CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

219876Orig1s000

PRODUCT QUALITY REVIEW(S)

Title:	NDA IQA Template Title Page- EXEC SUMMARY
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Template Revision: 03

Office of Pharmaceutical Quality

New Drug Application (NDA)
Integrated Quality Assessment Template

NDA Executive Summary

1. Application/Product Information

NDA Number	219876		
Applicant Name	CHIMERIX INC		
Drug Product Name	Dordaviprone		
Dosage Form	Capsule		
Proposed Strength(s)	125 mg		
NDA Classification	Type 1 - NME		
Route of Administration	Oral		
Maximum Daily Dose	625 mg		
Rx/OTC Dispensed	Rx		
Proposed Indication	(b) (4)		
Drug Product Description	supplied as white, opaque, hard capsules printed with “DDP” and “125” on the body and “CMRX” on the cap of the capsule. Each capsule contains 125 mg dordaviprone (equivalent to 148.8 mg dordaviprone dihydrochloride salt).		
Co-packaged product information	N/A		
Device information	N/A		
Storage Temperature/ Conditions	Store at 20°C to 25°C (68°F to 77°F); excursions permitted from 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Siva Mandadapu	Haripada Sarker
	Drug Product/ Labeling	Nan Yang	Xing Wang

			David Claffey (labeling)
	Manufacturing	Quamrul Majumder	Christine Falabella
	Biopharmaceutics	Rushikesh Sable	Anitha Govada
	Microbiology	Quamrul Majumder	Christine Falabella
	Other (specify)	None	
	RBPM	Janell Artis	
	ATL	Xing Wang	
Consults	None		

2. Final Overall Recommendation - Approval

3. Action Letter Information

a. Expiration Dating: An expiration dating period of 36 months may be granted when stored at the proposed storage conditions.

b. Additional Comments for Action

The following post-marketing commitment (PMC) will be issued to the applicant: Include a test and acceptance criterion for the (b) (4) in the drug product specifications at release and during stability studies.

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

The applicant has provided sufficient information to assure the identity, strength, purity, and quality of the proposed drug product. All associated manufacturing, testing, packaging facilities were deemed acceptable based on prior inspection history. The agency agrees with the applicant's proposal to continue performing (b) (4) testing on all three process validation batches on stability and at batch release for future commercial batches to establish an appropriate (b) (4) specification. A post-marketing commitment (PMC) will be issued. Based on the OPQ review team's evaluation of the information provided in the submission, OPQ recommends APPROVAL of NDA 219876 for dordaviprone capsules, for oral use.

b. Is the overall recommendation in agreement with the individual discipline recommendations? Yes

Recommendation by Subdiscipline:

Drug Substance	**-**	**Adequate**
Drug Product	**-**	**Adequate**
Quality Labeling	**-**	**Adequate**
Manufacturing	**-**	**Adequate**
Biopharmaceutics	**-**	**Adequate**
Microbiology	**-**	**Adequate**

Environmental Assessment: Categorical Exclusion - Adequate
QPA for EA(s): No

5. **Life-Cycle Considerations**

Established Conditions per ICH Q12: No
Comments: None

Comparability Protocols (PACMP): No
Comments:

Additional Lifecycle Comments: YES
The following post-marketing commitment (PMC) will be issued to the applicant: Include a test and acceptance criterion for the (b) (4) **in the drug product specifications at release and during stability studies.**

Refer to DP review for detail.

Application Technical Lead Name and Date:

Xing Wang *06/25/2025*

Xing Wang

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CHAPTER III: ENVIRONMENTAL

For more details about the items in this template, please see Chapter III (Environmental) of the NDA IQA Guide (OPQ-ALL-WI-0006)

R REGIONAL INFORMATION

Environmental

In accordance with 21 CFR 25.31(a), Chimerix, Inc. claims a categorical exclusion from the requirement to prepare an Environmental Assessment as the amount of waste to be generated is expected to be small. To our knowledge, no extraordinary circumstances exist.

The expected introduction concentration (EIC) is as follows:

EIC-Aquatic (ppb) = (b) (4) kg/year x 1/1.214 x (b) (4) L/day x year/365 days x (b) (4) µg/kg
= (b) (4) µg/liter
= (b) (4) ppb

Since the estimated EIC is lower than 1 ppb, the categorical exclusion is requested.

