CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205353Orig1s000

CHEMISTRY REVIEW(S)
NDA 205 353

Panobinostat

NOVARTIS

Danuta Gromek-Woods, Ph.D.

Review Chemist

Office of New Drug Quality Assessment
Division of New Drug Quality Assessment 1
Branch # 2

CMC REVIEW OF NDA 205 353
For the Division of Hematology Drug Products (DHP)
Table of Contents

Table of Contents .................................................................................................................. 2

CMC Review Data Sheet ......................................................................................................... 3

The Executive Summary ......................................................................................................... 9

I. Recommendations ............................................................................................................ 9
   A. Recommendation and Conclusion on Approvability .................................................... 9

II. Summary of CMC Assessments ....................................................................................... 9
   A. Description of the Drug Product(s) and Drug Substance(s) ......................................... 9
   B. Basis for Approvability or Not-Approval Recommendation ......................................... 10

III. Administrative ................................................................................................................. 13
CMC Review Data Sheet

1. NDA 205 353
2. REVIEW #: 2
3. REVIEW DATE: 25-Sep-2014
4. REVIEWER: Danuta Gromek-Woods, Ph.D.
5. PREVIOUS DOCUMENTS: Review #1
6. SUBMISSION(S) BEING REVIEWED:

<table>
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<tr>
<th>Submission</th>
<th>Document Date</th>
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<tbody>
<tr>
<td>Original Submission</td>
<td>23-mar-2014</td>
<td>0000</td>
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<td>Amendment (BC)</td>
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<td>18-Sep-2014</td>
<td>0043</td>
<td>Updated drug substance and drug product specifications, as requested in IR sent on 24-Aug-2014 and 26-Aug-2014.</td>
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7. NAME & ADDRESS OF APPLICANT:

<table>
<thead>
<tr>
<th>Name:</th>
<th>Novartis Pharmaceuticals Corporation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address:</td>
<td>One Health Plaza, East Hanover, 07936-1080, New Jersey, USA</td>
</tr>
<tr>
<td>Representative:</td>
<td>Jeannie Shen</td>
</tr>
<tr>
<td>Telephone:</td>
<td>(862) 778-3343</td>
</tr>
</tbody>
</table>

8. DRUG PRODUCT NAME/CODE/TYPE:

   a) Proprietary Name: Farydak
   b) Non-Proprietary Name: panobinostat
   c) Code Name/# (ONDQA only):
   d) Chem. Type/Submission Priority (ONDQA only):
      • Chem. Type: Type 1, NME
      • Submission Priority: Priority

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

10. PHARMACOL. CATEGORY: FARYDAK®, in combination with bortezomib and dexamethasone, is indicated for the treatment of patients with multiple myeloma, who have received at least 1 prior therapy.

11. DOSAGE FORM: Hard Gelatin Capsules

12. STRENGTH/POTENCY: 10 mg, 15 mg and 20 mg capsules

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: √Rx ___OTC

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

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

   Chemical Name: (2E)-N-Hydroxy-3-[4-((2-(2-methyl-1H-indol-3-yl)ethyl]amino)methyl]phenyl]prop-2-enamide 2-hydroxypropanolate (1:1)
**Structural Formula:**

![Structural formula image]

**Molecular Formula:** \(C_{21}H_{23}N_3O_2\), \(C_3H_6O_3\)

**Relative molecular mass:** 349.43 (free base) + 90.08 (lactic acid) = 439.51.

Salt/base ratio: 1.258

17. RELATED/SUPPORTING DOCUMENTS:

**A. DMFs:**

<table>
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</table>

1 Action codes for DMF Table:
1 - DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 - Type 1 DMF
3 - Reviewed previously and no revision since last review
4 - Sufficient information in application
5 - Authority to reference not granted
6 - DMF not available
7 - Other (explain under "Comments")
CMC Review Data Sheet

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:

<table>
<thead>
<tr>
<th>DOCUMENT</th>
<th>APPLICATION NUMBER</th>
<th>DESCRIPTION</th>
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<td>IND</td>
<td>69862 and 67091</td>
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18. STATUS:

