CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

218139Orig1s000

PRODUCT QUALITY REVIEW(S)

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Office of Pharmaceutical Quality

New Drug Application (NDA)
Integrated Quality Assessment Template

NDA Executive Summary

1. Application/Product Information

NDA Number	NDA 218139
Applicant Name	Novitium Pharma LLC
Drug Product Name	TEZRULY (terazosin) Oral Solution
Dosage Form	Solution
Proposed Strength(s)	1 mg/mL in a 150-mL bottle
NDA Classification	Type 3 - New Dosage Form and Type 5 – New Formulation or New Manufacturer
Route of Administration	Oral
Maximum Daily Dose	10 mg
Rx/OTC Dispensed	Rx
Proposed Indication	• The treatment of signs and symptoms of benign prostatic hyperplasia (BPH). • The treatment of hypertension alone or with other antihypertensive agents to lower blood pressure.
Drug Product Description	Novitium Pharma LLC has submitted this 505(b)(2) new drug application for TEZRULY® (terazosin) Oral Solution, 1 mg/mL intended for the treatment of signs and symptoms of benign prostatic hyperplasia (BPH) and the treatment of hypertension alone or with other antihypertensive agents to lower blood pressure. The active moiety terazosin has been approved as terazosin hydrochloride, the active ingredient of the drug product, Hytrin tablets under NDA 019057 on August 7, 1987. Since its first approval multiple generic drug products containing this active ingredient have been approved for marketing in the United States.

	TEZRULY® oral solution is a clear, cherry flavored solution, free from visible particulate matter. Each mL of contains 1 mg of terazosin supplied as 1.(b) (4) mg of terazosin hydrochloride as the active ingredient and artificial cherry flavor ((b) (4) citric acid anhydrous, glycerin, methylparaben, propylparaben, purified water, sodium citrate dihydrate, and sucralose as inactive ingredient. Inactive ingredients used in the composition of the drug product are all compendial materials and/or material previously used in approved oral drug products. The levels of the inactive ingredients are at or below the limit provided in the Agency's IID for oral products. TEZRULY® (terazosin) Oral Solution, 1 mg/mL is to be supplied in 150-mL HDPE bottle with a child-resistant (b) (4) closure that include a head induction foil laminate layer. This drug product should be stored at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) with currently granted expiration dating period of 24 months. The assigned expiration dating period is supported by the stability data submitted to the application.		
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 to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Sharon Kelly, Ph.D.	Lawrence Perez, Ph.D.
	Drug Product/ Labeling	Craig Bertha, Ph.D.	Nina Ni, Ph.D./Julia Pinto, Ph.D.
	Manufacturing	Khalid Khan, Ph.D.	Cassandra Abellard, Ph.D.
	Biopharmaceutics	N/A	N/A

	Microbiology	Paul Koushik, Ph.D.	Jesse Wells, Ph.D.
	Other (specify) Categorical Exclusion	Craig Bertha, Ph.D.	Nina Ni, Ph.D.
	RBPM	Stephanie Ngan, MPH	
	ATL	Hamid Shafiei, Ph.D.	
Consults	N/A		

2. Final Overall Recommendation - Approval

This application is recommended for approval from all OPQ review disciplines, and the final agreed labeling and container closure labels that have been communicated through the clinical team to the applicant and have been accepted. The revised labeling and container closure labels that reflect the recommended changes will be submitted to this application prior to PDUFA action date. Based on the acceptance by the applicant of recommended labeling/labels changes, the labeling review is now considered adequate although in the original labeling review chapter the PI labeling as well as container and carton labels were found as inadequate. Therefore, no additional labeling memorandum will be attached to the labeling review chapter.

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

- The applicant of this 505(b)(2) new drug application has provided sufficient CMC information to assure the identity, strength, purity, and quality of the drug substance, terazosin hydrochloride and the drug product, TEZRULY (terazosin) Oral Solution, 1 mg/mL.
- The Office of Pharmaceutical Manufacturing Assessment (OPMA) has made the overall recommendation of adequate for the facilities involved in this application.
- The CMC recommended changes to the labeling have been communicated to the Clinical Review Team and the proposed CMC revisions have been accepted.
- The applicant's request for categorical exclusion from the preparation of environmental assessment has been found adequate and is granted.

Therefore, this applicant is recommended for approval from the OPQ perspective with an expiration dating period of 24 months.

