

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

220295Orig1s000

PRODUCT QUALITY REVIEW(S)



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

NDA Executive Summary

1. Application/Product Information

NDA Number	220295
Applicant Name	GlaxoSmithKline, LLC
Drug Product Name	LYNAVOY (linerixibat) tablets
Dosage Form	Tablet
Proposed Strength(s)	40 mg
NDA Classification	Type 1 - NME
Route of Administration	Oral
Maximum Daily Dose	80 milligrams
Rx/OTC Dispensed	Rx
Proposed Indication	Treatment of cholestatic pruritis in adult patients with primary biliary cholangitis (PBC).
Drug Product Description	Purple biconvex film-coated round tablets containing 40.0 mg linerixibat; the tablets are debossed with “GS 3JG” on one side and are plain on the other side. GlaxoSmithKline (GSK) submitted this 505(b)(1) NDA for an immediate-release linerixibat tablet to treat cholestatic pruritis in adult patients with primary biliary cholangitis. Linerixibat (a bile acid transporter inhibitor) is a New Molecular Entity (NME). The NDA 220295 drug product is an immediate-release solid oral tablet containing 40 mg of linerixibat (as the neutral moiety); the other components of the tablets are compendial (microcrystalline cellulose, croscarmellose sodium, and magnesium stearate in the tablet core) and a film coat comprised of (b) (4). (b) (4) Each tablet has a mass of 230 mg. The drug product is stable through 36 months at USP controlled room temperature (25°C); the expiry was based on provision of 24 months of acceptable long-

	term ICH stability data, 6 months of acceptable accelerated ICH stability data, and extrapolation.		
Co-packaged product information	N/A		
Device information	N/A		
Storage Temperature/ Conditions	25°C (USP Controlled Room Temperature, CRT)		
Review Team	Discipline	Primary	Secondary
	<i>Drug Substance</i>	Sam Bain	Lawrence Perez
	<i>Drug Product/ Labeling</i>	Kaining Zhi	David Lewis
	<i>Manufacturing</i>	Miral Patel	Shu-Wei Yang
	<i>Biopharmaceutics</i>	Kalpana Paudel	Tapash Ghosh
	<i>Microbiology</i>	N/A	N/A
	<i>Office of quality surveillance</i>	Nyrma Cruz Ruiz	Mary Manibusan
	<i>RBPM</i>	Stephanie Ngan	
	<i>ATL</i>	David Lewis	
Consults	OQS (office of quality surveillance) Pharmaceutical Quality System (PQS)		

2. Final Overall Recommendation - Approval

3. Action Letter Information

a. Expiration Dating: 36 months at room temperature

b. Additional Comments for Action

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

The applicant for this 505(b)(1) NDA provided sufficient CMC information to ensure the identity, strength, purity, and quality of the drug substance (linerixibat) and the drug product, LYNAVOY (linerixibat) 40 mg tablets. OPMA has approved the facilities involved in the manufacture and control of the drug substance and drug product. The labeling, including the prescribing information (PI) and container label, was found to be adequate. The applicant's

request for a categorical exclusion from the preparation of an environmental assessment has been found valid; therefore, the request for categorical exclusion has been granted.

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 - N/A

Environmental Assessment: Categorical Exclusion - Adequate
QPA for EA(s): Yes

5. Life-Cycle Considerations

Established Conditions per ICH Q12: Yes

Comments:

Adequate per OPQA III's recommendation for the drug substance.
Adequate per OPMA's recommendation for the drug product facility and processing.

Comparability Protocols (PACMP): Yes

Comments:

Adequate per OPMA and OPQA III's recommendation.

Additional Lifecycle Comments:

None.

Application Technical Lead Name and Date: Rishi Thakur 02/23/2026 (signing for Dr. David B. Lewis)



Rishi
Thakur

Digitally signed by Rishi Thakur

Date: 2/24/2026 03:31:32PM

GUID: 5407887b000a1c7a2c99827ec2cd922d

Comments: Signing for Dr. David B. Lewis

62 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page



Title:	NDA IQA Template CHAPTER IV-LABELING
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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	<u>220295</u>
Assessment Cycle Number	<u>1</u>
Drug Product Name	<u>LYNAVOY (linerixibat)</u>

Assessment Recommendation: Choose an item.

Item	Assessment Conclusion	SDN # where labeling is adequate (“N/A” otherwise)
Prescribing Information Labeling	Adequate	1
Patient Information	Adequate	1
Instruction for Use (IFU)	N/A	N/A
Container Labels	Adequate	1
Carton Labeling	Adequate	1

Brief Description of Outstanding Issues:

- N/A

Submissions being reviewed:

Document Reviewed (eCTD #, SDN #)	Date Received	Information Provided
S/N 0001; SDN 01	03/24/2025	Prescribing Information Labeling (including Patient Information) Container Labels
S/N 0040; SDN 40	02/03/2026	Prescribing Information Labeling (including Patient Information) Container Labels
S/N 0043; SDN 43	02/20/2026	Prescribing Information Labeling (including Patient Information)

1.0 PRESCRIBING INFORMATION¹

Assessment of Product Quality Related Aspects of the Prescribing Information:

This assessment includes submissions S/N 0001, 0040, and 0043.

¹ [Labeling Review Tool \(LRT\) \(September 2025\)](#), 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)

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION



Item	Item in Proposed Labeling	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)	
Product Title in Highlights² [21 CFR 201.57(a)(2)]			
Established name(s) ³	Adequate	Must include proprietary name in UPPERCASE letters	"LYNAVOY" - properly in uppercase
		Must include nonproprietary name in parentheses	"(linerixibat)" - properly in parentheses
		Must include dosage form	"tablets" included
		All text in product title must be bolded	Product title appears to be bolded in formatting
		Proprietary name should be UPPERCASE, rest should be lowercase	"LYNAVOY (linerixibat) tablets, for oral use" - proper case formatting

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).