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<th>RECOMMENDATION</th>
<th>DATE</th>
<th>REVIEWER</th>
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<td>Biometrics</td>
<td>Adequate</td>
<td>06-Jun-2014</td>
<td>Sutan Wu, Ph.D.</td>
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<td></td>
<td>• 25°C/60%RH climate zone I and II)</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>For PVC/PCTFE package, the commercial package, the shelf life could be up to 36 month.</td>
<td></td>
<td></td>
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<tr>
<td>EES</td>
<td>Acceptable, see Attachment 1 for EER</td>
<td>11-Sep-2014</td>
<td>Dholakia, Vipul, Ph.D., Consumer Safety Officer / SPA, Office of Compliance, CDER/FDA</td>
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<tr>
<td>Pharm/Tox</td>
<td>NA</td>
<td></td>
<td></td>
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<tr>
<td>Biopharm</td>
<td>Recommended for Approval - See review in DARRTS</td>
<td>22-Sep-2014</td>
<td>Elsbeth Chihikhale, Ph.D.</td>
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<td>LNC</td>
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<tr>
<td>Methods Validation</td>
<td>We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified (as per email from Dr. Ali Al Hakim dated 13-Jun-2014).</td>
<td>Methods Validation Consult Request Form was sent on 13-Jun-2014 to FDA Division of Pharmaceutical Analysis, Attn: Michael Trehy, St. Louis, MO 63101, by Janice Brown, please refer to Consult request in DARRTS dated 13-Jun-2014</td>
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<td>DMETS</td>
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<tr>
<td>EA</td>
<td>The applicant certifies that this submission for qualifies for a categorical exclusion in</td>
<td></td>
<td>Danuta Gromek-Woods, Ph.D.</td>
</tr>
<tr>
<td>CONSULTS/CMC RELATED REVIEWS</td>
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<td>DATE</td>
<td>REVIEWER</td>
</tr>
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<tr>
<td></td>
<td>accordance with 21 CFR Part 25.31(b) as the concentration of the active moiety will be significantly &lt; 1 ppb.</td>
<td></td>
<td></td>
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<tr>
<td>Product Quality Microbiology</td>
<td>Recommended for Approval - See review in DARRTS</td>
<td>29-May-2014</td>
<td>Erica Pfeiler, Ph.D.</td>
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</table>
Chemistry Review for NDA 205 353

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This NDA has provided sufficient CMC information to assure the identity, strength, purity, and quality of the drug product. As indicated in the Risk Assessment table, pg. 11, the primary reviewer recommends an optimization of the drug product method “Assay and degradation products by HPLC” to improve the separation of impurity from Panobinostat, which can be addressed post approval. This issue does not preclude the approvability of NDA 202 353 at this time.

Labels/labeling are under discussion with the Review Team. An “Acceptable” recommendation was issued by the Office of Compliance for Novartis Farmaceutica, Barcelona, Spain on 11-Sep-2014. The Biopharmaceutics’ reviewer issued an “Adequate” recommendation on 22-Sep-2014.

Overall, NDA 205 353 is recommended for “Approval” from the CMC perspective.

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

None.

II. Summary of CMC Assessments

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

(1) Drug Substance

FARYDAK (panobinostat) is a histone deacetylase inhibitor. The Active Pharmaceutical Ingredient of the FARYDAK® hard gelatin capsules is panobinostat lactate anhydrous. This is a New Molecular Entity and the review process for this NDA submission is conducted “under the PDUFA V Program”.

The chemical name of panobinostat is 2-Hydroxypropanoic acid, compd. with 2-(E)-N-hydroxy-3-[4-[[2-(2-methyl-1H-indol-3-yl)ethyl]amino][methyl]phenyl]-2-propenamide (1:1). The structural formula is provided below:
Panobinostat lactate anhydrous is a white to slightly yellowish or brownish powder. The molecular formula is C_{21}H_{23}N_{3}O_{6}·C_{3}H_{6}O_{3} with a molecular weight of 439.51 as a lactate [349.43 (free base) + 90.08 (lactic acid)]. Panobinostat free base is not chiral and shows no specific optical rotation. Panobinostat lactate anhydrous is slightly soluble in water. Solubility of panobinostat lactate anhydrous is pH-dependent, with the highest solubility in buffer pH 3.0 (citrate).

Based on the drug substance stability data and ICH Q1E Guidance “Evaluation of Stability Data”, a 180 months re-test period for Panobinostat lactate, anhydrous when packed and stored is granted.

(2) Drug Product

LBH589 (Panobinostat) is a highly potent class I, II, and IV pan-deacetylase inhibitor (DACi) promoting increased acetylation of both histone and non-histone DAC. DAC inhibition affects targets in several different pathways that contribute to the malignant phenotype. LBH589 has the potential for broad anti-cancer activity as a combination partner.