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): Yes

5. Life-Cycle Considerations

Established Conditions per ICH Q12: No
Comments:

Comparability Protocols (PACMP): No
Comments:

Additional Lifecycle Comments: None

Application Technical Lead Name:

Hamid Shafiei, Ph.D.
Senior Pharmaceutical Quality Assessor
DPQA VII/OPQA II/OPQ

Important: Do Not Change the Header or Footer

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	218139
Assessment Cycle Number	1
Drug Product Name	Terazosin oral solution

Assessment Recommendation: Choose an item.

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

Brief Description of Outstanding Issues:

Submissions being reviewed:

Document Reviewed (eCTD #, SDN #)	Date Received	Information Provided
eCTD 0001, SDN 1	9/29/2023	Original application with labeling

1.0 PRESCRIBING INFORMATION[1]

Assessment of Product Quality Related Aspects of the Prescribing Information:

[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)

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

(b) (4)

[redacted]

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	**Inadequate**	Revise [redacted] (b) (4) [redacted] " to "TEZRULY (terazosin) oral solution"
Controlled drug substance symbol (if applicable)	N/A	

[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 (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Initial U.S. Approval [§201.57(a)(3)]	**Inadequate**	Revise to "1993"
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]	**Inadequate**	Revise to: "Oral solution: 1 mg per mL of terazosin" **Note:** that the USP currently includes two drug product monographs for: Terazosin Tablets Terazosin Capsules
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: ***Inadequate.***

1. Revise the Product Title to "(b) (4) to "TEZRULY (terazosin) oral solution."

[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)
[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>

2. Revise Initial U.S. Approval to "1993."

3. Revise the DOSAGE FORMS AND STRENGTHS in HIGHLIGHTS to "Oral solution: 1 mg per mL of terazosin."

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)[9]

(b) (4)

[redacted]

[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)

(b) (4)

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 the stability of the reconstituted or diluted product).	N/A	

[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)
Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food).	Adequate	Section 2.3 is appropriately included and indicates that the formulation should be measured with the enclosed calibrated dosing syringe and that household teaspoons should not be used to measure the formulation for dosing.
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.***

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

[11] §201.57(c)(3)(iv)
[12] USP General Notices 2.30 Legal Recognition
[13] See § 201.57(c)(4); Labeling Review Tool (March 2022, page 29)

(b) (4)

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.	**Inadequate**	Revise to "1 mg terazosin per mL (b) (4) "
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 imaging bulk package (see USP <659>).	N/A	

Assessment: ***Inadequate.***

1. Revise the DOSAGE FORMS AND STRENGTHS section as follows: "TEZRULY oral solution is a clear, cherry flavored solution, free from visible particulate matter available as 1 mg terazosin (b) (4) ."

1.2.3 Section 11 (DESCRIPTION)[14]

(b) (4)

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)].	**Inadequate**	Revise the established name in the DESCRIPTION section to "TEZRULY (terazosin)."
Dosage form(s) and route(s) of administration [§ 201.57(c)(12)(i)(B)].	**Inadequate**	Revise the DESCRIPTION section to include the dosage form and route of administration: "TEZRULY (terazosin) oral solution is supplied in…."
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	**Inadequate**	Revise the DESCRIPTION section to include the equivalency statement as per the USP salt policy, i.e., "TEZRULY contains 1 mg/mL of terazosin (equivalent to 1.1 mg/mL of terazosin hydrochloride)."

[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)
of drug-x (equivalent to 123.7 mg of drug-x hydrochloride)" [§ 201.57(c)(12)(i)(C)].		
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)].	**Inadequate**	Revise the DESCRIPTION section to list citric acid anhydrous as "anhydrous citric acid."
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)].	Inadequate	(b) (4)

[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 (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
		(b) (4)
Sterility statement (if applicable) [§ 201.57(c)(12)(i)(D)].	N/A	
Pharmacological/Therapeutic class[17] [§ 201.57(c)(12)(i)(E)].	Adequate	
Chemical name[18], structural formula, molecular weight [§ 201.57(c)(12)(i)(F)].	Adequate	
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)].	**Inadequate**	Revise the DESCRIPTION section to specify the pH of the product formulation (target and/or range).
For oral prescription drug products, include gluten statement[19] (if applicable).	Adequate	(b) (4)
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	

[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)

Assessment: ***Inadequate.***

1. Revise the established name in the DESCRIPTION section to "TEZRULY (terazosin)."
2. Revise the DESCRIPTION section to include the dosage form and route of administration: "TEZRULY (terazosin) oral solution is supplied in…."
3. Revise the DESCRIPTION section to include the equivalency statement as per the USP salt policy, i.e., "TEZRULY contains 1 mg/mL of terazosin (equivalent to 1.1 mg/mL of terazosin hydrochloride)."
4. Revise the DESCRIPTION and PATIENT INSTRUCTIONS sections to list citric acid anhydrous as "anhydrous citric acid." Revise the alphabetical order accordingly.
5. Revise the DESCRIPTION section to specify the pH of the product formulation (target and/or range).
6. Revise the DESCRIPTION section to remove the parenthetical remark: (b) (4) "