Assessment: *Adequate*

Dordaviprone is indicated for the treatment of a rare form of glioma. The chemical waste generated from the drug product is expected to be small. As the estimated EIC is lower than 1 ppb, the Applicant's request for categorical exclusion of an environment assessment is granted.

Primary Environmental Assessor Name and Date:

Yang Nan, Ph.D.

Secondary Assessor Name and Date (and Secondary Summary, as needed):

Xing Wang, Ph.D.

Yang Nan

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Xing Wang

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CHAPTER IV: LABELING

For more details about the items in this template, please see Chapter IV (Labeling) of the NDA IQA Guide (OPQ-ALL-WI-0006)

NDA Number	219876
Assessment Cycle Number	1
Drug Product Name	MODEYSO (dordaviprone) capsules, 125 mg

Assessment Recommendation: Adequate

Item	Assessment Conclusion	SDN # where labeling is adequate ("N/A" otherwise)
Prescribing Information Labeling	Adequate	N/A At the time of closing this review, labeling of USPI is still ongoing.
Patient Information	Adequate	N/A
Instruction for Use (IFU)	Adequate	N/A
Container Labels	Adequate	N/A
Carton Labeling	Adequate	N/A

Brief Description of Outstanding Issues: None

Submissions being reviewed:

Document Reviewed (eCTD #, SDN #)	Date Received	Information Provided
1	12/18/2024	Original
25	04/24/2025	Updated patient package insert
35	06/16/2025	Updated carton and container labeling
36	06/25/2025	Updated carton and container labeling

1.0 PRESCRIBING INFORMATION[1]

Assessment of Product Quality Related Aspects of the Prescribing Information:

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Refer to the original draft of the USPI for details.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Product Title in Highlights[2] [21 CFR 201.57(a)(2)]		
Established name(s)[3]	Adequate	
Route(s) of administration	Adequate	
Controlled drug substance symbol (if applicable)	N/A	
Initial U.S. Approval [§201.57(a)(3)]	Adequate	
Dosage Forms and Strengths Heading in Highlights [§ 201.57(a)(8)]		
Dosage form(s)[4] and strength(s) in metric system[5]	Adequate	
If the drug product contains an active ingredient that is a salt, clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride).[6]	Adequate	See the section 3 below.

[1] Labeling Review Tool (LRT) (March 2022), including use of consistent terminology for dosage form and unit of measure for strength in the product title and DOSAGE FORMS AND STRENGTHS heading in Highlights, in the DOSAGE AND ADMINISTRATION, DOSAGE FORMS AND STRENGTHS, DESCRIPTION, and HOW SUPPLIED/STORAGE AND HANDLING sections (see page 2 of LRT)

[2] Draft guidance: *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018)

[3] Established name = [Drug] [Route of Administration] [Dosage Form]. Do use not "USP" descriptor in the product title or within the Highlights (see page 3 of LRT).

[4] Draft guidance: *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018); USP <1151>; USP Nomenclature Guideline

[5] Labeling Review Tool (March 2022, page 13), include limited packaging information; USP <7>

[6] Guidance: *Naming of Drug Products Containing Salt Drug Substances* (June 2015); MAPP 5021.1

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."[7]	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.[8]	N/A	

Assessment: *Adequate*

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)[9]

Refer to the original draft of the USPI for details.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE AND ADMINISTRATION section		
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents and/or soft food[10], storage conditions needed to maintain	Adequate	

[7] Guidance: *Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation* (March 2013)
[8] Guidance: *Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use* (October 2018); USP <659>
[9] See § 201.57(c)(3); draft guidance: *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products — Content and Format* (January 2023); Labeling Review Tool (March 2022, page 25)
[10] Draft Guidance: Use of Liquids and/or Soft Foods as Vehicles for Drug Administration: General Considerations for Selection and In Vitro Methods for Product Quality Assessments