LBH589 was initially developed at Novartis Pharmaceuticals Corporation (NPC) and The process was subsequently transferred to Novartis Barbera, Spain for scale-up and commercialization. LBH589 has been developed as immediate release hard gelatin capsules for oral administration.

FARYDAK hard gelatin capsules contain 10 mg, 15 mg or 20 mg panobinostat free base. The inactive ingredients are magnesium stearate, mannitol, microcrystalline cellulose and pregelatinized starch. The capsules contain gelatin, FD&C Blue 1 (10 mg capsules), yellow iron oxide (10 mg and 15 mg capsules), red iron oxide (15 mg and 20 mg capsules) and titanium dioxide.

Based on drug product stability data and statistical analysis, the expiration dating period for the Panobinostat capsules is 36 months. Product should be stored at 20° to 25°C (68° to 77°F), excursions permitted between 15° and 30°C (59° and 86°F).

B. Basis for Approvability or Not-Approval Recommendation
CMC REVIEW OF NDA 205 353

Executive Summary Section

This NDA has provided sufficient CMC information to assure the identity, strength, purity, and quality of the drug product. As indicated in the Risk Assessment table, pg. 11, the primary reviewer recommends an optimization of the drug product method “Assay and degradation products by HPLC” to improve the separation of impurity from Panobinostat, which can be addressed post approval. This issue does not preclude the approvability of NDA 202 353 at this time.

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Overall, NDA 205 353 is recommended for “Approval” from the CMC perspective.

<table>
<thead>
<tr>
<th>CQAs</th>
<th>Factors that can impact the CQA</th>
<th>Risk Ranking</th>
<th>Risk Mitigation approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assay, stability</td>
<td></td>
<td>L</td>
<td>Suitability of analytical methodology:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>The reviewer found (and the applicant confirmed in response to the agency’s IR) that Assay and degradation products by HPLC method for the drug product is not specific enough to accurately quantify impurities and .</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Impurity is a</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Impurity is controlled as 'Any unspecified impurity' in the drug substance, at a level of NMT %.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Since the capsules are packaged in blisters and the blisters are packaged in a secondary carton container, the risk is minimal. As per label, the product has to be stored in an original container and protected from light.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Conclusion: Although impurities and are minimal, as per label, the product has to be stored in an original container and protected from light.</td>
</tr>
</tbody>
</table>

Taking in account the above considerations, this issue does not preclude the approvability of NDA 202 353 at this time.

<table>
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<tr>
<th>Lifecycle Considerations / Comments</th>
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</thead>
<tbody>
<tr>
<td>Drug product: Monitor level of individual and total impurities on stability, especially for the impurity controlled as 'Any unspecified impurity' (limit of NMT %). Optimization of the drug product method “Assay and degradation products by HPLC” to improve the separation of impurity from the active is recommended by the primary reviewer.</td>
</tr>
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</table>
## Executive Summary Section

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<thead>
<tr>
<th>CQAs</th>
<th>Factors that can impact the CQA</th>
<th>Risk Ranking</th>
<th>Risk Mitigation approach</th>
<th>Risk Evaluation</th>
<th>Lifecycle Considerations / Comments</th>
</tr>
</thead>
</table>
| Physical stability          | • Formulation  
• Crystallinity of drug substance (polymorphism)  
• Process parameters | L            | Anhydrous form of Panobinostat lactate is used:  
• See Review#1.pgs. 47-51 and 113-120 for polymorph characterization in drug substance and drug product.  
• XRPD test is included in drug substance specification | L              | If any changes in drug substance synthesis or drug product manufacturing process occur in the future, polymorphic stability should be re-visited. |
| Solid state                 |                                                                                               |              |                                                                                         |                 |                                                                                                                                                                   |
| Content Uniformity          | • Formulation  
• Raw materials  
• Process parameters  
• Scale/equipment | M            | Robust manufacturing process.  
• Adequate analytical methodology to test content uniformity. | L              |                                                                                                                                                                   |
| Microbial limits            | • Formulation  
• Raw materials  
• Process parameters  
• Site  
• Finished product | L            | See the Quality microbiology review in DARRTS.                                               | Acceptable      | Refer to the Microbiology Review.                                                                                                                                 |
| Dissolution                 | • Formulation  
• Raw materials  
• Exclude major reformulations  
• Process parameters  
• Scale/equipment  
• Site | M            | See Biopharmaceutics reviews in DARRTS dated 22-Sep-2014                                     | Acceptable      | Refer to the Biopharmaceutics Review.                                                                                                                                 |
Executive Summary Section

III. Administrative

A. Reviewer’s Signature:

(See appended electronic signature page)

Danuta Gromek-Woods, Ph.D., Chemistry Reviewer

B. Endorsement Block:

(See appended electronic signature page)

Ali Al Hakim, Ph.D., Branch Chief, Branch 2, ONDQA

C. CC Block: entered electronically in DFS

8 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

DANUTA E GROMEK-WOODS
10/07/2014

ALI H AL HAKIM
10/07/2014
NDA 205 353

Panobinostat

NOVARTIS

Danuta Gromek-Woods, Ph.D.