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

(b) (4)

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	

[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)
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.	**Inadequate**	Revise the HOW SUPPLIED/STORAGE AND HANDLING section to include the equivalency statement as per the USP salt policy, i.e., "TEZRULY contains 1 mg/mL of terazosin (equivalent to 1.1 mg/mL of terazosin hydrochloride)."
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	
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	(b) (4) [redacted]

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)
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature. (see USP <659>).	Adequate	
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: ***Inadequate.***

1. Revise the HOW SUPPLIED/STORAGE AND HANDLING section to include the equivalency statement as per the USP salt policy, i.e., "TEZRULY contains 1 mg/mL of terazosin (equivalent to 1.1 mg/mL of terazosin hydrochloride)." Refer to the Agency guidance entitled *Naming of Drug Products Containing Salt Drug Substances* (June 2015), available at https://www.fda.gov/media/87247/download.

1.2.5 Other Sections of Labeling

There may be other sections of labeling that contain product-quality related information. For example, there are specific required/recommended warnings for certain inactive ingredients [e.g., aspartame, aluminum in large and small volume parenterals, sulfites, FD&C Yellow Number 5 (tartrazine), and benzyl alcohol]. Please notify the prescription drug review division if the product contains any of these inactive ingredients.

[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)

Please include your comments about other sections of labeling if they contain product quality information.

N/A for the NDA 218139 labeling.

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

(b) (4)

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.	**Inadequate**	Include the street address for the distributor in the labeling.

Assessment: ***Inadequate.***

1. Include the street address for the distributor in the labeling.

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).	**Inadequate**	Revise the PATIENT I (b) (4) to include storage instructions.
If the product contains a desiccant, ensure the desiccant has a warning (e.g., "Do not eat.") and the size and shape of	N/A	

[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)
the desiccant differ from the dosage form.		
Active ingredient(s) (if applicable).	Adequate	
Alphabetical listing of inactive ingredients (if applicable).	Adequate	Will need to be rearranged once citric acid anhydrous is changed to "anhydrous citric acid" to be consistent with the USP.
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer.	**Inadequate**	See deficiency comment above under the DESCRIPTION section evaluation.

Assessment: ***Inadequate.***

1. Revision the PATIENT (b) (4) to include storage instructions.

3.0 CONTAINER AND CARTON LABELING[25]

[25] Carton and Container Labeling Resources

1 Page(s) of Draft Labeling has been Withheld in Full as B4 (CCI/TS) immediately following this page

(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	

[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)
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>].	**Inadequate**	Yes	Revise the carton and container labels to include the equivalency statements as per the USP salt policy, i.e., TEZRULY contains 1 mg/mL of terazosin (equivalent to 1.1 mg/mL of terazosin hydrochloride).
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	
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	Yes	
For injectable drug products for parenteral administration, use appropriate package type	N/A	Choose an item.	

[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)
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>).			
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	Choose an item.	
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	Yes	
Name of manufacturer/distributor	Adequate	Yes	

[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)
/packer [§ 201.1(a), 201.1(h)(5)].			
"Keep out of reach of children" statement, optional for Rx, required for OTC [§ 201.66(c)(5)(x)].	Adequate	Yes	
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.	
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.	N/A	Choose an item.	

[31] USP General Notices 3.20 Indicating Conformance

Assessment of Carton Labels and Container Labeling: ***Inadequate.***

1. Revise the carton and container labels to include the equivalency statements as per the USP salt policy, i.e., TEZRULY contains 1 mg/mL of terazosin (equivalent to 1.1 mg/mL of terazosin hydrochloride). Refer to the Agency guidance entitled *Naming of Drug Products Containing Salt Drug Substances* (June 2015), available at https://www.fda.gov/media/87247/download.