Item	Item in Proposed Labeling	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)	
		with limited exceptions	
		Should avoid abbreviations in product title	No abbreviations used (e.g., uses "hydrochloride" not "HCl")
Route(s) of administration	Adequate	Must include route of administration as "for [ROA] use" when ROA does not precede dosage form	"for oral use" - properly formatted
Controlled drug substance symbol (if applicable)	N/A	Controlled substance symbol must be included if applicable, preceded by comma	Not applicable - linerixibat is not a controlled substance
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	"40 mg" in metric system	
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	N/A	Linerixibat is not a salt.	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored." ⁷	N/A	Tablet is not scored.	
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	N/A	Product is oral dosage form.	

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

⁷ Guidance: [Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation \(March 2013\)](#)

Item	Item in Proposed Labeling	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)	
pharmacy bulk package and imaging bulk package. ⁸			

Assessment: *Adequate*

Per labeling review tool (updated in September 2025), the Highlights section is acceptable from CMC's perspective.

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>

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)⁹



Item	Item in Proposed Labeling	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 the stability of the reconstituted or diluted product).	N/A	No special instructions.	
Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food).	Adequate	Must include recommended dosage information including dose, dosing frequency, and duration	"40 mg orally twice daily. Swallow tablets whole at least 30 minutes before any food or beverage (other than water)"

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	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)	
		Must include administration instructions relative to food for orally administered drugs	
		Should include missed dose instructions when adequate information available	"If a dose is missed, take the missed dose as soon as possible and at least 30 minutes before your next meal, then resume the original dosing schedule. If a dose is missed by more than 6 hours, skip the dose and resume the original dosing schedule. Do not take a double dose to make up for a missed dose."
		Must include dosage modifications for drug interactions	" (b) (4) at least 4 hours before or 4 hours after taking a bile acid binding resin"
		Should use metric system and avoid error-prone abbreviations	Uses "mg" appropriately, no error-prone abbreviations identified
For parenteral products: include statement: <i>"Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."</i> ¹¹	N/A	Oral dosage form, not parenteral product.	
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	N/A	No USP monograph.	

¹¹ §201.57(c)(3)(iv)

¹² USP General Notices 2.30 Legal Recognition

Item	Item in Proposed Labeling	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
requirement may be applicable to another section of the PI (e.g., Section 11).		
For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s) who administer the drug	N/A	Not a radio active product.
For hazardous products, include the statement “ <i>DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.</i> ” ^x with x numerical citation to “OSHA Hazardous Drugs.”	N/A	Not hazardous.

Assessment: Adequate

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)¹³

(b) (4)

Item	Item in Proposed Labeling	Assessor's Comments
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Adequate	"Tablets"
Strength(s) in metric system	Adequate	"40 mg"
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	Drug substance is not a salt.
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	"purple, biconvex, round, film-coated tablets debossed with 'GS 3JG' on one side"
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state “functionally scored.”	N/A	Tablet is not scored.

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

Item	Item in Proposed Labeling	Assessor's Comments
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 imaging bulk package (see USP <659>).	N/A	Product is oral dosage form, not injectable.

Assessment: *Adequate*

1.2.3 Section 11 (DESCRIPTION)¹⁴



(b) (4)

Item	Item in Proposed Labeling	Assessor's Comments
DESCRIPTION section		

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

Item	Item in Proposed Labeling	Assessor's Comments
Proprietary and established name(s) ¹⁵ [§ 201.57(c)(12)(i)(A)].	Adequate	"LYNAVOY" and "limerixibat"
Dosage form(s) and route(s) of administration [§ 201.57(c)(12)(i)(B)].	Adequate	"tablet" and "for oral administration"
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)].	N/A	Drug substance is not a salt.
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	"croscarmellose sodium, magnesium stearate and microcrystalline cellulose" - alphabetical order maintained. "film-coating contains black iron oxide, hypromellose, polyethylene glycol, red iron oxide, and titanium dioxide." - alphabetical order maintained.
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	Oral dosage form, not injectable.
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	Alcohol is not present.

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).

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.

Item	Item in Proposed Labeling	Assessor's Comments
Sterility statement (if applicable) [§ 201.57(c)(12)(i)(D)].	N/A	Drug product is not sterile.
Pharmacological/Therapeutic class ¹⁷ [§ 201.57(c)(12)(i)(E)].	Adequate	"IBAT inhibitor"
Chemical name ¹⁸ , structural formula, molecular weight [§ 201.57(c)(12)(i)(F)].	Adequate	Chemical name: "3-((((3R,5R)-3-butyl-3-ethyl-7-methoxy-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydrobenzo[f][1,4]thiazepin-8-yl)methyl)amino)pentanedioic acid"; Molecular formula: C ₂₈ H ₃₈ N ₂ O ₇ S; Molecular weight: 546.68 g/mol; Structural formula referenced.
If radioactive, statement of important nuclear characteristics [§ 201.57(c)(12)(i)(G)].	N/A	Not radioactive.
Other important chemical or physical properties (such as pKa or pH) [201.57(c)(12)(ii)].	Adequate	"white to off-white solid. Its solubility in aqueous solutions is pH-dependent and varies from very slightly to slightly soluble"
For oral prescription drug products, include gluten statement ¹⁹ (if applicable).	N/A	Gluten was not used in excipients.
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity").	Adequate	No statement found.
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	No USP monograph available.

Assessment: *Adequate*

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.

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 \(December 2017\)](#)

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



(b) (4)

Item	Item in Proposed Labeling	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	"tablets, 40 mg" described
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	"40 mg"
Available units (e.g., bottles of 100 tablets) [§ 201.57(c)(17)(ii)].	Adequate	"bottles of 60 tablets"
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	"purple, biconvex, round, film-coated tablets debossed with 'GS 3JG' on one side" and "NDC 0173-0938-18"
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."	N/A	Tablet is not scored.