Review Chemist

Office of New Drug Quality Assessment
Division of New Drug Quality Assessment 1
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CMC REVIEW OF NDA 205 353
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   B. Description of How the Drug Product is Intended to be Used ....................... 11
   B. Basis for Approvability or Not-Approval Recommendation .......................... 11

III. Administrative ..................................................................................................... 14

CMC Assessment ........................................................................................................ 15

I. Review Of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body Of Data......15
   S DRUG SUBSTANCE ............................................................................................ 15
      S.1 General Information ...................................................................................... 15
      S.2 Manufacture .................................................................................................. 18
      S.3 Characterization ............................................................................................ 43
      S.4 Control of Drug Substance .......................................................................... 65
      S.5 Reference Standards or Materials ................................................................. 81
      S.6 Container Closure System ........................................................................... 84
      S.7 Stability ......................................................................................................... 84

   P DRUG PRODUCT .................................................................................................. 86
      P.1 Description and Composition of the Drug Product ....................................... 86
      P.2 Pharmaceutical Development ....................................................................... 88
      P.3 Manufacture .................................................................................................. 93
      P.4 Control of Excipients .................................................................................... 107
      P.5 Control of Drug Product .............................................................................. 110
      P.6 Reference Standards or Materials ................................................................. 134
      P.7 Container Closure System ........................................................................... 134
      P.8 Stability ......................................................................................................... 136

   A APPENDICES ...................................................................................................... 140
      A.1 Facilities and Equipment (biotech only) ......................................................... 140
      A.2 Adventitious Agents Safety Evaluation ......................................................... 140
      A.3 Novel Excipients ............................................................................................. 140

   R REGIONAL INFORMATION .............................................................................. 140
CMC REVIEW OF NDA 205 353

R1  Executed Batch Records.................................................................141
R2  Comparability Protocols.................................................................141
R3  Methods Validation Package...........................................................141

II.  Review Of Common Technical Document-Quality (Ctd-Q) Module 1 .........................141

Labeling & Package Insert are under discussion with the Review Team.........................141

III. List Of Deficiencies to be Communicated.................................................141

CMC Review #1

Page 3 of 144
CMC Review Data Sheet

1. NDA 205 353
2. REVIEW #: 1
3. REVIEW DATE: 10-Jun-2014
4. REVIEWER: Danuta Gromek-Woods, Ph.D.
5. PREVIOUS DOCUMENTS: NA
6. SUBMISSION(S) BEING REVIEWED:

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7. NAME & ADDRESS OF APPLICANT:

Name: Novartis Pharmaceuticals Corporation
8. DRUG PRODUCT NAME/CODE/TYPE:
   a) Proprietary Name: Farydak
   b) Non-Proprietary Name: panobinostat
   c) Code Name/# (ONDQA only):
   d) Chem. Type/Submission Priority (ONDQA only):
      - Chem. Type: Type I, NME
      - Submission Priority: Priority

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11. DOSAGE FORM: Hard Gelatin Capsules

12. STRENGTH/POTENCY: 10 mg, 15 mg and 20 mg capsules

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: ✔ Rx    ___ OTC

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

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

   Chemical Name: (2E)-N-Hydroxy-3-[4-([2-(2-methyl-1H-indol-3-yl)ethyl]amino)methyl]phenyl]prop-2-enamide 2-hydroxypropanoate (1:1)

   Structural Formula:
Molecular Formula: C_{21}H_{23}N_{3}O_{2}. C_{3}H_{6}O_{3}
Relative molecular mass: 349.43 (free base) + 90.08 (lactic acid) = 439.51.
Salt/ base ratio: 1.258

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<th>STATUS(^2)</th>
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<th>COMMENTS</th>
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<tr>
<td>(b)(c)</td>
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<td></td>
<td>4</td>
<td>Adequate</td>
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<td></td>
</tr>
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\(^1\) Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 – Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")
Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

