CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

218347Orig1s000

PRODUCT QUALITY REVIEW(S)

Office of Pharmaceutical Quality

New Drug Application (NDA) 218347
Integrated Quality Assessment

RECOMMENDATION

☒ Approval
☐ Approval with Post-Marketing Commitment
☐ Complete Response

NDA 218347
Assessment #1

Drug Product Name	Upadacitinib Oral Solution
Dosage Form	Oral solution
Strength	1.0 mg/mL
Route of Administration	oral
Rx/OTC Dispensed	Rx
Applicant	AbbVie, Inc.
US agent, if applicable	N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original (SD 1)	6/28/2023	All
Amendment (SD 2)	7/05/2023	Labeling
Amendment (SD 4)	7/14/2023	Labeling
Amendment (SD 6)	9/6/2023	Manufacturing/Microbiology
Amendment (SD 7)	9/15/2023	Drug Product
Amendment (SD 9)	11/8/2023	Drug Substance/Drug Product
Amendment (SD 10)	11/22/2023	Labeling
Amendment (SD 13)	12/20/2023	Drug Substance/Drug Product
Amendment (SD-16)	1/4/2024	Labeling
Amendment (SD 17)	1/5/2024	Manufacturing/Microbiology
Amendment (SD 18)	1/26/2024	Labeling
Amendment (SD 21)	2/9/2024	Labeling
Amendment (SD 23)	2/27/2024	Microbiology
Amendment (SD 24)	2/27/2024	Labeling

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessor	Secondary Assessor
Drug Substance	N/A	

Drug Product	Zhengfang Ge	Craig M. Bertha
Manufacturing	Pratibha Bhat	Shu-Wei Yang
Microbiology	Marijke Koppenol-Raab	Jesse Wells
Biopharmaceutics	N/A	
Regulatory Business Process Manager	Rajani Ranga/Stephanie Ngan	
Application Technical Lead	Craig M. Bertha	
ORA	Caryn McNab	
Laboratory (OTR)	N/A	
Environmental	N/A	

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Manufacturing

Microbiology

Labeling

QUALITY ASSESSMENT DATA SHEET

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	III		(b) (4)	Active	N/A	Sufficient information in NDA
	III			Active	N/A	Sufficient information in NDA
	III			Active	N/A	Sufficient information in NDA
	III			Active	N/A	Sufficient information in NDA

B. OTHER DOCUMENTS: *IND, RLD, RS, Approved NDA*

Document	Application Number	Description
IND	128180	Upadacitinib for atopic dermatitis, (b) (4)
IND	114717	Upadacitinib for rheumatoid arthritis (RA), psoriatic arthritis, axial spondyloarthritis, juvenile idiopathic arthritis, (b) (4)
IND	121783	Upadacitinib for Crohn's disease
IND	128249	Upadacitinib for ulcerative colitis
IND	(b) (4)	(b) (4)
IND	(b) (4)	
NDA	211675	Adults and pediatric patients 12 years of age and older with refractory, moderate to severe atopic dermatitis; Adults with: moderately to severely active rheumatoid arthritis, psoriatic arthritis, moderately to severely active ulcerative colitis, moderately to severely active Crohn's disease, active ankylosing spondylitis, active non-radiographic axial spondyloarthritis with objective signs of inflammation

2. CONSULTS

Discipline	Status	Recommendation	Date	Assessor
Biostatistics	N/A			
Pharmacology/Toxicology	N/A			

CDRH	N/A			
Clinical	N/A			
Other				

EXECUTIVE SUMMARY

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

N/A – All deficiencies have been resolved[1], thus, the application is recommended for approval.