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
the stability of the reconstituted or diluted product).		
Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food).	Adequate	
For parenteral products: include statement: *"Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."*[11]	N/A	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.[12] Note the labeling requirement may be applicable to another section of the PI (e.g., Section 11).	N/A	
For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s) who administer the drug	N/A	
For hazardous products, include the statement *"DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.*[x]*"* with x numerical citation to "OSHA Hazardous Drugs."	N/A	

Assessment: *Adequate*

[11] §201.57(c)(3)(iv)
[12] USP General Notices 2.30 Legal Recognition

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)[13]

The original proposed text is: "TRADENAME is supplied as white, opaque, hard capsules printed with "DDP" and "125" on the body and "CMRX" on the cap of the capsule. Each capsule contains 125 mg dordaviprone (equivalent to 148.8 mg dordaviprone dihydrochloride salt)."

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Adequate	
Strength(s) in metric system	Adequate	
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride). No equivalency statement.	Adequate	The original text is not acceptable as (b) (4) (b) (4) This section is recommended to the following: Capsules: 125 mg, white, opaque, hard capsules printed with "DDP" and "125" on the body and "CMRX" on the cap of the capsule. Each capsule contains 125 mg dordaviprone. The adequacy of this section is pending Applicant's accepting the revision as recommended.
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable.	Adequate	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and	N/A	

[13] See § 201.57(c)(4); Labeling Review Tool (March 2022, page 29)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
imaging bulk package (see USP <659>).		

Assessment: *Adequate*

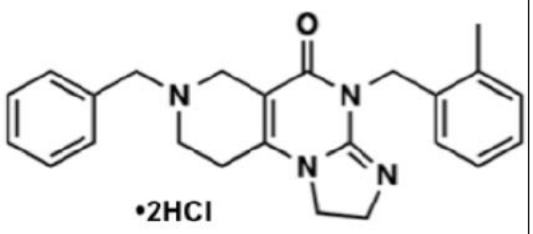
1.2.3 Section 11 (DESCRIPTION)[14]

Refer to the original draft of the USPI for details.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DESCRIPTION section		
Proprietary and established name(s)[15] [§ 201.57(c)(12)(i)(A)].	Adequate	
Dosage form(s) and route(s) of administration [§ 201.57(c)(12)(i)(B)].	Adequate	
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per Salt Guidance and MAPP. For example: "TRADENAME contains 100 mg of drug-x (equivalent to 123.7 mg of drug-x hydrochloride)" [§ 201.57(c)(12)(i)(C)].	Adequate	The original proposed text is not acceptable. The Applicant includes information (b) (4) (b) (4) which is confusing. The established USAN for the drug substance is "dordaviprone hydrochloride" which is also listed in "FDA's Global Substance Registration System". To be consistent with USAN, the chemical name is recommended to use "dordaviprone hydrochloride" (b) (4) (b) (4) There is no salt equivalency statement. Also, there is no description of capsule shell and printing ink. This section is revised to:

[14] See § 201.57(c)(12); Labeling Review Tool (March 2022, page 56)

[15] Use of "USP" descriptor is not required to be included next to the established name throughout Prescribing Information (PI) labeling. If an applicant wants to use the "USP" descriptor next to the established name in the PI, recommend limiting its use to the product quality sections of the Full Prescribing Information (FPI) (i.e., DOSAGE FORMS AND STRENGTHS, DESCRIPTION, HOW SUPPLIED/STORAGE AND HANDLING) (see page 3 of LRT).

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
		Dordaviprone is present as dordaviprone hydrochloride whose formula for dordaviprone hydrochloride is $C_{24}H_{26}N_4O \cdot 2HCl$. The molecular weight is 459.41. The full chemical name for dordaviprone hydrochloride is 7-benzyl-4-(2-methylbenzyl)-1,2,6,7,8,9-hexahydroimidazo[1,2-*a*]pyrido[3,4-e]pyrimidin-5(4*H*)-one dihydrochloride. Dordaviprone hydrochloride has the following chemical structure:  Dordaviprone hydrochloride is a white to off-white solid that is freely soluble in water. The 1% solution of dordaviprone hydrochloride is measured as pH 3.3. TRADENAME (dordaviprone) capsules are supplied as 125 mg strength capsules in an immediate-release oral formulation. Each capsule contains 125 mg of dordaviprone (equivalent to 148.8 mg of dordaviprone hydrochloride). The inactive ingredients in the capsule include magnesium stearate, microcrystalline cellulose, and sodium starch glycolate. The capsule shell consists of hypromellose and titanium dioxide. The black printing ink contains alcohol, D&C yellow#10,