**B. Other Documents:**

<table>
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<tr>
<th>DOCUMENT</th>
<th>APPLICATION NUMBER</th>
<th>DESCRIPTION</th>
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### CMC REVIEW OF NDA 205 353

**CMC Review Data Sheet**

18. **STATUS:**

#### ONDC:

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<th>CONSULTS/ CMC RELATED REVIEWS</th>
<th>RECOMMENDATION</th>
<th>DATE</th>
<th>REVIEWER</th>
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<td>06-Jun-2014</td>
<td>Sutan Wu, Ph.D.</td>
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<td>- 25°C/60%RH climate zone I and II)</td>
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<td><strong>For PVC/PCTFE package, the commercial package, the shelf life could be up to 36 month.</strong></td>
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<td>Dholakia, Vipul, Ph.D., Consumer Safety Officer / SPA, Office of Compliance, CDER/FDA</td>
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<td>Elsbeth Chihikhale, Ph.D.</td>
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<td><strong>Biopharm</strong></td>
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<td><strong>LNC</strong></td>
<td>We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified (as per email from Dr. Ali Al Hakim dated 13-Jun-2014).</td>
<td>Methods Validation Consult Request Form was sent on 13-Jun-2014 to FDA Division of Pharmaceutical Analysis, Attn: Michael Treby, St. Louis, MO 63101, by Janice Brown, please refer to Consult request in DARRTS dated 13-Jun-2014</td>
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<td>The applicant certifies that this submission for qualifies for a categorical exclusion in</td>
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<td>Danuta Gromek-Woods, Ph.D.</td>
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<td>Product Quality Microbiology</td>
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<td>29-May-2014</td>
<td>Erica Pfeiler, Ph.D.</td>
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Chemistry Review for NDA 205 353

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This NDA has provided sufficient CMC information to assure the identity, strength, purity, and quality of the drug product. Labels/labeling are under discussion with the Review Team. From a CMC perspective, this NDA is recommended for “Approval” pending an “Acceptable” recommendation from the Office of Compliance and an “Adequate” recommendation from the Biopharmaceutics’ reviewer.

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

None.

II. Summary of CMC Assessments

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

1) Drug Substance

FARYDAK (panobinostat) is a histone deacetylase inhibitor. The Active Pharmaceutical Ingredient of the FARYDAK® hard gelatin capsules is panobinostat lactate anhydrous. This is a New Molecular Entity and the review process for this NDA submission is conducted “under the PDUFA V Program”.

The chemical name of panobinostat is 2-Hydroxypropanoic acid, compd. with 2-(E)-N-hydroxy-3-[[2-(2-methyl-1H-indol-3-yl)ethyl]amino]methyl]phenyl]-2-propenamide (1:1). The structural formula is provided below:

![Chemical Structure of Panobinostat](image-url)
Panobinostat lactate anhydrous is a white to slightly yellowish or brownish powder. The molecular formula is C_{21}H_{23}N_5O_2•C_3H_4O_3 with a molecular weight of 439.51 as a lactate [349.43 (free base) + 90.08 (lactic acid)]. Panobinostat free base is not chiral and shows no specific optical rotation. Panobinostat lactate anhydrous is slightly soluble in water. Solubility of panobinostat lactate anhydrous is pH-dependent, with the highest solubility in buffer pH 3.0 (citrate).

Based on the drug substance stability data and ICH Q1E Guidance “Evaluation of Stability Data”, a 6 months re-test period for Panobinostat lactate, anhydrous when packed and stored is granted.

(2) Drug Product

LBH589 (Panobinostat) is a highly potent class I, II, and IV pan-deacetylase inhibitor (DACi) promoting increased acetylation of both histone and non-histone DAC. DAC inhibition affects targets in several different pathways that contribute to the malignant phenotype. LBH589 has the potential for broad anti-cancer activity as a combination partner.

LBH589 was initially developed at Novartis Pharmaceuticals Corporation (NPC) and . The process was subsequently transferred to Novartis Barbera, Spain for scale-up and commercialization. LBH589 has been developed as immediate release hard gelatin capsules for oral administration.

FARYDAK hard gelatin capsules contain 10 mg, 15 mg or 20 mg panobinostat free base. The inactive ingredients are magnesium stearate, mannitol, microcrystalline cellulose and pregelatinized starch. The capsules contain gelatin, FD&C Blue 1 (10 mg capsules), yellow iron oxide (10 mg and 15 mg capsules), red iron oxide (15 mg and 20 mg capsules) and titanium dioxide.