II. SUMMARY OF QUALITY ASSESSMENTS

A. Product Overview

The drug product upadacitinib oral solution is to be used for treatment of pediatric patients with juvenile idiopathic arthritis. The route of administration (RoA) is oral and the drug product includes a bottle adaptor and oral dosing syringe. The drug substance information is provided by reference to previously approved application NDA 211675. The drug product is (b) (4) contains sodium benzoate (b) (4) as well as sucralose as a (b) (4) Twelve months of stability data are provided and a **shelf-life of 24 months is granted.**

Proposed Indication(s) including Intended Patient Population	Juvenile idiopathic arthritis (JIA) for patients 2 years and older
Duration of Treatment	Chronic
Maximum Daily Dose	12 mg
Alternative Methods of Administration	N/A

B. Quality Assessment Overview

Drug Substance: N/A

Note: All drug substance (API) information is provided by cross-reference to approved NDA 211675. No API review team was assigned.

Drug Product : Adequate

The combination product (drug/device) is a multidose oral solution (180 mL target fill) containing upadacitinib 1 mg/mL in a 200 mL HDPE bottle fitted with a child-resistant (b) (4) cap, (b) (4) . An (b) (4) press-in bottle adapter and a 10 mL (b) (4) oral dosing syringe are co-packaged with the drug

[1]The labeling review decision is pending for this IQA due to ongoing negotiations with the applicant. There are only minor labeling deficiencies from the CMC perspective and we expect the applicant will accept our recommendations. Refer to the CMC sections of the final approved labeling.

product inside a carton. Upadacitinib was previously approved as extended-release tablets containing 15, 30, and 45 mg strengths under NDA 211675. The oral solution is for pediatric patients who are not able to swallow tablets and also provides dosing flexibility based on body weight. Upadacitinib oral solution contains common compendial grade (USP/NF) excipients that are all within maximum daily exposure levels in approved products for the oral route of administration.

The product specification includes typical tests for oral solutions and the acceptance criteria are supported by the batch analyses and stability data. The applicant has provided assessment, and has confirmed with batch data, that the potential existence of (b) (4) impurities (b) (4) in the product is low.

The application includes three registration stability batches of product manufactured at the proposed commercial site and packaged in the proposed container closure system. Twelve (12) months long-term stability data at 5°C±3°C and 30°C/35% RH and 6 months accelerated stability data at 40°C/20%RH are provided. Photostability testing was conducted according to ICH Q1B for one registration batch. In addition, temperature excursion and cycling studies were also conducted. In-use stability testing was performed over 60 days for samples from two product registration batches stored for 12-months at 30°C/35%RH, which supports an expected maximum in-use period of 30 days. Overall, the stability data demonstrate that no changes were observed for all the tests with the exception of the assay of the (b) (4) sodium benzoate, during the long-term storage at 5°C±3°C and 30°C/35% RH, however, the sodium benzoate assay remains within limits that assure its antimicrobial effectiveness. Thus, **a 24 month expiration dating period is granted for the product** when it is stored under the labeled conditions (2°C to 30°C (36°F to 86°F)).

Labeling: Inadequate

See footnote 1 and refer to the labeling chapter. Minor edits have been made to the Dosage Forms and Strengths section, the Description section, and the How Supplied/Storage Condition section. Note that it was initially recommended that the applicant change the storage condition statement to “store between 2°C to 25°C (36°F to 77°F), excursions permitted up to 30°C (86°F)” however, considering that the stability data provided do support the applicant’s proposed labeled storage condition statement, and the fact that there is no published Agency policy regarding the storage condition statements consistent with the applicant’s stability

program, the proposed storage conditions of 2°C to 30°C (36°F to 86°F) was accepted.

Manufacturing: Adequate

The commercial manufacturing process for Upadacitinib Oral Solution combination product is comprised of the three major unit operations:

(b) (4)

(b) (4)

. Secondary packaging involves the co-packaging of the drug product with a press-in bottle adapter and a 10 mL oral dosing syringe in a carton.

All of the unit operations were found to have a low risk in terms of the intermediate, and final product quality attributes. The proposed commercial batch size of Upadacitinib Oral Solution is (b) (4) which is same as that of clinical and primary stability batches.

All the facilities listed in the application are acceptable. Both the product and drug substance facilities are approved based on the firm's inspection history and manufacturing experience. There are also no major GMP issues raised based on the review of the submitted primary stability batches.