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
		FD&C blue #1, FD&C blue #2, FD&C red #40, ferrosoferric oxide, methyl alcohol, *N*-butyl alcohol, propylene glycol and shellac glaze (20% esterified).
List inactive ingredients (not required for oral use, except for colorant) by the USP/NF names in alphabetical order.[16] Avoid brand names. [§ 201.57(c)(12)(i)(C)].	Adequate	See above.
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)].	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol at 60 °F. (15.56 °C) [§ 201.10(d)(2)].	N/A	
Sterility statement (if applicable) [§ 201.57(c)(12)(i)(D)].	N/A	
Pharmacological/Therapeutic class[17] [§ 201.57(c)(12)(i)(E)].	Adequate	

[16] Per § 201.100(b)(5)(i) and (ii), flavoring and colorants may be designated as such without naming their components except for FD&C Yellow No 5 and FD&C Yellow No 6, which must be listed per § 201.20. Per § 201.100(b)(5)(iii), trace amounts of harmless substances added solely for individual product identification need not be named. If an applicant wants to use the National Formulary (NF) descriptor next to excipients, recommend limiting its use to the product quality sections of the FPI (see page 3 of LRT). Do not list brand names, e.g., Opadry, Eudragit, Polistirex, etc.

[17] Listed before "indicated for" in INDICATIONS AND USAGE of Highlights section [§ 201.57(a)(6)]; can also search the term "FDA EPC Text Phrases" in FDA's Labeling Resources for Human Prescription Drugs for the most recent EPC list.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Chemical name[18], structural formula, molecular weight [§ 201.57(c)(12)(i)(F)].	Adequate	See above.
If radioactive, statement of important nuclear characteristics [§ 201.57(c)(12)(i)(G)].	N/A	
Other important chemical or physical properties (such as pKa or pH) [201.57(c)(12)(ii)].	Adequate	See above.
For oral prescription drug products, include gluten statement[19] (if applicable).	N/A	
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity").	N/A	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled. Note the labeling requirement may be applicable to another section of the PI (e.g., Section 2).	N/A	

Assessment: *Adequate*

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)[20]

Refer to the original draft of the USPI for details.

[18] Chemical names do not need to be capitalized unless it appears at the beginning of a sentence (see *Preferred IUPAC Names Provisional Recommendation*, September 2004; Chapter 1, par. 16 Name writing, p.80-90).
[19] Draft guidance: *Gluten in Drug Products and Associated Labeling Recommendations* (December 2017)
[20] See § 201.57(c)(17); Labeling Review Tool (March 2022, page 70). Consider including proprietary name and established name.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s) [§ 201.57(c)(17)].	Adequate	
Strength(s) in metric system. [§ 201.57(c)(17)(i)] If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety. No equivalency statement.	Adequate	
Available units (e.g., bottles of 100 tablets) [§ 201.57(c)(17)(ii)].	Adequate	
Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s) [§ 201.57(c)(17)(iii)].	Adequate	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package (see USP <659>).	N/A	

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to "Dispense in original container," provide reason why (e.g., to protect from light or moisture, to maintain stability, etc.). For hazardous drugs, state "DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[x]" with x numerical citation to "OSHA Hazardous Drugs." [§ 201.57(c)(17)(iv)]	Adequate	For clarity, the "how supplied" section is revised to a tabular format containing the following components: Strength: 125 mg Description: White, opaque, hard capsules printed with "DDP" and "125" on the body and "CMRX" on the cap of the capsule Package configuration: Each bottle contains 10 capsules and desiccant with a child-resistant closure. NDC number: pending
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature. (see USP <659>).	Adequate	The storage condition is recommended to revise to:" Store at 20°C to 25°C (68°F to 77°F)."
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: *"Not made with natural rubber latex. Avoid statements such as "latex-free."*[21]	N/A	
Include information about child-resistant packaging[22] (if chosen by manufacturer).	Adequate	