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	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
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	Oral dosage form, not injectable.
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	"Store in the original package to protect from moisture. Keep the bottle tightly closed."
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature. (see USP <659>).	Adequate	"Store at 20°C to 25°C (68°F to 77°F); excursions are permitted between 15°C to 30°C (59°F to 86°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: " <i>Not made with natural rubber latex. Avoid statements such as "latex-free."</i> " ²¹	N/A	Drug product does not have latex in product itself or container closure systems. Applicant did not elect to include a statement.
Include information about child-resistant packaging ²² (if chosen by manufacturer).	Adequate	"white high density polyethylene (HDPE) bottles with polypropylene child-resistant closures and a polyethylene faced induction heat seal liner containing a HDPE canister with silica gel desiccant"

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)

Assessment: *Adequate*

1.2.5 Other Sections of Labeling

No other quality information found in other sections.

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	“Manufactured for  GlaxoSmithKline Durham, NC 27701 ©2026 GSK group of companies or its licensor.” Missing street address information.

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	“LYNAVOY [LIN-ah-voy]

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)
		(linerixibat) tablets, for oral use”
Special preparation instructions (if applicable).	Adequate	No special preparation instructions.
Storage and handling information (if applicable).	Adequate	"Store LYNAVOY at room temperature between 20° to 25°C (68° to 77°F), in the original package to protect from moisture. Keep the bottle tightly closed."
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	“Do not remove or swallow the desiccant canister (b) (4).”
Active ingredient(s) (if applicable).	Adequate	“What are the ingredients in LYNAVOY?”
Alphabetical listing of inactive ingredients (if applicable).	Adequate	Active ingredients: linerixibat 40 mg Inactive ingredients: croscarmellose sodium, magnesium stearate and microcrystalline cellulose. Tablet film-coating: black iron oxide, hypromellose, polyethylene glycol, red iron oxide, and titanium dioxide.”
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer.	Adequate	Manufactured for: GlaxoSmithKline, Durham, NC 27701

Assessment: Adequate

3.0 CONTAINER AND CARTON LABELING²⁵

3.1 Container Labels²⁶

Label for commercial packaging:

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.

Item	Item in Proposed Carton Labeling	Assessor's Comments about Container Labels and Carton Labeling
Proprietary name and established name ²⁷ , (font size and prominence) [§ 201.10(g)(2)].	Adequate	Lynavoy (linerixibat) Tablets for oral use.
Strength(s) in metric system [§ 201.100(b)(4) & 201.100(d)]. ²⁸	Adequate	40 mg
Route(s) of administration, not required for oral use [§ 201.100(b)(3)].	N/A	
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>].	N/A	Active ingredient is not a salt.
Net contents (e.g., tablet count, volume of liquid) [§ 201.51(a)]. ²⁹	Adequate	60 tablets for commercial packaging. (b) (4) tablets for sample.
"Rx only" displayed on the principal display [§ 201.100(b)(1)].	Adequate	"Rx only" is visible.
NDC (requested, but not required for all labels or labeling) [§ 201.2 & 207.35].	Adequate	NDC 0173-0938-18 for commercial packaging. NDC 0173-0938-63 for sample packaging.
Lot number and expiration date [§ 201.18 & 201.17].	Adequate	Room for lot number and expiration date is reserved in the right hand side with dark background.
Storage conditions. If applicable, include a space on the carton labeling for the user to write the beyond-use-date (BUD).	Adequate	"Store at 20°C to 25°C (68°F to 77°F); excursions are permitted between 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]."
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	N/A	Not injectable.

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

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	Assessor's Comments about Container Labels and Carton Labeling
a "Not for direct infusion" statement. (See USP <659>).		
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)].	N/A	Oral drug exception.
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	Not parenteral.
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	No alcohol included.
Linear Bar code [§ 201.25(c)(2)]. ³⁰	Adequate	Barcode is provided for commercial packaging, blank for sample packaging.
Adequate directions for use: "Recommended Dosage: See Prescribing Information" [§ 201.5 & 201.55].	Adequate	See prescribing information for dosage information.
Name of manufacturer/distributor /packer [§ 201.1(a), 201.1(h)(5)].	Adequate	Mfd. for: GSK, Durham, NC 27701
"Keep out of reach of children" statement, optional for Rx, required for OTC [§ 201.66(c)(5)(x)].	N/A	Not required for Rx drug.
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	N/A	No Medication Guide.
No text on Ferrule and Cap overseal of a vial of injectable products unless a cautionary statement is required. (USP <7>).	N/A	Not injectable.
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	No USP monograph.
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	No USP monograph.
And others if space is available.	N/A	

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.

³¹ USP General Notices 3.20 Indicating Conformance

Assessment of Carton Labels and Container Labeling: *Adequate*

4. OUTSTANDING ISSUES AND RECOMMENDATIONS

None.

Primary Labeling Assessor Name and Date: Kaining Zhi, 02/23/2026

Secondary Assessor Name and Date (and Secondary Summary, as needed): Rishi Thakur, 02/23/2026 (in proxy of David B. Lewis).