Biopharmaceutics: N/A

Microbiology (if applicable): Adequate

The applicant provided an adequate description of the drug product composition and the container closure system designed to maintain microbial control of the product. (b) (4) The tests and acceptance criteria related to microbiological quality included in the product specification are also found to be adequate. Note that the applicant has also confirmed

that they are testing the product for all three organisms recommended by USP <60> for *Burkholderia cepacian complex (BCC)*.

The stability protocol includes tests for Total Aerobic Microbial Content, Total Yeast and Mold Content, and BCC, in addition to assay for the [redacted] (b) (4) at appropriate time points. In addition, for the registration stability batches, the applicant performed [redacted] (b) (4) which satisfies the commitment [redacted] (b) (4) In addition, the sponsor updated the stability protocol to include testing for *E. coli* as per USP<62> for primary stability batches starting at 24 months with storage at 30°C/35%RH. From a microbiological perspective, **the 24 month expiration dating period is acceptable for the product.**

Risk Assessment

Refer to the Drug Product chapter of the IQA

D. List of Deficiencies for Complete Response

1. Overall Quality Deficiencies *(Deficiencies that affect multiple sub-disciplines)*

N/A

2. Drug Substance Deficiencies

N/A

3. Drug Product Deficiencies

N/A

4. Labeling Deficiencies

Refer to the labeling review chapter of the IQA.

5. Manufacturing Deficiencies

N/A

6. Biopharmaceutics Deficiencies

N/A

7. Microbiology Deficiencies

N/A

8. Other Deficiencies *(Specify discipline, such as Environmental)*

N/A

Application Technical Lead Name and Date: Craig M. Bertha, 3/5/2024

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CHAPTER VII: MICROBIOLOGY

IQA NDA Assessment Guide Reference

Product Information	
NDA Number	218347
Assessment Cycle Number	MR01
Drug Product Name/ Strength	Upadacitinib oral solution, 1mg/mL
Route of Administration	Oral
Applicant Name	AbbVie Inc.
Therapeutic Classification/ OND Division	CDER/OND/OII/DRTM
Manufacturing Site	AbbVie Inc. 1 N Waukegan Rd. North Chicago, IL 60064 USA
Method of Sterilization	(b) (4)

Assessment Recommendation: **Adequate**

Assessment Summary: The proposed drug product is a non-sterile liquid formulation of upadacitinib intended for oral administration. The drug product is filled into plastic bottles and supplied with a press-in bottle adapter and oral syringe for administration.

List Submissions being assessed (table):

Document(s) Assessed	Date Received
0001 Original Submission	28 June 2023
0006 Quality IR Response	6 September 2023
0017 Quality IR Response	5 January 2024
0024 Quality IR Response	27 February 2024

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

Remarks: This NDA is for an oral solution formulation of upadicitinib (Rinvoq®) to allow for administration to patients unable to swallow solid dosage forms.

Concise Description of Outstanding Issues
(List bullet points with key information and update as needed): N/A

Supporting Documents: N/A

S DRUG SUBSTANCE

The drug product is non-sterile. The drug substance will not be reviewed here.

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

Description of drug product – Clear, colorless-to-light yellow, multi-dose solution in a plastic bottle containing 1mg/mL upadicitinib (fill volume 180mL per bottle). The product is co-packaged with one 10mL syringe used for oral dosing and a press-in bottle adaptor (PIBA), which are supplied by (b) (4)

Drug product composition –

Ingredient	Function	Concentration (mg/mL)
Upadacitinib (anhydrous)	Active Ingredient	1.0
Sodium Benzoate, USP/NF	(b) (4)	
Citric Acid Anhydrous, USP		
Sodium Citrate, Dihydrate, USP		
Sucralose, USP/NF		
Purified water, USP		

Description of container closure system –

Component	Description	Manufacturer
Bottle	200 mL high-density polyethylene bottle	(b) (4)
Cap	28 mm (b) (4) child-resistant cap and (b) (4)	

Assessment: *Adequate*

The applicant provided an adequate description of the drug product composition and the container closure system designed to maintain microbial control of the product.