Assessment: *Adequate*

[21] Guidance: *Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex* (December 2014)
[22] Guidance: *Child-Resistant Packaging Statements in Drug Product Labeling* (August 2019)

1.2.5 Other Sections of Labeling

N/A

1.2.6 Manufacturing Information After Section 17 (for drug products)[23]

Item	Item in Proposed Labeling (choose "Adequate" or "Inadequate")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Manufacturing Information After Section 17		
Name and location of business (street address, city, state, and zip code) of the manufacturer, distributor, and/or packer.	Adequate	

Assessment: *Adequate*

2.0 PATIENT LABELING

Assessment of Product Quality Related Aspects of Patient Labeling (e.g., Medication Guides, Instructions for Use, Patient Information):

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[24]	Adequate	
Special preparation instructions (if applicable).	Adequate	
Storage and handling information (if applicable).	Adequate	
If the product contains a desiccant, ensure the desiccant has a warning (e.g., "Do not eat.") and the size and shape of the desiccant differ from the dosage form.	Adequate	Verified.
Active ingredient(s) (if applicable).	Adequate	The active ingredient has been revised to dordaviprone hydrochloride (b) (4)
Alphabetical listing of inactive ingredients (if applicable).	Adequate	Revised.

[23] § 201.1(h)(5) and 201.1(i); Labeling Review Tool (March 2022, page 74)
[24] Established name = [Drug] [Route of Administration] [Dosage Form]

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer.	Adequate	

Assessment: *Adequate*

The provided Patient Information and IFU (Instruction for Use) have been reviewed. The identified deficiencies will be provided to the Applicant.

3.0 CONTAINER AND CARTON LABELING[25]

3.1 Container Labels[26] (updated as of 6/25/2025)

(b) (4)

[redacted]

[25] Carton and Container Labeling Resources

[26] Per § 201.10(h)(2)(i)(1), if the drug container is too small to bear all labeling information required by section 502(e)(1)(A)(ii) and (B) of the FD&C Act, the container label should bear: proprietary name, established name, lot number, the name of the manufacturer, packer, or distributor of the drug.

3.2 Carton Labeling (updated as of 6/25/205)

(b) (4)

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
Proprietary name and established name[27], (font size and prominence) [§ 201.10(g)(2)].	Adequate	Yes	Dosage form is missing. It is recommended to include "capsules" at the end of the nonproprietary name. The following information request was sent to the Applicant on June 23, 2025: Regarding the carton and container labeling for NDA 219876, dosage form is missing. We recommend inclusion of "capsules" at the end of the

[27] Established name = [Drug] [Route of Administration] [Dosage Form]

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
			nonproprietary name dordaviprone, so the product name and dosage form read: "MODEYSO (dordaviprone) capsules" on the carton and container labeling to be consistent with USPI. The Applicant accepted the recommendation on June 25, 2025.
Strength(s) in metric system [§ 201.100(b)(4) & 201.100(d)].[28]	Adequate	Yes	
Route(s) of administration, not required for oral use [§ 201.100(b)(3)].	Adequate	Yes	
If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP [§ 201.10(d)(1) & 201.100(b)(4), USP <1121>].	Adequate	No	The equivalency statement is included in the carton labeling. Due to limited space on the container label, there is no salt equivalency statement on the container label. This is acceptable.
Net contents (e.g., tablet count, volume of liquid) [§ 201.51(a)].[29]	Adequate	Yes	
"Rx only" displayed on the principal display [§ 201.100(b)(1)].	Adequate	Yes	

[28] Express as " XX mg per tablet" or "XX mg per capsule" for strength of professional samples of solid oral dosage form with small net quantities per container (e.g., 5 or less) or blister pack/carton. See Guidance: *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)

[29] § 201.51(h): A drug shall be exempt from compliance with the net quantity declaration required by this section if it is an ointment labeled "sample", "physician's sample", or a substantially similar statement and the contents of the package do not exceed 8 grams.