Kaining
Zhi

Digitally signed by Kaining Zhi
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Rishi
Thakur

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BIOPHARMACEUTICS

Product Background:

NDA: NDA-220295-ORIG-1

Drug Product Name / Strength: Linerixibat (GSK2330672) Tablet 40 mg

Route of Administration: Oral

Applicant Name: GlaxoSmithKline LLC (GSK)

Submission:

GlaxoSmithKline LLC (GSK) has submitted NDA 220295 for the approval of linerixibat tablet 40 mg for the treatment of cholestatic pruritus in adult patients with Primary Biliary Cholangitis (PBC). Linerixibat (GSK2330672) is a potent and selective small molecule that reversibly inhibits the IBAT. Linerixibat has been designed to have poor cellular permeability, complete dissolution at relevant GI pHs, chemical stability within the GI contents to facilitate interaction with its target at the brush border of enterocytes and to be minimally absorbed from the GI tract with minimal systemic exposure. Linerixibat has negligible metabolism and no major human-specific metabolites. Absolute oral BA is 0.05% and plasma concentrations were often BLQ in clinical studies. Due to its minimal absorption leading to minimal systemic exposure, and target site of action, linerixibat plasma concentrations are neither required nor relevant to its efficacy.

The intended commercial linerixibat dose is 40 mg taken BID approximately 30 minutes before food or beverage (other than water) (b) (4) to ensure that the drug reaches the target site in the ileum for optimal efficacy prior to the surge of bile into the GI lumen as a result of gall bladder contraction in response to eating.

Review Recommendation: Adequate

Review Summary:

The Biopharmaceutics review is focused on the evaluation of dissolution method and acceptance criterion for linerixibat tablet and bridging between the pivotal clinical trial and to-be-marketed formulation.

Dissolution Method and Acceptance Criterion: Adequate

The following dissolution method and acceptance criterion are approved for the release of linerixibat from oral tablet:

USP Apparatus	Speed (RPMs)	Medium/Temperature	Volume (mL)	Acceptance criterion
II (Paddle)	65	Sodium Acetate pH 3.7 + 0.1% CTAB)/37°C ± 0.5°C	900	NLT (b) (4)% (Q) in 30 minutes

The applicant provided sufficient scientific rationale for the selection of the proposed dissolution method parameters, demonstrating that the method is appropriately designed for the intended purpose. The dissolution method exhibits sensitivity to critical quality attributes, specifically to (b) (4) (b) (4) particle size variations and the effects of (b) (4) during stability storage conditions. Given that packaging operations can influence dissolution performance as a critical quality attribute during stability studies, a comprehensive control strategy has been implemented that includes the (b) (4) and rigorous in-process control monitoring (b) (4).

The dissolution method demonstrated excellent robustness across all evaluated parameters. The comprehensive Design of Experiments study confirmed that deliberate variations in buffer molarity, paddle rotation speed, buffer pH, CTAB concentration, and dissolution medium volume had no practically significant impact on method performance, with all results meeting the stringent (b) (4) acceptance criteria and RSD values below 6%, thereby validating the method's suitability for routine quality control testing.

The Applicant noted that there are no Critical Bioavailability Attributes (CBAs) due to linerixibat's mode of action and unique properties. It is designed for oral delivery as rapidly disintegrating immediate release tablet, highly soluble at relevant GI pHs, exhibits minimal absorption from GI tract, all released drug available in GI tract, reaches site of action in lower ileum. Thus, while the dissolution method is discriminative for relevant parameters, the unique properties of linerixibat mean dissolution is not a critical bioavailability factor, and the acceptance criteria are appropriately set for quality assurance rather than bioavailability concerns.

Overall, the proposed dissolution method is suitable for quality control purposes in both release and stability testing of linerixibat tablets. The proposed dissolution acceptance criterion of *Not less than* (b) (4)% (Q) dissolved in 30 minutes for linerixibat tablets is acceptable based on the dissolution profile data submitted.

Bridging of Formulations: Adequate

The commercial product formulation is identical to the Phase 3 clinical study tablet formulation, with the sole difference being the debossing. Therefore, no bridging studies are required. The dissolution profiles for all clinical and registration batches demonstrate similarity.

Biowaiver Request: Not applicable

Only one strength (40 mg) of the drug product is proposed in the application.

List of Submissions reviewed:

Application 220295 - Sequence 0001/Multiple Categories/Subcategories

Application 220295 - Sequence 0024/IR response- July 08, 2025

Application 220295 - Sequence 0028/IR response-10/10/2025

Highlight Key Outstanding Issues from Last Cycle: None. This is the first review cycle.

Concise Description of Outstanding Issues Remaining: None. Please refer to Appendix for the deficiencies conveyed to the Applicant in the current review cycle.

Conclusion: From Biopharmaceutics perspective, NDA 220295 for Linerixibat tablet 40 mg is recommended for APPROVAL.

BCS Designation

Reviewer's Assessment: Adequate

The Applicant has not claimed or requested any BCS classification for their drug product in the current submission. The Applicant stated that linerixibat is a BCS Class 4 drug (low permeability/solubility minima at pH 3.7). However, linerixibat is highly soluble at relevant gastro-intestinal (GI) pHs and exhibits minimal absorption from the GI tract. High solubility at relevant gastrointestinal pHs ensures that complete dissolution occurs before reaching the target site in the ileum of the small intestine. Given that linerixibat was designed to act locally in the ileum with minimal systemic absorption, it exhibits intermittently measurable plasma concentrations that result in high inter-participant variability in both plasma exposure (AUC) and maximum concentration (C_{max}), which is typical for minimally absorbed drugs. Consistent with its design for local gastrointestinal activity, linerixibat demonstrates an exceedingly low absolute oral bioavailability of approximately 0.05%.

In humans, pHs close to 3.7 are only transiently experienced in the upper small intestine (duodenum), with most drug dissolution for an immediate release product occurring at lower pHs in the stomach or at higher pHs in the jejunum and ileum. Since the site of action for linerixibat is the ileum, there is sufficient time in a high solubility environment (either in the stomach at lower pH or in the intestine at higher pH than 3.7) for drug dissolution to occur during gastrointestinal transit prior to reaching the target site. Consequently, drug concentrations at the target site will be insensitive to minor changes in dissolution rate. Nevertheless, to account for any perceived risks generally associated with a BCS Class 4 drug, employing a dissolution method at the lowest solubility—specifically, the pH profile where sensitivity to drug product parameters is greatest—offers the highest level of assurance that batches meeting specification will perform similarly in vivo.