4. OUTSTANDING ISSUES AND RECOMMENDATIONS

The following comments cover labeling deficiencies that need to be addressed by the applicant:

1. Revise the Product Title to "(b) (4)" to "TEZRULY (terazosin) oral solution."
2. Revise Initial U.S. Approval to "1993."
3. Revise the DOSAGE FORMS AND STRENGTHS in HIGHLIGHTS to "Oral solution: 1 mg per mL of terazosin."
4. Revise the DOSAGE FORMS AND STRENGTHS section as follows: "TEZRULY oral solution is a clear, cherry flavored solution, free from visible particulate matter available as 1 mg terazosin per mL (b) (4)."
5. Revise the established name in the DESCRIPTION section to "TEZRULY (terazosin)."
6. Revise the DESCRIPTION section to include the dosage form and route of administration: "TEZRULY (terazosin) oral solution is supplied in…."
7. Revise the DESCRIPTION section to remove the parenthetical remark: (b) (4)."
8. Revise the DESCRIPTION, HOW SUPPLIED/STORAGE AND HANDLING sections as well as the carton and container labels to include the equivalency statement as per the USP salt policy, i.e., "TEZRULY contains 1 mg/mL of terazosin (equivalent to 1.1 mg/mL of terazosin hydrochloride).")." Refer to the Agency guidance entitled *Naming of Drug Products Containing Salt Drug Substances* (June 2015), available at https://www.fda.gov/media/87247/download.
9. Revise the DESCRIPTION and PATIENT (b) (4) sections to list citric acid anhydrous as "anhydrous citric acid." Revise the alphabetical order accordingly.

10. Include the street address for the distributor in the labeling.

Primary Labeling Assessor Name and Date: Craig M. Bertha

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

Craig Bertha

Digitally signed by Craig Bertha
Date: 2/12/2024 12:50:35PM
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Julia Pinto

Digitally signed by Julia Pinto
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CHAPTER VII: MICROBIOLOGY

IQA ANDA Assessment Guide Reference

Product Information	Treatment of symptomatic benign prostatic hyperplasia (BPH), Treatment of hypertension can be used alone or in combination with other antihypertensive agents such as diuretics or beta-adrenergic blocking agents
NDA Number	218139
Assessment Cycle Number	MR01
Drug Product Name / Strength	Terazosin Oral Solution, 1 mg/mL
Route of Administration	Oral solution.
Applicant Name	Novitium Pharma LLC.
Method of Sterilization	Non-Sterile.

Assessment Recommendation: **Adequate**

Theme:

☒ N/A	☐ Depyrogenation Validation Data
☐ Product Sterility Assurance	☐ Product Release and/or Stability Specifications
☐ Media Fill Data	☐ Validation for Product Release and/or Stability Test Method
☐ Validation of Product Test	☐ Other (Requires Division Director Approval)
☐ Due to Consult	

Justification: *view justification statements found at:* **Justification Statements**

N/A
Other (Requires Division Director Approval) – *Assessor writes-in justification here if "other" selected as theme.*

Assessment Summary: (b) (4)

List Submissions Being Assessed (table):

Document(s) Assessed	Date Received
eCTD Seq #0001	09/29/2023

eCTD Seq #0005	01/26/2024

Highlight Key Issues from Last Cycle and Their Resolution: N/A

Remarks: The submission is **recommended** for approval on the basis of sterility assurance.

Concise Description of Outstanding Issues: None.

Supporting Documents: None.

Select Number of Approved Comparability Protocols: 0

P.1 Description of the Composition of the Drug Product

Description of the Composition of the Drug Product

(*32p1-description--composition.pdf)*

The Terazosin Oral Solution is a clear, cherry flavored solution, free from visible particulate matter, which is available as 1mg/ml in bottles of 150ml with child resistant closure. The composition of the drug product is provided below.

Item #	Ingredients	Functions	Amount Per Unit, mg /mL	%w/v	%w/w
1	Terazosin Hydrochloride, USP	Active	(b) (4)	0.11	0.11
2	Methylparaben, NF	(b) (4)			(b) (4)
3	Propylparaben, NF				
4	Glycerin, USP				
5	Sucralose, NF				
6	Citric acid anhydrous, USP				
7	Sodium citrate dihydrate, USP				
8	Artificial Cherry Flavor (b) (4)				
9	Purified water, USP				
					(b) (4)

Description of container closure system –

(*32p7-container-closure-summary.pdf)*

The container closure system for the drug product is provided in the below table:

Strength	Fill Volume	Packaging
Terazosin Oral Solution, 1 mg/mL	150 mL	(b) (4)

A complete description of the container/closure system including COA is provided in.P.7.

Reviewer's Assessment: Based on the above information the reviewer has concluded that the applicant has provided adequate description of the drug product composition and the packaging system to support the manufacturing process for the drug product.

Acceptable

P.2 Pharmaceutical Development

P.2.5 Microbiological Attributes:

(b) (4)

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Jesse Wells

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Koushik Paul

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