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
NDC (requested, but not required for all labels or labeling) [§ 201.2 & 207.35].	Adequate	Yes	
Lot number and expiration date [§ 201.18 & 201.17].	Adequate	Yes	
Storage conditions. If applicable, include a space on the carton labeling for the user to write the beyond-use-date (BUD).	Adequate	No	The initial storage temperature "Store temperature (b) (4) (b) (4) is not correct. It should be 20°C - 25°C (68°F to 77°F). The issue has been communicated to DMEPA. Due to limited space on the container label, there is no storage condition on the container label. This is acceptable
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package, and these products require a "Not for direct infusion" statement. (See USP <659>).	N/A	Choose an item.	
Name of all inactive ingredients, in alphabetical order [§ 201.10(a)] [except for oral drug per § 201.100(b)(5) or limited space per § 201.10(i)(2)].	Adequate	No	The Applicant included all the inactive ingredients in the capsule on the carton labeling (see SD#36). No names of inactive ingredients are on the container label, which is acceptable per CFR 201.100(b) .

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
For parenteral injectable dosage forms, include quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)].	N/A	Choose an item.	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol at 60 °F. (15.56 °C) [§ 201.10(d)(2)].	N/A	Choose an item.	
Linear Bar code [§ 201.25(c)(2)].[30]	Adequate	Yes	
Adequate directions for use: "Recommended Dosage: See Prescribing Information" [§ 201.5 & 201.55].	Adequate	No	Due to limited space on the container label, no direction for use is listed.
Name of manufacturer/distributor /packer [§ 201.1(a), 201.1(h)(5)].	Adequate	Yes	
"Keep out of reach of children" statement, optional for Rx, required for OTC [§ 201.66(c)(5)(x)].	N/A	Choose an item.	
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	N/A	Choose an item.	
No text on Ferrule and Cap overseal of a vial of injectable products unless a cautionary statement is required. (USP <7>).	N/A	Choose an item.	

[30] See § 201.25(b)(1)(i) for a list where bar code is not required, e.g., prescription drug samples, medical gases, radiopharmaceuticals, etc.

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	Choose an item.	
When a drug product differs from the relevant USP standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.[31]	N/A	Choose an item.	
And others if space is available.	Adequate	Yes	

Assessment of Carton Labels and Container Labeling: *Adequate*

4. OUTSTANDING ISSUES AND RECOMMENDATIONS

None. The USPI, carton and container labeling are adequate provided that the Applicant accepts all the above-mentioned recommendations.

[31] USP General Notices 3.20 Indicating Conformance

Primary Labeling Assessor Name and Date:

Yang Nan, Ph.D.

Secondary Assessor Name and Date (and Secondary Summary, as needed):

David Claffey, Ph.D.

Yang Nan

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David Claffey

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CHAPTER VI: BIOPHARMACEUTICS

NDA Number	NDA 219876
Assessment Cycle Number	1 (Original NDA)
Drug Product Name/ Strength	Dordaviprone Capsules 125 mg
Route of Administration	Oral
Applicant Name	Chimerix Inc.
Therapeutic Classification/ OND Division	Anti-Cancer Division of Oncology 2 (DO2)
Proposed Indication	For the treatment of H3 K27Mmutant diffuse glioma in adult and pediatric patients

Assessment Recommendation: Adequate.

Assessment Summary:
The Applicant Chimerix Inc. is seeking approval of NDA 219876 for Dordaviprone Capsules 125 mg under 505(b)(1) regulatory pathway. Dordaviprone exhibits the characteristics of a BCS-II (low solubility, high permeability) drug substance. The proposed drug product exhibit rapid dissolution across the physiologic pH range. Dissolution testing method was assessed at IND stage (IND136090 review).

Review Objective: The focus of the current Biopharmaceutics review is to assess the dissolution method, drug release specifications and bridging (if required) for the proposed drug product quality control (QC).

Recommendation: Based on the totality of data/information provided, the following dissolution testing method and acceptance criterion are approved for the QC of the proposed drug product at batch release and throughout stability program/shelf-life.

Final Dissolution Method and Acceptance Criterion:

Apparatus Type	Rotation Speed	Medium/ Volume	Temperature	Acceptance Criterion
USP apparatus I (Basket)	100 rpm	0.1N HCl / 500 mL	37.0 ± 0.5 °C	Q= (b)(4)% in 20 minutes

Bridging: Not required as the commercial formulation is identical to the clinical formulation.