Linerixibat is designed to be gut restricted through minimal systemic absorption, which enables local action in the lower ileum. The low permeability of linerixibat is demonstrated by the very low fraction absorbed and extremely low oral bioavailability reported in human mass balance study 205895, a summary of which is provided in Module 2.7.1, Summary of Biopharmaceutics Studies, Section 2.1.1.

Although linerixibat has good solubility across most of the physiological range, it has solubility that is marginally lower than that required to be classified as good solubility by BCS at its pH solubility minimum (pH (b) (4)). Linerixibat is therefore classified as a BCS Class 4 (low solubility/low permeability) locally acting drug.

Drug Product

The composition of the drug product is provided below.

Table 1: Composition of Linerixibat Tablets, 40 mg

Component	Quantity mg/tablet	Function	Reference to Standard ¹
Linerixibat	40.0	Active	GSK
Microcrystalline Cellulose	(b) (4)	(b) (4)	USP/NF, Ph. Eur., JP
Croscarmellose Sodium			USP/NF, Ph. Eur., JP
Magnesium Stearate			USP/NF, Ph. Eur., JP
Core Unit Dose			-
(b) (4)	(b) (4)	(b) (4)	USP/NF, Ph. Eur., JP, ChP
Total Unit Dose	229.8	-	-

Notes:

1. Details of the specification of the active ingredient are provided in S.4.1. Specification. Details of the specifications of the excipients are provided in P.4.1. Control of Excipients
2. (b) (4)
3. (b) (4)
4. (b) (4)

Dissolution Method and Acceptance Criterion

Reviewer’s Assessment: Adequate

The Biopharmaceutics review is focused on the evaluation of dissolution method and acceptance criterion for linerixibat tablets.

Proposed dissolution method and acceptance criterion

The following dissolution methods and acceptance criteria were initially proposed:

Table 2: Dissolution method for linerixibat tablets

USP Apparatus	Speed (RPMs)	Medium/Temperature	Volume (mL)	Acceptance criterion
II (Paddle)	65	Sodium Acetate pH 3.7 + 0.1% CTAB)/37°C ± 0.5°C	900	NLT (b) (4)% (Q) in 30 minutes

Dissolution method development

(b) (4)

Discriminating ability of the dissolution method

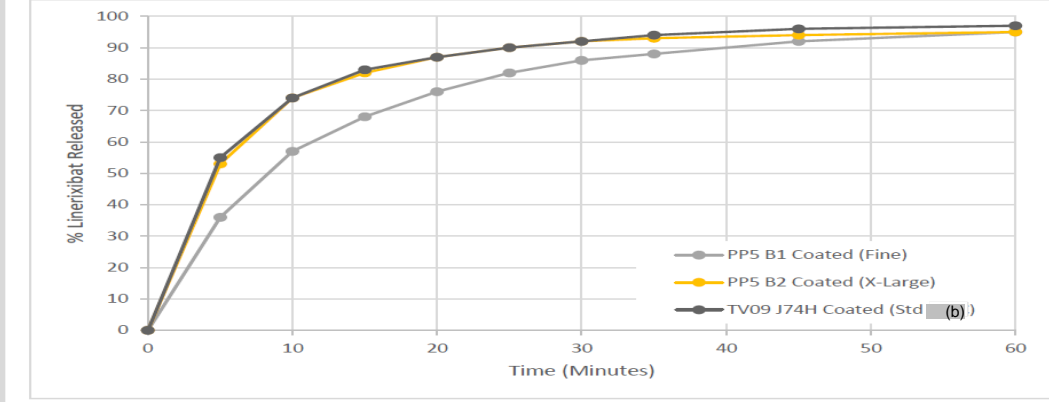
The final method was validated for its ability to discriminate against critical parameters as follows:

(b) (4) particle size:

The specification for particle size distribution (PSD) (b) (4) used in linerixibat tablets, 40 mg establishes an X50 specification range of (b) (4) microns. To assess the impact of (b) (4) particle size on dissolution performance, tablets were manufactured using two batches of (b) (4) that fell outside the standard particle size range: one batch containing extra-large particles (PSD X50 = (b) (4) μm) and another batch with fine particles (PSD X50 = (b) (4) μm). The resulting dissolution profiles are presented in the figure below. The mean dissolution profiles from batches manufactured with extra-large and standard particle size (b) (4) demonstrated similar release characteristics; however, the batch produced using fine particle size (b) (4) exhibited a notably slower dissolution rate. While both tested batches met the proposed dissolution specification, the batch formulated with fine particle size (b) (4) would have necessitated stage 2 testing. This reviewer's calculation of the similarity factor (f_2) using the initial 5 time points (up to 25 minutes when one batch

reaches $\geq 85\%$) yielded a value of ≤ 50 (b) (4), indicating that the dissolution profiles are not similar. This data demonstrates that the proposed dissolution method discriminates for variations in (b) (4) particle size. Further, (b) (4) particle size distribution is controlled to an approved supplier specification, in line with USP/NF monograph requirements.