Based on drug product stability data and statistical analysis, the expiration dating period for the Panobinostat capsules is 36 months. Product should be stored at 20° to 25°C (68° to 77°F), excursions permitted between 15° and 30°C (59° and 86°F).

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

FARYDAK hard gelatin capsules are intended for oral administration.

B. Basis for Approvability or Not-Approval Recommendation

This NDA has provided sufficient CMC information to assure the identity, strength, purity, and quality of the drug product. Labels/labeling are under discussion with the Review Team. From a CMC perspective, this NDA is recommended for “Approval” pending an “Acceptable” recommendation from the Office of
Executive Summary Section

Compliance and an "Adequate" recommendation from the Biopharmaceuticals' reviewer.

Initial Risk Assessment

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<td>Release (1)</td>
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<td>Per biopharm: No BCS classification. The aqueous solubility is low, and the permeability is moderate, so it could be a BCS class II or IV.</td>
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Risk Assessment

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CMC Review #1 Page 12 of 144

Reference ID: 3617102
Conclusion:
Adequate controls for drug substance and raw materials are in place, manufacturing processes are robust and adequately controlled, specifications ensure the identity, strength, quality, and purity of the drug product. The container/closure system is adequate to protect the drug product. Stability data assure that the product will be stable through the expiration date. Based on provided stability data and statistical analysis the expiration dating period of 36 months is granted for the for the FARYDAK capsules packages in PVC/PCTFE when stored @25°C (77°F); excursions permitted to 15-30°C (59-86°F). For details, please refer to the Biometrics Consult in DARRTS dated 06-Jun-2014, prepared by Dr. Sutan Wu, both at

Labeling has been under discussion with the Review Team. The EES Report indicates a “Pending” recommendation for Novartis Farmaceutica, Barcelona, Spain.

From the CMC perspective, NDA 205 353 has provided sufficient information to assure the identity, strength, purity, and quality of FARYDAK over the proposed shelf life when stored as prescribed in labeling.

This NDA is recommended for “Approval” from the CMC perspective pending an “Acceptable” recommendation from the Office of Compliance and an “Adequate” recommendation from the Biopharmaceutics reviewer.
III. Administrative

A. Reviewer's Signature:

(See appended electronic signature page)

Danuta Gromek-Woods, Ph.D.

B. Endorsement Block:

(See appended electronic signature page)

Ali Al Hakim, Ph.D., Branch Chief, Branch 2, ONDQA

C. CC Block: entered electronically in DFS
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

DANUTA E GROMEK-WOODS
08/27/2014

JANICE T BROWN
08/27/2014
Janice Brown, MS for Ali Al-Hakim, Ph.D.
FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 205353/000
Org: 161
Priority: 1
Stamp Date: 24-MAR-2014
PDUFA Date: 24-NOV-2014
Action Goal: 
District Goal: 24-JUL-2014

Sponsor: NOVARTIS PHARMS CORP
1 HEALTH PLAZA BLDG 339 RM 1113
EAST HANOVER, NJ 079361080

Brand Name: PANOBINOSTAT (LBH589)

Generic Name: 

Product Number; Dosage Form; Ingredient; Strengths
001; CAPSULE; PANOBINOSTAT HYDRATE; 10MG
002; CAPSULE; PANOBINOSTAT HYDRATE; 15MG
003; CAPSULE; PANOBINOSTAT HYDRATE; 20MG

FDA Contacts: D. GROMEK-WOODS Prod Qual Reviewer 3017961217
E. PFEILER Micro Reviewer (HF-22) 3017960642
T. AGOSTO Product Quality PM 2404023777
D. HANNER Regulatory Project Mgr (HFD-006) 3017964058

Overall Recommendation: ACCEPTABLE on 11-SEP-2014 by R. MOORE () 2404029988
PENDING on 08-APR-2014 by EES_PROD

Establishment: CFN: 9617362 FEI: 3002910506
NOVARTIS FARMACEUTICA SA
RONDA SANTA MARIA 158
BARBERA DE VALLES, BARCELONA, BARCELONA, SPAIN

DMF No: AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER
FINISHED DOSAGE STABILITY TESTER

Profile: CAPSULES, PROMPT RELEASE

OAI Status: NONE

Last Milestone: OC RECOMMENDATION
Milestone Date: 11-SEP-2014
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Reference ID: 3709088
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