Biowaiver: The Applicant has proposed only one strength (Dordaviprone Capsules 125 mg). Biowaiver is neither requested nor needed.

Overall recommendation: From a Biopharmaceutics perspective, NDA 219876 for Dordaviprone Capsules 125 mg is recommended for APPROVAL.

CQAs	Initial Risk Ranking	Comments	Updated Risk Ranking after Assessment Cycle #	Comments
Dissolution	Medium	Low Solubility (per BCS Criteria)	Low	Acceptable dissolution specifications

List Submissions Being Assessed (table):

Document(s) Assessed	Date Received
SN-1 (original NDA)	12/18/2024
SN-19 (Response to Biopharm IR)	03/28/2025

Concise Description of Outstanding Issues:

(None from the Biopharmaceutics perspective)

B.1 BCS DESIGNATION

The Applicant considers Dordaviprone as a BCS-II compound. Thus, there was no request to designate Dordaviprone Capsules 125 mg as a high solubility (BCS-1 or BCS-3) drug substance/drug product.

Assessment: Not applicable

Solubility: *Not High*
Based on the provided solubility data[1], the drug substance exhibits pH dependent solubility, specifically the data shows high solubility (>60mg/mL) in the pH range of 1 to 4.5, and the solubility drops significantly from pH 4.5 to 5 and then less dramatically from ~pH 5 to ~pH 6 and low solubility beyond pH 6.0. Overall, the proposed drug product strength 125 mg is completely soluble in 250 mL between range pH 1.0 to pH 5.0.

[1] \\CDSESUB1\EVSPROD\nda219876\0001\m3\32-body-data\32s-drug-sub\dordaviprone-all\32s1-gen-info\general-properties.pdf

Saturation solubility of Dordaviprone (37 °C)

pH	Solubility (mg/mL)
1.0	62.2
4.0	92.1
4.5	98.6
5.0	6.02
6.0	0.26
6.8	0.062
7.8	0.065

Dordaviprone exists as a di-hydrochloride salt and is a variable hydrate. The desired and controlled morphic form for drug product manufacturing is (b) (4)

(b) (4)

Permeability: The results of *in vitro* Caco-2 bidirectional studies displayed high permeability in both A to B and B to A direction. The study also showed that Dordaviprone is not a substrate of efflux transporters in Caco-2 cells.

Dissolution: The proposed drug product exhibits rapid dissolution in the physiological pH range (b) (4)

[2] \\CDSESUB1\EVSPROD\nda219876\0001\m3\32-body-data\32p-drug-prod\dordaviprone-capsule-all\32p5-contr-drug-prod\32p56-justif-spec\justification-of-specifications.pdf

B.2 DISSOLUTION METHOD AND ACCEPTANCE CRITERIA

Assessment: *Adequate.*

Dissolution Method:

At IND stage (IND136090[3]), the Applicant originally proposed the following quality control dissolution method and acceptance criterion for Dordaviprone Capsules, 125 mg:

(b) (4)

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Upon review of the dissolution method development information and data submitted on 10/19/2023 and 6/19/2024, FDA recommended, and the Applicant subsequently accepted, the QC dissolution method [USP Apparatus I (Basket) 40 mesh, 100 rpm, 500 mL of 0.1 N HCl, 37.0 ± 0.5°C] for Dordaviprone Capsules, 125 mg. Refer to the FDA Advice Communication as described in the review of IND 136090 amendment.

Dissolution Acceptance Criteria:

The Applicant initially proposed an acceptance criterion of "Q= (b)(4)% in (b)(4) minutes" for the drug product release and stability specifications. However, based upon dissolution profiles of pivotal batches, this proposed dissolution acceptance criterion found to be too permissive and therefore not acceptable. Consequently, a data-driven acceptance criterion of "Q = (b)(4)% in (b)(4) minutes" was recommended in the Information Request[5] (IR) issued on 03/06/2025.

Subsequently, the Applicant requested a modification to widen the acceptance criterion from "Q = (b)(4)% in (b)(4) minutes" to "Q = (b)(4)% in 20 minutes." This request was made (b)(4) (b)(4) (b)(4) Based on the review of totality the data/information submitted, the revised criterion was found to be acceptable.