Figure 10: Comparison of Batches Prepared with Differing (b) (4) Particle Size



(b) (4)

Figure 11: Dissolution Profile of Linerixibat Tablets, 40 mg (b) (4)

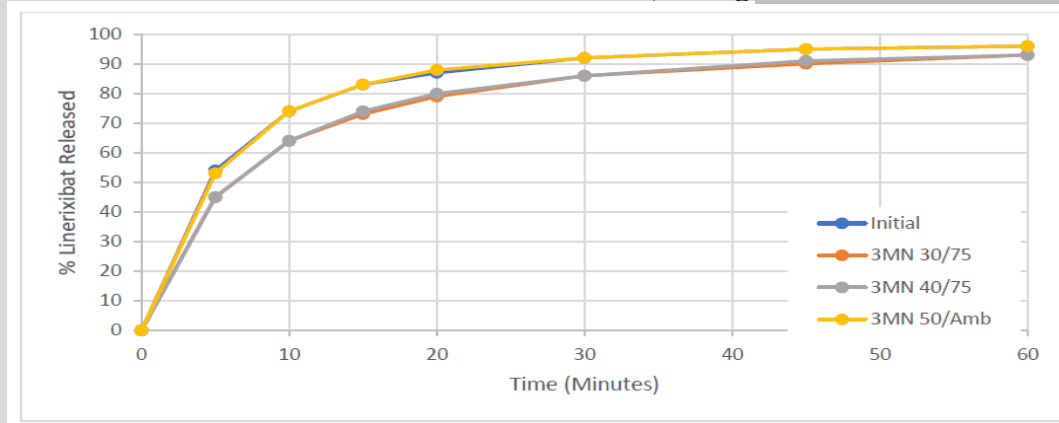


Table 5: (b) (4) on Linerixibat Tablets, 40 mg (b) (4)

Condition	Initial	3 months 30°C/75%RH	3 months 40°C/75%RH	3 months 50°C/AmbH
(b) (4)				

In response to an information request, the Applicant submitted individual dissolution data and similarity testing results (f2 values) for the study. The f2 values were >50, indicating that the profiles are considered statistically equivalent to the initial profile; however, clear visual differences between dissolution profiles were observed despite this statistical equivalence, with higher (b) (4) resulting in slower dissolution rates. The Applicant acknowledged that (b) (4) fall outside their established control strategy and are mitigated through (b) (4) (b) (4). Additionally, the Applicant noted that the conditions under which discrimination was observed are systematically eliminated through their comprehensive product control strategy, ensuring that (b) (4) dissolution changes do not occur under normal storage conditions.

The FDA requested an explanation for the behaviors observed in the discriminating ability data, where batches manufactured with fine particle size (b) (4) or (b) (4) demonstrated slower dissolution profiles. The Applicant provided detailed scientific rationale for both effects. For (b) (4) particle size, variations can alter tablet disintegration behavior, (b) (4) (b) (4), leading to longer disintegration times and delayed dissolution rates. Regarding (b) (4) effects, (b) (4) results in longer disintegration times and slower dissolution (b) (4) (b) (4), both contributing to extended disintegration times and subsequently slower drug release.

Critical Bioavailability Attributes (CBAs)

In response to an IR, the Applicant noted that there are no CBAs due to linerixibat's mode of action and unique properties:

- o Designed for oral delivery as rapidly disintegrating immediate release tablet
- o Highly soluble at relevant GI pHs
- o Exhibits minimal absorption from GI tract
- o All released drug available in GI tract, reaches site of action in lower ileum
- o No need for targeted release formulation

Thus, while the dissolution method is discriminative for relevant parameters, the unique properties of linerixibat mean dissolution is not a critical bioavailability factor, and the acceptance criteria are appropriately set for quality assurance rather than bioavailability concerns.

Control Strategy and Quality Assurance

The Applicant's control strategy identifies that only the (b) (4) affects dissolution as a Critical Quality Attribute (CQA) on stability, which is controlled through (b) (4) (b) (4) and in-process control of (b) (4). Other typical process parameters

and attributes with potential dissolution impact were systematically assessed using Quality by Design (QbD) principles, demonstrating no or minimal impact, including (b) (4), tablet hardness, (b) (4) (b) (4) coat weight gain, and drug substance particle size distribution. For drug substance particle size distribution, no relationship was identified between linerixibat particle size and drug product performance or manufacturability, and per ICH Q6A (b) (4), particle size is not considered a CQA. Therefore, no specification limits or acceptance criteria are required for particle size control. Regarding solid state form, (b) (4) is the most (b) (4) stable form selected for linerixibat drug substance, while (b) (4) can form (b) (4) (b) (4) in commercial batches. (b) (4) demonstrates similar properties to (b) (4) and remains stable under storage conditions, and following ICH Q6A (b) (4), solid state form is not considered a CQA based on (b) (4) stability, similar properties (b) (4), linerixibat's local mode of action, and acceptable drug product performance with batches containing up to (b) (4). Similarly, manufacturing controls systematically remove variability through (b) (4) excipient specifications and in-process controls, with comprehensive batch release processes ensuring compliance with registered specifications.

Dissolution method validation: Robustness and Ruggedness

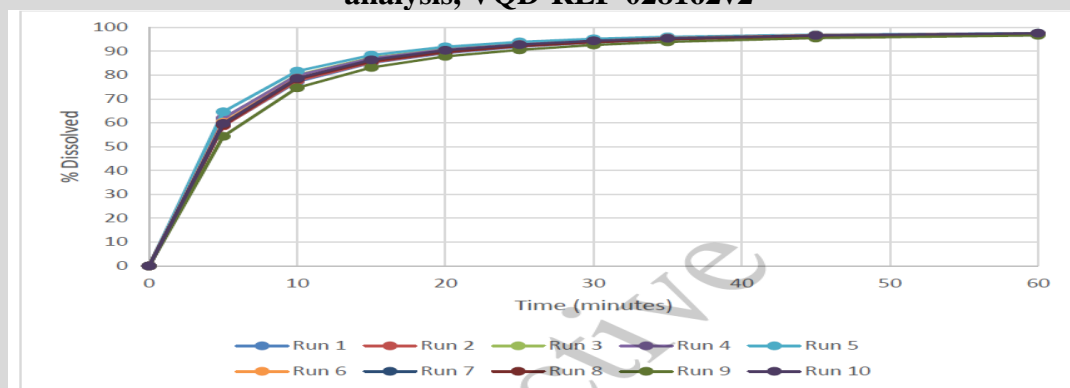
In response to an IR, the Applicant submitted dissolution method validation report including robustness, and ruggedness of the proposed dissolution method as summarized below.