P.2 PHARMACEUTICAL DEVELOPMENT

(b) (4)

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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

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information:

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

(b) (4)

Item	Items 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		
Established name(s)[1]	Adequate	- "upadacitinib"
Route(s) of administration	Adequate	- "oral solution"
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system	Adequate	- "oral solution" - "1 mg/mL"
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 parental 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.	N/A	
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).	N/A	

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

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

(b) (4)

(b) (4)

(b) (4)

Item	Items 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, storage conditions needed to maintain the stability of the reconstituted or diluted product)	Adequate	-provided in section 2.2 "Important Administration 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	- provided in section 2.2 "Important Administration Instructions"

For parenteral products: include statement: *"Parenteral drug products must be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit"*	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 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	

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

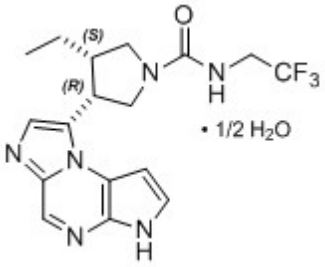
(b) (4)

Item	Items 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)	Inadequate	- Change to read "oral solution: 1 mg/mL upadacitinib as a clear, colorless to light yellow solution in bottles of 180 mL"
Strength(s) in metric system	Adequate	- 1 mg/mL
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 (Tablets: 10 mg of drug-x hydrochloride).	N/A	
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	- "clear, colorless to light yellow solution"
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 parental 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.	N/A	

1.2.3 Section 11 (DESCRIPTION)

(b) (4)

Item	Items 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)	Inadequate	- Established name not included in the 1st sentence. Revise to include established name as "RINVOQ (b) (4) (upadacitinib) oral solution"
Dosage form(s) and route(s) of administration	Inadequate	- Add "oral solution"
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)"	N/A	
List names of all inactive ingredients. Use USP/NF names in alphabetical order. Avoid brand names.	Adequate	- "citric acid anhydrous, purified water, sodium benzoate, sodium citrate dihydrate, and sucralose"
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.	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Sterility statement (if applicable)	N/A	
Pharmacological/Therapeutic class	Adequate	- "a JAK inhibitor"

Chemical name, structural formula, molecular weight	Adequate	- chemical name: (3S,4R)-3-Ethyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-N-(2,2,2-trifluoroethyl)pyrrolidine-1-carboxamide hydrate (2:1). - molecular formular: $C_{17}H_{19}F_3N_6O$ •½ H_2O. - molecular weight: 389.38 g/mol - molecular structure: 
If radioactive, statement of important nuclear characteristics.	N/A	
Other important chemical or physical properties (such as pKa or pH)	Adequate	- "The strength of upadacitinib is based on anhydrous upadacitinib. The solubility of upadacitinib in water is 38 to less than 0.2 mg/mL across a pH range of 2 to 9 at 37°C", same as the approved drug product.
For oral prescription drug products, include gluten statement (if applicable)	N/A	
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity")	N/A	

If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled. Note the labeling requirement may be applicable to another section of the PI (e.g., Section 2).	N/A	

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING

Item	Items 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)	Inadequate	- change to read "RINVOQ (b) (4) (upadacitinib) oral solution is supplied as:…"
Strength(s) in metric system	Adequate	- "1 mg/mL"
Available units (e.g., bottles of 100 tablets)	Adequate	- (b) (4)
Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s)	Inadequate	- Add "each bottle contains … clear, colorless to light yellow oral solution"
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 parental 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.	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."	Adequate	- "Discard remaining oral solution 60 days after opening the bottle".
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Inadequate	- Change to "2°C to 25°C (36°F to 77°F), excursions permitted up to 30°C (86°F)." per recommendation from OPQ Labeling committee
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."*	N/A	
Include information about child-resistant packaging	Inadequate	- Add "child-resistant cap" per information in section 3.2.P.7

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.