Based on the overall dissolution method development data and the clinical data provided, the following dissolution method and acceptance criterion is approved for the QC of the proposed drug product at batch release and stability specifications:

Final Approved Dissolution Method Acceptance Criterion:

Apparatus Type	Rotation Speed	Medium/ Volume	Temperature	Acceptance Criterion
USP apparatus I (Basket)	100 rpm	0.1N HCl / 500 mL	37.0 ± 0.5 °C	Q= (b)(4)% in 20 minutes

Stability Testing:

In accelerated stability testing for some drug product registration batches, a (b)(4) was observed. The Applicant conducted a separate *in-vivo* bioequivalence / bioavailability study and claimed that (b)(4) are bioequivalent (which will be reviewed by Office of Clinical Pharmacology) and will have minimal impact on bioavailability of the Dordaviprone. The Applicant submitted dissolution data for the batches (b)(4) of Dordaviprone which found to be comparable which mitigates the risk to low.

[5] \\CDSESUB1\EVSPROD\nda219876\0010\m1\us\111-information-amendment\quality-information-amendment-cmc-march-2025.pdf

B.12 BRIDGING OF FORMULATIONS

Not Applicable. The proposed commercial drug product will have the same formulation and manufacturing process/site/batch size/controls/supply chain as the registration/primary stability lots.

B. 13 BIOWAIVER REQUEST

Assessment: *Not Applicable*

There is only one strength (125 mg) proposed for marketing, and this strength was evaluated in the pivotal clinical trial (as well as in registration/stability studies).

R. REGIONAL INFORMATION

Comparability Protocols

None

Post-Approval Commitments

None

Lifecycle Management Considerations

The drug substance Dordaviprone demonstrates pH-dependent solubility; however, the proposed drug product, Dordaviprone Capsules 125 mg, exhibits rapid dissolution across the physiological pH range. While the drug substance has a propensity (b) (4) the Applicant has asserted that this presents a low risk. To support this claim, the Applicant has provided bioequivalence data and comparable dissolution profiles for batches containing (b) (4) These data serve to mitigate the potential risk associated with (b) (4) changes to a low level.

BIOPHARMACEUTICS LIST OF DEFICIENCIES

None

Primary Biopharmaceutics Assessor's Name and Date:
Rushikesh Sable, Ph.D. 05/15/2025

Secondary Assessor Name and Date (and Secondary Summary, as needed):
Anitha Govada, Ph.D. 05/16/2025

Appendix

Biopharmaceutics Information Request[6] (3/20/2025)

1. Based on the dissolution data submitted, on 12/18/2024 in SDN 001, the dissolution method using Apparatus: USP-I (Basket), 100rpm, 500 mL of 0.1N HCl at 37 ± 0.5oC is acceptable for quality control testing of the proposed drug product. However, based on totality of dissolution data/information submitted, a tighter acceptance criterion of Q = (b) (4) % at (b) (4) minutes is recommended for batch release and stability testing of proposed drug product Dordaviprone Capsules, 125 mg.

2. Implement the revised dissolution acceptance criterion and update the drug product's specifications for batch release and stability testing and other relevant sections of your NDA accordingly. Note that the setting of the dissolution acceptance criteria is based on (b) (4) (b) (4) Please note that all batches should meet the revised dissolution acceptance criterion throughout the stability program. If any dissolution failures occur on stability these should be reported to the agency. Discuss any corrective actions to avert such dissolution failures if needed.

Applicant's Response: Based on the comparative dissolution data of the drug product batches (b) (4) the Applicant requested a modification to widen the acceptance criterion from "Q = (b) (4) % in (b) (4) minutes" to "Q = (b) (4) % in 20 minutes." This request made (b) (4) (b) (4) (b) (4)

Reviewer assessment: Based on the review of totality of the data/information submitted, the revised acceptance criterion was found to be acceptable.

[6] \\CDSESUB1\EVSPROD\nda219876\0019\m1\us\111-information-amendment\quality-information-amendment-cmc-march-2025.pdf

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Xing Wang

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/s/

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