The dissolution robustness study evaluated method VQD-OPS-068018 for determining linerixibat release by dissolution in pH 3.7 media with 0.1% CTAB using offline HPLC detection. This comprehensive robustness assessment was conducted using a Design of Experiments (DoE) approach on a fully automated ATF platform that has been transferred to (b) (4) for registration stability testing. The study examined five critical factors identified as having the highest risk potential. These parameters included buffer molarity (tested from (b) (4) mM), rotation speed ((b) (4) RPM), buffer pH ((b) (4)), CTAB amount ((b) (4) %), and dissolution medium volume ((b) (4) mL).

The experimental design consisted of 8 fractional factorial runs plus 2 center points, totaling 10 runs with 12 replicates each. All testing was performed using linerixibat 40 mg tablets from batch SJ8X, which was manufactured using target processing parameters and is representative of the final commercial product. The acceptance criteria required that differences in means of drug release remain within $\pm 5\%$ of standard conditions, with RSD for sample preparations at the 30-minute timepoint not exceeding 6%.

The dissolution method demonstrated excellent ruggedness across all tested analytical parameters. The method remained robust (Figure 12) when subjected to deliberate variations in five critical factors as mentioned above: buffer molarity, paddle rotation speed, buffer pH, CTAB concentration, and dissolution medium volume. Statistical analysis confirmed that no significant factor effects were observed at the 5% level for any response except at the early 5-minute timepoint, which was attributed to inherent early-timepoint variability rather than method weakness. The method consistently met acceptance criteria with factor effects well within the $\pm 5\%$ limit and RSD values below 6% at all critical timepoints. Buffer pH was identified as the most influential parameter but remained within acceptable limits, confirming that the existing method controls are sufficient to maintain analytical performance under normal operational variations.

Figure 12: The Mean Dissolution profiles for the 10 runs performed for statistical analysis, VQD-REF-028162v2



The ruggedness of the dissolution method was demonstrated through evaluation of intermediate precision, reproducibility, and analytical procedure equivalence as per USP <1092>, rather than through a separate dedicated ruggedness study as shown below.

HPLC Method

The intermediate precision was evaluated using two different analysts working on different days with different equipment sets. Both analysts achieved mean dissolution values of 91-92% at the 30-minute specification timepoint with RSDs of 1.7% and 2.8% respectively. The 90% confidence interval for the difference between analysts (b) (4) was completely contained within the predetermined acceptance criteria of (b) (4), demonstrating acceptable intermediate precision.

A comprehensive reproducibility study was conducted across two different laboratories using four different analysts, each testing twelve replicate samples. The study included different HPLC systems and dissolution baths at each site. All analysts achieved mean dissolution values between 93-94% with excellent RSDs ranging from 0.8% to 1.5%. The statistical analysis using Two One-Sided Tests (TOST) confirmed that the 90% confidence interval for mean differences was within the (b) (4) acceptance criteria, demonstrating successful reproducibility across laboratories and analysts.

UV Method

The UV method was evaluated using two analysts working on different days with different equipment sets. Both analysts achieved identical mean dissolution values of 92% at the 30-minute timepoint with RSDs of 1.7% and 1.8% respectively. The 90% confidence interval for the difference between analysts (b) (4) was well within the (b) (4) acceptance criteria, confirming acceptable intermediate precision for the UV detection method.

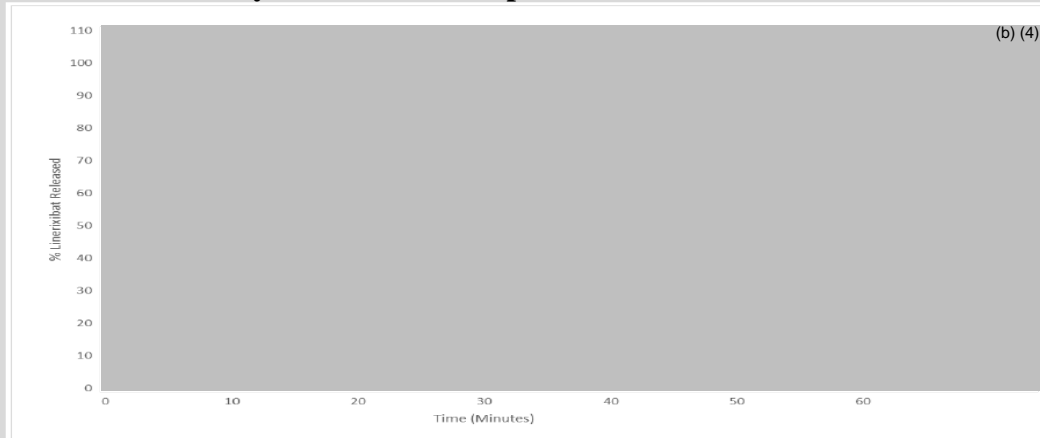
Both methods demonstrated excellent precision and reproducibility, with all results meeting the stringent acceptance criteria and showing minimal variability across different analysts, equipment, and laboratory conditions.

Dissolution acceptance criterion

The Applicant has proposed dissolution acceptance criterion of *Not less than* (b) (4)% (*Q*) dissolved in 30 minutes for linerixibat tablets. Dissolution profiles (Figure 13) of pivotal clinical batches and registration/stability batches using the validated method demonstrates consistent performance that

supports this specification. The individual dissolution data provided in response to the information request (detailed in the Appendix) shows minimal variability across dissolution profiles, indicating robust and reproducible tablet performance. The proposed dissolution acceptance criterion for linerixibat tablets is acceptable.

