovan Capsules.

7. Container Closure System

Provide results of the USP Container Test <671> for water vapor permeation for each combination of bottle and cap intended for commerce (b) (4)

8. P.8.1 Stability Summary and Conclusions

Provide clarification regarding your statement in “

9. P.8.2 Post-approval stability protocol and commitment

Include the first three commercial production scale batches in blister packaging into your post-approval stability commitment.


Include NDC numbers (differentiated by potency and package) in the ‘How Supplied’ section.

III. Administrative
Executive Summary Section

A. Reviewer’s Signature

B. Endorsement Block

ChemistName/Date: Prafull Shiromani, Ph.D.
ChemistryTeamLeaderName/Date: Ramesh Sood, Ph.D.
ProjectManagerName/Date: Lori Wachter

C. CC Block

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/s/

Prafull Shiromani
4/8/2009 12:17:58 PM
CHEMIST

Ramesh Sood
CHEMIST
Summary
This is an e-CTD submission for a fixed dose combination drug product of valsartan, an angiotensin receptor blocker and aliskiren hemifumarate, a direct renin inhibitor. Both valsartan and aliskiren are approved monotherapy products under Novartis’ NDAs 20-665 (Diovan) and 21-985 (Tekturna). Clinical trials for this combination drug product were carried out under IND 76,045. There have been no CMC specific meetings with Novartis in connection with this NDA. A multi-disciplinary pre-NDA meeting was held on Feb 22, 2007 and only one quality related question about the amount of product stability data at submission and the timing of stability updates was discussed.

Drug Substance
Since both drug substances in this combination drug product are the subject of NDAs held by Novartis, all CMC information is cross-referenced to these applications and their supplements. Both valsartan and aliskiren hemifumarate are chiral synthetic compounds and are enantiomerically pure. Valsartan is described in the USP.

Drug Product
Two strengths, 150 mg/160 mg and 300 mg/320 mg of aliskiren and valsartan have been developed for commercialization as immediate release film coated tablets. Standard compendial excipients are used in the formulation. The premixes used for film coating are composed of compendial ingredients or colors that meet 21CFR. After clinical efficacy was established using free combinations of aliskiren and valsartan, fixed dose combinations of the two actives were developed. However, pharmacokinetic studies showed that the formulation was not bioequivalent to the free forms so additional formulations were investigated. After developing 5 new formulations, Novartis selected a...
Standard oral dosage form specifications have been proposed for Valturna tablets. The product will be packaged in both HDPE bottles and Alu/Alu blisters and up to 6 months long term and accelerated data have been submitted. 12 months long term data will be provided during the review period. An initial expiration date of \( (p) \) is proposed for the drug product packaged in both bottle and blister configurations.

**Critical Review Issues**

**Drug Product**

- Have the two drug substances shown to be compatible with each other? Stability studies on the finished product may not be sufficient to answer this question since this is a bilayer tablet.
- Homogeneity of the tabletting mixture and of the cores over the compression run has been demonstrated by blend uniformity testing of the tabletting mixture and content uniformity testing of the cores and film coated tablets performed during development of the manufacturing process. Is this sufficient especially since no routine in-process tests for this attribute are proposed?
- Indigotin blue lake is not a compendial article but is said to comply with 21 CFR. This should be verified.
- Has the dissolution method shown to be discriminatory? An informal consultation with Dr Marroum and his team is recommended for the dissolution method and acceptance criteria. The biowaiver request for the 150/160 mg strength should also be brought to their attention.
- Higher limits have been proposed for the degradation impurities of aliskiren than in the NDA for aliskiren monotherapy. Why? Since the new acceptance criteria are above the qualification threshold, have these been re-qualified? Pharm/Tox input may be needed.
- Is the skip-lot microbial testing proposed acceptable?
- In the post-approval stability commitment for the first 3 production batches, Novartis has not included testing of the product in blister packaging. Why?
Comments and Recommendations
The application is fileable. Manufacturing, testing and packaging facilities have been entered into EES and the reviewer should verify the accuracy and completeness of the entries. Since an environmental assessment has been submitted a consult has been requested from the OPS EA staff. A single CMC reviewer is recommended.

Kasturi Srinivasachar
Pharmaceutical Assessment Lead

Ramesh Sood, Ph.D.
Branch Chief

Dec 11, 2008
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/
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Kasturi Srinivasachar
12/11/2008 02:12:15 PM
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