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

1.2.6 Manufacturing Information After Section 17 (for drug products)

(b) (4)

Item	Items 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)
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	

2.0 PATIENT LABELING

(b) (4)

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[2]	Adequate	- provided
Special preparation instructions (if applicable)	N/A	
Storage and handling information (if applicable)	Inadequate	- Change to "store RINVOQ (b) (4) between 2°C to 25°C (36°F to 77°F), excursions permitted up to 30°C (86°F)."
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 differs from the dosage form.	N/A	
Active ingredient(s) (if applicable)	Adequate	- provided
Alphabetical listing of inactive ingredients (if applicable)	Adequate	- provided
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer	Adequate	- provided

Any deficiencies should be listed at the end in the "ITEMS FOR ADDITIONAL ASSESSMENT."

3.0 CONTAINER AND CARTON LABELING

3.1 Container Labels

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

2 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[3], (font size and prominence)	Adequate	- "upadacitinib"
Strength(s) in metric system	Adequate	- "1 mg/mL, Each mL contains 1 mg of upadacitinib".
Route(s) of administration	Adequate	- "for oral use only"
If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP.	N/A	
Net contents (e.g., tablet count, volume of liquid)	Adequate	- "180 mL per bottle"
"Rx only" displayed on the principal display	Adequate	- provided
NDC	Adequate	- provided
Lot number and expiration date	Adequate	- provided
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new beyond-use-date (BUD).	Inadequate	- change to "store between 2°C to 25°C (36°F to 77°F), excursions permitted up to 30°C (86°F)." - Add space for patient to write "beyond use date" after the instruction of (b) (4)
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package, and these products require a "Not for direct infusion" statement.	N/A	
For parenteral injectable dosage forms, include the name and quantities of all active and inactive ingredients in alphabetical order. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.	N/A	

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

If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Linear Bar code	Adequate	

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Name of manufacturer/distributor /packer	Adequate	- provided
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	Adequate	- "Before use, read the accompanying instruction for use" provided
No text on Ferrule and Cap overseal, unless a cautionary statement is required.	N/A	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	
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.	N/A	
And others, if space is available.	Adequate	- "Insert bottle adaptor on 1st use. Do not remove after insertion" provided on c/c labels. - "Store the bottle upright, in a cool dark place" provided on c/c labels. - "Keep out of sight and reach of Children" provided on c/c labels. - "Only use the oral syringe provided" on c/c labels. - "Contents of Carton:1 Bottle, 1 Adapter, 1 Reusable Oral Syringe (10 mL), Full Prescribing Information, Instructions for Use" provided on carton label.

Assessment of Carton and Container Labeling: *{Adequate}*

2. ITEMS FOR ADDITIONAL ASSESSMENT

Make the following Change for PI in SharePoint:

- 3. Dosage Form and Strengths: change to read “oral solution: 1 mg/mL upadacitinib as a clear, colorless to light yellow solution in bottles of 180 mL”
- 11. Description: add “oral solution”.
- 16. How Supplied/Storage Condition:
    - change storage condition to “stored at “2°C to 25°C (36°F to 77°F), excursions permitted up to 30°C (86°F).”
    - add “each bottle contains 180 mL clear, colorless to light yellow oral solution”.
    - add “child-resistant cap”.

Communicate to the applicant for the following c/c label change:

- change the storage condition to “store between 2°C to 25°C (36°F to 77°F), excursions permitted up to 30°C (86°F).”
- Add space for patient to write “beyond use date” after the instruction of (b) (4)

Overall Assessment and Recommendation:

The NDA is now recommended for Approval from the labeling perspective with the above recommendation. Dr. C. Bertha, the ATL, will add the final labels to the combined CMC assessment once the labels are finalized.

Primary Labeling Assessor Name and Date:

Zhengfang Ge, Ph. D.
Reviewer, BRANCH IV/DIVISION II
OFFICE OF NEW DRUG PRODUCT

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

Julia Pinto, Ph. D.
SPQA, BRANCH IV/DIVISION II
OFFICE OF NEW DRUG PRODUCT

Zhengfang Ge

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Date: 1/30/2024 05:24:21PM
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Julia Pinto

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