Figure 13: Dissolution Profiles for Linerixibat Release from Linerixibat Tablets, 40 mg-Clinical and Stability batches with Proposed Commercial Formulation and Process



Bridging of Formulations

Reviewer's Assessment: Adequate

Initial formulation development:

During the initial formulation development phase, early clinical studies utilized oral solution formulations with linerixibat concentrations ranging from 0.06 to 2.0 mg/g or mg/mL. The development program subsequently transitioned to solid dosage forms, specifically immediate-release tablets containing 10 mg and 45 mg of linerixibat that were manufactured using (b) (4) technology.

Bridging between Phase 2 and Phase 3 formulations:

A 40 mg tablet formulation was developed for Phase 3 clinical studies based on the 45 mg formulation used in Phase 2, with several minor modifications to optimize manufacturability and dosing. The tablet core weight was adjusted to achieve the target 40 mg strength, while the linerixibat (b) (4) to improve manufacturing processes. To compensate for the (b) (4) quantity, the amount of (b) (4) was correspondingly adjusted. Additionally, the (b) (4) (b) (4) to enhance manufacturability, and the coating was changed (b) (4) (b) (4).

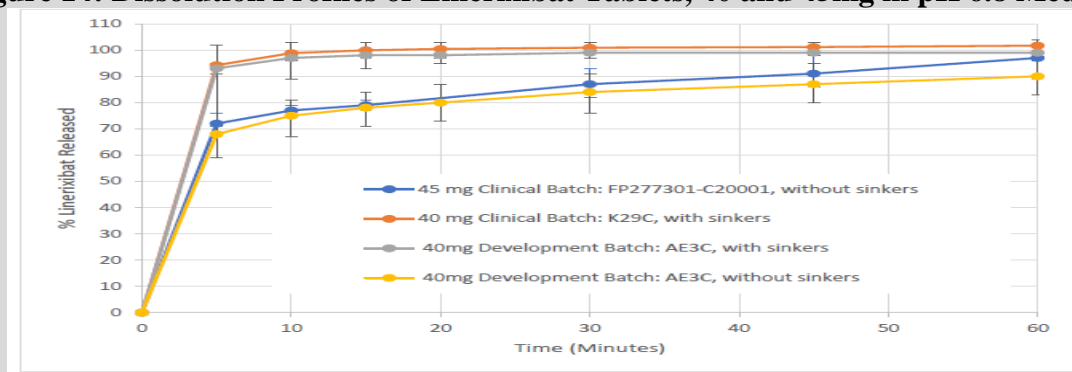
In the Summary Biopharm (2.7.1) document, the Applicant provided dissolution profile generated on a Phase 3 clinical batch (40 mg) and stated that data are not shown for the Phase 2 tablet formations (45 mg), as these are not used to support any efficacy claims, which was discussed in the CMC End of Phase 2 briefing package [FDA reference 4778138 and confirmed in IND 130391, Seq

0084; SN 0081]. However, the applicant stated that dissolution profiles of Phase 3 linerixibat tablets were comparable to earlier formulations but did not provide comparative data to support this claim. When requested to provide multi-point comparative dissolution profiles using the proposed commercial method for both the 40 mg Phase 3 tablets and the earlier 45 mg tablets, the applicant clarified that both formulations had been tested using a pH 6.8 dissolution methodology that was employed during early clinical development stages, as this pH was considered most physiologically relevant for the locally acting drug in the lower ileum. 45 mg tablets were never tested using the proposed commercial dissolution method.

The comparative dissolution testing revealed some methodological differences between the 40 mg and 45 mg tablet evaluations. The 40 mg tablets were tested using pH 6.8 medium at 50 rpm paddle speed with tripod sinkers, while the 45 mg tablets were tested under the same conditions but without tripod sinkers. (b) (4)

(b) (4) To bridge this methodological gap, the applicant used a development batch (AE3C) of 40 mg tablets that was tested both with and without sinkers. The results (Figure 14) demonstrated that the 40 mg development batch without sinkers showed comparable dissolution profiles to the clinical 45 mg tablets, while the same batch with sinkers was comparable to clinical 40 mg tablets. Based on this bridging study, the dissolution profiles of the clinical 40 mg and 45 mg tablets were considered comparable, supporting the formulation transition from Phase 2 to Phase 3 studies.

Figure 14: Dissolution Profiles of Linerixibat Tablets, 40 and 45mg in pH 6.8 Medium



Note: error bars represent minimum and maximum values

Bridging between Phase 3 and commercial formulations:

The to-be-marketed commercial formulation is essentially identical to the Phase 3 clinical study tablet formulation, with the only difference being the addition of debossing for product identification. The commercial linerixibat tablets are manufactured as 40 mg purple film-coated round tablets featuring 'GS 3JG' debossed on one side while the other side remains plain. Since the formulation composition and manufacturing process remain unchanged between the Phase 3 clinical tablets and the commercial product, no formal bridging studies are required to demonstrate equivalence.

The dissolution profiles of all clinical and registration batches demonstrate similar performance characteristics as seen in Figure 13, providing additional confirmation of formulation consistency throughout development. Importantly, the pivotal Phase 3 Study 212620 (GLISTEN) and the majority of Phase 3 Study 212358 (LLSAT) were conducted with the to-be-marketed formulation further supporting the clinical foundation for the commercial product without requiring additional bridging studies.

Biowaiver Request

Reviewer's Assessment: Not applicable

Conclusions and recommendation

From Biopharmaceutics perspective, NDA 220295 for Linerixibat Tablet 40 mg is recommended for APPROVAL.

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Ghosh

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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

RISHI THAKUR
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